Juvenile Diabetes Cure Research Tax Check-Off Program Annual Report

January 1 - December 31, 2011

pennsylvania
DEPARTMENT OF HEALTH

Tom Corbett, Governor

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Juvenile Diabetes Cure Research Tax Check-Off Program

Created in September 2004 with the passage of Act 133, Juvenile Diabetes Cure Research, the Juvenile Diabetes Cure Research Tax Check-Off Program provides a state income tax check-off option for individuals to contribute a portion of their state tax refund to support research for juvenile diabetes, more commonly known as type 1 diabetes. The Program funds research grants focused on restoring normal blood levels, preventing and reversing complications of the disease, and/or prevention of juvenile diabetes.

Tax Check-Off/Private Contributions

Tax Year 2010 (Calendar Year 2011) was the sixth year in which contributions were collected for this fund. Contributions to the fund in 2011 totaled $54,758.81. The cumulative balance, as of December 31, 2011, was $272,438.13. These annual contributions are displayed below in Figure 1.

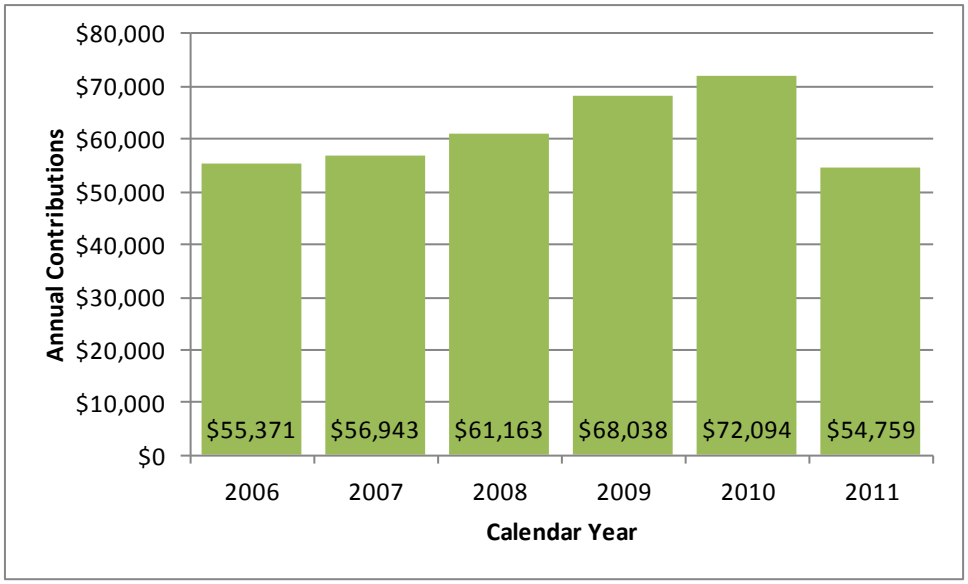


Figure 1: Annual contributions made in calendar years 2006-2011

Administration of the Program

The Pennsylvania Department of Health Diabetes Prevention and Control Program is responsible for the administration of the Juvenile Diabetes Cure Research Tax Check-Off Program. A $100,000 grant was awarded to The Pennsylvania State University College of Medicine to conduct vision impairment diabetic retinopathy research for patients with type 1 diabetes. Research began January 1, 2009, and ended on December 31, 2010. A second grant was awarded to The Pennsylvania State University Department of Pharmacology to conduct vision impairment diabetic retinopathy research for patients with type 1 diabetes. Research will begin July 1, 2012, and will end on June 30, 2014.

The eventual significance of this research on public health outcomes could be enormous. Significant progress has been made using these funds. The results of these studies have led to published manuscripts that describe roles for altered lipids and enzyme inhibition in diabetic retinopathy and complications. See Appendix 1.

The Pennsylvania State University College of Medicine has leveraged their findings for additional extramural funding as a bridge to national research funding from the National Institutes of Health (NIH) and American Diabetes Association (ADA):

1. National Institutes of Health National Eye Institute – The Role of Glycosphingolipids in Diabetic Retinopathy.

2. American Diabetes Association – Therapeutically modulating glycosphingolipid metabolism in a model of type 1 diabetes.

3. We are presently seeking extramural funding to further explore the role of diminished caveolin-1 in ocular inflammation and vascular leakage.

Type 1 Diabetes Overview

Type 1 diabetes, previously known as insulin-dependent diabetes mellitus (IDDM), or juvenile-onset diabetes, is an auto-immune disease in which the immune system destroys the insulin-producing beta cells of the pancreas that regulate blood glucose. As a result, the pancreas no longer produces insulin, the hormone needed to convert sugar (glucose), starches and other foods into energy needed for living. This form of diabetes usually strikes children and young adults, although disease onset can occur at any age. In adults, type 1 diabetes accounts for approximately 5 percent of all diagnosed cases of diabetes. Risk factors may be autoimmune, genetic or environmental, but the exact cause of type 1 diabetes is unknown with no known way to prevent it. In addition, there is no cure.

Type 1 diabetes is the third most prevalent childhood chronic disease in the United States. Type 1 diabetes has been diagnosed in children of all races, ages 10 to 19.[1] The disease comes on suddenly, causes dependence on injected or pumped insulin for life, and carries the constant threat of devastating complications. While insulin injections or infusions allow a person with type 1 diabetes to stay alive, they do not cure diabetes, nor do they necessarily prevent the possibility of the disease's devastating effects, which may include kidney failure, blindness, nerve damage, heart attack, stroke and amputations. Research focused on type 1 diabetes provides hope to detect its causes and to find a cure.

The Scope of Diabetes: In the U.S., a new case of diabetes is diagnosed every 30 seconds; more than 1.9 million people are diagnosed each year.[2]

The Cost of Diabetes: Nearly one-third of every Medicare dollar is spent on people with diabetes.[3]

The Harm Caused by Diabetes: Damage to many organ systems (Diabetes is the leading cause of kidney failure, adult blindness, non-traumatic amputations and nerve damage.); increased heart disease risk (People with diabetes are two to four times more likely to have a heart attack or stroke.); and shortened life.[1]

Type 1 Diabetes Statistics

On April 27, 2011, The World Health Organization reported that non-communicable diseases (NCDs) caused more than half of all deaths in 2008 and now pose a greater threat than infectious diseases, such as malaria, HIV and tuberculosis. NCDs, including diabetes, accounted for 36 million, or 63 percent, of the 57 million deaths worldwide in 2008.[4]

- According to the Centers for Disease Control and Prevention (CDC), it is estimated that 25.8 million people of all ages in the United States have diabetes (with 18.8 million diagnosed and seven million undiagnosed).[5]
- It is estimated that 5 to 10 percent of diabetic adults have type 1.[5]
- The American Diabetes Association estimates that about one in every 400 children and adolescents has type 1 diabetes.[6]
- Diabetes is one of the costliest chronic diseases.[7]
- Diabetes was the seventh leading cause of death listed on U.S. death certificates in 2007[5] and the seventh leading cause of death in 2009 in Pennsylvania.[8]
- In 2009, an estimated 14 percent (95 percent Confidence Interval: 10-20) of Pennsylvania adults age 18 and older with diabetes had type 1 diabetes.[9]

In an effort to gain a better understanding and a better statistical picture of diabetes in children, the CDC and the National Institute of Diabetes and Digestive and Kidney Diseases funded the SEARCH for Diabetes in Youth study, a multi-center study focusing on children and youth with diabetes in the United States. This five-year study was a $22 million national research project that ended in October 2005 and identified the number of children and youth under the age of 20 who have diabetes, both type 1 and type 2. The study provided the opportunity to learn more about the disease, its complications and its effects on the everyday lives of those who have it. It examined a diverse population of children and youth under age 20 from six geographic locations across the country. The published findings indicate:

- The majority of new cases of diabetes in youth are type 1, with most occurrences in children under age 10.
- Of participants with type 1 diabetes, 56 percent had a first degree relative – a parent, sibling, or grandparent – with the disease.
- Children diagnosed with type 1 diabetes had higher rates of obesity than children without diabetes.[4,10]

About 215,000 people younger than 20 years had diabetes (type 1 or type 2) in the United States in 2010.[11] See Figure 2 for the rates of new cases of diagnosed type 1 and 2 diabetes for non-Hispanic whites, non-Hispanic blacks, Hispanics, Asians/Pacific Islanders and American Indians. The CDC 2011 National Diabetes Fact Sheet reports:

- "Estimates of undiagnosed diabetes are unavailable for this age group."
- "During 2002–2005, 15,600 youth were newly diagnosed with type 1 diabetes annually, and 3,600 youth were newly diagnosed with type 2 diabetes annually."
- "Among youth aged less than ten years, the rate of new cases was 19.7 per 100,000 each year for type 1 diabetes and 0.4 per 100,000 for type 2 diabetes."
- "Among youth aged ten years or older, the rate of new cases was 18.6 per 100,000 each year for type 1 diabetes and 8.5 per 100,000 for type 2 diabetes."

Rate of new cases of type 1 and type 2 diabetes among youth aged < 20 years, by race/ethnicity, 2002-2005

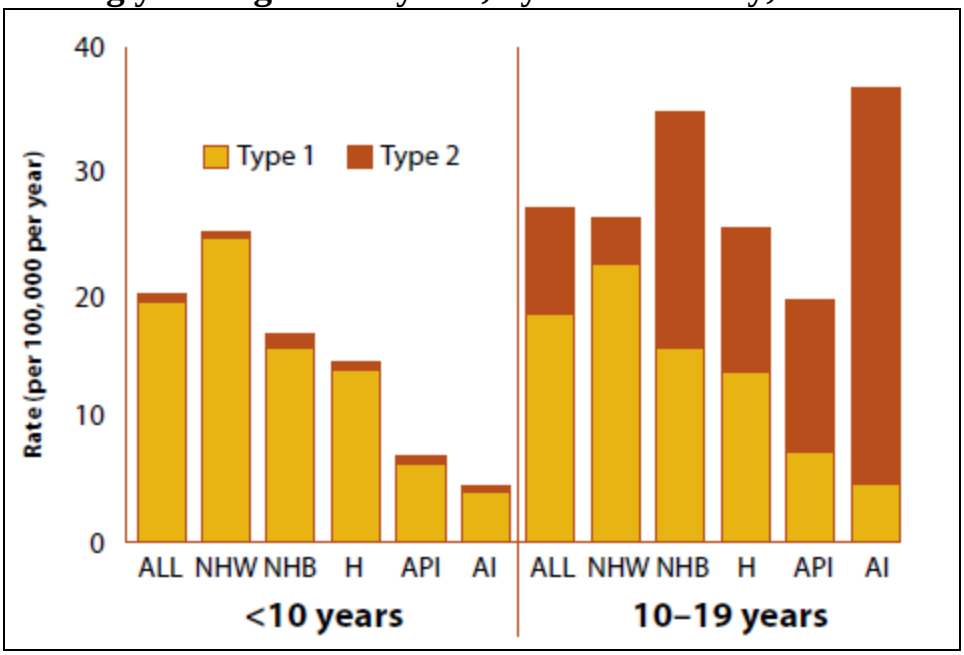


Figure 2: New Cases of Diagnosed Diabetes
Source: SEARCH for Diabetes in Youth Study
NHW=non-Hispanic whites; NHB=non-Hispanic blacks; H=Hispanics; API=Asians/Pacific Islanders; AI=American Indians

Diabetes Costs Overview

Diabetes is one of the costliest chronic diseases, and timely investment in the diagnosis and treatment of diabetes is an excellent medical and economic decision. The number of new diagnosed cases of diabetes does not show the whole picture, since a large study reported that there may be a large percent of undiagnosed cases of diabetes. "In 2005-2006, the crude prevalence of total diabetes in people aged > or =20 years was 12.9%, of which approximately 40% was undiagnosed … Over 40% of individuals had diabetes or pre-diabetes. Almost one-third of the elderly had diabetes, and three-quarters had diabetes or pre-diabetes." [12] The ramifications of undiagnosed and untreated diabetes can be serious, and the projected cost of not treating diabetes is expensive.

- National Estimated Diabetes Costs for 2007
  - ✓ Total (direct and indirect): $174 billion
  - ✓ Direct medical costs: $116 billion
  - ✓ Indirect costs: $58 billion (disability, work loss, premature mortality)

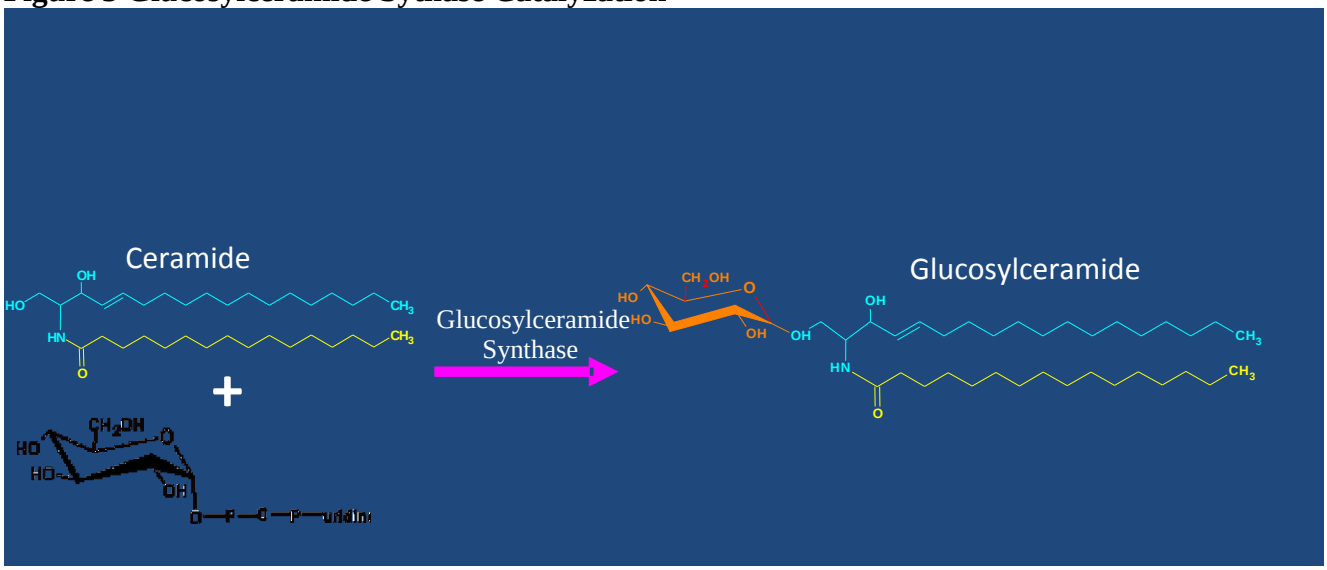
- Pennsylvania Estimated Diabetes Costs for 2006 (American Diabetes Association's Diabetes Cost Calculator)
  - ✓ The total cost of diabetes for people in Pennsylvania in 2006 was estimated at $6.789 billion.
  - ✓ This estimate includes excess medical costs of $4.496 billion attributed to diabetes and lost productivity valued at $2.293 billion.

- 2010 Pennsylvania Health Care Cost Containment Council (PHC4) Total Charges and Medicaid Charges for Type 1 and Type 2 Diabetes (see PHC4 disclaimer on page 11):
  - ✓ Totals for type 1 diabetes principal diagnosis hospital charges in Pennsylvania during 2010 have reached more than $225 million, including over $80 million in Medicaid charges. [8]
  - ✓ Totals for type 2 diabetes principal diagnosis hospital charges in Pennsylvania during 2010 have reached more than $723 million, including over $143 million in Medicaid charges. [8]

Research Results from the Program

Research Summary: Thanks to the first grant, medical science now knows that too much of a type of glycolipid in the type 1 diabetic retinas of both rat and mouse models causes insulin to fail to be processed properly, as well as causing detrimental effects of inflammation, vascular dysfunction and neuronal cell death. An enzyme called glucosylceramide synthase (GCS) catalyzes the reaction that creates glucosylceramide in the retina. See Figure 3. Juvenile Diabetes Cure Research Tax Check-Off Program grant funds were successfully used to identify and validate GCS as a target in reducing or eliminating diabetic complications.

Figure 3 Glucosylceramide Sythase Catalyzation



Research Next Steps: A potential next step of this research would involve "knocking down" the production of the enzyme that catalyzes the reaction of the glycolipid by delivering small segments of ribonucleic acid (RNA) to locations where the enzyme is produced. These small segments can be encapsulated using recently developed nanotechnology techniques and can make the reduction or elimination of the type 1 diabetic complications (improperly functioning insulin receptor, inflammation, vascular dysfunction and neuronal cell death) in the retina extremely likely.

This type of molecular-based therapy will become an important part of the health care industry. There are many diseases that are prime candidates to be cured by molecular-based therapies, especially autoimmune illnesses, such as asthma, rheumatoid arthritis and type 1 diabetes.

Future Research Needs/Prospects: These would include 1) to determine if polymorphisms in the GCS gene are associated with diabetes and/or metabolic syndrome; 2) to determine the upstream regulators of GCS; 3) to develop a non-labile, non-toxic small interfering ribonucleic acid (siRNA) formulation that targets GCS as a therapeutic to ameliorate diabetic complications.

Research Implications: Should research to create an encapsulated siRNA – one that remains stable in the body and turns off the malfunctioning gene(s) producing the GCS enzyme – be successful, the same techniques could be applied to other autoimmune illnesses by identifying the enzymes causing the problems in other autoimmune diseases and developing siRNA and delivery mechanisms to turn off those malfunctioning genes.

The American Autoimmune Related Diseases Association lists more than 100 autoimmune illnesses, including type 1 diabetes.

Plans for Fiscal Year 2012-2013

The Diabetes Prevention and Control Program released a Request for Application (RFA) in 2011. The purpose of the resulting grant is to conduct research that focuses on juvenile diabetes as it relates to restoring normal blood levels, preventing and reversing complications from the disease and/or preventing juvenile diabetes. Research funds from the program will allow researchers to initiate their research with the intention of seeking sustainable funding from national funding sources. The title of the new grant is, "Studies to Verify Dysfunctional Toll-like Receptor Signaling and Diabetic Retinopathy."

This report was prepared by the Diabetes Prevention and Control Program, Division of Nutrition and Physical Activity, Bureau of Health Promotion and Risk Reduction, Pennsylvania Department of Health. For more information, contact:

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To contribute to the Program Fund:
Individuals may indicate the amount of their state tax refund they wish to contribute to the Juvenile (Type 1) Diabetes Cure Research Fund. Contributions may be payable to the Juvenile Diabetes Cure Research Fund and sent to:

Pennsylvania Department of Health
Bureau of Administrative & Financial Services
Division of Budget
625 Forster St.
Health and Welfare Building
Harrisburg, PA 17120

For Additional Information

For additional information regarding type 1 diabetes, including managing the disease and current research being conducted, please visit the following:

- Centers for Disease Control and Prevention, http://www.cdc.gov/diabetes
- American Diabetes Association, http://www.diabetes.org
- Juvenile Diabetes Research Foundation, http://www.jdrf.org
- SEARCH for Diabetes in Youth, http://www.searchfordiabetes.org

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Appendix 1

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3. Fox TE, Young MM, Kester M, Gardner TW. "Insulin Signaling in Retinal Neurons is Regulated Within Cholesterol-enriched Membrane Microdomains" (American Journal of Physiology) First published 4 January 2011.

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5. Fox TE, Young MM, Pedersen MM, Han X, Gardner TW, Kester M. "Diabetes diminishes phosphatidic acid in the retina: implications for reduced mTOR signaling and increased neuronal cell death in diabetic retinopathy" (under peer review at Investigative Ophthalmology and Visual Science).

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PHC4 Disclaimer

The Pennsylvania Health Care Cost Containment Council (PHC4) is an independent state agency responsible for addressing the problem of escalating health costs, ensuring the quality of health care and increasing access to health care for all citizens regardless of ability to pay. PHC4 has provided data to the Pennsylvania Department of Health in an effort to further PHC4's mission of educating the public and containing health care costs in Pennsylvania. PHC4, its agents, and staff, have made no representation, guarantee or warranty, express or implied, that the data -- financial, patient, payor and physician specific information -- provided to this entity, are error-free, or that the use of the data will avoid differences of opinion or interpretation. This analysis was not prepared by PHC4. This analysis was done by the Pennsylvania Department of Health. PHC4, its agents and staff, bear no responsibility or liability for the results of the analysis, which are solely the opinion of this entity.