Diabetes Mellitus Interagency Coordinating Committee

Fiscal Year 2001 | **Annual Report**

Diabetes Mellitus Interagency Coordinating Committee

CONTENTS

INTRODUCTION

In accordance with Section 429 of the Public Health Act, the Diabetes Mellitus Interagency Coordinating Committee (DMICC) prepares an annual summary report of its activities as well as other Federal research activities in the field of diabetes. It is submitted to the Secretary, Department of Health and Human Services (DHHS), and the Director of the National Institutes of Health (NIH). This is the annual report of the DMICC for Fiscal Year (FY) 2000.

LEGISLATIVE MANDATE

The DMICC was authorized by Public Law 93-354 and established in fall 1974; subsequent legislation modified some of the charges to the Committee. The legislative authority of the Committee is presented in Appendix A. The charge to the DMICC is to coordinate the research activities of the NIH and other Federal agencies relating to diabetes mellitus and its complications and to contribute to the adequacy and technical soundness of these activities by providing a forum for communication and exchange of information.

The Committee includes representatives from Federal agencies whose programs are relevant to diabetes mellitus and its complications. The chairman, designated by the Director, NIH, is the Director, Division of Diabetes, Endocrinology, and Metabolic Diseases, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). In FY 2000, the DMICC membership included representatives of 21 Federal organizations. A roster of Committee members as of the close of the fiscal year is included as Appendix B.

ACTIVITIES OF THE DMICC

The DMICC facilitates cooperation, communication, and collaboration among agencies that conduct or support diabetes-related activities. These activities may range from support for biomedical research to direct provision of health care services. The DMICC provides both a forum for initiating interactions and a mechanism for tracking progress.

ACTIVITIES OF MEMBER ORGANIZATIONS

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Agency for Healthcare Research and Quality (AHRQ)

The Agency for Healthcare Research and Quality continues to be involved in a broad range of activities related to improving the quality of health care,reducing its costs, improving patient safety, decreasing medical errors, and broadening access to essential services related to diabetes. These activities include the support of research and collaborations with others in the public and private sectors to improve outcomes for those with diabetes and to prevent the condition across the population.

Current Activities

The Agency is funding and involved with a large number of studies related to diabetes. A number of recent RFAs (Requests for Applications) have specifically identified diabetes as a priority condition. These RFAs include one focused on the translation of research into practice (TRIP II) and one aimed at establishing Excellence Centers to Eliminate Ethnic/Racial Disparities (EXCEED). Under these initiatives, researchers are examining why disparities exist in the care and outcomes of minorities with diabetes and what can be done to reduce or eliminate these disparities. Projects include an examination of the association between diabetes education programs and quality of care indicators in the Indian Health Service; implementation of successful managed care models of diabetes care in underserved populations; a community-based participatory research study to improve processes of care for elderly African-American diabetics; an evaluation of the impact of point-of-service testing of Hemoglobin A1c on care and outcomes; and the development and evaluation of a culturally sensitive multimedia education program aimed at increasing diabetes-related knowledge, self-efficacy, and self-care for African-American and Latino populations. Other studies that are being funded include an assessment of diabetes care in community health centers, the effects of Navajo interpreters on diabetes outcomes, the effectiveness of an automated telephone disease-management system for English- and Spanish-speaking patients, and an evaluation of the impact on utilization and outcomes of changes in managed care policy toward reimbursement for glucose self-monitoring.

Staff at AHRQ are also involved in a number of intramural studies of diabetes. Investigators are using data from the Medical Expenditure Panel Survey (MEPS) to develop national estimates for medical visits, individual expenditures, and sources of payment for people with diabetes. Another group is studying factors associated with multiple hospitalizations of diabetics.

AHRQ continues to work with individuals and organizations to ensure that the evidence-base is being employed. The Office for Health Care Information has recently released two syntheses presenting findings from AHRQ-supported research on diabetes and on racial and ethnic disparities in diabetes.

The Diabetes Quality Improvement Project (DQIP), based in large part on the AHRQ-supported Diabetes Patient Outcomes Research Team (PORT), is a collaboration of AHRQ with the Centers for Medicare and Medicaid Services (CMS), the National Committee for Quality Assurance, the Department of Veterans Affairs, the American Diabetes Association, and others. It continues to develop core measures of diabetes performance that allow benchmarking across organizations and identify opportunities for improvement among health plans and providers. Reporting on DQIP measures is now required of managed care organizations by CMS and results will be made publicly available.

AHRQ is also collaborating with the Juvenile Diabetes Research Foundation International and other private and public sector partners in efforts to improve rates of screening and treatment fordiabetes retinopathy.

Future Activities

Much of the work mentioned above will continue during the next fiscal year. It is expected that additional work will be funded under the agency's program announcements (PAs) and RFAs. Specifically, the PA calling for applications to enhance the evidence on patient-centered care is aimed at chronic conditions including diabetes.

Current Activities

Under the above research support application mechanisms, pertinent areas that are covered fall into two main categories: Basic and Clinical Research. Areas include: Beta Cell Biology, Islet and Pancreas Transplantation, Insulin Action , Insulin Resistance, Pathogenesis of Type 1 and Type 2 Diabetes, and also the study of pathogenesis of obesity. These studies invoke molecular genetic, metabolic, and histochemical approaches.

These applications are reviewed in several Scientific Review Groups(SRGs) within which individual subcommittees are located. Each of these subcommittees (study sections) has definite expertise to review specific areas relevant to diabetes and obesity.

Center for Scientific Review (CSR)

The Center for Scientific Review is a center within the National Institutes of Health, where a majority of investigator-initiated applications in diabetes and obesity areas are reviewed. The mechanisms of application support are the investigator-initiated individual project applications (R01s), High Risk/High Impact Pilot grant applications (R21s), Small Business Investment Research Applications or Technology Transfer (SBIR/STTR,) and Individual Fellowship Applications: Predoctoral (F31)
Postdoctoral (F32)
and Senior Fellowships(F33).

Thus, the mission of CSR relevant to activities of DMICC is central and pivotal through help in maintaining the quality of diabetes and obesity research in the nation. The knowledge gained through these NIH-supported projects would help control/treat type 1 diabetes and type 2 diabetes and obesity in areas of the world where these endocrine and metabolic disorders are prevalent.

Centers for Disease Control and Prevention (CDC)

The mission of CDC's diabetes programs is to document and reduce the burden of diabetes through public health action. This mission is directed to all populations within the United States and associated territories and consists of surveillance and epidemiology science; health services research; population-based diabetes control programs; and translation efforts that convert important diabetes research findings into clinical and public health programs.

Current Activities

- National and territorial surveillance activities for diabetes and associated complications, with public health programs in all 50 States, the U. S. territories, and the District of Columbia.

- Targeted surveillance and epidemiologic programs that focus on youth with diabetes (type 1 and type 2), ethnic and racial minority communities, women with or at risk for diabetes, and members of managed care organizations.

- Health services and economic research, including evaluation of the structure and function of managed care organizations within the United States and cost-effectiveness analyses of diabetes, associated complications, and preventive treatment.

- Expansion of State-based Diabetes Control Programs (DCPs) to include surveillance activities, programs that target high-risk ethnic and racial minority communities, and State/territorial policies that facilitate/impair diabetes prevention programs.

- Partnerships with Federal and State-based diabetes organizations (e.g., with National Institutes of Health through the National Diabetes Education Program, Health Services and Resources Administration (HRSA) through the Diabetes Collaborative, Indian Health Service through the National Diabetes Prevention Center; and others) as well as the private sector (e.g., Washington Business Group on Health, American Association of Health Plans, and others).

Major Accomplishments in FY 2001

Diabetes Burden in the United States. CDC validated and published surveillance information regarding the past, present, and future burden of diabetes prevalence through use of the Behavioral Risk Factor Surveillance System (BRFSS) and computer modeling, documenting the dramatic and disconcerting increase in type 2 diabetes, in association with increasing obesity and decreasing physical activity.

Programs Addressing Diabetes in Special Populations. The agency implemented several scientific and programmatic activities that specifically target special populations, including:

- *Youth With Diabetes:* through the SEARCH project, established six (6) regional sites that have created registries for prevalence and incidence of diabetes among youth (< 20), as well as quality of care.

- *Women With/At Risk for Diabetes:* established a public health initiative to address social, economic, and cultural barriers to diabetes prevention and management among all women across the life-spectrum.

- Solidified and implemented programs that address a public health program for all American Indians with the National Diabetes Prevention Center in Gallup, New Mexico.

- Expanded interactions among public health (State-based DCPs) and clinical programs (Community Health Centers (CHCs)/HRSA) to improve the "safety net" for disadvantaged persons with diabetes to > 400 CHCs and > 40 DCPs.

Diabetes in Managed Care. CDC finalized data collection procedures and initiated information accumulation for diabetes preventive care practices and outcomes among large managed care organizations within the United States through the TRIAD (Translating Research Into Action for Diabetes) Project.

Economic Dimensions of Diabetes. CDC initiated economic analyses of primary prevention of type 2 diabetes, interventions to prevent diabetic renal disease, and preventive strategies to reduce the incidence and seriousness of cardiovascular disease (CVD) among persons with diabetes.

Future Activities

- Develop "Action Plan" for the Public Health Initiative on Women with Diabetes.
- Develop strategies and programs that address primary prevention for type 2 diabetes, including screening, economic, and public health interventions with CDC's projects.
- Expand surveillance activities that address health disparities, quality of life dimensions to the diabetes burden, and economic aspects of diabetes.
- Through the National Diabetes Education Program, expand broad-based activities that address cardiovascular disease among persons with diabetes, as well as initiate science-based interventions to improve primary prevention for type 2 diabetes.
- Expand the programs of the State-based DCPs so that adequate support and advice would be provided to all programs.

Centers for Medicare & Medicaid Services (CMS) [formerly HCFA]

Diabetes activities at CMS in 2001 fell into several broad categories: evaluation of the quality of care provided to Medicare beneficiaries, national and State-level quality improvement projects designed to improve care for Medicare beneficiaries; reimbursement and coverage policies to support quality care; beneficiary educational campaigns; and research to support quality diabetes care.

Current Activities

Evaluation of quality of care provided to Medicare beneficiaries was conducted for beneficiaries in both Medicare fee-for-service and in managed care. These data, based on the Diabetes Quality Improvement Project (DQIP), a project initiated and funded by CMS, allow identification of opportunities for improvement and focus for quality improvement projects. A Medicare quality surveillance system was developed in 2001 that will allow ongoing assessment of the characteristics of beneficiaries with diabetes, quality of care and outcomes of care for diabetes, and monitoring of the impact of key regulations and coverage decisions.

National and State-level quality improvement projects included the National Eye Project to improve eye exam rates in conjunction with the American Academy of Ophthalmology and the American Optometric Association. All Medicare managed care plans were required to conduct quality improvement activities in diabetes. State-level efforts conducted by Quality Improvement Organizations in collaboration with individual practitioners, medical specialty groups, and other partners occurred in all 50 States and three territories. In the fee-for-service setting, remeasurement demonstrated significant improvement of quality during the time period during which these efforts were implemented (ranging from a 3 percent increase in eye exam rates to a 15 percent increase in lipid testing). Improvements in quality of diabetes care in Medicare managed care plans were also impressive.

Payment and coverage policies to support quality care included publication of the final regulations about the diabetes self-management training benefit authorized under the Balanced Budget Act of 1997. Regulations governing the new medical nutrition benefit for patients with diabetes or renal disease were also published and the benefit will go into effect on January 1, 2002.

Two new coverage policies were announced. The first modified the coverage requirements for use of a subcutaneous insulin pump to broaden eligibility to include more persons with type 1 and some with type 2 diabetes. The second policy will reimburse providers for beneficiaries with diabetes and diabetic peripheral neuropathy with loss of protective sensation to have up to two foot exams per year.

Beneficiary education campaigns in 2001 attempted to encourage beneficiaries to control their blood sugar and publicized the expanded Medicare benefit for blood sugar management. Over 3.2 million people were reached via print media and 2.2 million people via television campaigns. A new campaign for 2002, in conjunction with the National Diabetes Education Program, entitled "Be Smart About Your Heart: Control the ABCs of Diabetes" will build on the successes of the "Power to Control Diabetes is in Your Hands" campaign launched in 2001 and will further promote the new diabetes self-management training benefit and the nutrition therapy benefit and educate older adults about the high risk of heart attack or stroke if they have diabetes. An upcoming campaign in conjunction with the National Institutes of Health's National Eye Institute will promote the new Medicare benefit for glaucoma detection that will provide coverage for an annual dilated eye exam for Medicare beneficiaries at high risk for glaucoma (including those with diabetes).

Research to support quality diabetes care has included examination of the factors in both the fee-for-service environments and in managed care plans that influence quality. For example, there are significant relationships between rates of eye exams and the proportion of plan members who have a personal physician. Another research project underway in 2001 is exploring characteristics and systems in place in managed care plans consistently reporting the highest quality diabetes care.

Food and Drug Administration (FDA)

FDA is charged to approve safe and efficacious agents for public use. This is especially important with regard to therapeutic agents in the treatment of diabetes mellitus.

Current Activities

Insulin resistance is the hallmark of type 2 diabetes. A new class of insulin-sensitizing agents, the thiazolidinediones, decrease hyperinsulinemia by alleviating insulin resistance. Troglitazone, the prototype, had been approved and withdrawn from the market due to liver toxicity. Two newer members of the thiazolidinedione class have since been approved—rosiglitazone in May and pioglitazone in July 1999. Careful monitoring for possible hepatic adverse effects are being followed as for troglitazone. Numerous clinical trials are now reporting multiple cardiovascular benefits of this class of agents, which decrease hyperinsulinemia by alleviating insulin resistance.

Other non-thiazolidinedione peroxisome proliferator-activated receptor (PPAR) dual agonists, active at both alpha and gamma PPAR receptors, are being developed by various pharmaceutical companies. Currently, there are more than a dozen such agents in various phases of the drug development process. They have been demonstrated to have both glucose and lipid lowering activities.

Lantus (insulin glargine (rDNA origin)) was approved this year for adult patients with type 2 diabetes and pediatric patients (> 6 years of age) with type 1 diabetes. This insulin analog provides 24-hour basal glucose-lowering activity. Lantus insulin must not be diluted or mixed with any other insulin or solution.

NovoLog Mix 30/70 was also approved. This insulin preparation may provide adequate glucose control with one shot daily.

Health Care Financing Administration (HCFA)
See **Centers for Medicare & Medicaid Services (CMS)**

Health Resources and Services Administration (HRSA)

The Health Resources and Services Administration manages several health care systems programs that include diabetes identification, education, prevention, or treatment.

Current Activities

Bureau of Primary Health Care. HRSA's Bureau of Primary Health Care (BPHC) established two strategic goals: to move toward the elimination of health disparities and toward a 100 percent access system for all Americans. The Health Disparities Collaboratives, started in FY 1999, seeks to (1) generate and document improved health outcomes for underserved populations, (2) transform clinical practice through new models of care, (3) develop infrastructure, expertise, and multidisciplinary leadership to improve health status, and (4) build strategic partnerships.

The initiative originally focused on diabetes mellitus—to delay or decrease disease complications—by implementing an evidence- and population-based model of care, which relies on knowing which patients have the illness and helps them participate in their own care. It has six basic elements: support of patient self-management, clinical decisions support, delivery system redesign, a clinical information system, organization of health care, and strong partnerships with local government and community organizations.

BPHC activities include:

- A total of 270 health centers participated in the initial year-long diabetes collaboratives. Eighty-eight centers in 1999, 118 centers in 2000, and 62 centers are currently participating in the Diabetes 3 Collaborative.
- After completing the year-long collaborative, health centers continue to receive support to promote the model of care throughout their organizations, bring change to clinics, and measure its impact on the health of underserved patients.
- Orientation and training videos and a brochure describe the initiative.
- A software program was developed to meet the need for a comprehensive clinical information system. It combines patient information management of diabetes with the comorbidity of cardiovascular disease by looking at multiple disease registries.
- Depression screening is included in the care of diabetes patients.
- Partnerships with other Federal agencies, State diabetes control programs, and private-sector organizations continue to grow stronger.

BPHC outcomes include:

- Health centers continue to report on the shared key goal that 90 percent of patients with diabetes will receive two HbA1c tests annually, at least 3 months apart. Starting in 2000, a shared health outcome measure was added to all the collaboratives (Diabetes 1, Diabetes 2, and Diabetes 3 collaborative participants) requiring them to report on control of glucose levels (average HbA1c) and a self-management support measure. Additional measures focus on prevention of cardiac as well as microvascular complications, the latter including eye, kidney, and lower extremity disease.

- There are over 41,000 persons with diabetes in electronic registries that enable centers to track and manage the health of these patients.

- The average HbA1c has decreased from 9.2 to 8.5 for more than 12,200 patients in the Diabetes 1 Collaborative.

- The average HbA1c has decreased from 8.9 to 8.3 for more than 22,000 patients in the Diabetes 2 Collaborative.

- Average percentage of patients with two HbA1c tests in 12 months increased from 24 percent to 48 percent in Diabetes 1 and 2 Collaboratives as they disseminated the care model throughout the organization and the registry size grew.

- Forty percent (40%) of patients have documented collaboratively set self-management goals.

BPHC strategic partnerships and infrastructure development highlights include:

- Six cluster directors and five information systems specialists are employed by the five lead Primary Care Associations. Five Sate-based cluster coordinators and two information systems specialists were added this year to the cluster infrastructure.

- A national BPHC director of the collaboratives started in April 2000.

- Primary Care-Public Health partnerships are highlighted as a programmatic success. The partnership with CDC Division of Diabetes Translation continues to be strengthened. In 1999, 15 initial partnerships were established between State health department Diabetes Control Programs (DCP) and health centers working on the diabetes collaborative. Direct support to health centers from DCPs was $1.3 million. In 2000, health centers received $2.7 million in support.

- The Agency for Health Research and Quality is assisting with the program evaluation strategy.

Maternal and Child Health Bureau. The Maternal and Child Health Bureau (MCHB) administers maternal and child health (MCH) Block Grants to States to support programs that promote the health of all the Nation's mothers and children and ensure statewide systems of health care for the MCH population. Diabetes screening, education, prevention, and treatment programs may be supported under these grants.

Additional Title V activities, such as MCH research, training, genetic services, and MCH improvement projects, are supported under Special Projects of Regional and National Significance. While these activities may not specifically target Diabetes Mellitus, core elements of community systems of care serving children with special health care needs are addressed. MCHB, in concert with the March of Dimes, the American Academy of Pediatrics, and Family Voices, has developed a 10-Year Action Plan to achieve community-based systems for children and youth with special health care needs and their families, including children with diabetes. The Healthy Start Initiative to significantly reduce infant mortality in targeted communities also includes services addressing diabetes in mothers and children. In addition, MCHB promotes diabetes detection and care through school-based and school-linked health programs.

The MCH Training Program provides training grants to graduate programs and professional schools to support teaching, research, and service activities that focus on women and children. Its Leadership Education in Adolescent Health (LEAH), public health nutrition, and pediatric nutrition grantee programs include diabetes education. The Eighth Annual Pediatric Update in May 2001, sponsored by the Department of Pediatrics at the University of Alabama at Birmingham, addressed "Type 2 Diabetes in Children and Youth." A national videoconference in September 2001, sponsored by the Indiana University

School of Medicine, included an intensive workshop on "Treatment Challenges for Children and Adolescents with Type 2 Diabetes."

Bureau of Health Professions. The Bureau of Health Professions (BHPr), which provides national leadership in establishing the Nation's health personnel, charges its Division of Health Careers Development to provide technical assistance to community groups to improve the health status of diverse and disadvantaged populations significantly affected by Diabetes Mellitus; Type 2 in particular.

Office of Rural Health Policy. The Office of Rural Health Policy funds approximately 18 grantees through its Outreach and Network Development program, including a component that addresses the diabetic population. Projects receive 3years of funding—from approximately $40,000 to $200,000 per year. Seven projects were funded in 1999, seven in 2000, and an additional five in 2001. Some focus on the diagnosis, treatment, education, or prevention, while others focus on a goal that deals with diabetes. Projects focusing primarily on diabetes, include:

- The Diabetes Prevention and Care Project, a collaborative effort coordinated and overseen by the Chiricahua Community Health Center, Elfrida, Arizona, focuses on the provision of treatment and education about diabetes for at-risk individuals in a predominately Hispanic community (68%).

- The Sunset Diabetes Outreach and Education Project works to improve access to health care services for the target population of mostly Hispanic migrant farm workers and their families in Yuma County, Arizona.

- The Park County Diabetes Project was established at Livingston Community Health Care System, Inc., in Livingston, Montana, to address the needs of individuals with diabetes in rural communities.

Office of Special Programs. HRSA has been working with the Organ Procurement and Transplantation Network, the national system for matching donated organs with patients on the transplantation waiting list, to facilitate the allocation of pancreatic organs for use in pancreatic islet cell transplants in treating patients with type I diabetes mellitus. Five transplant centers are now performing islet cell transplants.

Indian Health Service (IHS)

The mission of the IHS National Diabetes Program (NDP) is to develop, document, and sustain a public health effort to prevent and control diabetes in American Indian and Alaska Native (AI/AN) people. The agency promotes collaborative strategies for the prevention of diabetes and its complications in the 12 IHS Administrative Service Areas through a network of 19 Model Diabetes Programs and 13 Area Diabetes Consultants. The agency also disseminates current information about all aspects of diabetes surveillance, treatment, education, and prevention.

Diabetes was the most frequently identified health problem in IHS Area consultation workshops for FY 2002 planning. Type 2 diabetes disproportionately affects AI/AN adults who are over three times more likely to have diabetes than the general U.S. population. A recent alarming trend is the increase in prevalence of type 2 diabetes in AI/AN young persons. Over a 9-year period, from 1990–1998, the prevalence of diabetes rose 68 percent in AI/AN adolescents and young adults. Recent data show that diabetes mortality is 4.3 times higher in the AI/AN population than in the U.S. population. There was a 24 percent increase in the American Indian age-adjusted death rate from diabetes from 1991–1993 to 2000. There is clear evidence that for Indian people the health disparity related to diabetes is increasing.

Significant Activities in 2001

Special Diabetes Program for Indians, 1997 Balanced Budget Act and 2001 Consolidated Appropriations Act. The IHS Diabetes Program administered Year 4 of the Special Diabetes Program for Indians of the 1997 Balanced Budget Act (BBA). Thirty million dollars per year have been distributed from the BBA funds through 286 non-competitive grants administered at 318 sites throughout Indian country. In December 2000, Congress appropriated an additional $70 million to the Special Diabetes Program for Indians through the Consolidated Appropriations Act of 2001. Over 96 percent of these funds are distributed through grants to tribes, IHS facilities, and urban Indian centers while 3.8 percent are withheld for administration of the grant program. Tribal entities are the direct recipients of 81 percent of the grants. The IHS National Diabetes Program (NDP) works closely with the Tribal Leaders Diabetes Committee to administer this program. The new Request for Application developed by the IHS NDP this year included a Best Practices approach with 14 strategies identified, researched, and compiled for use by applicants.

IHS Standards of Care & Education; IHS to become a Deeming Entity for Diabetes Education Certification.

Education Standards. The IHS National Diabetes Program, with agency and tribal leader support, has established an Indian Health Diabetes Education Accreditation Program and has received notification from the Centers for Medicare and Medicaid Services (formerly HCFA) that the IHS NDP application to become a deeming entity will soon be approved. This process will allow Indian health diabetes education programs to become certified and thus seek Medicare reimbursement for diabetes education.

Clinical Standards (Diabetes Care and Outcomes Audit). The IHS National Diabetes Program updated the IHS Standards of Care for Diabetes in 2001 to reflect new science and best practices. The Annual IHS Diabetes Care and Outcomes Audit, a voluntary medical records review of 87 clinical care and public health practices and outcomes, is based on these standards. These standards and audit summary results are distributed to providers IHS-wide through a network of regional Area Diabetes Consultants and local Diabetes Coordinators and are used as quality indicators at the local, regional and national levels to identify specific problems and to determine policy and practice.

Obesity Prevention. The IHS National Diabetes Program is coordinating an obesity prevention initiative targeting Head Start children (0–5 years), families, Head Start staff, and AI communities. Five tribal Head Start pilot sites, in collaboration with their respective community health partners, have developed obesity and diabetes prevention interventions in their local communities. Each Head Start site community action plan includes multifaceted program activities and milestones focusing on healthy eating, physical activity, healthy behavior, and community partnerships. The core component of the initiative is to develop and sustain local community partnerships in the implementation of each program's interventions. The five pilot sites are developing outcome measure and evaluation methods for each of their individual action plans. The sites evaluate their progress every 6 months and modify interventions as appropriate.

Joslin Vision Network Teleophthalmology Project. In FY 2002, Congress increased to $1.5 million the IHS appropriation to address screening for diabetic retinopathy through a collaborative project with the Joslin Diabetes Center using the Joslin Vision Network (JVN). JVN is a remote site diabetes retinopathy screening system that uses low-level illumination and does not require pupil dilation. The acquired retinal image is sent electronically to a reading center and the analysis sent back to the remote site. IHS has established demonstration sites at the IHS Phoenix Indian Medical Center (PIMC), which serves as the central reading station, and the Tohono O'odham (formerly Papago) Reservation at Sells Public Health Service Indian Hospital. Staff have been hired to implement the process and active screening is taking place at both sites. The addition of remote screening station sites at five additional locations throughout the country is currently underway. Acquired retinal images from these remote sites will be electronically sent to the central reading station at PIMC. Primary challenges to future site development in remote locations beyond these demonstration sites include availability of communication lines and staffing.

NIDDK/IHS/TLDC/AIHEC collaboration to Recruit AI/AN Students into Biomedical Science Research and Diabetes Careers. In FY 2001, at the request of tribal leaders serving on the Tribal Leaders Diabetes Committee (TLDC), IHS and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) collaborated on a project to encourage young AI/AN students to consider careers in biomedical research and diabetes. This project also involves the American Indian Higher Education Consortium (AIHEC), which represents the 34 tribal colleges around the country, and will target students in elementary, middle, and high schools. Resources have been identified, a planning committee formed, and NIDDK plans to release an RFA in FY 2002.

CDC/IHS Collaboration on Redesign of the National Diabetes Prevention Center. The IHS National Diabetes Program worked closely with the Centers for Disease Control (CDC) Division of Diabetes Translation (DDT) in FY 2001 to redefine and re-establish the National Diabetes Prevention Center (NDPC) in Gallup, New Mexico, consistent with NDPC's original mission to provide diabetes outreach, information, and technical assistance to tribes throughout the United States. In addition, the CDC DDT provides diabetes educational and epidemiologic support to the IHS National Diabetes Program with two full time positions and close collaboration on projects of mutual concern.

Collaboration and Partnership With Other Federal Agencies and Organizations. The IHS NDP Director serves as a member of the newly formed Translation Committee of the Diabetes Prevention Program, an NIH-sponsored study showing that type 2 diabetes can be prevented. The IHS NDP Director also serves as a member of the Steering Committee of the National Diabetes Education Committee, a joint effort of the National Institutes of Health and CDC to promote national awareness about diabetes.

IHS NDP supports the American Diabetes Association's outreach initiative program for AI/AN communities: *Strong in Body and Spirit*. Provides expert guidance related to diabetes program development and modification based on participant evaluation.

IHS NDP participates in the AI subcommittee of the National Diabetes Education Program. IHS NDP provides regular representation to the committee and helps with distribution of program materials. IHS NDP partners with the National Indian Council on Aging on a diabetes monograph series, newsletters for tribal leaders, and development of an electronic automated diabetes audit.

A partnership has been established with the American Indian Higher Education Consortium (AIHEC) Board to help build tribal college and university capacity and infrastructure for diabetes training and program activities in AI/AN communities.

Future Directions

IHS NDP plans to hold a national diabetes conference in collaboration with the TLDC in Denver, Colorado, in December 2002. The conference will feature successful grant programs and results of the Diabetes Prevention Program study. IHS NDP will hold regional meetings with diabetes programs around the country to discuss Best Practices and successful models for implementation of diabetes prevention and treatment in AI/AN communities.

IHS is planning for more training (for health professionals, tribal leadership, administrators, paraprofessionals, and patients) and increased awareness regarding new diabetes prevention findings through media, booklets, internet, and other avenues of communication.

National Center for Health Statistics (NCHS), CDC

NCHS's mission as it relates to diabetes is to monitor and provide national diabetes statistics in the form of summary health measures and individual level data for research. This information originates from vital records, interview and examination surveys, medical records, and patient encounters (such as ambulatory care visits).

Highlights of FY 2000–2001 Activities

The National Health and Nutrition Examination Survey (NHANES) continued to collect information on the prevalence of diagnosed and undiagnosed diabetes and assessment of the following measures among people with diabetes (HbA1c, cholesterol, blood pressure, visual acuity, lower extremity neuropathy and vascular insufficiency, renal function, oral health, anthropometry, diet, and functional status).

In November 2000, NCHS published the baseline tracking measures for the 2010 Health People national health objectives. This included 17 diabetes objectives, which are the key diabetes health goals for the U.S. (http://www.cdc.gov/nchs/hphome.htm)

The NCHS Research Data Center now contains a followup data file, which was created by matching participants from NHANES II and the Centers for Medicare and Medicaid Services (CMS) (formerly HCFA) end-stage renal disease (ESRD) program. People with diabetes accounted for much of the ESRD. (http://www.cdc.gov/nchs/r&d/rdc.htm)

NCHS published numerous reports that included diabetes health statistics including trends in avoidable hospitalizations for DKA (diabetic ketoacidosis) or coma and urbanization patterns for the diabetes risk factors of obesity and sedentary leisure time lifestyle.

Future Plans and Ongoing Initiatives

Release of the 1999–2000 NHANES data (see above) is scheduled for early 2002.

NHANES will be releasing fact sheets on the risk of chronic renal disease among people with diabetes, which is based on the matched NHANES–CMS data file.

Plans by the National Health Interview Survey (NHIS) to periodically collect diabetes-related questions on preventive measures related to diabetes including diabetes education and frequency of vision, foot, or HbA1c evaluations will be suspended until additional funds are obtained by NCHS. 1999 was the last time this NHIS information was obtained. In addition, no plans exist to repeat the 1989 diabetes supplemental survey in NHIS.

National Center for Research Resources (NCRR)

The National Center for Research Resources (NCRR) develops and supports research technologies and shared resources that are critically important to the research efforts directed at maintaining and improving the health of our Nation's citizens. To facilitate health-related research, NCRR supports the development and use of sophisticated instrumentation and technologies, animal models of human disease, and clinical research environments. NCRR programs also provide support for the career development of clinical and veterinary biomedical investigators. The current NCRR diabetes research portfolio includes approximately 680 basic and clinical research subprojects. Selected highlights of NCRR-supported research activities and future plans that relate to diabetes are presented below.

Current Activities

NCRR established a network of 10 Islet Cell Resource (ICR) centers to isolate, purify, and characterize human pancreatic islets for subsequent transplantation into patients with type 1 diabetes.

Scientists are using electron microscopy to image the Golgi apparatus, a cellular component that is essential for insulin secretion in beta cells, to study its fine structure and function, and to gain a fundamental understanding of insulin secretion.

New nuclear magnetic resonance methods are being developed in humans and mice to analyze and understand in vivo metabolic changes that occur in type 2 diabetics. A recent study in humans showed that three separate pathways of glucose production in the liver could be monitored in a single experiment.

At the University of California Davis Regional Primate Research Center (RPRC), xenografts of islet cells from pigs to diabetic macaques were successful in 50 percent of the animals and showed functionality for at least 3 months.

Researchers at the University of Washington RPRC have been investigating pancreatic islet cell allograft survival in macques and baboons. They found that transplanting islets without immuno-suppression followed by a second graft with immuno-suppression facilitates allo-tolerance of the second graft.

Porcine models are being used to investigate the significance of coronary artery disease in type 2 diabetics.

Advances at General Clinical Research Centers (GCRCs) have been made in understanding the relationship between insulin peptides and type 1 diabetes pathogenesis. Approximately 75 percent of the subjects in the Diabetes Prevention Trial–1 study are cared for through GCRCs. Many of the participating Centers use their core laboratories to measure plasma insulin levels and use their dieticians to analyze dietary histories.

Several GCRC investigators are studying the genetic polymorphisms that predispose patients to type 2 diabetes while others are exploring the complications that the disease causes in the vascular bed and blood clotting mechanism.

Diabetes-related research is being conducted at five NCRR-supported Research Centers at Minority Institutions (RCMIs): University of Hawaii at Manoa, Howard University, University of Puerto Rico Medical Sciences Campus, Charles R. Drew University, and the University of Texas El Paso.

The Charles R. Drew RCMI has established the Center of Urban Research and Education in Diabetes and Metabolism (CUREDM), which is in its second year of funding, and continues to attract established research investigators and provide them with resources they need to study diabetes and its complications in disproportionately affected indigenous populations.

The Howard University RCMI is starting Project DiSH (Diabetes, Stroke and Hypertension) at two at-risk urban minority school systems, which will provide a school-based program to increase awareness of medical and lifestyle factors responsible for diabetes.

The Shaping Health Behaviors Through Science Enrichment project at Colorado State University focuses on students in grades K–6, using science education enrichment as a model for behavioral change to reduce type 2 diabetes by improving nutrition and reducing the rate of childhood and adolescent obesity.

Future Activities

NCRR will increase support for ICR centers that will procure whole human pancreases, isolate the islets, optimize the quantity and quality of the islet preparations, and distribute islets to investigators conducting approved research.

Collaborations with other components of NIH and private organizations will continue and expand for studies that enroll diabetic and prediabetic patients for research into the etiology and treatment of diabetes. This will in part be through continued support of national cooperative diabetes programs such as DPP, DPT–1, EDIP, and EDIC as well as corporate-sponsored drug trials.

Expand resources will be expanded to maintain and supply genetically-engineered mouse models for diabetes mellitus research including hyperglycemia, hyperinsulinemia, and insulin resistance.

NCRR plans to link the newly established diabetes mutant mouse resource at the Jackson Laboratory with the existing NCRR-funded Mutant Mouse Regional Resource Center. The Jackson Laboratory will house models that are standard inbred and hybrid mice as well as mice with spontaneous and induced mutations serving as models for diabetes and obesity. A coordinated database will form the backbone of this diabetes mouse resource.

Efforts to develop a non-human primate model for diabetes will continue. The advent of molecular tools enables the search for naturally occurring diabetes in non-human primates as well as the detection of genes involved in diabetes.

The Charles R. Drew CUREDM will continue to develop its research infrastructure, including the provision of support for pilot projects. The Center will be expanding to house a telemedicine remote site and exercise physiology center, and has received approval to create an Ophthalmology CUREDM satellite.

National Center on Minority Health and Health Disparities (NCMHD)

The mission of the National Center on Minority Health and Health Disparities is to lead, coordinate, support, and assess the NIH effort to reduce and ultimately eliminate health disparities. In this effort NCMHD will conduct and support basic, clinical, social and behavioral research, promote research infrastructure and training, foster emerging programs, disseminate information, and reach out to minority and other health disparity communities. The NCMHD envisions an America in which all populations will have an equal opportunity to line ling, healthy and productive lives.

Building on the work of the former Office of Research on Minority Health (ORMH) through its partnerships with the NIH institutes and centers (ICs), the NCMHD has made remarkable achievements since its establishment just over one year ago. NCMHD is particularly committed to continuing its partnerships with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and other NIH ICs, supporting diabetes research and training. While diabetes affects all groups in the U.S. population, Native Americans, Mexican Americans, Puerto Ricans and African Americans suffer disproportionately compared to the general population. Findings in a recent National Eye Institute/NCMHD funded study indicated that increased efforts are needed to improve diabetes detection in Mexican Americans.

The Center is addressing disparities in health status in racial and ethnic minorities with respect to diabetes through the support of research in three broad areas: preventing or delaying the early onset of diabetes through diabetes education and lifestyle changes, improving the management of and therapies for diabetes, and the identification of biological and genomic risk factors for diabetes. Addressing one of the barriers to racial and ethnic minority individuals' participation in clinical trials – lack of racial and ethnic minority clinical investigators and researchers —NCMHD is continuing to support research training at minority health professional schools. Two such programs include a clinical trials faculty development program and a research training alliance through one of NIDDK's Diabetes Research and Training Centers.

National Eye Institute (NEI)

The National Eye Institute's mission is to conduct and support research, training, health information dissemination, and other programs concerned with blinding eye diseases, visual disorders, mechanisms of visual function, preservation of sight, and the special health problems and requirements of the blind. Diabetes is responsible for diabetic retinopathy, an eye disease that is the leading cause of blindness in people between the ages of 24 and 70 years. This disease is characterized by a progressive breakdown of the normal retinal vascular system.

Current Activities

NEI sponsorship of the workshop entitled ""Genetics of Diabetic Retinopathy" on September 21–22, 2000, in Bethesda, Maryland, resulted in publication of a program announcement (PA–02–020), entitled "Strategies to Identify the Genetic Basis of Diabetic Retinopathy." This PA seeks grant applications on gene discovery; genetic epidemiology; methodological studies of phenotypic assessment of retinopathy, including possible surrogate markers; and the development and application of novel statistical methods relevant to analyzing genetic data on diabetic retinopathy. This PA is co-sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). In addition, NEI is participating with other NIH institutes in a PA entitled "The Role of Antioxidants in the Prevention of Diabetic Complications." The intent of this PA is to solicit applications on the role of antioxidants in preventing, delaying, or ameliorating the micro- or macrovascular complications of diabetes as well as the mechanism(s) by which antioxidants might prevent diabetic vascular disease.

NEI has joined with other NIH institutes in several RFAs (Requests for Applications). RFA–DK–02–016, "Surrogate Endpoints for Diabetic Macular Complications," invites applications to develop biological endpoints that can be used to predict risk and assess progression of microvascular complications of diabetes. RFA–DK–02–023, "Innovative Partnerships in Type 1 Diabetes Research," is intended to support collaborations between investigators already engaged in diabetes research and researchers from other areas with expertise relevant to type 1 diabetes research. RFA–DK–02–022, "Bench to Bedside Research on Type 1 Diabetes and Its Complications," seeks applications involving partnerships between clinical and basic biomedical researchers with the goal of translating advances of the molecular basis of type 1 diabetes into new therapies.

NEI continues to participate with NIDDK, the National Institute of Dental and Craniofacial Research (NIDCR), the National Institute of Neurological Disorders and Stroke (NINDS), and the National Heart, Lung and Blood Institute (NHLBI) in a program announcement (PA–99–159) on "The Role of Growth Factors in the Development of Diabetic Complications." This PA encourages grant applications on the role of growth factors in the etiology and pathogenesis of the micro- and macrovascular complications of diabetes.

NEI is helping to co-sponsor ACCORD (Action to Control Cardiovascular Disease Risk in Diabetes), a large multicenter trial supported by NHLBI and NIDDK to assess treatments to reduce risk of cardiovascular disease in type 2 diabetes. For this trans-NIH effort, NEI is sponsoring an eye examination component in order to collect epidemiological data.

Through its National Eye Health Education Program (NEHEP), NEI coordinated the National Diabetes Month (NDM) Eye Health Initiative in November 2000. This initiative was designed to increase awareness of diabetic eye disease and the importance of dilated eye exams for the 10 million people diagnosed with diabetes. The NEHEP Partnership, which represents more than 60 leading public and private organizations, sponsored the awareness month. Community resource guides and educational materials were distributed to health professionals and community organizations nationwide for use in conducting local programs and events. In addition, diabetic eye disease information was disseminated to both English and Spanish print and radio media and to Spanish language television stations.

Consistent with the recommendations of the congressionally established Diabetes Research Working Group (DRWG), NEI is supporting an initiative on the evaluation of new treatments for diabetic macular edema, a major cause of visual loss in patients with diabetes. An RFA (EY–01–001) entitled "Diabetic Macular Edema Clinical Research Network" was issued in June 2001 and calls for cooperative agreement applications to support core centers to plan, implement, and conduct clinical trials on the treatment of diabetic macular edema. Clinical centers will be added to the network during the first year of operation. The overall goal of this RFA is to develop an infrastructure to accelerate the development and conduct of clinical trials of the treatment of diabetic macular edema. These include both medical and surgical approaches. A pilot study is being developed at the NEI clinical center to pilot methods to evaluate less intense photocoagulation, vitamin E supplementation, COX–2 inhibitors, and lipid lowering. The pilot study is intended to set the stage for a major multicenter randomized clinical trial for the treatment of diabetic macular edema.

Another initiative seeks to identify genetic associations in patients with microvascular complications of diabetes. NEI is supplementing the FIND (Family Investigation of Nephropathy and Diabetes) study funded by NIDDK to investigate the genetics of individuals and special populations of patients with renal disease. NEI is supporting detailed eye examinations for these patients and will search for genetic associations with microvascular disease.

Future Activities

NEI will continue to incorporate the scientific priorities outlined in the Report of the Congressionally Established Diabetes Research Working Group in making funding decisions.

NEHEP will continue to develop and implement outreach activities for people with diabetes.

NEI will continue to encourage experienced investigators from outside vision research to apply their expertise to develop novel strategies for increasing knowledge about the pathophysiology and treatment of diabetic retinopathy.

National Heart, Lung and Blood Institute (NHLBI)

NHLBI has continued to pursue a comprehensive research program to understand the pathogenesis, improve treatment, and develop effective prevention strategies to address the cardiovascular complications of diabetes, the major cause of death in patients with diabetes. Despite reductions in cardiovascular disease (CVD) mortality in the general population, patients with diabetes continue to have 2–4 times the CVD rates of non diabetics of the same age and gender. In addition, recent studies indicate that current treatments to prevent these complications may be somewhat less effective among those with diabetes than in the non-diabetic population.

Current Activities

During the past year, NHLBI has initiated recruitment for two major clinical trials that will evaluate several therapeutic approaches designed to reduce cardiovascular complications of diabetes. The Action to Control Cardiovascular Disease Risk in Diabetes (ACCORD) trial is conducting a 1,000 patient vanguard phase. If the vanguard is successful, ACCORD will study 10,000 patients over the next 5 years to evaluate the benefits of intensified control of hyperglycemia over more conventional glucose control and also test the benefits of aggressive blood pressure control and intensified control of the dyslipidemia associated with diabetes upon CVD rates.

The Bypass Angioplasty Revascularization Investigations II Diabetes (BARI 2D) trial will study 2,800 patients and evaluate whether elective coronary artery revascularization plus optimal medical management of cardiovascular risk factors and symptoms is superior to optimal medical management alone. It will also evaluate the important issue of whether reducing insulin resistance provides protection against cardiovascular complications by testing whether insulin- sensitizing drugs are superior to injected insulin or to oral drug regimens that stimulate insulin secretion at levels of glycemic control that are attainable with current conventional treatments. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is providing partial support for both of these trials.

NHLBI is also helping to fund the NIDDK-sponsored Action for Health in Diabetes (Look AHEAD) trial, which will evaluate the effect of obesity treatment on cardiovascular complications in type 2 diabetic patients.

While these trials should lead to clinical approaches that reduce cardiovascular complications of both type 1 and type 2 diabetes, additional more basic research is necessary to identify other ways in which this major complication of diabetes can be retarded or prevented. In view of the complexity of the available treatments and the burden they place on patients with diabetes, it is particularly important to develop new therapies that can reduce the adverse effects of diabetes on the heart and large vessels without requiring intensive efforts at glucose control. NHLBI has expanded basic research related to macrovascular complications of diabetes including large program project grants originally cosponsored with the Juvenile Diabetes Foundation.

NHLBI has also participated, in collaboration with NIDDK, in the program of small, innovative grants aimed at improved understanding of diabetic macrovascular complications. These have involved studies of the effects of diabetes on vascular smooth muscle cells, its effect on circulating growth factors, and the effect of salt restriction on insulin sensitivity. Last year, a new initiative was funded to understand the etiology of diabetes-associated cardiomyopathy, an abnormality that may contribute to the high rates of congestive heart failure in diabetic patients.

A major recommendation of the 1997 Diabetes Research Working Group report was to develop improved animal models of diabetic complications, a crucial limiting factor in expanding studies of how diabetes produces chronic micro- and macrovascular changes. During the past year, new Requests for Applications (RFAs) were released to stimulate development of these models. While collaborating on the NIDDK-led mouse model initiative, NHLBI sponsored an initiative to develop larger animal models for studies of vascular complications of diabetes.

Finally, it is important to recognize that many of the other research efforts supported by NHLBI may help to reduce or improve treatment for cardiovascular diseases occurring in patients with either type 1 or type 2 diabetes. This is because the effect of diabetes on macrovascular disease is, at least in part, to accelerate progression of the underlying atherosclerosis that is also common in non-diabetic individuals in middle and older ages. Thus, studies on treatment of congestive heart failure, treatment of arrhythmias, including public access to defibrillation, stent implantation, regeneration of cardiac muscle, and other treatments may have major benefits for patients with diabetes.

NHLBI support for studies of diabetes-related macrovascular disease has continued to increase. Funding for this work expanded further as the major clinical trials began actively recruiting participants in FY 2001. Taken together, these clinical and basic studies should provide better guidance for physicians to reduce cardiovascular complications of diabetes in the near future and provide easier to use, more effective therapies to achieve this goal in later years.

National Human Genome Research Institute (NHGRI)

The National Human Genome Research Institute supports two ongoing diabetes projects being conducted by investigators in the Division of Intramural Research and their collaborators. Both studies aim to identify genetic variations that lead to increased susceptibility to type 2 diabetes mellitus.

Current Activities

Africa America Diabetes Mellitus Study (AADM). During the past several years, the National Center for Minority Health and Health Disparities, formerly the Office of Research on Minority Health, and NHGRI have supported an innovative research collaboration between investigators from Howard University and scientists in NHGRI's Division of Intramural Research. The collaboration involves support for a project aimed at finding the genetic contribution to type 2 diabetes in African Americans. To achieve this and other research goals, NHGRI assisted Howard University in establishing a Center for collaborative research on genomic analyses of diseases that disproportionately affect African Americans. The National Human Genome Center at Howard University was dedicated on May 1, 2001. Initial efforts to define the scientific focus and objectives of the Center's diabetes research efforts were addressed through peer-reviewed contracts with Howard University as the Coordinating Center for the Africa America Diabetes Mellitus Study.

Because of the high frequency of environmental risk factors for diabetes in the African-American population, it is potentially more powerful to study genetic risk factors in West Africans, since they are thought by many anthropologists to be the founding population of modern African Americans and have fewer dietary and nutritional confounding variables. To establish recruitment sites for the study, five sites were selected through a peer review process from a total of 24 applications, three of them from diabetologists in Nigeria and two of them from diabetologists in Ghana. Because of logistical challenges involved in doing a study of this type in West Africa, the study was planned in stages to allow assessment of the sites' ability to recruit appropriate patients and collect blood, urine, and other clinical data and successfully send the samples and data to the Coordinating Center at Howard University. The 1-year pilot project fully met its goal of recruiting 15 affected sibling pairs/site. Based on this experience, a full-scale study was implemented in September 1998 to recruit 400 affected sibling pairs and 200 spouse

controls from West Africa by the end of the study period; this goal has also been fully met. Genetic analysis of the blood samples was performed this year at the Center for Inherited Disease Research (CIDR); a centralized facility established by NIH to provide genetic services for investigators seeking to identify genes that contribute to human disease. The services for the AADM study were awarded through a competitive application process. The data generated at CIDR are currently under analysis at Howard University. The study has not only started to yield high quality data, but has assisted in the recruitment of several top-flight scientists to the National Human Genome Center at Howard University.

Finnish US Investigation Of NIDDM Genetics (FUSION). NHGRI assisted in the development of a consortium of groups who have agreed to pool their linkage data on type 2 diabetes in order to study the genetic factors involved in this disease. The consortium currently has support from the National Institute of Diabetes and Digestive and Kidney Diseases and includes all of the major groups in the United States with large family collections as well as a few European groups. The consortium already has completed an analysis of chromosome 20, and is moving on to look at the rest of the genome.

NHGRI's intramural research program includes a major project, known as the Finland-United States Investigation Of Non-Insulin Dependent Diabetes Mellitus (abbreviated FUSION), which aims to identify susceptibility genes for type 2 diabetes and for the related intermediate quantitative traits in a Finnish population. The data from the FUSION project represents a major component of the type 2 diabetes consortium's effort. A genome search for genes conferring susceptibility to diabetes, or intermediate traits such as insulin resistance, was completed on DNA from approximately 3,280 individuals using more than 400 genetic markers. The project already has identified regions on chromosomes 20 and 11 that seem to harbor susceptibility genes. Further statistical evaluations of the data, including quantitative trait linkage and association analyses, have identified additional chromosomal locations that may contain susceptibility genes. These and several other potential gene locations are being followed up by candidate gene evaluation and linkage disequilibrium analysis in this unique population.

Future Activities

Technology Development for Natural Genetic Variation. NHGRI started a program to establish new academic Centers for advanced genome research. These Centers of Excellence in Genomic Science (CEGS) will support multi-investigator, interdisciplinary teams to develop innovative genomic approaches to address biological problems. One of the CEGS aims to develop and apply tools for studying natural genetic variation directed toward developing an improved understanding of the molecular basis of genetic susceptibilities to type 1 diabetes, progressive supranuclear palsy, and neutropenia.

Cultural and Ethical Issues Associated with Genetic Family Studies. The Institute's Ethical, Legal and Social Implications (ELSI) Program was designed to provide a novel approach to scientific research by identifying, analyzing and addressing the ethical, legal, and social implications of human genetics research at the same time that the basic scientific issues are being studied. This specific project aims to examine cultural and ethical issues associated with participation in genetic family studies by patients with a family history of type 2 diabetes mellitus in order to enhance the ascertainment process and establish strategies for genetic counseling of patients and relatives with a family history of type 2 diabetes and diabetic neuropathy.

National Institute of Allergy and Infectious Diseases (NIAID)

Fiscal Year 2001 (FY2001) information was not available.

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

Fiscal Year 2001 (FY2001) information was not available.

National Institute of Biomedical Imaging and Bioengineering (NIBIB)

The mission of the National Institute of Biomedical Imaging and Bioengineering (NIBIB or EB) is to improve health by promoting fundamental discoveries, design and development, and translation and assessment of technological capabilities in biomedical imaging and bioengineering, enabled by relevant areas of physics, chemistry, mathematics, materials science, information science, and the computer sciences.

Current Activities

The Institute plans, conducts, fosters, and supports an integrated and coordinated program of research and research training that can be applied to a broad spectrum of biological processes, disorders and diseases, and organ systems.

The Institute coordinates with the biomedical imaging and bioengineering programs of other agencies and NIH Institutes to support imaging and engineering research with potential medical applications and facilitates the transfer of such technologies to medical applications.

Within this mission, NIBIB supports hypothesis-, design-, technology- or problem-driven research relating to the discovery, design, development, translation, and physical assessment of new knowledge in biomedical imaging and bioengineering. The knowledge gained and the technologies developed in this endeavor will be transferred to other Institutes for the refinement and optimization that is uniquely organ- or disease-specific.

Future Activities

Diabetes research supported by NIBIB will encompass investigation of future methods to image and cope with this disease. The potential applicability of these research results will enable diabetes researchers to improve the well being of individuals with diabetes.

National Institute of Child Health and Human Development (NICHD)

The mission of the National Institute of Child Health and Human Development is to promote the development of healthy children. Understanding genetic and environmental factors that contribute to the development of diabetes is consistent with this mission, given the prevalence of both type 1 and type 2 diabetes in children and the serious complications of diabetes later in life. NICHD focuses its efforts on the earliest pathogenesis of type 1 diabetes and on optimizing insulin therapy in children with type 1 diabetes. In addition, NICHD has targeted research on the origins of type 2 diabetes in adolescents and on improving the outcome of pregnancy in women with gestational diabetes mellitus.

Current Activities

In efforts to prevent type 1 diabetes, NICHD has pioneered methods in stratifying levels of risk for type 1 (juvenile) diabetes mellitus according to genetic and immunologic markers. This work forms the basis of the Diabetes Prevention Trial for Type 1 Diabetes, a major collaborative, trans-NIH study aimed at preventing or delaying the onset of type 1 diabetes. NICHD also continues its collaboration with the Juvenile Diabetes Research Foundation International (JDRF) to co-fund a large prospective study of infants who have relatives with type 1 diabetes, to ascertain the earliest changes in gene expression in those children who become diabetic.

Recently NICHD completed a clinical research study entitled "Tolerability and Pharmacokinetics of Inhaled Insulin in Children 6–11 Years of Age with Type 1 Diabetes." Up to 36 units of insulin can be delivered through the airway system of the lungs. This study showed that inhaled insulin is as efficacious as insulin injected subcutaneously and represents a new departure in the treatment of diabetes, overcoming children's fear of injections and difficulty in complying with intensive insulin therapy.

NICHD is currently supporting a 16-site, prospective, international study of hyperglycemia and adverse pregnancy outcomes. This study of gestational diabetes mellitus will enroll 25,000 women early in their pregnancy and will follow them through their gestation, delivery, and postpartum period. Their infants will be studied as well. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is co-funding this large study. In 2001, NICHD funded eight new grant applications in response to Requests for Applications (RFAs) in the areas of fetal origins of adult disease and prevention of type 2 diabetes in adolescents. Both of these initiatives focus on early pathogenesis of insulin resistance and glucose intolerance prior to the onset of clinical diabetes.

Congressional Report 106–293 encourages NICHD to work with the National Institute of Allergy and Infectious Diseases (NIAID) and NIDDK on efforts to develop a vaccine to prevent juvenile or type 1 diabetes. In response to this Report, NICHD joined NIDDK in co-funding TrialNet, a Network of 14 centers designed to perform clinical trials of new immunomodulatory agents to treat, delay, or prevent the onset of type 1 diabetes. NICHD also joined NIDDK and NIAID in co funding the Cooperative Study Group for Autoimmune Disease Prevention, a network of investigators who are developing new methods to induce immune tolerance to self-antigens of the beta cells of the pancreas. Ultimately, this collaborative research promises to mitigate or reverse the autoimmune process that leads to type 1 diabetes.

NICHD also initiated a Cooperative Multicenter Research Network to test glucose sensors in children with type 1 diabetes. This effort is designed to reduce the incidence of hypoglycemic attacks in diabetic children on intensive insulin therapy. This multicenter trial of glucose sensors in children will utilize funds appropriated by Congress for research in type 1 diabetes for the first 3 years and will then be co-funded by NICHD and NIDDK.

NICHD's Intramural Research Program is following children in a 15-year study designed to understand the earliest pathogenesis of insulin resistance and glucose intolerance in obese children and in non-obese children of obese parents. These investigators are also studying the effects of metformin and orlistat in obese insulin-resistant children.

Future Activities

NICHD's Intramural program plans to initiate a case-control study of new-onset type 1 diabetes to elucidate the genetic and environmental factors that interact to initiate the autoimmune attack on the beta cells of the pancreas. The Pediatric Pharmacology Research Unit Network plans to augment its Phase 1 and Phase 2 studies of new molecular entities designed to ameliorate glucose intolerance in children and adolescents.

The incidence of type 1 diabetes has increased steadily over the past 30 years. It is presumed that environmental factors account for this striking increase in incidence. Epidemiologic studies and animal models implicate cow milk antigens in infant formula as an environmental agent that may trigger the autoimmune attack. Screening will begin next year to find 2,800 infants at high genetic risk of type 1 diabetes, based on HLA genotype. The infants will be randomized to standard infant formula or to Nutramigen" a casein hydrolysate. The investigators will follow the development of autoantibodies in these children through 2005. Meade-Johnson will provide the standard formula and the Nutramigen". The study will be funded by NICHD, NIDDK, the Juvenile Diabetes Research Foundation International, The Canadian Institutes of Health Research, the European Foundation for the Study of Diabetes, and the Netherlands Diabetes Foundation.

National Institute of Dental and Craniofacial Research (NIDCR)

The mission of NIDCR is to support research on the causes, prevention, diagnosis, and treatment of oral and craniofacial diseases and conditions, including oral complications associated with diabetes. These complications include greater prevalence and severity of periodontal diseases, increased susceptibility to oral mucosal infections, impaired wound healing, salivary gland dysfunction, and neuropathies resulting in loss or alteration of taste, smell, and mucosal sensory perception. NIDCR also supports research on the effects of oral diseases and conditions on metabolic control of blood glucose.

Current Activities

NIDCR and the American Academy of Periodontology co-sponsored a conference "The Periodontal – Systemic Diseases Connection," which addressed relationships between oral health and diabetes (Bethesda, Maryland; April 18–20, 2001). This meeting identified research gaps including a need for clinical intervention studies to better determine the connection between periodontitis and diabetes. Proceedings of the meeting will be published in the *Annals of Periodontology* in 2002.

NIDCR support for diabetes research in FY 2001 included support for six new Exploratory Grants (R21s) to develop new approaches for the study of the microbiology and immunology of type 1 diabetes.

Ongoing NIDCR-supported basic research included studies on:

- The role of non-enzymatic glycation of extracellular proteins in periodontal diseases.
- Impaired macrophage/monocyte function in patients with diabetes.
- Mechanisms underlying gingival connective tissue destruction in patients with diabetes.
- Regulation of B-cell autoimmunity by Interleukin-10.
- Characterization of diagnostic pancreatic autoantigens in serum and saliva of type 1 diabetes patients

Translational and clinical research/clinical trials supported included studies on:

- Salivary gland dysfunction in animals and humans with diabetes .
- Diabetes as a risk factor for periodontitis.
- A randomized clinical trial to evaluate the effect of treating periodontal infection on improving glycemic control in type 2 diabetes patients.

In addition, epidemiological studies were initiated on oral complications and oral health status in type I diabetics and on the associations between periodontitis, diabetes, and heart disease. A training and career development program to develop researchers with skills needed to study relationships between oral and systemic diseases, including diabetes, also received FY 2001 support.

Future Activities

NIDCR continues to participate in two active program announcements (PAs), "The Role of Growth Factors in the Development of Diabetes Complications" and "Enhancing Adherence to Diabetes Self-Management Behaviors." The National Institute of Diabetes and Digestive and Kidney Diseases and NINR, respectively, were the lead Institutes on these PAs issued collaboratively with several other Institutes. No additional initiatives are planned.

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

The National Institute of Diabetes and Digestive and Kidney Diseases is the lead agency of the Federal Government for research efforts to combat diabetes and its complications. The Division of Diabetes, Endocrinology, and Metabolic Diseases has responsibility for extramural programs related to diabetes research and research training. The Division of Intramural Research, the Division of Digestive Diseases and Nutrition, and the Division of Kidney, Urologic and Hematologic Diseases support additional diabetes-related activities. In addition, NIDDK is responsible for overseeing the deployment of special funds to support research on the prevention and cure of type 1 diabetes provided through the Balanced Budget Act of 1997 (P.L. 105–33) and its subsequent extension in Section 931 of the Benefits Improvement and Protection Act of 2000 (P.L. 106–554).

Current Activities

NIDDK supports a vigorous program of both basic and clinical research to further understanding of the development, treatment, prevention, and cure of diabetes and its complications. To maximize research on diabetes, the Institute has fostered collaborations among the many Institutes and Centers of the

National Institutes of Health (NIH), as well as with the Centers for Disease Control and Prevention (CDC), the Juvenile Diabetes Research Foundation International (JDRF), and the American Diabetes Association (ADA). Some examples of ongoing activities and new initiatives for FY 2001 follow.

Type 1 Diabetes. Type 1 diabetes most often occurs in children, but can appear at any age. Formerly known as insulin-dependent or juvenile-onset diabetes, it accounts for 5 to 10 percent of all diabetes in the U.S. It occurs equally among males and females, but is more common in Caucasians than in non-Caucasians. Type 1 diabetes develops when the immune system turns against itself in a disease process termed "autoimmunity." The immune system destroys clusters of cells in the pancreas called islets, which contain the body's insulin-producing beta cells. Once these cells are destroyed, type 1 diabetes patients require either lifelong insulin injections, often multiple times throughout the day, or infusion of insulin via a pump to control their blood glucose levels. Insulin therapy, however, is not a cure, nor can it always prevent the long-term complications of the disease.

NIDDK is spearheading a major clinical trial, the Diabetes Prevention Trial for Type 1 Diabetes (DPT–1), to prevent the development of type 1 diabetes in people at risk. DPT–1 is now testing whether oral insulin can prevent type 1 diabetes in people with a moderate risk of developing type 1 diabetes within 5 years. The same study group recently completed a separate trial that found that low-dose insulin injections do not prevent type 1 diabetes in people with impaired insulin secretion who have a high risk of developing the disease within 5 years. The oral insulin trial is testing a different scientific approach to preventing type 1 diabetes in individuals whose insulin production is not yet impaired. The National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Child Health and Human Development (NICHD), the National Center for Research Resources (NCRR), JDRF, ADA, and industry also support DPT–1.

A new NIDDK initiative that will facilitate additional clinical research on type 1 diabetes is the Type 1 Diabetes TrialNet. Spearheaded by NIDDK, this effort is co-sponsored by NIAID and NICHD. TrialNet will include clinical centers, recruitment networks, and a coordinating center. It will provide the research infrastructure needed for future design and execution of pilot studies and expanded clinical research. TrialNet will permit more rapid clinical testing of novel approaches to treatment and prevention of type 1 diabetes. TrialNet will also enable efficient performance of intervention studies to preserve pancreatic beta cell function in new-onset cases of type 1 diabetes, and ultimately to prevent onset of the disease.

The Diabetes Control and Complications Trial (DCCT) established the importance of intensive diabetes control in type 1 diabetes to dramatically reduce the devastating complications that can result. However, with current treatment modalities, tight control remains an unattainable goal for many people with diabetes. Episodes of severe hypoglycemia are the major obstacle to the achievement of euglycemia and the prevention of long-term complications. Hypoglycemia is frightening to the patients and their families. Diminished brain function during a hypoglycemic episode poses potential physical danger to the patient. In addition, recurrent hypoglycemia may impose long-lasting damaging effects on the brain, resulting in impairment of memory or other cognitive functions. This is especially concerning in the early childhood years when the nervous system is still developing. Over time, individuals may not be aware of the significant drop in blood glucose levels—a condition known as hypoglycemia unawareness. To highlight the problem of hypoglycemia in individuals with diabetes, JDRF, ADA, NIDDK, the National Institute of Neurological Disorders and Stroke (NINDS), NICHD, and the National Aeronautics and Space Administration (NASA), co-sponsored a workshop entitled "Hypoglycemia and the Brain." An initiative developed from recommendations of the workshop will define the mechanisms underlying the loss of hypoglycemia awareness in patients with diabetes and develop novel approaches to prevent or reverse

hypoglycemia unawareness. Related research will define the scope and nature of hypoglycemia in individuals with diabetes and develop and test strategies to prevent the development of hypoglycemia or to ameliorate its effects.

In related research, NIDDK is co-sponsoring the creation of a Type 1 Diabetes in Children Research Consortium, led by NICHD. The Consortium will develop and implement a protocol using continuous glucose monitoring devices in children with type 1 diabetes to evaluate the utility of the devices and to determine if continuous monitors are useful in improving glycemic control and preventing hypoglycemia in children with the disease. This study should complement knowledge gained about the risks and benefits of intensive therapy in adolescents and adults during and after the DCCT.

The Beta Cell. Gaining knowledge about the beta cells of the pancreatic islets is important to both type 1 and type 2 diabetes because they are the key to insulin production and resulting glucose control. Two major conferences addressed this important research area in diabetes. NIDDK, along with ADA and JDRF, sponsored a conference entitled "Pancreatic Development, Proliferation, and Stem Cells." This 2-day workshop brought together investigators from multiple disciplines doing state-of-the-art research in developmental biology of the pancreas, islet cell biology, and stem cells. A second conference, "Beta Cell Biology in the 21st Century: Engineering a Pathway to Greater Understanding," was sponsored by NIDDK, JDRF, ADA, and Lilly Research Laboratories. This workshop showcased recent progress in beta cell biology and exciting new results in other systems that will impact future work in the beta cell. It also provided a forum to explore new research directions provided by emerging genomic and proteomic information.

One of the extraordinary research opportunities recommended by the congressionally established Diabetes Research Working Group was to better define signaling in the beta cell and to use this increased knowledge of beta cell biology to develop novel treatments for diabetes. To this end, NIDDK has initiated the "Comprehensive Beta Cell Project," which includes the "Functional Genomics of the Developing Endocrine Pancreas" project and the "Beta Cell Biology Consortium." Together these projects are designed to enumerate all the protein coding regions uniquely expressed in the developing and adult beta cells from human and mouse, to clone the associated mRNAs, and to gain a better understanding of beta cell development and differentiation in hopes of obtaining an unlimited supply of new beta cells or islets for use in long-term treatment of type 1 diabetes.

NIDDK has also initiated a functional genomics program, the Diabetes Genome Anatomy Project (DGAP), which has initially focused on the endocrine pancreas and has as a major goal development of tools that are targeted to restoration of pancreatic beta cell function. This program involves a consortium of investigators at Washington University, the University of Pennsylvania, and Harvard University with expertise in pancreatic development, functional genomics and bioinformatics. This program will catalog all genes expressed in the developing mouse pancreas and make clones available through the IMAGE consortium. The Center for Bioinformatics at the University of Pennsylvania will soon release a Web-based database that will contain tools to aid researchers in expression profiling, gene discovery, and promoter analysis.

Microarrays developed by this consortium should prove valuable for studies of islet cell development, bioengineering of beta cells, and stem cell biology.

Little is known about the natural history of beta cell mass, turnover, and cell lifetime, or the course of inflammation in diabetes. This is principally because the pancreas is a highly heterogeneous organ that is difficult to biopsy, and beta cell mass comprises only 1 to 2 percent of the organ. Imaging technology has advanced rapidly in recent years, making it possible to image small or deep structures that have until now been impossible. It would be of great benefit to the diabetes community to be able to image the cells of the pancreatic islets. NIDDK has re-issued a solicitation to further stimulate the development of techniques or reagents leading to the ability to image or otherwise non-invasively detect pancreatic islet beta cells in vivo, and to measure their mass, function, or evidence of inflammation, or to monitor engraftment of transplanted pancreatic islets. It is anticipated that research in this area will lead to eventual development of a clinical exam that can be used for monitoring disease progress and response to therapy in diabetics and in people at risk for diabetes.

Islet Transplantation for Type 1 Diabetes. For decades, researchers have been searching for ways to treat, prevent, and ultimately cure type 1 diabetes. They have pursued means other than the external administration of insulin to regulate blood glucose levels and/or to restore insulin-producing capacity. Successful transplantation of the whole pancreas is the most common procedure to re-establish normal blood glucose regulation; however, this procedure entails major surgery and is usually done only in conjunction with a kidney transplant in those individuals with end-stage renal disease. Moreover, it is not a feasible therapy for young children with type 1 diabetes. Therefore, scientists have been concentrating on methods for replacing only the insulin-producing islets isolated from a donor pancreas.

In pursuing this area of research, NIDDK, in a collaborative effort with NIAID and JDRF, has supported numerous centers to develop improved protocols for islet transplantation in humans. In complementary research, NIDDK, in conjunction with the Department of the Navy, has established a Transplantation and Autoimmunity Branch that will explore new approaches to both kidney and islet transplantation for diabetes. The Walter Reed Army Medical Center and the University of Miami's Diabetes Research Institute are also collaborating on this research.

NIDDK and JDRF are also co-sponsoring the Immune Tolerance Network (ITN), a collaboration involving numerous research institutions spearheaded by NIAID. The ITN will solicit, develop, implement, and address clinical strategies, including biological assays, for the purpose of inducing and maintaining immune tolerance in patients receiving kidney and islet transplants. The Transplantation and Autoimmunity Branch of the NIDDK Division of Intramural Research is one of 11 centers participating in ITN's testing of the "Edmonton Protocol" in performing transplant procedures in a larger number of patients. This clinical research will further assess the effectiveness of the technique and identify any long-term risks associated with steroid-free immunosuppressive therapies. Researchers hope the study will serve as a platform for testing new treatments in which the permanent reversal of diabetes can be achieved without the lifelong need for immunosuppressive drugs. In addition, NIDDK will support two additional studies to determine if one pancreas can provide sufficient islets for transplantation into one patient. In support of all of these efforts, NCRR is establishing several centers aimed at maximizing islet harvesting processes.

One barrier to widespread islet transplantation is the limitation in the supply of islets from donor pancreata. Ex vivo gene transfer approaches may be one method to engineer beta cells or to alter islets to enhance viability that could have advantages for transplantation. NIDDK and NIAID are soliciting pilot and feasibility studies to explore gene transfer techniques that could be applied to enhance islet transplantation.

Type 2 Diabetes. Type 2 diabetes is the most common form of the disease. Once known as non-insulin-dependent or adult-onset diabetes, it affects about 90 to 95 percent of people with diabetes. Two factors play an important role in the growing public health burden of type 2 diabetes—the changing demographics of America in terms of age, ethnicity, and race and the increasing prevalence of obesity, a major risk factor for the disease. Diabetes is the sixth leading cause of death in the U.S. and the third leading cause of death in some minority groups. It places an especially heavy burden on growing segments of the U.S. population—elderly and minority groups. NIDDK is spearheading NIH-wide research efforts to combat diabetes and obesity in order to stem the tide of this devastating disease.

For those at risk for type 2 diabetes, results from a major NIDDK clinical trial are providing important knowledge about prevention strategies. The results of the Diabetes Prevention Program (DPP) demonstrate that individuals with IGT at high risk of developing type 2 diabetes can prevent or delay disease onset and improve their blood glucose through modest improvements in diet and exercise. Of the over 3,200 participants in the DPP, 45 percent are from minority populations that suffer disproportionately from type 2 diabetes—African Americans, Hispanic/Latino Americans, Asian Americans, Native Hawaiians and other Pacific Islanders, and American Indians/Alaska Natives. All participants were overweight with impaired glucose tolerance and were randomly assigned to one of the following groups: intensive lifestyle changes, treatment with the medication metformin, or a placebo control. The lifestyle intervention aimed to reduce weight by 7 percent through a low-fat diet and exercising for at least 150 minutes per week. Patients in the lifestyle intervention group were 58 percent less likely to develop diabetes than those in the control group. The lifestyle intervention was effective for both men and women and in all of the racial/ethnic groups. Lifestyle intervention also worked well in people over age 60, reducing the development of diabetes by 71 percent in this group. Participants randomized to treatment with metformin reduced their risk of developing the disease by 31 percent. The DPP was co-sponsored by NICHD, the National Institute on Aging (NIA), the National Center for Minority Health and Health Disparities (NCMHD), NCRR, the NIH Office of Research on Women's Health (ORWH), and the Office of Behavioral and Social Science Research (OBSSR). CDC, ADA, and industry provided additional support.

A post-DPP study will enable investigators to continue a long-term followup of the DPP cohort.

Another clinical trial of great significance to type 2 diabetes is "Look AHEAD—Action for Health in Diabetes." This large, multicenter trial is designed to determine whether interventions to produce sustained weight loss in obese individuals with type 2 diabetes will improve health. The trial is expected to recruit a patient population whose overall ethnic and racial composition will reflect the prevalence rates for diabetes in the U.S. NIDDK is sponsoring this trial along with the National Heart, Lung and Blood Institute (NHLBI), the National Institute of Nursing Research (NINR), NCMHD, ORWH, and CDC.

It is well recognized that there are major differences in the prevalence of type 2 diabetes among racial-ethnic groups in the U.S. A research solicitation entitled, "Racial and Ethnic Differences in the Etiology of Type 2 Diabetes in Minority Populations," will determine, through studies in representative U.S. populations, the reasons for disparities in the incidence of type 2 diabetes in minority racial-ethnic populations. Additionally, information that could emerge from these studies would be important for devising cost-effective approaches to phenotyping patients with type 2 diabetes and individuals at risk for the disease.

Type 2 Diabetes in Children. Type 2 diabetes has traditionally been considered a disease of adults because the age of onset is frequently after age 40 and it is often associated with obesity. Children with diabetes usually have been presumed to have type 1 diabetes; however, in recent years, an increasing number of children who appear with elevated blood glucose levels are being diagnosed with type 2 diabetes. The increase in reports of type 2 diabetes among children parallels a similar rise in the adult population, as obesity has become a major public health concern. In children, the increased incidence of type 2 diabetes appears to be occurring largely in minority populations—Hispanic/Latino Americans, African Americans, and Native Americans—again paralleling the disproportionate burden this disease places on the same minority populations in adulthood.

To combat type 2 diabetes in children, NIDDK, along with NICHD, is supporting research to promote greater understanding of its causes, to refine diagnostic criteria, to define metabolic abnormalities, and to formulate treatment options. In addition, NIDDK has recently awarded support for a coordinating center and clinical centers to develop community- or school-based primary prevention programs that can be applied in a cost-effective manner to decrease the risk factors for type 2 diabetes and to reduce the incidence of this disease in children and adolescents. Treatment options will be studied to determine the safest, most effective, and cost-effective strategies to achieve and maintain normal blood glucose levels in the pediatric population.

Genetics of Diabetes and Its Complications. Diabetes and its complications have strong genetic determinants. Even though diabetes appears to develop as a result of many factors, virtually all forms appear to have genetic influences, with the likely involvement of multiple genes. NIDDK is involved in major initiatives to capitalize on new knowledge about the human genome and the genetics of diabetes. The Institute is a leading partner in support of the International Type 2 Genetic Linkage Analysis Consortium. The purpose of the Consortium is to combine data from multiple genome scans and thus increase the probability of gene discovery. The groups involved in the Consortium are pursuing a fine mapping effort of potential susceptibility genes for type 2 diabetes located on several chromosomes. Intensified support for the Consortium will also permit additional analyses to determine whether unique susceptibility genes exist in African Americans, who are disproportionately affected by type 2 diabetes.

NIDDK and JDRF are working closely to establish a Type 1 Diabetes Genetics Consortium. The initial objective would be to pursue the results of three genome-wide scans for type 1 diabetes, which have recently been completed. These scans have identified several genetic regions as likely to contain diabetes susceptibility genes. A combined analysis of these three datasets could identify the most promising areas for further study of genes that confer susceptibility to type 1 diabetes.

To identify the genes responsible for the kidney complications of diabetes, the Institute is now launching a new genetics initiative called "FIND"—the Family Investigation of Nephropathy and Diabetes. This initiative will focus on family studies designed to uncover candidate genes associated with type 1 or type 2 diabetes, genes associated with development of complications, and genes relevant to those identified in animal models. A specific objective will be to search for susceptibility genes in subpopulations of Caucasians, African Americans, Hispanic/Latino Americans, and American Indians/Alaska Natives across the U.S.

In FY 2001, NIDDK issued a solicitation to establish a cross-disciplinary Mouse Models of Diabetic Complications Consortium that will develop innovative mouse models of diabetes complications that closely mimic human disease. The consortium will generate animal models that will be useful for the study of disease pathogenesis, prevention and treatment and test the role of candidate genes or chromosomal regions that emerge from genetic studies of human diabetic complications, particularly diabetic kidney disease and accelerated cardiovascular disease. When a model is sufficiently characterized and validated, the mice will be distributed to the research community for individual investigator-initiated projects.

Complications of Diabetes. The complications of diabetes affect virtually every system of the body. Diabetes is the leading cause of kidney failure, new blindness in adults, and non-traumatic amputations. It is a major risk factor for heart disease, stroke, and birth defects; shortens average life expectancy by up to 15 years; and costs the nation in excess of $100 billion annually in health-related expenditures. NIDDK is undertaking several new and expanded initiatives designed to further understanding of the key mechanisms involved in development of the complications of diabetes and the means to reduce or prevent them. Some examples of research solicitations in this area follow.

Diabetes is the leading cause of non-traumatic lower extremity amputations in the U.S. Foot ulcers are a major predictor of future amputation in patients with diabetes. Even without amputation, diabetic foot ulcers contribute a major economic burden to society and impair quality of life for the individual. Despite advances in wound care, the incidence of diabetic foot ulcers, and of amputations, remains high. An initiative entitled "New Therapies for Diabetic Foot Disease" encourages research on the etiology and pathogenesis of diabetic foot ulcers and development of effective prevention and treatment modalities. It is hoped that this solicitation will lead to new diagnostic, prognostic, and therapeutic strategies to reduce the burden of diabetic foot disease. NINR is also supporting this initiative.

Extant information on the incidence of complications in the U.S. is often based on community populations or large clinic populations in which the onset of diabetes occurred several decades ago. These studies generally found a striking and large excess of microvascular disease in minority racial and ethnic groups, including American Indians/Alaska Natives, African Americans, Hispanic/Latino Americans, Asian Americans, Native Hawaiians and other Pacific Islanders. Whether these disparities in diabetes complications continue to occur in contemporary diabetic patients is not known. A solicitation entitled "Race/Ethnic Disparities in the Incidence of Diabetes Complications" will investigate differences among contemporary populations in the U.S., categorized by race, ethnicity, and other factors, in risk factors for the development and rates of complications in diabetes. Research supported through this initiative may also aid in determining the extent to which other factors, including metabolic and genetic variations, medical care, socioeconomic status, and behavior account for these differences.

Over 60 percent of individuals with diabetes suffer from some form of neuropathy, and in many patients the symptoms are serious enough to interfere with daily activities. Diabetic peripheral neuropathy is often associated with peripheral vascular disease and impaired wound healing. Symptoms of diabetic autonomic neuropathy can include heart rate abnormalities, blood pressure dysregulation, dizziness, digestive disturbances, and impotence. Autonomic neuropathy is thought to be an important cause of sudden cardiac death in patients with diabetes. Effective therapies for the prevention and treatment of diabetic neuropathy are not currently available. An initiative sponsored by the National Institute of Neurological Disorders and Stroke (NINDS), and supported by NIDDK and JDRF, may lead to increased understanding of the mechanisms by which diabetes results in painful, disabling peripheral neuropathy, autonomic neuropathy, impaired counterregulation and hypoglycemia unawareness, and other neurologi-

cal complications. It is the intent of this initiative to attract basic neuroscientists to the study of diabetic neuropathy and neurobiology relevant to diabetes and enhance interdisciplinary approaches to research in this area.

In November 1999, NIDDK, NIAID, NHLBI, NCRR, JDRF, and ADA sponsored a meeting entitled, "Gene Therapy Approaches for Diabetes and Its Complications." One of the recommendations from the meeting was to support additional studies to develop novel approaches using gene therapy for the treatment of diabetes and its complications. There are many approaches to interfering with the development of type 1 diabetes and to treating the complications resulting from both type 1 and type 2 diabetes that would appear to be amenable to gene therapy technology. A solicitation spearheaded by NIDDK also encourages development of gene therapy approaches for type 1 diabetes and its complications and to their application in appropriate animal models or small pilot studies.

Prevention and treatment of long-term complications remain critical problems in the management of both type 1 and type 2 diabetes. Identification of patients at risk for the development of complications, with the hope of early intervention, is a public health priority. Early intervention is essential, because by the time symptoms of disease are recognized, irreparable damage to organs may have already occurred. NIDDK, in collaboration with the National Eye Institute (NEI) and NINDS invites basic and clinical research to develop biochemical, cellular, physiologic, and genetic surrogate endpoints that can be used to predict risk, aid in early diagnosis, and assess the progression of complications of diabetes. The overall aim of this solicitation is to develop biomarkers that could be used as diagnostic tools for the individual patient, or as outcome measures to be used in clinical trials testing new therapeutic agents.

In the U.S., diabetes is the leading cause of new cases of end stage renal disease. Large-scale interventional trials have established that blockade of the renin-angiotensin system and good glycemic control both slow the progression of diabetic kidney disease. Nonetheless, many patients with diabetes develop progressive kidney disease in spite of adequate management of these factors, and new strategies, both to prevent disease and to slow its progression, are needed urgently. NIDDK has issued a solicitation for clinical research trials using novel agents or drug combinations in patients to prevent the appearance or slow the progression of diabetic kidney disease. The goal of this initiative is to evaluate therapies that might potentially be taken to large, phase III interventional trials.

Bench-to-Bedside—Translation of Research into Clinical Practice. One initiative, spearheaded by NIDDK, will support partnerships between clinical and basic biomedical researchers with the goal of translating advances in understanding of the molecular basis of type 1 diabetes and its complications into new therapies for the prevention, treatment, and cure of this disease. In the "bench to bedside" research partnerships, a team of clinical and basic scientists will conduct collaborative research that, if successful, will bring basic research advances from the laboratory to a point where potential new therapy can be tested in patients or in preclinical studies in animal models.

Education and Outreach.
Refer to NDEP Section (pg. 45)

Diabetes has long been used in teaching biomedical sciences as a model for understanding the physiology and cell biology of organ systems, since it affects so many systems. Diabetes is an especially relevant model for teaching biology to younger students, particularly in communities adversely impacted by the disease. Moreover, education focused on diabetes could serve several purposes in such communities, such as fostering science education, encouraging students to select science and health-related career paths, and providing information that may influence healthy lifestyle choices in children and families at risk for diabetes. Through this, Tribal youth can be instrumental in preventing the development of and promoting better management of diabetes for themselves and in their own communities. A recent solicitation resulted in support for seven Tribal Colleges or Universities for planning grants to develop educational programs to enhance understanding and appreciation of diabetes and related science in elementary, middle and high schools serving American Indian/Alaska Native communities.

National Institute of Environmental Health Sciences (NIEHS)

Many environmental agents have been investigated as contributing to the risk of type 1 diabetes. Environmental components have been suggested because concordance rates between identical twins, where one twin has type 1 diabetes, remain at 30 to 50 percent. NIEHS is pursuing research in several areas relevant to the etiology of type 1 diabetes, as summarized below.

Current Activities

Recent studies have raised the possibility that certain chemicals in the environment, such as nitrates in well water, increase the risks of juvenile diabetes. Studies in the United Kingdom, Finland, and Colorado indicate that the incidence of childhood diabetes is higher in areas with elevated levels of nitrate in the drinking water. This finding is significant for agricultural communities because well water can have elevated nitrate levels in areas where there is extensive use of fertilizers. Current and future activities in this area by NIEHS intramural scientists include:

- Further investigation of the possible association between nitrates and juvenile diabetes in a rigorous prospective study, such as the Agricultural Health Study.

- Evaluation of diabetes along with other health outcomes in the Agricultural Health Study.

In other studies, intramural investigators at NIEHS have reported an association between the body burden of a persistent organic pollutant (polychlorinated biphenyls) and type 1 diabetes. Current and future studies in this area include further studies to examine the relation between diabetes and body burden of persistent organic pollutants are either underway or being planned. For example, DNA is being collected from a cohort of men so that polymorphisms in the Ah-receptor (binds with dioxin-like polychlorinated biphenyls) can be examined in relation to body burden of persistent pollutants and risk of diabetes.

In extramural studies supported by NIEHS, investigators are studying the possibility that arsenic in drinking water causes an increase in diabetes risk. Elevated levels of arsenicals in drinking water are common throughout the world, and oxidative forms of arsenic are known to have cytotoxic effects. These studies will:

- Investigate the effects of trivalent arsenicals and related compounds on glucose- stimulated insulin secretion in pancreatic islets and cell culture systems.

- Examine the effects of these compounds on insulin sensitivity in insulin-sensitive peripheral tissues and in intact animals.

NIEHS intramural investigators are also investigating the role of menstrual and reproductive risk factors in diabetes and are looking at mechanisms of how environmental agents can affect pancreatic cancer cells.

National Institute of General Medical Sciences (NIGMS)

The National Institute of General Medical Sciences supports research and research training in the basic biomedical sciences that provide the foundation for a better understanding of fundamental life processes. Some of this work has relevance to understanding and treating diabetes.

Current Activities

NIGMS supports the Human Genetic Cell Repository, a collection of over 6,600 cell lines from individuals with a wide variety of genetic disorders, including diabetes, and from normal individuals. Cell lines in the collection include those from individuals with various types of diabetes, including insulin-dependent diabetes mellitus (IDDM) and diabetes mellitus and insipidus with optic atrophy. The repository includes an extensive collection of cell lines from members of an extended pedigree with maturity-onset diabetes of the young. This collection is of value in studies designed to map and characterize the gene(s) responsible for the disorder.

NIGMS has an interest in understanding how genetic and environmental components interact to result in complex diseases such as diabetes. The Institute supports a portfolio of grants to develop better statistical methods for mapping and identifying genes underlying complex traits, to develop mathematical models for studying gene-gene and gene-environment interactions, to investigate DNA sequence variation and its evolution, to examine gene activities and the consequences of abnormalities in these activities, and to optimize sampling strategies. NIGMS also supports pre- and postdoctoral training that emphasizes statistical and computational skills and workshops to provide additional training in statistical methods to biologists.

NIGMS support for research on the mechanisms underlying individual variations in drug response, while not specifically targeting diabetes, has the potential to have an impact on the treatment of diabetes and its complications. Researchers are studying the structural features of a powerful peripheral vasodilator related to insulin identified as an important prospective drug for peripheral angiopathies associated with diabetes.

NIGMS, in conjunction with several other Institutes, is supporting a mouse mutagenesis and phenotyping center whose emphasis is the high-throughput generation and identification of mice with mutations in developmental defects, including those that affect organogenesis.

NIGMS is also participating in the Trans-NIH Zebrafish Initiative, whose goal is to improve the genomic resources for the zebrafish, a potentially valuable model for diabetes.

For many of the cell lines in the Human Genetic Cell Repository, DNA is also available. In a major new initiative, the Repository has cooperated with the National Human Genome Research Institute to acquire a collection of cell lines, and DNA, from 500 unrelated individuals representative of the diversity of the U.S. population. This resource has already been of great value to researchers for the discovery of DNA polymorphisms, an important step in identifying genes involved in complex genetic disorders such as diabetes.

Future Activities

In the future, NIGMS will continue to support basic research that focuses on underlying mechanisms and principles that are expected to shed light on both normal and disease processes and to lead to the development of new modes of treatment and prevention.

National Institute of Mental Health (NIMH)

The National Institute of Mental Health (NIMH) supports research on the processes and mechanisms underlying co-morbid mental disorders and diabetes. It also supports research to develop and test preventive, treatment, and rehabilitative interventions for mental disorders in people with diabetes—the interventions may be pharmacologic, behavioral, or psychosocial.

Current Activities

In FY 2000–2001, NIMH and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) co-sponsored a major research conference, "Depression and Mental Disorders in Patients with Diabetes, Renal Disease, and Obesity/Eating Disorders," on January 29–30, 2001 at the Natcher Conference Center, National Institutes of Health. The papers resulting from the conference are currently in preparation for journal publication in 2002.

Future Activities

NIMH and NIDDK have jointly released a Request for Applications with a set aside of $1.5 million to fund new research projects in FY 2002. In addition, NIMH will re-issue in FY 2002, its program announcement calling for research applications on co-morbid mental and physical disorders, including diabetes.

National Institute of Neurological Disorders and Stroke (NINDS)

The National Institute of Neurological Disorders and Stroke supports a portfolio of research to study the neurological complications of diabetes. Over 60 percent of people with diabetes are affected by neuropathy, and in many patients symptoms such as pain, numbness, weakness, or even paralysis are serious enough to interfere with daily activities. Symptoms of diabetic autonomic neuropathy can include heart rate abnormalities, hypertension, dizziness, digestive disturbances, and impotence. Autonomic neuropathy is an important cause of sudden cardiac death in people with diabetes. Prevention and treatment of neurological complications is a central therapeutic problem in diabetes mellitus, as well as ancillary research in the areas of metabolism, sensory disorders, impaired wound healing, and pain.

Current Activities

NINDS has participated in nine initiatives related to the type 1 diabetes appropriations, three as the lead Institute. As the result of three RFAs (Requests for Applications) published each year between FY 1998 and FY 2000, NINDS has greatly expanded its research into neurological complications of diabetes. New areas of study include early detection of diabetic neuropathy, gene transfer for prevention of neuropathy, autonomic neuropathy, behavioral effects of hyperglycemia, and mechanisms of neuropathic pain.

NINDS continues to support a large epidemiological study of neurological complications of diabetes in the Rochester, Minnesota, area in the Caucasian and Mdewakanton Dakota Native American populations.

Future Activities

In FY 2002, applications in response to a new RFA, "Effects of Hypoglycemia on Neuronal and Glial Cell Function," will be received. This RFA solicits basic studies (1) to define the effect of varying glycemic levels on cerebral metabolism, transport of glucose across the blood brain barrier, and astrocytic regulation of substrates for neuronal metabolism, and (2) to determine pathological consequences of acute and recurrent hypoglycemic insult on cells of the central nervous system.

In addition to the Caucasian and Mdewakanton Dakota Native American populations, the Rochester epidemiological study will be expanded to include Hispanic subjects. Diabetes is characterized by large disparities in prevalence among ethnic groups, but little is known about the extent of neurological complications in these populations. This study will be the first to document the extent and progression of neurological complications in a longitudinal multiethnic cohort.

National Institute of Nursing Research (NINR)

The National Institute of Nursing Research supports and conducts research and research training on the biological and behavioral processes that underlie promotion of health, amelioration of illness and its sequelae, and effective delivery of care. One purpose of this research, specific to diabetes, is to understand how to promote health-sustaining behavior and to improve quality of life by relieving the effects of disease processes and their progression. Nursing research focuses on how physical and psychological responses to diabetes symptoms and treatment of the disease affect health throughout the lifespan. NINR research programs pay particular attention to special populations affected by diabetes.

Current Activities

In response to three Program Announcements (PAs) either directly or indirectly related to diabetes research, NINR had a significant increase in diabetes funding in FY 2000 and FY 2001. The three PAs were published in January and June of 2000. Two were specific to diabetes research and the third included diabetes research opportunities.

The announcements were "Enhancing Adherence to Diabetes Self-Management Behaviors," "Diabetes Self-Management in Minority Populations," and "Self-Management Strategies Across Chronic Diseases." These PAs are consistent with the congressionally mandated Diabetes Research Working Group (DRWG) recommendations (NINR was a participant in this working group).

In response to increased congressional support for type 1 diabetes research, NINR also joined three requests for applications: "Innovative Partnerships in Type 1 Diabetes Research," "New Approaches to Prevent Hypoglycemia in Patients with Diabetes," and "Understanding Hypoglycemia Unawareness in Patients with Diabetes."

Funded grants related to diabetes research included career development, postdoctoral training, and research. Diabetes-specific topics included ethnic variations in type 2 diabetes prevention knowledge, cardiac risk factors in type 1 and 2 adolescents, autonomy and self-care in type 1 adolescents, Spanish language self-management programs, intervention studies in several ethnic groups, a description of the integration of diabetes self-care in Mexican-Americans with type 2 diabetes in the southwest, an intervention for parents of young children with newly diagnosed diabetes, biophysical determinants of diabetes foot ulcer healing, weight loss in diabetes, and children's response when a sibling has type 1 diabetes.

Future Activities

NINR plans to continue to support research that focuses on problems experienced in diabetes populations. Research efforts will be guided by the following goals:

- FY 2002: NINR plans to focus support on promising ongoing and new diabetes research areas, while building on recent nursing science advances.

- FY 2003: NINR will work collaboratively with other Institutes and organizations to increase and facilitate diabetes research activities.

In summary, NINR activities are designed to support research related to diabetes interventions, self-management, quality of life, special and diverse population needs, problems of defined age groups and across the lifespan, basic research, genetics, and other initiatives relevant to clinical practice and client outcomes. Advances in science leading to translation to the practice setting will be encouraged.

National Institute on Aging (NIA)

The mission of NIA as it relates to diabetes research and related issues is to support biomedical and behavioral research leading to improved therapies to prevent diabetes and its complications, as well as improved quality of life of older diabetic patients.

Current Activities

NIA continues to support studies of potential metabolic mechanism(s)/factors that contribute to and/or underlie deleterious changes in body composition that can lead to metabolic disorders in old age.

Ongoing studies in animal models have found that surgical removal of visceral fat results in increased insulin sensitivity similar to that seen with caloric restriction. It has also been noted that insulin-mediated suppression of hepatic glucose production during hyperinsulinemia is diminished with aging in ad lib fed rats. By preventing an increase in visceral fat, or fat mass, or with caloric restriction, there can be marked improvement in the ability of insulin to suppress hepatic glucose production.

Ongoing clinical studies are focusing on the development of interventions to reduce abdominal fat and on the factors mediating regional differences in body fat noted in older NIDDM patients.

Insulin resistance is a metabolic disorder that may precede the development of type 2 diabetes in older adults. Ongoing studies in aging rats have shown that insulin resistance is characterized by elevated insulin release as well as increased glucose effectiveness (the latter reflecting primarily enhanced hepatic action of glucose to suppress endogenous glucose production).

It also appears that free fatty acids (FFA) play a key role in endogenous glucose production. Acute glucose elevation induces a marked decline in plasma FFA. Such findings suggest that at basal insulin, inhibition of endogenous glucose production by hyperglycemia may be mediated by glucose-induced suppression of FFA.

NIA was a cosponsor of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and DMICC workshop, "Diabetes and Aging, From Basic Biology to Clinical Care: New Research Directions for Understanding Diabetes in Older Age."

NIA was also a cosponsor of the NIDDK study, Diabetes Prevention Program (DPP).

NIA participated in the DMICC Task Force to develop a Diabetes Prevention Initiative.

Future Activities

Data from animal models suggest that caloric restriction (CR) can prevent and/or delay the onset of age-related pathologies, including insulin insensitivity. Moreover there are data that demonstrate that physical activity can decrease body weight and body fat comparably to CR and have similar effects on glucose tolerance and insulin sensitivity, but physical activity has significantly less effect on life span.

In March 1999, NIA and NIDDK co-sponsored the meeting of the Caloric Restriction Clinical Implications Advisory Group. Based on the scientific recommendations from the Caloric Restriction Advisory Group, NIA issued the Request for Applications (RFA), "Exploratory Studies of Sustained Caloric Restriction in Non-Obese Persons: Physiologic Effects and Comparisons/ Interactions with Physical Activity." Briefly, the purpose of this RFA was to solicit applications for cooperative agreements (U01s) for exploratory controlled human intervention studies on the effects of caloric restriction (CR) interventions on physiology, body composition, and risk factors for age-related pathologies in non-obese persons. Studies of similarities, differences, and/or potential interactions between the effects of CR and of physical activity (PA) on these outcomes were also invited. Three sites will be awarded from this RFA, and this group of U01 projects will be known as CALERIE (Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy). It is anticipated that the CALERIE studies will begin in early 2002.

National Institute on Alcohol Abuse and Alcoholism (NIAAA)

The National Institute on Alcohol Abuse and Alcoholism encourages research to understand the role of alcohol consumption as a risk factor in the development of diabetes mellitus. NIAAA also supports research to determine the effects of moderate alcohol consumption on diabetes. Several studies suggest that alcohol consumption may directly or indirectly contribute to the development of type 1 diabetes. This contention is based on following observations: (a) alcohol may impair the release of insulin from the pancreas; (b) chronic alcohol intake can increase plasma levels of TNF, which has been shown to cause apoptosis of pancreatic beta cells that in turn may decrease beta cell number and insulin secretion; and (c) chronic alcohol consumption may impair beta cell function by eliciting immunotoxicity.

Chronic alcohol consumption also has been implicated in the development of type 2 diabetes based on the following findings: (a) chronic alcohol feeding in rats reduces the number of insulin binding sites on isolated hepatocytes; (b) alcohol impairs insulin-mediated tyrosine phosphorylation of insulin receptors in a tumor cell line; (c) chronic alcohol exposure blunts tyrosine phosphorylation of insulin receptor substrate-1 in rat hepatocytes and a tumor cell line; and (d) chronic alcohol exposure inhibits the activity of rat hepatocyte phosphotidylinositol-3kinase, which stimulates glucose transport. These effects of alcohol may lead to insulin resistance and impaired glucose transport.

Current Activities

Currently, NIAAA supports three projects that investigate the relationship between alcohol intake and diabetes. The following research areas are under investigation:

- Impact of moderate alcohol consumption on the risk of diabetes mellitus.
- Effects of fetal alcohol exposure on the biochemical and physiological changes in the insulin response and glucose homeostasis.
- Molecular mechanisms of disruption of insulin-mediated glucose transport by ethanol.

National Library of Medicine (NLM)

In particular, NLM seeks to learn how the use of NLM's MEDLINEplus Web site, and other computer-based health information resources, can be helpful to patients, their families, and members of the public to learn about and understand the latest research news on diabetes, nutritional requirements, tests, devices, secondary prevention techniques, and for obtaining answers to patient-specific questions.

In the clinical setting, the principal hypothesis is that MEDLINEplus can reinforce and supplement the information provided by physicians, nurses, and health educators. A related hypothesis is that a combination of individualized training and access to publicly available computer resources at hospital libraries and elsewhere in the community can help bridge the "digital divide" experienced by minority populations who have less ready access to computers in the home, school, and workplace than the majority population.

Current Activities

NLM's objectives are to develop, design, implement, and evaluate a comprehensive program of diabetes-focused outreach initiatives in collaboration with academic health science centers and libraries, clinical centers, community-based organizations, and voluntary health organizations.

Project A. In collaboration with the Naomi Berrie Diabetes Center at Columbia/Presbyterian Hospital in New York City, this project studies the benefits of MEDLINEplus and the Center's own Web site with Hispanic and African-American teenage type 1 diabetes patients who are on the insulin pump. These new resources are intended to reinforce and supplement the information provided by the Center's physicians, nutritionists, and educators. The Center is also working with the medical informatics department at Columbia to build a type 1 diabetes module for a promising telemedicine system now under development for patients and hospital staff.

Project B. In collaboration with the Children's Hospital of Los Angeles, this project studies how a diverse patient population of Hispanic and African-American teens and the families of newly diagnosed type 1 patients can benefit from using MEDLINEplus to learn about and understand the latest research news, nutritional requirements, and uses of new medical devices for promoting better diabetes management and control.

Project C. In collaboration with the Medical University of South Carolina health sciences library, this project studies how third-year medical students and their preceptors equipped with portable laptop computers can use the technology to access needed diabetes and other health information at the time of need. The students are enrolled in a clerkship that serves rural indigent patients, many of whom suffer from type 2 diabetes and its complications.

Project D. This study will provide a followup with the King/Drew Medical Center in Los Angeles and their efforts to promote continuity of care with the aid of a diabetes "smart card" that enables access to a centralized medical record and diabetes-related test results for a type 2 Hispanic and African-American population that is seen variously at different health centers across the county.

Project E. In collaboration with the University of Texas Health Science Center at San Antonio, and at its regional health center and clinics in the Lower Rio Grande Valley, this project studies how a computer workstation installed in the clinic waiting room can provide Hispanic patients with diabetes-related information. To encourage use of MEDLINEplus, the health care providers will use prescription pads.

Project F. This project will collaborate with the Juvenile Diabetes Research Foundation International (JDRF) in a variety of mutually supportive uses of new information technologies. These include enhancement of NLM's MEDLINEplus diabetes content for children and teens; user evaluations of MEDLINEplus; inclusion of JDRF-sponsored trials in NLM's ClinicalTrials.gov database; creation of Spanish language resources based on JDRF's Countdown research magazine; experimentation with informatics tools to lessen the probability of misdiagnosis of type 1 diabetes, particularly in emergency departments serving minority and other medically underserved populations; and experimentation with informatics and distance education tools for science teachers and nurses in low income high schools.

The Veterans Health Administration (VHA), Department of Veterans Affairs

The mission of the Veteran's Healthcare System is to serve the needs of America's veterans by providing primary care, specialized care, and related medical and social support service. To accomplish this mission, VHA needs to be a comprehensive, integrated healthcare system that provides excellence in healthcare value, excellence in service as defined by its customers, and excellence in education and research, and it needs to be an organization characterized by exceptional accountability and by being an employer of choice.

The mission of the VHA diabetes program is to improve the health of veterans with diabetes by decreasing the incidence of adverse health outcomes, especially macrovascular and microvascular disease. This will be accomplished through systems-level integration of guidelines, performance measurement, and data feedback to promote the increased use of evidence-based preventive and treatment processes. VHA research service supports this mission through clinical, basic science, and health services research. VHA reports the following progress in FY 2001:

Current Activities

Performance Measurement (Office of Quality and Performance, OQP). In FY 2001, VHA, through its External Peer Review Program, collected data from a random sample of 40,095 charts of veterans with diabetes. Eligible patients must have accessed VHA for care some time during the previous 12 months. OQP data analysis showed that the percentage of patients having chart documentation of the following Diabetes Quality Improvement Project (DQIP) measures using DQIP abstraction criteria within 12 months (or as noted) of chart review is as follows:

- HbA1c test (93%); 80% of HbA1c values less than 9.5%; 61% less than 8.0%; 38% less than 7%.
- Lipid profile within 2 years (91%); 68% of LDL–C values less 130 mg/dl, 40% less than 100 mg/dl.
- Blood pressure control, 55% less than 140/90.
- Dilated retinal examination (66%).
- Nephropathy screening within 2 years (72%).
- Visual examination of feet (91%); palpation of pedal pulses (83%); sensory examination of feet (78%); referral of patients with "high risk feet" to a foot care specialist (85%).

Since VHA uses DQIP measures, comparison to the private sector is possible. FY 2000, VHA national adherence to most measures was at the 90th percentile of the individual private sector plans included in the NCQA Quality Compass Report.

VHA Diabetes Registry (Office of Policy and Planning). VHA has developed a nationwide diabetes registry derived from administrative data. Veterans are identified as having diabetes using one inpatient or two outpatient codes with a diabetes-specific code, or receipt of an oral agent or insulin. The denominator is defined as veterans who had at least one clinical visit during the year. For FY 2000, 639,323 veterans with diabetes were identified out of 3, 318,158 veteran users, yielding a prevalence of 19.3 percent. This cross-sectional calculation technique probably yields an underestimate compared to the prevalence calculated from a longitudinal analysis.

Based on registry data analysis, the mean HbA1c for FY 2000 was 7.61%; and the mean LDL–C was 108 mg/dl. In addition to cardiovascular disease, the cohort had a high prevalence of co-morbid conditions, including about 30 percent mental health conditions, which is an underreport if one considers self reports as the reference standard.

Lower Extremity Amputation Programs (Offices of Policy and Planning and Patient Care Services). In collaboration with the Centers for Disease Control and Prevention Division of Diabetes Translation, a 12-year Lower Extremity Amputation (LEA) Registry has been created by the Office of Policy and Planning. From FY 1997–FY 2000, the age-adjusted rate (standardized to the VHA 1998 User Population) of LEA in the entire veteran population has decreased from 2.18 (0.78 major amputations [e.g., below knee or above knee]) to 1.42 (0.65 major amputations) per 1000 VHA users in FY 2000.

On May 11, 2001, the Under Secretary for Health reissued the VA Preservation, Amputation Care, and Treatment Directive (PACT), which mandates multidisciplinary foot care programs, including screening, surveillance and salvage components, at all VHA facilities.

VHA recently participated as a full partner with the American Diabetes Association, the Centers for Medicare and Medicaid Services (CMS), the American Podiatric Medical Association and the Centers for Disease Control in an initiative to improve foot care for Medicare beneficiaries with diabetes. CMS's comprehensive decision memorandum cites five VHA research papers as providing scientific evidence to support the requested coverage benefit. The results of the VA PACT Program were also submitted as evidence.

Guideline Development (Offices of Quality and Performance and Patient Care Services). VHA, in partnership with the Department of Defense, issued a revision (2/00) of its Diabetes Clinical Practice Guidelines. The guidelines, covering outpatient management of glycemia, blood pressure, hyperlipidemia, diabetic retinopathy, foot care, and renal disease, emphasize transparency of the evidence underlying clinical recommendations as well as principles of absolute risk reduction and patient-clinician target (HbA1c) value negotiations. Version 1.0 was developed in collaboration with the executive committee of the National Diabetes Education Program. VA has developed concise, pocket-size clinical guideline information for nationwide distribution.

Research Service. There are three VA Diabetes Centers of Excellence focused on diabetes research co-funded by Medical Research Service and the Juvenile Diabetes Research Foundation International. Investigators at these sites are investigating the effects of diabetes on the vascular system; mechanisms of insulin resistance; cellular and molecular processes by which intensive therapy reduces insulin resistance; the role of exercise in modulating the effectiveness of therapy; and mechanisms responsible for defective low blood sugar regulation.

VHA funded a 5-year cooperative study (VA Diabetes Trial (VADT), CSP #465) to evaluate the effect of near-normal glycemic control on cardiovascular outcomes in type 2 diabetes. VADT will enroll 1,700 men and women from 20 VHA sites randomized to intensive versus conventional control. The outcome will be assessed by evaluating composite cardiovascular events.

The VHA Quality Enhancement Research Initiative (QUERI) has been cited as a model by the Institute of Medicine. The goals of QUERI initiatives are to translate research into improvements in patient care and outcomes. The primary focus of the Diabetes Mellitus-QUERI program is on more aggressive treatment of modifiable risk factors and the prevention of progressive complications among veterans with diabetes. These activities range from the implementation of interventions to assist "front-line" clinicians with targeting high-risk patients to the design and evaluation of alternate methods for constructing diabetes care quality indicators. QUERI–DM is also working with partners outside VA, including the Centers for Disease Control and Prevention (Translating Research into Action for Diabetes). This project will produce a structural and organizational analysis of VHA diabetes care and allow direct comparisons with diabetes care in the private sector.

Joslin Vision Eye Network (Office of Patient Care Services). The VHA is a participant in the Telemedicine Project for Non-Mydriatic Retinal Examination in partnership with the Joslin Vision Network. The Joslin Vision Network is a congressionally mandated project, which currently includes the VHA, the Department of Defense, and the Indian Health Service. The project involves imaging the retina with a non-mydriatic camera and transmitting the images to a reading center. VHA has established centers in the New England and North West regions and is planning further expansion to the Sunbelt region. A recent VHA teleopthamology (digital imaging) consensus conference made recommendations on the technical aspects of data acquisition.

Standardization of Glycated Hemoglobin Testing. Consistent with a directive from the Under Secretary for Health, all VHA facilities use methodology traceable to the Diabetes Control and Complications Trial (DCCT) standard as recommended by the National Glycosylated Hemoglobin Standardization Program.

Education. Thirty VHA facilities have obtained American Diabetes Association recognition of their patient education programs—more than any other national system of health care. VHA hosted the 3rd annual National Diabetes Symposium for over 250 endocrinologists and primary care clinicians, as well as the annual VA Diabetes Educators Conference for nearly 300 VHA clinician educators. These conferences represent an institutional commitment to translating agency priorities and research findings into results at the field level.

Future Activities

VHA remains committed to improving outcomes for veterans with diabetes. A nationwide approach to more aggressive blood pressure control, instituted last year, remains a priority. Research service has issued requests for proposals for research to improve eye care and blood pressure control. The Under Secretary for Health, in the reissued PACT directive, has directed that senior management review network amputation rates. A national Web-based learning center is being pilot tested. VHA has a national Computerized Patient Record System (CPRS), with clinical reminders, and improvements to CPRS to support all clinical care, including diabetes, are ongoing.

THE NATIONAL DIABETES EDUCATION PROGRAM

THE NATIONAL DIABETES EDUCATION PROGRAM

Fiscal Year 2001 Accomplishments

INTRODUCING THE NATIONAL DIABETES EDUCATION PROGRAM

The National Diabetes Education Program (NDEP) is jointly sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the Centers for Disease Control and Prevention (CDC) and is a subcommittee of the DMICC. The program speaks to a national audience of people with diabetes and their families, health care providers, payers and purchasers of health care, health care system policy makers, and the general public, including people with undiagnosed diabetes and those at risk for the disease.

The NDEP's efforts are aided by a Steering Committee comprised of representatives from diabetes-related, health care, racial/ethnic, and voluntary service organizations. Federal liaisons to the NDEP Steering Committee include several representatives from the DMICC. Members of the Steering Committee also serve on NDEP work groups that provide direction and help implement NDEP initiatives.

The NDEP also has developed a Partnership Network of about 200 organizations to help disseminate program messages through the mass media, community groups, and health systems serving people with diabetes. A new web site, called "Team Diabetes," has been launched to provide an interactive, online site for NDEP partners to exchange resources and information.

In June 2001, the NDEP published *Changing the Way Diabetes Is Treated, A Progress Report from the National Diabetes Education Program* that reviewed the NDEP's accomplishments since its inception in 1997 through Fiscal Year 2000. This booklet details the origins, development, activities, and future priorities of NDEP and has been distributed widely in the diabetes community. To obtain copies of this publication, please contact Joanne Gallivan, Program Director, NDEP, NIH at *Joanne_Gallivan@nih.gov.*

During FY 2001, NDEP supported a variety of activities to promote awareness about the importance of diabetes control and to add an important new message about comprehensive diabetes care. Highlights of NDEP's activities during the past year are summarized below.

NDEP Steering Committee

The Steering Committee met twice--in October 2000 in Miami, Florida, and in April 2001, in Washington, D.C. The purpose of the meetings was to coordinate and advise on program policies, initiatives, and goals and to help coordinate efforts. The April meeting was planned to help coordinate efforts in conjunction with the June launch of the NDEP Comprehensive Care Campaign.

During FY 2001, the NDEP worked with the Steering Committee to modify the program's organizational structure. A key outcome of that effort was the creation of an Operations Committee that will provide guidance on strategic planning and address cross-cutting issues and opportunities within the NDEP work groups. Several Steering Committee members also completed their term of service during the past year and will be replaced with new representatives.

Mass Media Campaigns

From June 1998, when NDEP launched its first PSA campaign, through FY 2001, NDEP's campaigns have obtained well over $13 million in free advertising time or print media space. The NDEP initiated several new mass media campaigns in FY 2001. NDEP carried out extensive market research prior to initiating these campaigns and developed the materials in conjunction with appropriate NDEP Work Groups. The program also provided ongoing support for continuing campaigns targeted to African Americans, Hispanic/Latino Americans, American Indians, and Asian Americans and Pacific Islanders.

The Jerry Stackhouse "Discipline and Control" campaign featured a Detroit Pistons basketball player whose family has been hit hard by diabetes. The TV, radio, and print ads addressed the importance of diabetes control and demonstrated a son's social support for his parents who have diabetes.

"It's More Than Food, It's Life!" is the theme of FY 2001's Hispanic/Latino nutrition awareness campaign. The campaign is designed to educate Hispanics and their families, that food is a powerful tool in diabetes control and to dispel the myth that healthy eating means sacrificing taste and tradition. Campaign materials include television, radio, and print PSA's, posters, and a meal planner featuring mouth-watering traditional Hispanic dishes.

"The Power to Control Diabetes Is in Your Hands" is NDEP's campaign targeted to older Americans. The campaign educates older adults with diabetes about the importance of self-monitoring blood glucose to control diabetes and promotes the availability of Medicare benefits for self-monitoring equipment and supplies. Launched with a video news release in May 2001, Older Americans Month, campaign materials include press kits, print ads, brochures, posters, and community outreach and health care practitioners kits.

"Move It!" is the call to action of the American Indian Youth Campaign, which addresses the rising prevalence of Type 2 diabetes in American Indian young people. The campaign includes a series of 3 posters, a print ad, and a fact sheet and promotes the importance of physical activity to reduce risk of diabetes.

"Be Smart About Your Heart: Control the ABCS of Diabetes" creates awareness about the link between diabetes and heart disease and promotes comprehensive diabetes care to control blood glucose, blood pressure, and cholesterol—the ABCs of diabetes. The "Be Smart" campaign was launched at the annual meeting of the American Diabetes Association in June.

Media Outreach

In conjunction with these PSA campaigns, NDEP continued to conduct media outreach to obtain coverage about diabetes in the print and broadcast media. Program messages were featured in a number of national media outlets. Examples of health care professional journal articles NDEP placed were "The National Diabetes Education Program—Changing the Way Diabetes Is Treated: Comprehensive Diabetes Care," editorial in Diabetes Care, April 2001 and "Current Treatment Goals for Type 2 Diabetes," in the Home Health Care Journal, June 2001. In terms of consumer media, NDEP placed several articles about diabetes in HealthQuest magazine. NDEP messages were also broadcast on the Russ Parr Morning Radio Show and AARP Prime Time Radio.

NDEP Conference Participation

Program spokespersons gave presentations and represented NDEP at several meetings in FY 2001. Conferences included the American Dietetic Association's annual meeting in October 2000; the Urban League of Nebraska's "Lift Every Voice" diabetes training workshop in January; the ADA Postgraduate Course in January; the Diabetes

Health and Wellness Expo in March; the American Association of Diabetes Educators Leadership Conference in April and their annual meeting in August; the CDC's Diabetes Translation Conference in May; the Virginia Dietetic Association meeting in August; the annual meeting of the ADA in June; and the annual meeting of the American Academy of Nurse Practitioners in July.

In addition, the NDEP continues to conduct workshops on the Diabetes Community Partnership Guide. The workshops introduce participants to the Guide's various community tools and activities, which are designed to mobilize communities into action. Eighteen workshops have been conducted to date across the country; three of them in Spanish.

NDEP Speakers' Kits

In FY 2001, the NDEP developed a speaker's kit, comprised of eight slide/script presentations that are intended for use by partners at conferences and public events. The presentations include the same core information about diabetes and the NDEP but they have been tailored for various racial/ethnic audiences, people with diabetes, health care professionals, and health care purchasers and payers. In Fiscal Year 2002, these presentations will be placed on the NDEP web site for partners to access.

Diabetes at the Worksite

NDEP's Business and Managed Care Work Group has designed a web-based resource that employers, human resource, and health professionals can use to assess the scope of the diabetes problem in their workforces and to conduct diabetes education at the worksite. This resource will be launched in Fiscal Year 2002.

Diabetes in Children and Adolescents

This work group is completing a set of resource materials for health care professionals, parents, and others concerned about diabetes in children and adolescents. Materials include fact sheets, an annotated bibliography, and a resource directory. In addition, a subcommittee of this work group is developing a guide for "Managing Diabetes in the Schools" that will be published and distributed in Fiscal Year 2002.

Health Care Professional Work Group Activities

NDEP's Health Care Provider work group provided guidance for the Comprehensive Care Campaign and selecting the "ABCs of Diabetes" message. The group is exploring various approaches to improve the quality of diabetes care; clinical practice tools will be developed in 2002. The Pharmacy, Podiatry, Optometry, and Dentistry (PPOD) work group is developing a diabetes primer to expand PPOD professionals' understanding of their role in care for people with diabetes beyond their own specialty and to include education about the need for glycemic, blood pressure, and cholesterol control for people with diabetes.

During Fiscal Year 2002, NDEP will not only continue to promote diabetes control but it also will take the lead on translating and promoting the findings of the recently completed Diabetes Prevention Program (DPP) clinical trial. The DPP demonstrated that the onset of diabetes could be prevented or delayed among people at risk for the disease through modest lifestyle changes such as 150 minutes of moderate activity per week and losing 5 to 7 percent of one's body weight. This important prevention message will add a new dimension to the NDEP and its goal of "changing the way diabetes is treated."

For more information about the National Diabetes Education Program, please visit our web sites at *http://ndep.nih.gov and www.cdc.gov/team-ndep* on the Internet.

MEETING SUMMARIES

MEETING SUMMARIES

DIABETES AND AGING CONFERENCE

February 12-13, 2001
National Institutes of Health
Bethesda, Maryland

DAY 1

WELCOME
– Allen Spiegel, Richard Hodes

The purpose of this conference was to bring together researchers from the fields of gerontology and diabetology to examine issues surrounding the etiology, impact and responses to diabetes in the aging population. Traditionally, researchers in these two disciplines have worked independently, though their research interests often overlap. However, the rapid growth of the population over sixty, taken together with the increasing incidence of type 2 diabetes in that population, seem to call for a more collaborative effort. Therefore, we have invited laboratory and clinical researchers from both disciplines to tell us about what they are learning and to help us to define the next phase of needed research.

PRESENTATIONS

Overview of the Problem

The Evolution of the "Disease vs. Aging" Controversy – Reubin Andres

Since gerontologists and diabetologists approach the fact of diabetes in the elderly from different points of view, it may be helpful to articulate the basic differences. In general, diabetologists regard the development of type 2 diabetes in the elderly as the result of a disease process. Gerontologists are more inclined to see the same development of diabetes as a fundamental consequence of aging. So the question is whether the decline in glucose tolerance seen in elderly diabetics is a primary biological reaction to a given stimulus or set of events, or whether there are other characteristics about getting old that result in such a decline.

This is not an easy question to address, much less answer. Older people develop a large number of medical problems and take a wide array of medications. Further, they are likely to have changes in diet and activity patterns, as well as body composition when compared to their earlier lives. Any of these variables, alone or in combination, have potential for affecting the body's ability to tolerate glucose. We must then be very careful to be comparing apples with apples as we approach the question.

This leads us to the issue of how we measure glucose tolerance. Over time, our ability to measure glucose tolerance has improved, but there is still a divergence of measures used to diagnose the condition in clinical practice and in research. In order to draw meaningful conclusions from the data we collect we need to have some common reference points. We need to know if the same measure of glucose tolerance means the same thing in twenty year olds, fifty year olds and eighty year olds. We need to follow subjects longitudinally if we hope to be able to develop standard reliable measures that may be used as reasonable predictors for diagnosis and management of diabetes in the future. Combining the efforts of the gerontologists and diabetologists can only benefit this research.

Scope and Impact of Diabetes in the Elderly – Maureen Harris

Data from a survey conducted in 2000 indicate that there are 17 million diabetics in the US, half of which are over 60 years of age. This means that almost 18% of those aged 60 and older have diabetes. According to the survey, nearly a third of all cases of diabetes go undiagnosed. Rates of incidence are higher among non-white populations than among whites.

The implications of this epidemic can be seen in the increase in risk factors for macro and micro vascular disease. Half the diabetics in the study had BBP exceeding 140/90, or uncontrolled. More than half also failed to meet the ADA goals for total cholesterol of 200, and half failed to meet the goal of LDL lower than 130. Additional impact from diabetes in those over age 65 can be seen in the incidence of lower extremity amputation, which increases with age. End stage renal disease is another condition experienced by elderly diabetics at a rate much higher than non-diabetics.

Another area where we see the impact of diabetes in the elderly population is in physical disability. When we look at rates of inability to manage ordinary physical tasks such as walking, climbing stairs, and housework, we see that diabetic women had twice the rate of disability as women without diabetes. The final place where the impact shows is in the significantly higher rate of mortality from all causes in diabetic men and women over age 65, when compared to their non-diabetic counterparts.

Pathophysiology of Diabetes in Aging – Josephine Egan (Chair)

In order to avoid developing diabetes the body must maintain a balance between insulin secretion and insulin sensitivity. In Type I diabetes there is an absolute decline in insulin secretion. type 2 diabetes occurs when insulin sensitivity declines for any reason and insulin secretion fails to increase to restore the balance. type 2 diabetes is a progressive disease, so control is an ongoing challenge, often requiring an increase in numbers of medications, finally going to insulin.

The progressive nature of the disease is the result of a continuing Beta cell failure inside the islets. In various studies, researchers found that after the rodents reached middle age, the islets no longer enlarged. The number of Beta cells actually declines, and the remaining Beta cells hypertrophy, so the islet size does not decrease. At the same time, there is a decline in the insulin messenger RNA in the islets and a decline in the total pancreatic insulin. There is also a decline in the sensing mechanism of the Beta cells with age in rodents, so that the specific glucose transporter, as well as glucokinase, the message and the protein levels, both decline with age.

Factors Determining Glucose Tolerance in the Elderly – Marilyn Ader

Without trying to account for the reason, we know that insulin sensitivity decreases with aging and that this decrease in insulin sensitivity is associated with increased mortality from all causes. In spite of the number of studies done to try to determine whether the increase in insulin resistance in the elderly is a natural consequence of aging, or a disease process, controversy still exists. In fact, the body of research produces conflicting data on the question.

We see from the literature that investigators approached the question in various ways, each focusing on different variables. They used animal and human subjects, dynamic and steady state measures, and longitudinal as well as cross-sectional data. They focused on insulin sensitivity in both hepatic and peripheral tissue, as well as insulin secretion under a variety of conditions. They used both lean and obese subjects, and they compared old vs. young, as well as healthy elderly subjects vs. diabetic elderly subjects. Though they were all trying to understand the etiology of increasing insulin resistance with age, they were actually asking different questions. It is not surprising then that the data give us conflicting conclusions.

Though there are differences in the literature, there are also some common conclusions we can draw.

- Peripheral insulin resistance likely exists during the sustained hyperinsulinemic conditions of the glucose CLAMP.

- Under dynamic conditions of the OGTT or the IVGTT, the magnitude of the insulin resistance may be greater.

- Hepatic resistance, impaired suppression of glucose production, may be evident in the dynamic condition.

- Visceral adiposity does increase with age, but there have not yet been enough studies done that have corrected the insulin sensitivity for central fat. We need to know more about age-associated changes in insulin sensitivity associated with visceral adiposity.

- We need to pay close attention to how secretory function is measured. All measures are not equal. We get different results for diagnosis and incidence depending on what measure we use.

- Secretory function needs to be assessed in terms of rising insulin resistance with age.

Basic Mechanisms of Insulin Resistance – Nir Barzilai

We are looking for a cause and effect relationship between aging and insulin resistance. We know that the insulin resistance syndrome in the elderly is associated with obesity, disease, and mortality from all causes. In the rodent model we see that visceral fat appears to pose a much greater risk for morbidity than does the total fat in the body mass index.

We are looking at the hypothesis that longevity is limited by lipotoxicity. Rodents in the wild are lean, extremely active, and survive on far fewer calories than do ad libinum fed animals in the laboratory. This kind of caloric thrift gives the genes the greatest chance of being reproduced. If the animal eats more calories than it needs for survival, and begins to accumulate excess fat, the metabolic system is required to compensate for the excess demand. It is important to note here that the greatest increase in risk of insulin resistance occurs with an increased distribution of fat to the visceral area.

We see in obese rodents that when we remove the visceral fat, their insulin sensitivity improves significantly, even when less than 15% of total fat is removed. Since it is possible for a lean looking individual to have a high concentration of body fat in the abdominal region, it is important that we understand the processes at work in both the increased risk for insulin resistance as it relates to visceral fat, and in the decreased risk generally seen in caloric restriction.

Insulin Secretory Deficits in the Elderly with and without Diabetes – Graydon Meneilly

In spite of the number of studies done in this field, there still exists a large amount of controversy regarding the cause and impact of insulin secretory deficits in the elderly. When life style factors, such as diet, activity level, and body composition are adjusted for in community dwelling older subjects by multiple regression analysis, the effects of aging per se in the OGTT is very small. One area of concern is the European study that showed that there is a decrease in insulin clearance in older individuals. This would mean that the ability to maintain physiological levels of glucose in the aging may be due to a reduced rate of insulin clearance, not to an appropriate rate of insulin production. There also seem to be changes in more subtle measures in the elderly involving the burst mass and regularity of insulin pulses, both in rapid and ultradian insulin responses, under both fasting and hyperglycemic conditions.

Lean older people with diabetes tend to have a profound impairment in glucose induced insulin secretion when compared to age matched non-diabetic controls. Obese older people with type 2 diabetes have an absence of first phase insulin secretion, but they have a relatively modest impairment in second phase insulin secretion when compared to age matched non-diabetic controls. All older people with type 2 diabetes have marked defects in insulin secretion. The magnitude of the secretory defect is greater in lean patients than it is in obese patients, but all older patients have a defect in Beta cell secretion of insulin for various reasons. With GLP, and potentially with many other interventions that we have at our disposal, we can partly or completely reverse some of the defects in insulin secretion that occur in older people in association with diabetes.

Basic Defects in Insulin Secretion and the Beta Cell with Age – Peter Butler

The traditional belief has been that humans do not grow new islets over time, yet we have autopsy evidence that new islet production occurs even in those over 90 years of age. There is also speculation that Beta cell mass inevitably decreases with aging, but this has not been demonstrated. However, we still see a typical decline insulin sensitivity for various reasons in humans as they age. Some of this can be attributed to possible genetic defects at the level of the islet. We know that there is a minimum Beta cell mass needed to avoid the development of diabetes. We are beginning to learn what happens inside the Beta cell and the islet that may help to explain Beta cell death and the consequent decline in insulin producing capacity.

There are striking similarities between the decline of Beta cells seen in type 2 diabetes and the decline of brain cells seen in Alzheimer's. There is consistent evidence in both diabetes and Alzheimer's research to indicate that amyloid material exists inside the cells prior to their deaths. The protein is found only in pathological circumstances. Cell death in both diseases is highly correlated with small intra-cellular aggregates of amyloid. In both diseases there seem to be deficits of chaperone proteins necessary to protect the secretory protein from aggregating as it moves within the cell. The processes of cell destruction in both type 2 diabetes and Alzheimer's are so similar that it is quite possible that if we find the cause for one, we will also find the cause for the other.

Molecular Events of Insulin Signal Transduction – Mark Lane (Chair)

The Possible Role of Insulin Signaling in Aging and the Retardation of Aging and Age-related Disease by Caloric Restriction – Mark Lane

There is essentially no literature about molecular events in the development of diabetes in aging. We have a lot of questions, but few answers about the role of insulin signaling in caloric restriction and its relationship to aging and age related disease. We know that there are many genes and processes that are responsive to insulin within the cell. We also know that ad libidum fed animals die earlier and have higher rates of morbidity than do those on caloric restriction. So there is a high correlation between caloric restriction and extended lifespan. The insulin pathway is a major sensor and transducer of the energetic status of the animal, and we may speculate that this pathway plays a significant role in the benefits seen in caloric restriction.

Caloric restriction reduces "energy" intake and may extend lifespan by altering carbohydrate metabolism or stress resistance. When animals can find more than adequate food, more of their energy can be devoted to growth, development, and reproduction. When food is scarce, a higher proportion of energy needs to be devoted to repair, maintenance and survival. In caloric restriction, the energy expenditure ratio changes to emphasize maintenance and survival, making the organism more resistant to stress. So it appears that stress response is greatly enhanced in caloric restriction and may be significant in life extension.

The DAF-2 Pathway of the Nematode Caenorhabditis elegans as a Homolog of the Insulin Signaling Pathway in Mammals: Similarities and Differences – Thomas Johnson

C. elegans is an excellent organism for the study of aging. It has only 1000 cells and is thoroughly mapped. In addition, it is optically transparent, enabling researchers to tag particular proteins and track them in the animal. C. elegans offers several classes of gerontogenes for study. The generation length is only three days. When the animals are fed ad libidum, they multiply from one egg to 100,000 worms in a week.

When food supplies are exhausted, the animal form an alternative form called "dauer larvae", a migratory stage during which metabolism continues. When food is inadequate, this condition is sensed by a series of genes, whose basic output is the formation of dauers. These DAF (dauer formation defective) genes are involved in a coordinated pathway that starts with a putative insulin receptor, such as DAF-2 that has very high homology to the insulin IGF-1 receptor in mammals. Proteins in the insulin signaling pathways in c. elegans are homologous to a great degree with identifiable proteins filling similar functional roles in mammals. There is a signal transduction cascade driven by kinase action whose ultimate output is the DAF-16 gene, which is closely associated with stress resistance and extended lifespan in the worm.

While the c. elegans model is very useful helping us understand the interaction of the genes in this pathway, the output of these different pathways is quite different. Worms respond to the output by forming dauers, while mammals probably experience some metabolic shift in response to the absence of food. In worms, there is an obvious trade off between dauer formation and reproduction. In mammals, the output from this pathway is perhaps more likely to be expressed in terms of the animal's ability to resist stress, which then has implications for morbidity and lifespan.

The Role of IRS Proteins in Growth and Metabolism – Morris White

Insulin action has an enormous influence on mammalian physiology beyond what we ordinarily think of as glucose metabolism measured by glucose uptake in fat and muscle. In mammalian systems up to 80 or 90% of insulin signals are mediated through IRS (insulin receptor signal) proteins. We have identified a range of IRS proteins and other receptors and understand some of their roles in insulin signaling and response.

The insulin signaling pathway involves a large number of proteins that all need to function in a coordinated way in order to achieve optimum gluco-regulation. These proteins perform the additional function of coordinating the physiology and growth in brain, liver, ovary, adipose and muscle tissues. We need, therefore, to look at the impact of this pathway beyond the disease processes we typically think of in association with diabetes. We need to examine the specific ways that age related alterations in the insulin signaling pathway influence the development of a wide range of age associated diseases and related disability.

Insulin Signaling and Action in Skeletal Muscle: Effects of Age and Caloric Restriction – Gregory Cartee

Muscle is important for disposing of blood glucose in response to insulin. Muscle insulin resistance is an early defect in type 2 diabetes, and muscle function is highly dependent on metabolism. Insulin signaling is therefore, very important to muscle function. In order for insulin to enter the muscle cell, a GLUT 4 transporter must move to the cell surface. We set out to describe the calorie restriction effect on glucose transport in animals at various ages in both calorie-restricted groups and ad libidum fed groups. We used isolated muscle cell preparations for our analyses.

We looked at both long and short- term calorie restriction and found that there were significant improvements in glucose transport in both cases. Though there are declines in GLUT 4 abundance with age, we see significantly more cell surface insulin in elderly CR animals than in the elderly ad libidum fed animals at the same insulin levels. We have reason to believe then, that age related insulin resistance in skeletal muscle likely involves altered insulin signaling.

Old animals do respond to single session and chronic exercise with a substantial increase in insulin stimulated glucose transport. Skeletal muscle remains responsive to calorie restriction and to exercise induced improvements and insulin sensitivity during old age. The underlying mechanisms for improved insulin signaling and action with calorie restriction and exercise appear to be different, yet both likely involve amplified insulin signaling.

Prevention and Treatment – James Meigs (Chair)

Carbohydrate Metabolism in Dietary Restriction and Aging – Mark Lane

We are testing the hypothesis that caloric restriction will extend life span, prevent or delay onset of age related diseases, and slow the rate of aging in rhesus monkeys. The work is being done at a three labs, using a range of diets, feeding protocols and ages of the animals at the initiation of restriction. In calorie restricted animals we find a decline in total body fat, body weight, and abdominal fat. CR animals have a significant reduction in the peak level of glucose. This goes up with age. Glucose tolerance goes down with age.

When we surveyed the medical records of the monkeys for chronic disease and mortality in both the calorie restricted populations and the controls, preliminary data indicate that calorie-restricted animals have only half the deaths due to chronic disease seen in the control animals. Data from both rodents and monkeys indicate that caloric restriction is an effective means for improving glucose tolerance and increasing insulin sensitivity. The effects of calorie restriction and gluco-regulation can occur after only a short time on restriction and may not be entirely dependent on changes in body composition.

Glycemia and Risk for Cardiovascular Disease – James Meigs

We used the Framingham Heart Study to look at the relationship between glycemia and risk for CVD. We looked at data from both the original cohort study and the offspring study and asked the following questions:

1. What is the prevalence of diabetes with age using various diagnostic criteria?

2. What is risk for CVD associated with hyperglycemia among older persons? What is the association between hyperglycemia and CVD?

3. What is the risk for CVD associated fasting and 2-hour hyperglycemia measures according to different thresholds?

Though the data are limited in a number of ways, we are able to draw some conclusions.

- Diabetes is common, even among the very old subjects. If that is true, and people with diabetes tend to die young, then new cases are continually developing, even in the very old.

- Isolated post challenge hyperglycemia is very common in older people, so a fasting plasma glucose screening would fail to identify many in this population at increased risk for CVD.

- Hyperglycemia is an independent CVD risk factor in older people.

- Hypertension is an important modifiable CVD risk factor in the elderly.

- Hypertension is a highly prevalent concomitant of diabetes.

- Post- challenge hyperglycemia is an independent risk factor for CVD, especially in older subjects. In thinking about interventions to reduce CVD, it may be worth focusing on post- challenge hyperglycemia is an attractive target.

The Pathway from Diabetes to Disability: Optimal Targets for Intervention in the Elderly – Helen Hazuda

This talk presents a series of statistical analyses using data from the San Antonio Longitudinal Study on Aging (SALSA). The study contains a nested, case controlled study that follows incidence of functional decline in subjects with and without diabetes. The aim of the study is to better understand the pathways between disease and disability in order to identify optimal targets for intervention. We are using a basic model identifying the stages leading to disablement, which include pathology, impairment, functional limitation, and disability. Data was collected at three different times over 18 months, looking for both trends and causes of disablement.

As different variables are included, the model becomes very complex. We tested the various hypothesized pathways by first adjusting for contextual variables of age, gender, ethnic group, education, and household income. We then begin to see involvements that we did not expect, such as the significant decline in musculo-skeletal function in the presence of diabetes. Although the percent of disability found to be due to diabetes was modest when compared to that attributable to context, even small percentages have a large public health impact in a population of 8.3 million diabetics. It is therefore important to be able to identify and understand the modifiable variables so that we can begin to develop effective interventions.

Pharmacological Treatment of Diabetes in Elderly People: Challenges and Opportunities – Jeffery Halter

Establishing appropriate, effective pharmacological treatment for elderly people with diabetes is a challenge because we don't know who has this condition, why they have it, or what we are trying to accomplish for them. We don't have uniform protocols or measures for diagnosis. Our main concerns are the range and rate of development of complications seen in elderly people with type 2 diabetes, as well as the increase in risk factors for other diseases. Many elderly people with diabetes have co-existing health problems, and are on several medications, some with side effects, so controlling hyperglycemia and establishing clear treatment priorities becomes extremely complex.

The clinical and research picture is further complicated by the varying perceptions of this population held by practitioners. Diabetologists tend to view these people as likely to be frail, dependent, and poor candidates for aggressive intervention, while the image held by most gerontologists is that most older people with diabetes are quite functional, independent, interested in their health and pursuing their interests in life. Clearly, this difference in perception leads to different levels of aggression in treatment, so we need to develop criteria to help clinicians make decisions about appropriate types and degrees of treatment in response to the actual overall condition of the patient.

type 2 diabetes is hard to treat over time. It is a progressive disease and requires an increasing number and dose of medications as the patients age. We generally fail to achieve ADA goals in screening for frequently seen complications in this population. For some common circumstances, we have thinly researched guidelines or none at all, as in the case of post-prandial hyperglycemia. With improved screening and diagnosis, we could much more adequately address the needs of the elderly who have diabetes than we now do.

Clearly, the treatment goals appropriate for an independent, active older person with diabetes need to be different from those for a patient in a skilled nursing setting. We have a variety of pharmacological treatment options including the standard collection of sulfonylureas, a growing number of specifically targeted insulins, as well as the newer combination therapies. We need to work harder to establish and promote appropriate treatment goals for all elderly persons with diabetes. We should not be excluding people from treatment arbitrarily because of age.

Clinical Overview of Diabetes and Aging – Robert Schwartz

This is a personal view of the current state of diabetes and aging. We can see that the population over age 65 is increasing rapidly as is the incidence of type 2 diabetes in that population. This increase carries with it a substantial burden of medical complications, cost, and disability. At present, type 2 diabetes in the elderly is seriously under diagnosed, so it is also under treated. We do an inadequate job of employing the tools we have available to screen for and diagnose the disease. We lack a commonly accepted protocol for diagnosis and treatment in the elderly population.

Treatment of diabetes in the elderly is complicated because of the changes in physiology seen in aging, the increase in risk factors for other diseases, the frequent occurrence of other medical conditions, and multiple medications. type 2 diabetes is a progressive disease, making it very difficult to treat over the long term. Available treatments typically have either high cost or considerable risk of hypoglycemia associated with them, and they are often inadequate to control the condition in the elderly. We do see promise in the new drug, Metformin.

Finally, appropriate treatment is frustrated by the belief on the part of many clinicians that individuals in this population are frail and have very limited life expectancies, so it is inappropriate to pursue aggressive treatment of their diabetes. In fact, at age 65 many women can expect to live for 19 years and many men can expect to live for 15 years. Undertreatment for diabetes and associated conditions may contribute substantially to portion of the remaining lifespan that will be spent in a dependent state. The public health consequences of untimely and inadequate care of the elderly with diabetes will be enormous unless we can work together to improve both the timeliness of intervention and the level of that care.

DAY 2

WORK GROUPS

Conference participants divided into three topic groups to design and compile lists of questions and topics that describe the most pressing research needs in the emerging field of diabetes and aging. Each group then presented its work to the full conference. The work group reports follow.

Patho-physiology Work Group Report

1. What is the role of body fat distribution in age-related peripheral and hepatic insulin action and glucose intolerance?

2. What is the role of insulin independent processes in age-related glucose intolerance?

3. What are the metabolic consequences of fat products such as free fatty acids and fat derived peptides, and how do they change with aging?

4. What are the metabolic consequences of age-related changes in glucose levels?

5. What are the mechanisms contributing to postprandial hyperglycemia, that are seen as a function of age?

6. Does Beta cell function change with age, and what are the mechanisms of change?

7. How does Beta cell mass change with age, and what are the mechanisms?

8. Can adverse changes in function and mass be ameliorated?

9. Should we establish a cooperative group in order to obtain human autopsy tissues such as pancreas, liver, fat, muscle?

10. Is there a mechanism whereby we in the type 2 DM field can obtain human islet cells for study?

11. What are the mechanisms underlying the change in the relationship between insulin secretion and insulin action with age? Can they be reversed?

12. Given the comparable pathology seen in Alzheimer's disease and type 2 diabetes, are the mechanisms leading to the neural and Beta cell dysfunction related?

Insulin Signal Transduction Group Report

General considerations

1. In addition to diabetes, insulin and insulin action are likely to be involved in many age associated diseases and pathologies.

2. It is important to more specifically define the role of insulin action on various age associated pathologies including syndrome x, Alzheimer's, etc.

3. Alzheimer's literature is beginning to discuss Alzheimer's as "diabetes of the brain".

Recommendations

1. We need to describe changes in insulin signaling that occur with aging in rodent models first. This is not necessarily looked upon favorably by study sections, and review boards, etc. Therefore it may require different funding mechanisms than usual.

2. Once the descriptive studies are done, the next step is to utilize those findings to develop targets for enhancing insulin action in peripheral tissues of older and /or diabetic individuals.

3. We need to define the role of tissue specific changes (other than those we typically think of as being involved in diabetes) in insulin action with age, independent of those changes involved solely in carbohydrate metabolism.

4. We need to understand the impact of aging and hyperglycemia, both independently and together on Beta cell function. Then we need to develop targets for improving Beta cell function in older individuals.

Models and Model Systems

1. We need to identify genes and mutations in humans associated with insulin resistance in aging, looking at micro-array and classic epidemiological studies.

2. Once those genes are identified, they could then be used in rodent models to do more mechanistic studies, either by inserting the human gene, or by altering the expression of a rodent homology to determine the effects or significance of that gene.

3. Non-human primates offer some advantages for this work because most of the variables can be controlled in a laboratory setting.

4. More functional (physiological/ biochemical) studies in c. elegans are needed to relate genetic studies in the worms to mammalian aging and disease.

Interventions

Both calorie restriction and exercise have been shown to improve insulin action, perhaps even in older individuals, and should be utilized in studies of aging and insulin action.

Miscellaneous

1. Is it better in aging to be more or less insulin sensitive?

2. Are there separate contributions of insulin level vs. insulin sensitivity to age-associated disease? Is it only insulin sensitivity, or is there some worth in considering the impact of hyper-insulinemia or insulin level in the blood itself?

3. If diabetes is a disease of signal transduction, maybe glucose has been over-emphasized in its importance. Should we consider insulin and insulin action in greater detail in diabetes as well as other diseases of aging?

4. We need to better understand the role of signal transduction mechanisms in relation to regulation of insulin secretion.

5. What is the role of nutrient sensing pathways in a variety of age related changes and diseases?

Prevention and Treatment Work Group Report

How do we define type 2 diabetes in the elderly?

Research Questions

1. Are there fast vs. slow progressors?

2. Should OGTT screening be performed?

3. Can a combination of fasting plasma glucose and HbA1c be used to identify at risk subjects?

4. Is fasting insulin a useful marker of disease? Goldberg's paper emphatically said no for older people.

5. Should, and how should, insulin assays be standardized?

6. Are there existing population data bases that can be exploited to advance knowledge?

7. What new data should be collected?

What causes the complications of diabetes in the elderly?

- Hyperglycemia is common.
- Coexistent risk factors are common.
- Treating hyper-lipidemia and hypertension is beneficial.

Research Questions

1. What is the significance of isolated post-challenge hyperglycemia as a risk factor? Is this true for hyperglycemia that happens after a meal?

2. What is the marginal benefit of controlling hyperglycemia beyond control of lipids and BP?

3. Are lifestyle interventions (exercise and weight loss) sage and effective in the elderly?

4. Is the observational data sufficiently complete that RCTs can now be recommended?

How should we prevent /treat diabetes in the elderly?

- Goals for treatment overall may not be applicable in the elderly. One size does not fit all.
- We know a lot about how to prevent complications.
- Evidence-based recommendations are not being applied in clinical practice.

Research Questions

1. What are appropriate goals for glycemic control in sub-groups of elderly aimed at preventing death or increasing function?

2. When should treatment be started, with prevention, with onset of symptoms, or with the appearance of complications?

3. What are appropriate goals of treatment? Prevention of mortality? Prevention of complications? Quality of overall life?

4. Poly-pharmacy is a problem with respect to cost, adherence, and side effects.

5. How can we address this?

6. Can we package drugs together to minimize the number of pills?

7. How can evidence be translated into practice?

8. What types of studies will inform better evidence-based care? We need to fund research to study care in managed care settings.

9. How can modern informatics/technology be used to enhance care?

10. How can we develop the clinical, geneological, and epidemiological data to better tailor treatment to individual differences in older patients?

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DIABETES MELLITUS INTERAGENCY COORDINATING COMMITTEE MEETING ON DIABETES AND AGING

February 12-13, 2001
National Institutes of Health
Bethesda, Maryland

WELCOME

Program Activities in Diabetes and Aging – Sanford Garfield (Chair)

This afternoon we will hear presentations from DMICC agencies telling us what they are working on and what opportunities are available in their organizations for further research.

PROGRAM ACTIVITIES AND RESEARCH OPPORTUNITIES

A summary of the presentations by representatives from DMICC member organizations. It gives a brief description of activities being carried on in each, as well as resources available in the organization for further research. It details available databases, populations, funding sources, etc. mentioned by the presenters. Contacts for each organization are included.

Centers for Disease Control

Program Activities

- Surveillance and epidemiology of incidence of disease, and its causes, treatments, complications and resulting disability.

- Translation research- study of whether, how, and to what degree of success efficacious interventions are being implemented at the clinical level.

- Implementation of research findings- Serve as clearinghouse for wide range of research so that it is made available and can be put into practice at the clinical level.

Current Study

Translating Research Into Action in Diabetes- a multi-center of diabetes treatment in managed care settings.

Indian Health Service

Characteristics of Native American Populations

- Strong cultural identity
- High rate of poverty and underinsurance
- Generally poor health with high rates of alcoholism
- High incidence of diabetes in young and old
- Existing diabetes care, prevention, and education programs emphasize service to the elderly.

Research needs

HIS needs data of all kinds related to diabetes in these communities, especially in the elder population.

Veterans Health Administration

Program Description

- Covers 9.3 million people over age 65, primarily male
- Largest integrated health care program in the country, comprising 22 regional networks
- 13% of $21 billion yearly budget spent on geriatrics
- All patients linked to primary care practitioner
- Performance measures in place for management of patient care

Research Opportunities

Data mining of completely computerized patient records, as well as information on income and demographics.

National Diabetes Education Program

Program Description

- Public and private partners working together to reduce the pain suffering and death due to diabetes.
- Trying to reach diabetics and their families as well as those who treat and pay for care
- Want to increase awareness of diabetes to improve diagnosis, treatment, lifestyle and testing

Current Activity

"Control Your Diabetes for Life" Campaign, aimed at promoting the message that diabetes is treatable, and that successful treatment is dependent on the involvement of patients in their own care.

American Diabetes Association

Program Description

Mission is to prevent and cure diabetes and improve the lives of people affected by diabetes through

- Supporting research - especially for novel approaches, new investigators, and supplemental studies
- Providing information to professionals: professional programs, journals, clinical practice recommendations, and recognition and accreditation programs for physicians and organizations.
- consumers – website, including all journals and clinical recommendations, call center, publications, and referrals to recognized programs. Outreach focus on children, African Americans, Hispanic Americans, and Native Americans.
- Advocacy- to increase funding for diabetes research, improve insurance coverage, end discrimination in schools and in work places.

Opportunities

At present trying to expand limited activity on diabetes in aging. Looking for volunteers to serve on a professional council on aging.

National Institute on Aging

Biology of Aging Program funds research in

- Non-enzymatic glycation
- Caloric restriction
- Insulin signaling

Research Opportunities

New animal model – Dwarf mice, extremely long lived, having defective genes involved with pituitary development. Lower blood glucose, higher insulin sensitivity, lower insulin levels than other laboratory animals.

Geriatrics Program funds research on

- Body composition changes
- Metabolic changes
- Caloric restriction

Research Opportunities

Currently waiting to award funds for study of caloric restriction in non-obese elderly people.

National Institute of Diabetes and Digestive and Kidney Diseases

Program Activities

Supports research across divisions that contribute to understanding of diabetes and the aging process

Division of Diabetes and Endocrinology supports

- Diabetes Prevention Program: Multi-center randomized controlled trial to determine whether interventions can be designed that can prevent the development and onset of type 2 diabetes

- Investigator-initiated grants

Division of Digestive Diseases and Nutrition supports

- Look AHEAD study following the consequences of intentional weight loss in population of individuals with type 2 diabetes over the course of the aging process. Recruitment of 45-75 yrs olds, to begin in June 2001.

Division of Kidney, Urologic and Hematologic Diseases supports

US Renal Data System in developing the database that follows population with endstage renal disease.

National Heart, Lung and Blood Institute

Program Activities

- Honolulu Heart Study – observational study started in 1965, including over 8000 Japanese American men. Looking at stroke in men age 45 to 65 at study entry.

- Strong Heart Study – study of three geographically diverse groups of 4500 Native Americans age 45-74. Currently in year 12. Plan to study 3600 people from 120 families for genetic linkage analyses.

- Cardiovascular Health Study – four US communities, aged 65 and older.

- Framingham Heart Study

- Action to Control Cardiovascular Risk in Diabetes - multi-center trial to assess rate of major CVD events that can be reduced by intensive control of blood sugar. New study intended to have 10,000 participants. Will compare blood pressure control and diabetes control for individuals aged 45 and older in Native Americans, 55 and older in Asian and Hispanics, and 65 and older in Caucasian and African Americans. Expect 60% of study population will be 65 and older.

Research Opportunities

- Public use data sets available for data collected up to 1996 on longitudinal study of Japanese men in Honolulu.

- Cardiovascular Health Study – four US communities, aged 65 and older. Substantial amount of data available for mining. Active diabetes working group.

DIABETES MELLITUS INTERAGENCY COORDINATING COMMITTEE (DMICC)

August 8, 2001
NIH Campus, Lister Hill Auditorium
Bethesda, Maryland

WELCOME

Dr. Allen Spiegel, Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and Chairman of the Diabetes Mellitus Interagency Coordinating Committee (DMICC), welcomed all to a meeting that he characterized as a unique event. The DMICC is charged with coordinating Diabetes research, not only throughout NIH but throughout all Department of Health and Human Services (DHHS) agencies, and will be integrally involved in the followup of the Diabetes Prevention Program (DPP). Dr. Spiegel explained that the DPP presentation would include a background overview and reports on the results and implications of the study. He took the opportunity to acknowledge all the people involved in the DPP, including the Principal Investigators, Program Coordinators, and, most importantly, the volunteers who participated, some of whom were in the audience. He then introduced the Chair of the DPP Study Group, Dr. David Nathan of Massachusetts General Hospital.

Dr. Nathan reported that the DPP was initiated in 1994 with a planning phase that lasted about 18 months. Recruitment was initiated in mid-1996 and completed 3 years later, ahead of schedule. The original plan was to conclude the treatment phase in 2002, but this phase was ended about 1 year early based on the recommendation of the independent Data Monitoring Board, which concluded in May 2001 that the DPP had succeeded in answering the major study questions.

STUDY RESULTS

See HHS News Release as follows:

At least 10 million Americans at high risk for type 2 diabetes can sharply lower their chances of getting the disease with diet and exercise, according to the findings of a major clinical trial announced by HHS Secretary Tommy G. Thompson today, August 8, 2001, at the National Institutes of Health (NIH).

"In view of the rapidly rising rates of obesity and diabetes in America, this good news couldn't come at a better time," said Secretary Thompson. "So many of our health problems can be avoided through diet, exercise and making sure we take care of ourselves. By promoting healthy lifestyles, we can improve the quality of life for all Americans, and reduce health care costs dramatically."

The same study found that treatment with the oral diabetes drug metformin (Glucophage®) also reduces diabetes risk, though less dramatically, in people at high risk for type 2 diabetes. Participants randomly assigned to intensive lifestyle intervention reduced their risk of getting type 2 diabetes by 58 percent. On average, this group maintained their physical activity at 30 minutes per day, usually with walking or other moderate intensity exercise, and lost 5-7 percent of their body weight. Participants randomized to treatment with metformin reduced their risk of getting type 2 diabetes by 31 percent.

The findings came from the Diabetes Prevention Program (DPP), a major clinical trial comparing diet and exercise to treatment with metformin in 3,234 people with impaired glucose tolerance, a condition that often precedes diabetes. On the advice of the DPP's external data monitoring board, the trial ended a year early because the data had clearly answered the main research questions.

Smaller studies in China and Finland have shown that diet and exercise can delay type 2 diabetes in at-risk people, but the DPP, conducted at 27 centers nationwide, is the first major trial to show that diet and exercise can effectively delay diabetes in a diverse American population of overweight people with impaired glucose tolerance (IGT). IGT is a condition in which blood glucose levels are higher than normal but not yet diabetic. (See also Diabetes Prevention Program: Questions & Answers.)

Of the 3,234 participants enrolled in the DPP, 45 percent are from minority groups that suffer disproportionately from type 2 diabetes: African Americans, Hispanic Americans, Asian Americans and Pacific Islanders, and American Indians. The trial also recruited other groups known to be at higher risk for type 2 diabetes, including individuals age 60 and older, women with a history of gestational diabetes, and people with a first-degree relative with type 2 diabetes.

"Lifestyle intervention worked as well in men and women and in all the ethnic groups. It also worked well in people age 60 and older, who have a nearly 20 percent prevalence of diabetes, reducing the development of diabetes by 71 percent. Metformin was also effective in men and women and in all the ethnic groups, but was relatively ineffective in the older volunteers and in those who were less overweight," said DPP study chair Dr. David Nathan of Massachusetts General Hospital, Boston.

DPP volunteers were randomly assigned to one of the following groups:

- intensive lifestyle changes with the aim of reducing weight by 7 percent through a low-fat diet and exercising for 150 minutes a week.

- treatment with the drug metformin (850 mg twice a day), approved in 1995 to treat type 2 diabetes.

- a standard group taking placebo pills in place of metformin. The latter two groups also received information on diet and exercise.

A fourth arm of the study, treatment with the drug troglitazone combined with standard diet and exercise recommendations, was discontinued in June 1998 due to the potential for liver toxicity. DPP participants ranged from age 25 to 85, with an average age of 51. Upon entry to the study, all had impaired glucose tolerance as measured by an oral glucose tolerance test, and all were overweight, with an average body mass index (BMI) of 34. About 29 percent of the DPP standard group developed diabetes during the average follow-up period of 3 years. In contrast, 14 percent of the diet and exercise arm and 22 percent of the metformin arm developed diabetes. Volunteers in the diet and exercise arm achieved the study goal, on average a 7 percent--or 15-pound-- weight loss, in the first year and generally sustained a 5 percent total loss for the study's duration. Participants in the lifestyle intervention arm received training in diet, exercise (most chose walking), and behavior modification skills.

Can the interventions prevent diabetes altogether? "We simply don't know how long, beyond the 3-year period studied, diabetes can be delayed," says Dr. Nathan. "We hope to follow the DPP population to learn how long the interventions are effective." The researchers will analyze the data to determine whether the interventions reduced cardiovascular disease and atherosclerosis, major causes of death in people with type 2 diabetes.

"Every year a person can live free of diabetes means an added year of life free of the pain, disability, and medical costs incurred by this disease," said Dr. Allen Spiegel, director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), which sponsored the DPP. "The DPP findings represent a major step toward the goal of containing and ultimately reversing the epidemic of type 2 diabetes in this country."

Diabetes afflicts more than 16 million people in the United States. It is the main cause of kidney failure, limb amputations, and new onset blindness in adults and a major cause of heart disease and stroke. Type 2 diabetes accounts for up to 95 percent of all diabetes cases. Most common in adults over age 40, type 2 diabetes affects 8 percent of the U.S. population age 20 and older. It is strongly associated with obesity (more than 80 percent of people with type 2 diabetes are overweight), inactivity, family history of diabetes, and racial or ethnic background. Compared to whites, black adults have a 60 percent higher rate of type 2 diabetes and Hispanic adults have a 90 percent higher rate.

The prevalence of type 2 diabetes has tripled in the last 30 years, and much of the increase is due to the dramatic upsurge in obesity. People with a BMI of 30 or greater have a five-fold greater risk of diabetes than people with a normal BMI of 25 or less.

To date, the cost of the DPP is $174.3 million. The DPP is funded by the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Child Health and Human Development, the National Institute on Aging, the National Center on Minority Health and Health Disparities, the National Center for Research Resources, the Office of Research on Women's Health, and the Office of Behavioral and Social Science Research within the NIH. Additional funding and support was provided by the Centers for Disease Control and Prevention, the Indian Health Service, and the American Diabetes Association. The study also is funded in part through a Cooperative Research Development Agreement (CRADA) with Bristol Myers Squibb. Other sources of corporate support include Merck and Company, Merck Medco, Hoechst Marion Roussell, Lifescan, Slimfast, Nike, and Health-O-Meter.

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DIABETES PREVENTION INITIATIVES: THE DMICC TASK FORCE

August 9, 2001
NIH Campus, Lister Hill Auditorium
Bethesda, Maryland

BACKGROUND

At the request of Bill Raub, Deputy ASPE, a meeting of the DMICC was held on August 6, 2001, to discuss diabetes prevention initiatives for presentation to the Secretary. Dr. Raub explained the background of this request and defined two parallel activities: a) a longer term effort to develop a set of coordinated initiatives for consideration as part of the FY'03 budget; b) a "fast-track" effort to develop bold new initiatives in which the Secretary could play a personal role and which could be implemented by 2002. Dr. Raub requested that responses for the latter effort be sent to Lily Engstrom, OS, by Monday August 13th.

The following DMICC members (N. Armstrong, NINR, P. Dudley, NEI, C. Dutta, NIA, M. Eberhardt, CDC, J. Fradkin, NIDDK, S. Garfield, NIDDK and Executive Secretary of the DMICC, G. Grave, NICHD, R. Knazek, NCRR, P. Savage, NHLBI, with B. Bowman, M. Engelgau, and F. Vinicor, CDC by conference call) met on August 9th to develop a coordinated response. A. Spiegel, Director of NIDDK and Chair of the DMICC, cconvened the meeting that also included J. Gallivan, NIDDK and codirector of the National Diabetes Education Program (NDEP), and W. Johnson-Taylor, NIDDK and NIH Division of Nutrition Research Coordination. Not present but included on the Task Force are K. Acton, IHS, P. Blackshear, NIEHS, and D. Stryer, AHRQ.

The group agreed that any initiative proposed should have a solid scientific basis, and as emphasized by Dr. Raub, should have an evaluation component. The group felt that evaluation measures should first assess the degree to which a message or program had reached its target audience, and second, assess the degree to which members of the target audience had put the message or program into action. Given the time frame involved and the nature of the initiatives, more definitive health outcome measures such as incidence of obesity and diabetes would only be assessed as part of ongoing efforts such as NHANES.

The group also agreed that primary prevention of diabetes should be a major focus of the initiative based on the recent results of the Diabetes Prevention Program (DPP). In fact, the Secretary, in announcing the results of the DPP, stated that he was creating a Task Force to make recommendations on how to implement these results on a wider scale. The DMICC working group constitutes that Task Force. The group also identified some possible short-term initiatives directed toward optimization of diabetes management, i.e. secondary and tertiary prevention, but concluded that more definitive efforts in this area, as well as on the issue of recommendations for screening for impaired glucose tolerance and undiagnosed diabetes, should be part of the longer-term effort directed toward the FY'03 budget. Also deferred was consideration of health coverage issues for such screening and for programs in diet and exercise counseling.

The initiatives proposed below focus largely on programs to increase physical activity in Americans of all ages based on the rationale that combating the epidemic of obesity and type 2 diabetes will require significant changes in lifestyle across all age groups, and that exercise programs lend themselves better to direct involvement of the Secretary than do programs focused on dietary change.

PROPOSED INITIATIVES

1. An HHS-wide initiative to increase physical activity of all employees. Such a program lends itself best to direct involvement of the Secretary, but could be extended by having him challenge other Cabinet Departments, as well as companies in the private sector. If successfully broadened, such an initiative could target a very large population of working-age adults. A number of suggestions regarding specific components included provision of additional time during or outside of lunch periods for group exercise, and provision of incentives for increases in physical activity which could include help in defraying cost of health club membership. Also provision of increased exercise facilities, showers, etc. on site. Additional ideas included making stairs in workplaces more user-friendly and more heavily used.

2. An effort to reinstate physical education programs in schools at all levels. The elimination of such programs correlates with the upsurge in obesity among youth. While this of course does not prove causality, most members of the group felt that this would be an important goal. The Secretary's challenge to Governors of each state to reinstate physical education in schools would be a dramatic step that could achieve significant results.

3. Consideration of the Head Start program as a venue for instruction in the importance of physical activity (and if possible, good diet). The Head Start program involves children 3-5 and their parents who typically come from groups disproportionately affected by diabetes. The program, moreover, is administered by HHS, offering the Secretary a ready opportunity to shape it. There may be barriers relating to cost (the program already costs in excess of $4 billion/year), but close scrutiny of the program may offer cost-effective approaches to incorporating exercise and diet instruction.

4. Several representatives offered suggestions regarding school and community-based programs involving instruction in healthy lifestyles. Some of these may lend themselves better to the initiatives to be suggested for FY'03, but one example suggested an award from the Secretary (similar to the "All-American town concept) for those communities achieving certain goals in terms of increased physical activity and/or decreased obesity. A more detailed description of school and community-based programs is included as an attachment.

5. Older Americans represent a group at highest risk for diabetes and therefore an important target for prevention efforts. I attach two documents: one that outlines the rationale for targeting the elderly, and another, as an example of a specific intervention program, that details a well-developed exercise program from NIA targeting those over 50. For the latter, I have omitted a lengthy set of references, but these can be provided if so desired. Dr. Dutta, NIA, will also be sending separately to L. Engstrom the exercise book and video described in the attachment. Similar programs targeting other age groups can be developed and fuller descriptions provided if so desired.

6. The National Diabetes Education Program (NDEP), a joint program of NIH and CDC, plans a major expansion of its activities. A major goal is to improve management of diabetics by launching a "Know your ABC's" campaign (hemoglobin A1C, blood pressure, and cholesterol). An attached document lists a number of bullet items in which the Secretary could promote NDEP activities.

7. CDC reps propose that the Secretary publicly launch the Diabetes and Women's Health initiative at the 2001 Annual Meeting of the American Public Health Association in Atlanta, GA in Oct. 2001.

PROGRAM PROPOSALS SUMITTED BY PARTICIPATING AGENCIES AND INSTITUTES

Proposal 1:
Exercise: It Works At Any Age

The health picture of older Americans improved steadily through the last century. But many of those age 65 and older still face chronic health conditions. In general, African Americans, Native Americans, and Hispanics are disadvantaged relative to whites on most health indices. Moreover, our national preoccupation with youth makes seniors almost invisible when it comes to messages of healthy lifestyles.

As the number of older people explodes, now is the time to change outmoded attitudes and to promote disease prevention to older people, especially members of special populations. It is a fact that you are never too old to start a healthier lifestyle. And, as one Director of the National Institute on Aging has said, "If you could pack exercise in a pill, it would be the single best medicine available."

Substantial research data exist to document the benefits of exercise (Tab 1 omitted for the sake of brevity). These include the role of exercise in preventing heart disease, type II diabetes, stroke, colon cancer, osteoporosis, depression, falls and disabling injuries, and even changes in cognition and possibly the onset of Alzheimer's disease. Despite the growing list of benefits of exercise, statistics show that few older people engage in regular physical activity. Most people know that exercise is good for them. Somehow, though, older adults have been left out of the picture. Now is the time to change this picture!

Within the HHS, the National Institute on Aging (NIA) has already developed the disease-prevention message and the tools (Tabs 2 and 3) to begin a major exercise and physical activity campaign targeted to seniors and, particularly, members of special populations. The NIA has a research-based, road-tested exercise program designed especially for older adults. Supporting materials include a complete exercise guide and fact sheets in Spanish and English, an exercise video, a Spanish-language exercise fotonovela, a special internet website designed for seniors based on NIA cognitive research done in conjunction with the National Library of Medicine (Tab 4), posters, shoelaces, and prescription pads for health providers. The prestige of the Secretary and the authority of his office hold great sway with older Americans. A sustained 1-year effort by the Secretary to promote the health message – *Exercise: It Works at Any Age* – would further this important effort to promote lifestyle change. How? In support of Secretary Thompson's deep commitment to preventive measures and a healthy lifestyle, the NIA proposes the development of the *Secretary's Fitness Calendar for Seniors.* The calendar, with a slogan and suggested spokesperson for each month, would include a message from the Secretary. Promotional radio spots will be produced and distributed in concert with other HHS agencies such as the Administration on Aging and the Center for Medicare Services. The calendar (Tab 5) would be annotated with suggestions for increasing physical activities during the month, a suggested regimen, model schedules, and even a certificate of acknowledgement from the Secretary. The NIA has also outlined potential strategies to evaluate the outcome of this initiative, should it go forward (Tab 6). The commitment to promote the exercise message to special populations of seniors would bring much-needed disease-prevention messages to frequently ignored seniors.

TAB 2

Statistics on Current Distribution of Exercise Program

Exercise: A Guide from the National Institute on Aging

(80-page book)
441, 900 books printed since 1998
397,018 books disseminated to date

Exercise: A Video from the National Institute on Aging

(48 minute, close-captioned VHS)
33,572 videotapes sold (cost recovery)

Marketing tools used to promote the book

Promotional shoelaces
Print ad slicks
Press releases
Film clip on NIA Website
Partial animation of exercises on NIA website
Exercise poster with Senator John Glenn
Public service announcement (Emmy nomination)
Prescription pads for health professionals
Flyers
Postcards
Exhibit

TAB 3

Exercise: A Guide from the National Insitute on Aging

NIA's exercise program targets aging baby boomers and seniors – 71 million Americans are 50 years or older. Research shows that staying active is essential to overall good health in aging. Increasingly, scientists are learning that regular exercise prevents many of the disabilities and illnesses common in older people.

NIA's exercise program emphasizes:

- endurance exercises, which increase stamina and help delay or prevent diabetes, colon cancer, heart disease and stroke.

- strength exercises, which increase metabolism, help control weight, and regulate blood sugar. Studies show that they also may help prevent osteoporosis.

- flexibility exercises, which help prevent and aid recovery from injuries.

- balance exercises, which help prevent falls – a major cause of broken hips and other injuries that lead to disability and loss of independence.

Despite the growing list of benefits of exercise for older adults, statistics show that few older people engage in regular physical activity. By age 75, for example, about one in three men and one out of every two women do not engage in any of the types of physical activities that help prevent disease and disability. Research has shown that even very frail older people in nursing homes can increase their strength by more than 100 percent through simple muscle-building exercises. The long list of benefits that aerobic exercise confers on cardiovascular health is well established. Recent studies also have shown a possible connection between exercise and prevention of dementia.

The guidelines and exercises included *Exercise: A Guide from the National Institute on Aging* have been scientifically approved. To ensure the most accurate and comprehen-sive information possible, NIA convened a panel of internationally renowned experts in the field of exercise and aging. This guide is based on their recommendations and is recognized as a state-of-the-art guide to exercise for older people. It includes exercises that older adults can perform at home, without expense, to improve strength, endurance, flexibility, and balance, as well as a detailed plan to develop a safe, effective exercise program. Other chapters provide information about safety, nutrition, motivation, and how to monitor progress. An updated appendix provides a list of resources for readers with special health concerns, such as diabetes and arthritis, and organizations that offer exercise programs especially for older people.

An accompanying 48-minute video takes viewers through an easy-to-follow workout of stretching, balance, and strength-training exercises found in *Exercise: A Guide from the National Institute on Aging*. The video features Margaret Richard, star of *Body Electric*, PBS television's popular exercise show.

TAB 4

Description of Project Teens Teaching Elders on the Internet

In January 2002, the National Institute on Aging (NIA) will become part of an intergenerational program by which teenagers teach older people how to use the Internet and gain access to senior-friendly Web Sites. The interactive Web Site on exercise for older people is being developed by the NIA and the National Library of Medicine. It will include online videos showing various exercises being done by the Department of Health and Human Services Secretary Tommy G. Thompson, if willing, and eight Directors from the National Institutes of Health. It will also include videos on exercise motivation, correct form, and frequency. The Website navigation, readability and teaching methods are based on sound research and use ability tests done on technology and older people. The Web Site will serve as a prototype for Web Sites geared toward older people.

Teens Teaching Internet Skills was developed by the USDA Cooperative State Research, Education and Extension Service (CSREES), the Center for Medicare/Medicaid Services (CMS) and local 4-H Youth Technology Team leaders. USDA-CSREES coordinates national 4-H programs and HCFA administers the federal Medicare program. Between September 1999 and April 2000, 4-H Youth Technology Corps members led successful pilot training sessions in Connecticut, Florida, Iowa, Virginia, Maryland and Washington State. Based on the success of the pilot sessions, leaders from USDA, CMS and 4-H are working to bring TTIS programs to communities around the country.

TAB 5

The Secretary's Fitness Calendar for Seniors

Exercise: It Works At Any Age

(month, slogan, suggested spokesperson)

Oct. *Don't Play Tricks On Yourself – Exercise* – Bill Cosby

Nov. *Exercise – Your Body Will Thank You* – Tina Turner

Dec. *Give Yourself A Holiday Gift* – Ruby Dee & Ossie Davis

Jan. *Resolve To Exercise* – Dick Clark

Feb. *Have A Healthy Heart – Exercise* – Maria Tallchief

Mar. *Get In Training – Exercise* – Hank Aaron

April *Exercise – It's Not Too Taxing* – JC Watts

May *Increase Your Independence – Exercise* – Rita Moreno

June *Graduate To A Higher Level Of Exercise* – Josefina Carbonell, Ass't Secretary for Aging

July *Burst Into Fitness* – Lee Trevino

Aug. *Don't Take A Vacation From Exercise* – Pat Morita

Sept. *Fall In Step: Start an Exercise Program* – Former President George Bush

TAB 6

Evaluation Plan

Exercise: It Works At Any Age

In addition to tracking the distribution of the exercise guide and video, NIA currently is conducting a number of projects to evaluate these materials and their use. Similar strategies would be planned to evaluate the Secretary's Calendar and public awareness campaign.

Current Projects to Evaluate Exercise:
A Guide from the National Institute on Aging

- Duke University Medical Center currently is conducting an evaluation of NIA's exercise guide as part of a larger study to evaluate whether a telephone-counseling program is effective in improving physical activity and diet among elderly cancer patients with early-stage disease – behavior changes that should ultimately improve their physical function. Specifically, they are evaluating whether the exercise book is easy to understand, whether the graphics in the book clearly demonstrate how to perform the exercises correctly, and whether the book motivates participants to exercise. Approximately 420 early-stage breast and prostate cancer patients 65 and older are participating in this evaluation project.

- NIA currently is conducting a feasibility study to determine the methodology for an evaluation of the exercise book and videotape, specifically to discover how the book/video are being used, its role in changing behavior (both short-term and long-term behavior changes), and whether modifications to the book/video might have a positive impact on users' ability to maintain exercise as part of a healthy lifestyle. This feasibility study focuses on developing a study to answer questions such as: how are people using the exercise book/video, who are they, how do the book/video alter users' personal exercise routines, what other exercise-related materials might help users sustain a healthy

lifestyle, and what suggestions do users have for improving these products.

Proposed Evaluation Strategies for Exercise:
It Works At Any Age, The Secretary's Calendar for Seniors

- The NIA Information Center will track numbers of calendars distributed and requests generated by the Calendar for copies of NIA's exercise book/video.

- The NIA Information Center will track the number of Certificates from the Secretary distributed in response to mail-back forms provided in the Calendar.

- NIA will develop a separate web page to record and respond to feedback/ suggestions for improving the exercise book/video, as well as collect comments about the usefulness of the Calendar in promoting fitness and healthy lifestyles.

- NIA will work with AoA to develop a community-based approach to evaluate how people are using the Calendar and its usefulness in motivating older people to adopt exercise as part of their daily routine. This project also will include component to evaluate performance and measure progress (for example, are older people exercising, how long, how often, and how much is it affecting their overall health).

- NIA will track media reports of the Secretary's promotional appearances on Oprah and other talk shows and will use a broadcast monitoring service to track print stories relating to this public awareness campaign.

Proposal 2:
Prevention of type 2 diabetes and its complications in elderly men and women

Type 2 diabetes is very common in the elderly and is projected to become an even greater problem. There are reasons to think it could be prevented or at least postponed by interventions similar to those which were so successful in the recently completed Diabetes Prevention Trial.

Using the WHO criteria for diabetes and impaired glucose tolerance, approximately 50% of U.S. adults aged 65 years and older have abnormal glucose tolerance. Approximately 20% have diabetes and 30% have impaired glucose tolerance. These numbers are even higher among many minority populations. While the number of people with diabetes will be somewhat less using the current US ADA criteria for diabetes, there is little doubt that the elderly are a group at high risk for progression to diabetes. Moreover, while diabetes increases the risk for eye and kidney disease, both diabetes and impaired glucose tolerance increase the risk for development of cardiovascular disease, the major cause of death in older persons. Older patients with type 2 diabetes represent a significant component of patients receiving care for end stage renal disease and a significant portion of those with serious visual impairment. Diabetes is a major risk factor for myocardial infarction and death in this age group.

It is important to note that the problem is increasing and, unless something is done, will be substantially greater in future years. There are several factors which will inevitably increase the numbers of older women and men with diabetes. The U.S. population is aging and the numbers of the "old old", i.e., over 85, will continue to increase. As life expectancy increases, more members of minority groups at high risk for diabetes will join the ranks of the elderly. Increasing obesity and lack of exercise among the middle aged population will also lead to more people at high risk for developing diabetes joining the elderly in the decades to come.

Despite the magnitude of the problem, however, other factors make the elderly a good group to target for prevention efforts. Although diabetes is common, in many instances it is mild in older persons, making them good candidates for responding to diet and lifestyle changes. Such interventions may be even more effective in those with impaired glucose tolerance, the milder abnormality treated in the diabetes prevention trial. It is noteworthy that the best results in the prevention trial occurred among those over 60 years of age. Older patients are frequently concerned about their health and often have the time and motivation to participate in activities which will be beneficial. In addition, their membership in organizations such as the American Association of Retired Persons and participation in activities at local senior centers, churches, recreation facilities, etc. may facilitate reaching them with public information campaigns and programs to adopt a healthier lifestyle. Even if such programs only succeed in postponing the development of diabetes or temporarily improving control of their glucose levels, the anticipated delay in developing complications of diabetes may give them several more years of a healthy life.

There may be a need to develop modifications in the prevention program to maximize its effectiveness among an elderly population. This is particularly true if it is provided to the older elderly where the existence of symptomatic heart and vascular disease is more common. Guidelines will need to be developed to identify participants who are most likely to benefit from the program and to also identify those who might not be able to tolerate the full intervention. Collaboration with local health care providers will be important, both to assure patient safety and to attain their cooperation in encouraging patient participation.

It is proposed that there be two components to the program 1) a public information campaign encouraging older women and men to eat a healthy diet and engage in regular physical activity and 2) a group of demonstration centers (or communities) where a more systematic effort to assess the best ways to achieve participation in the intervention (evaluating both communication methods and cost of the effort) and any possible adverse effects of participation.

A critical component of the overall program is to document its effectiveness. While there is no doubt that the diabetes prevention trial was a remarkable success, it is crucial to evaluate the ability to translate such research interventions into programs that are practical and affordable for use in the health care practice or community setting. The NIH and CDC should collaborate to develop goals for the program, methods to evaluate its success and procedures for modifying strategies and incorporating new relevant information as it becomes available. Translation problems may differ in different communities - the local environment may have a major effect upon the ability to successfully implement the prevention program.

A final advantage of an effort at diabetes prevention in older women and men is that a good diet and moderate exercise are likely to have several beneficial effects in this population beyond the prevention of diabetes. On the basis of existing scientific studies, beneficial effects may be anticipated on blood pressure, cardiovascular disease and the individual participant's sense of well being.

Proposal 3:
School and Community-based Interventions

Type 2 diabetes is now a health problem for all age groups, although it continues to be more prevalent in the adult and older adult years. Children who develop type 2 diabetes, however, have a longer life span to cope with a complex and difficult disease and to develop complications at an earlier age. Prevention or delay of the onset of type 2 diabetes in those at risk is an important societal concern. The following are some potential approaches that lend themselves to immediate implementation. These suggestions may be used to target at-risk populations or be opened to the community citizens as a whole.

1. Encourage schools to lead their community in leading healthier lifestyles through good nutrition and physical activity. Encourage whole community involvement. Communities could show, through common measures, their degree of achievement of their healthy living goals each year. Communities showing the most improvement might be awarded certificates of achievement and be recognized in the news. A healthy lifestyle achievement award could be given to the most improved communities by Secretary Thompson. One example of a school activity to encourage community involvement is to hold family "healthy living" evenings during the Fall or Spring months each year to reach parents, children, and all community citizens. Make it attractive enough to encourage attendance by all groups (including low income and minorities). Speakers or panel presentations could provide information about nutrition and physical activity and how a healthier lifestyle will improve fitness, emotional well-being, and help prevent/delay type 2 diabetes. Entertainment portion could include fun physical activity events/how to count pulses/other useful skills. Community businesses may want to show support in various ways including financing community-based physical activity events. Grocery stores could place clever signs over healthy foods. The communities would undoubtedly be creative in developing motivation enhancements and social support.

2. Develop an interactive computer program to install in school or home computers. The program would be based on many that are already available to the public. This program would focus on helping the child or adolescent to develop food and physical activity goals and track their progress. For example, the youngster might enter their weight and target weight, their current minutes of physical exercise and their target minutes, exercise type, and various other information. The program would allow periodic (daily or weekly) entry. Charts and graphics could display progress towards the goal. Refinement of goals and other inputs would be possible as the youngsters learn more about their lifestyle behaviors. A certificate of achievement should pop up and be available to print at the achievement of each goal.

3. Develop a public health information program for schools that targets all grades from preschool to 12th grade. The program should combine food intake and exercise in tandem as opposed to separate programs for each. For example,

   - Develop charts aimed at school-agers that show how much physical activity (duration, intensity) is required to burn various calorie amounts (100, 200, 300, etc.). The charts could be 3 ring binder size so students could place them in a notebook.

   - Develop menus for each major ethnic group showing realistic but healthy portion sizes of common ethnic foods. Portion sizes could be varied by age groupings

   - The menus in school cafeterias should reflect recommended food intake (type and calories). Unhealthy food choices in vending machines should be limited.

   - Physical activity should be re-instated as a required activity in all schools. Healthy food choices should be a part of the physical activity curriculum content.

4. Develop an educational program to teach teachers how to integrate healthy lifestyle content and behaviors in their curriculum. Schools could choose an integrated approach (healthy lifestyle content in all appropriate courses) or specific classes for students (physical activity and nutrition classes).

Proposal 4:
National Diabetes Education Program

The purpose of the National Diabetes Education Program (NDEP), a joint initiative of the NIH and CDC, is to improve the treatment and outcomes of people with diabetes, to promote early diagnosis, and ultimately, to prevent the onset of diabetes. The NDEP has embarked on public and private education and information programs focusing on increasing diabetes awareness, with emphasis on prevention of complications, and dissemination of recent research findings. Through its partnership network, the NDEP will provide support and promote findings from the Diabetes Prevention Program (DPP), similar to activities that have promoted results of the Diabetes Control and Complications Trial (DCCT) and other clinical trials.

For people with diabetes:

- Secretary Thompson challenges all Americans with diabetes to know their ABC numbers and take action to lower their risk of diabetes complications, particularly heart disease and stroke. People with diabetes would have A1C, blood pressure and blood cholesterol tests done and schedule a visit with an appropriate health care provider to begin to take steps to lower these numbers toward target levels that have been proven effective in preventing complications.

- Worksite programs would be available in all federal agencies to provide diabetes education, support groups and physical activity opportunities for people with diabetes. Federal agencies could use the NDEP diabetes worksite kit that will provide tools for businesses to use for creating and supporting diabetes education programs as well as motivation for implementation of these activities by assessing the impact of diabetes on their business.

For people at risk for diabetes Secretary Thompson would issue challenges for communities and organizations and provide incentives and awards to those that report accomplishments:

- Partner with corporations to provide support and resources for exercise programs in the workplace

- Partner with local community centers and neighborhood groups to provide opportunities to exercise in a safe environment without costly membership fees. Partner with YMCA, Girl/Boy Scouts, Boys and Girls Clubs to support/subsidize programs for children.

- Provide education and training for lifestyle interventions (diet, physical activity, behavior modification) that were successful in DPP with services to be covered by Insurance companies, beginning with Medicaid, Medicare.

- Schools to provide structured physical activity through physical education and/or after school programs, and support services for children to attend sessions (buses, supervision, etc.). Recreational group and individual sports should be encouraged and supported, not only competitive sports. Partner with President's Council on Fitness, Head Start.

- America Walks Program. Neighborhoods organize evening group walks. Low cost pedometers distributed through schools, communities with recognition for miles walked.

- School Lunch Program to promote healthy eating through school lunch, snacks, etc. Partner with PTSA, Association of School Board, Dept. of Education

- Partner with WIC, Food stamps, 5 -A- Day to get fresh fruits and vegetables available-Dept. of Agriculture

- National Community fitness day- held in communities across the country to encourage and support family fitness

- National Worksite fitness programs - fitness contests/programs among offices and agencies. "Take the stairs" day- one day per week to encourage activity.

- National Diabetes Prevention Day/Week in cities and communities across the country. Include fitness events, walk-a-thons, healthy eating activities, community gardening, etc. Get kids involved.

- Diabetes Prevention All-Stars – Sec. Thompson meets with baseball, basketball, Olympians, etc. commissioners, players to encourage fitness and working out with children

- President Bush promotes fitness/diabetes prevention during baseball on White House lawn

- Include Prevention education for diabetes and other diseases in President's Education Plan

- Partner with Office on Aging, AARP etc. to support fitness and healthy eating for older adults. Retirement communities, military programs to support fitness programs for adults of all ages.

- The "Sisters Together" project has developed a complete community health awareness program to encourage African American women to be more physically active and eat better to prevent obesity. The NIH launch of this national program will be held on Sept. 15 in D.C. at the Franklin D. Reeves Center. Secretary Thompson could use this event to challenge communities to adopt the Sisters Together program, enlist local community champions to promote the program and provide incentives/recognition for communities who enlist and complete local fitness events planned throughout the year. Sisters Together also encourages families to exercise together.

APPENDICES

APPENDIX A

PUBLIC HEALTH SERVICE:
Interagency Coordinating Committees

Sec.429. [285c—3]

(a) For the purpose of—

(1) better coordination of the research activities of all the national research institutes relating to diabetes mellitus, digestive diseases, and kidney, urologic, and hematologic diseases; and

(2) coordinating those aspects of all Federal health programs and activities relating to such diseases to assure the adequacy and technical soundness of such programs and activities and to provide for the full communication and exchange of information necessary to maintain adequate coordination of such programs and activities;

the secretary shall establish a Diabetes Mellitus Interagency Coordinating Committee, a Digestive Diseases Interagency Coordinating Committee, and a Kidney, Urologic, and Hematologic Diseases Coordinating Committee (hereafter in this section individually referred to as a "Committee").

(b) Each committee shall be composed of the Directors of each of the national research institutes and divisions involved in research with respect to the diseases for which the Committee is established, the Division Director of the Institute for the diseases for which the Committee is established, the Chief Medical Director of the Veterans' Administration,[1] and the Assistant Secretary of Defense for Health Affairs (or the designees of such officers) and shall include representation from all other Federal departments and agencies whose programs involve health functions or responsibilities relevant to such diseases, as determined by the Secretary. Each Committee shall be chaired by the Director of NIH (or the designee of the Director). Each committee shall meet at the call of the chairman, but not less often than four times a year.

(c) each Committee shall prepare an annual report for—

(1) the Secretary;

(2) the Director of NIH; and

(3) the Advisory Board established under section 430 for the diseases for which the Committee was established, detailing the work of the Committee in carrying out paragraphs (1) and (2) of subsection (a) in the fiscal year for which the report was prepared. Such report shall be submitted not later than 120 days after the end of each fiscal year.

[1] The reference is deemed to be a reference to the Under Secretary for Health of the Department of Veteran Affairs.
See section 302 (e)(1) of Public Law 102-405(106) Stat. 1985 and section 10(4) of Public Law 100-527 (102 Stat.2641).

APPENDIX B

DIABETES MELLITUS INTERAGENCY COORDINATING COMMITTEE

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