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BREAKTHROUGHS IN BRAIN RESEARCH: A NATIONAL STRATEGY TO SAVE BILLIONS IN HEALTH CARE COSTS

HEARING

BEFORE THE

SPECIAL COMMITTEE ON AGING UNITED STATES SENATE

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BREAKTHROUGHS IN BRAIN RESEARCH: A NATIONAL STRATEGY TO SAVE BILLIONS IN HEALTH CARE COSTS

TUESDAY, JUNE 27, 1995

U.S. SENATE,
SPECIAL COMMITTEE ON AGING,
Washington, DC.

The Committee met, pursuant to notice, at 9:35 a.m. in room 216, Hart Senate Office Building, Hon. William S. Cohen (Chairman of the Committee) presiding.

Present: Senators Cohen, Feingold, Pryor, Jeffords, and Burns.

Also present: Mary Berry Gerwin, staff director; Priscilla H. Hanley, professional staff; Victoria H. Blatter, professional staff; Sally J. Ehrenfried, chief clerk; Elizabeth M. Watson, system administrator; Theresa M. Forster, minority staff director; T. Paul Kim, professional staff; and David Jacobstein, intern.

OPENING STATEMENT BY SENATOR WILLIAM S. COHEN, CHAIRMAN

The CHAIRMAN. The Committee will come to order.

Last week the Nation mourned the death of Doctor Jonas Salk, one of the world's most revered scientists. Doctor Salk's dedication to finding a vaccine for polio turned this devastating disease from every parent's nightmare and a cause of national hysteria into a word that most school-aged children hardly recognize.

The commitment of Doctor Salk and the Nation's support for his research is a stunning example of how research of a chronic disease can pay for itself many times over in health care savings. The lifetime cost to maintain just two children stricken with polio is greater than all the money spent on the research that virtually eliminated the disease.

Our goal today is to show how applying the vigor of Doctor Salk and his colleagues to curing diseases that now ravage the elderly can once again produce miracles and can save us billions of dollars in health care and long-term care costs in the process.

The soaring cost of health care and long-term care in this Nation are the cause of enormous concern and frustration, especially as we try to balance the budget by the year 2002. If we consider health care costs to be out of control now, we should brace ourselves for the next 25 years.

Currently, over 33 million Americans are 65 or older. This number is going to more than double to over 70 million by the year 2030. The oldest old, those 85 and older, is the fastest-growing seg-

ment of our population and is going to rise from the current 3.3 million to 9 million 25 years from now, and more than double again by the year 2050.

This aging factor has enormous implication for health care costs. Less than a decade from now, over half of the Nation's total health care bill may be spent on senior citizens. These figures are not new. What is shocking, however, is that these demographics and a strategy for dealing with them are noticeably absent from the current debate on how to keep Medicare solvent and how to contain health care costs.

We battle over where and what to cut in Medicare and Medicaid just to stay afloat, but we are turning our backs to the tidal wave of an aging population that will drown us under the shear force of its health care costs.

We have two choices on how to meet the challenge of these staggering costs of aging. We can sit back and simply pay the bills, or we can develop a national strategy toward preventing, delaying, and even curing the diseases and conditions of aging. Only by choosing the latter course do we have any meaningful hope of staying afloat on this ocean of aging health care costs.

Our particular focus this morning is brain research, one of the most productive and important types of research now being conducted.

One in five Americans is struggling with a brain-related problem. Virtually every one of us at some point in our lives will struggle with our own or a loved one's battle with a brain-related problem.

Two recent events that have captured the hearts of millions of Americans illustrate the devastation and toll that these problems can take.

Last November the entire Nation was saddened by the news that former President Ronald Reagan had been diagnosed with Alzheimer's Disease, a cruel and devastating affliction that robs over 4 million Americans of their last years of dignity and independence.

Just weeks ago, the image of actor Christopher Reeve being thrown from his horse and sustaining a major spinal cord injury pointed out most vividly how each of us, no matter how vibrant and strong, can be touched by a neurological disability that can, within minutes, change our lives forever.

The economic costs of brain-related diseases and injuries to our society are enormous. They are estimated to exceed over a half a trillion dollars in health care costs, lost productivity, care-giving, and other economic costs.

The true costs of brain disorders, of course, cannot be measured in dollars alone. The heartbreak of parents whose child has been born with Down's Syndrome, the pain felt by a son watching his father lose his speech to a stroke, the exhaustion and loneliness of a spouse caring for an Alzheimer's Disease patient, or the frustration and fear felt by an individual being overtaken by Parkinson's Disease—none of these can be assigned a price tag or scored for budgetary purposes.

There is, however, exciting promise on the horizon. As we are going to hear this morning from leading neuroscientists in testimony, in the last 5 years significant progress has been made to

unlock the mysteries of the brain, and there is a strong consensus among the scientific community that the next 5 years will bring even more exciting breakthroughs in brain research.

As we are going to hear today, the potential for savings through brain research is enormous. The Alliance for Aging Research, for example, recently estimated that a 5-year delay in the onset of Alzheimer's Disease could cut health care spending by as much as $50 billion annually. A 5-year delay in the onset of stroke could save $15 billion annually. A 5-year delay in the onset of Parkinson's Disease could save as much as $3 billion each year in health care costs.

With savings like these within our grasp, we cannot afford to put the brakes on research spending; instead, we have to accelerate our investment in research that is going to pay for itself many times over in health care and long-term care savings for many years to come.

In addition to exploring breakthroughs in brain research, today the Committee is going to consider other means of reducing health care costs brought on by our aging population.

We are going to hear testimony describing the findings of a major report of the Task Force on Aging Research that I'm releasing today that sets for a blueprint on how to prioritize and fund aging-related problems and research.

In these times of fiscal restraint, finding adequate dollars to fund research is not an easy task, but funding is only part of the solution. We also have to find better ways to promote private sector research initiatives and to disseminate information about the latest, most cost-effective techniques in treating chronic diseases.

We are pleased today to have a most distinguished list of witnesses.

First, we are truly honored to have with us our distinguished colleague from Oregon, Senator Mark Hatfield, who is the Chairman of the Appropriations Committee and for many years has been in the forefront, a true leader in the fight for research funding.

We are then going to hear the personal experiences of individuals whose lives have been touched by brain-related disorders. These courageous people give us a glimpse of the faces behind the numbers.

We are also honored to have before us today some of the Nation's leading neuroscientists, who will tell us how close we are to finding cures or treatments for these major diseases of aging, and experts to testify on the savings we can achieve in this area.

Perhaps the best tribute we can pay to Doctor Salk and other scientific heroes like him is to recognize the importance of investing in research. Undoubtedly, we are going to reap its benefits in human and economic terms millions of times over.

I want to thank all of the witnesses who will be testifying this morning. We look forward to hearing their testimony.

Before turning to Senator Hatfield, who I'm told has to be out of here by 10, I yield to my distinguished colleague and friend, Senator Pryor, the former Chairman of the Aging Committee.

[The prepared statement of Senator Cohen follows:]

PREPARED STATEMENT OF SENATOR WILLIAM S. COHEN, CHAIRMAN

Good morning. This morning the Senate Special Committee on Aging is holding a hearing on the billions of dollars that could be saved in health care costs through finding cures and treatments for diseases of aging.

Last week, the nation mourned the death of Dr. Jonas Salk, one of the world's most revered scientists. Dr. Salk's dedication to finding a vaccine for polio turned this devastating disease from every parent's nightmare and a cause of national hysteria into a word that most school-aged children hardly recognize.

The commitment of Dr. Salk and the nation's support for his research is a stunning example of how research of a chronic disease can pay for itself many times over in health care savings: the lifetime cost to maintain just two children stricken with polio is greater than all the money spent on the research that virtually eliminated the disease.

Our goal today is to show how applying the vigor of Dr. Salk and his colleagues to curing diseases that now ravage the elderly can once again produce miracles—and can save us billions of dollars in health care and long-term care costs.

For the past several months, the Senate Special Committee on Aging has been examining how we can help Medicare, Medicaid, and other parts of our health care system better prepare for the dramatic aging of our population.

The soaring costs of health care and long-term care in this nation are the cause of enormous concern and frustration, especially as we try to balance the budget by the year 2002. The financial forecast for Medicare is bleak: the Medicare Trustees recently announced that the Medicare trust fund is "severely out of financial balance" and will collapse in about seven short years. The prediction for Medicaid is just as grim. State budgets are bursting under the weight of long-term care expenses, and families cannot bear the crushing burden of nursing home costs.

If we consider health care costs be out of control now, however, we should brace ourselves for the next 25 years.

Currently, over 33 million Americans are age 65 or older. This number will more than double to over 70 million by the year 2030. The "oldest old", those age 85 and older, is the fastest growing segment of our population, and will rise from its current 3.3 to 9 million Americans 25 years from now, and more than double again by the year 2050.

This "aging factor" has enormous implications for health care costs. In 1992, for example, per capita health care spending for persons over 65 was nearly four times the amount spent per person under 65. Less than a decade from now, over half of our nation's total health care bill may be spent on senior citizens.

These figures themselves are not new. What is shocking, however, is that these demographics, and a strategy for dealing with them, are noticeably absent from the current debate over how to keep Medicare solvent and how to contain health care costs.

We battle over where and what to cut in Medicare and Medicaid just to stay afloat. But we are turning our backs to the tidal wave of an aging population that will drown us under the sheet force of its health care costs.

Our nation spends billions of dollars each year directly and indirectly to treat and care for diseases of the aging. Here are just a few estimates:

Cardiovascular diseases cost us $138 billion each year.

Alzheimer's Disease costs about $100 billion each year, mostly in nursing home, and other costs of long-term care.

Strokes among older persons result in health-care costs of almost $30 billion each year.

Parkinson's Disease costs our society about $6 billion annually.

Cancer alone accounts for 10 percent of the total cost of disease in this country, costing over $104 billion each year.

The annual cost of osteoporosis has been estimated at $10 billion. Without intervention, these costs could reach as much as $60 billion over the next 25 years.

We have two choices on how to meet the challenge of these staggering costs of aging:

We can sit back and simply pay the bills, or we can develop a national strategy toward preventing, delaying, and even curing, the diseases and conditions of aging. Only by choosing the latter course do we have any meaningful hope of digging out from under the avalanche of aging health-care costs.

Today this Committee is holding the first in a series of hearings on how investment in research into the causes and courses of diseases most effecting the elderly is a vital component in the national strategy to bring health-care costs under control.

Our particular focus this morning is brain research, one of the most productive and important types of research now being conducted. One in five Americans is struggling with a brain-related problem—and virtually each one of us, at some point in our lives, will struggle with our own, or a loved one's, battle with a brain-related problem.

Two recent events that have captured the hearts of millions of Americans illustrate the devastation and toll of brain-related problems. Last November, the entire nation was saddened by the news that former President Ronald Reagan had been diagnosed with Alzheimer's Disease, a cruel and devastating affliction that robs over 4 million Americans of their last years of dignity and independence.

Just weeks ago, the image of actor Christopher Reeve being thrown from his horse and sustaining a major spinal cord injury has pointed out most vividly how each of us, no matter how vibrant or strong, could be touched by a neurological disability that would, within minutes, change our lives forever.

The economic costs of brain-related diseases and injuries to our society are enormous—they are estimated to exceed over half-a-trillion dollars a year in health care, lost productivity, caregiving, and other economic costs. Brain-related disorders account for the majority of our nation's long-term care costs, and, when combined with psychiatric disorders, these conditions account for more hospitalization and prolonged care than almost all other diseases combined.

The true costs of brain disorders cannot, of course, be measured in dollars alone. The heartbreak of parents whose child has been born with Down's Syndrome, the pain felt by a son watching his father lose his speech to a stroke, the exhaustion and loneliness of a spouse caring for an Alzheimer's disease patient, or the frustration and fear felt by an individual being overtaken by Parkinson's disease—none of these can be assigned a price tag or "scored" for budgetary purposes.

As we will learn from the personal experiences of today's first panel of witnesses, in addition to costing our nation billions of dollars, these diseases and injuries cost victims and their families far more in human terms. For them and for millions of others nationwide, research is often the only hope for arresting or reversing the devastation of brain-related disabilities.

There is, however, exciting promise on the horizon. As we will hear from leading neuroscientists in testimony today, in the last 5 years significant progress has been made to unlock the mysteries of the brain, and there is a strong consensus among the scientific community that the next 5 years will bring even more exciting breakthroughs in brain research.

Three years ago, for example, over 130 of the world's outstanding neuroscientists made a commitment to do all they can to deliver major scientific progress by the year 2000, and set an aggressive agenda of ten major goals of brain research for the 1990's, the so-called "Decade of the Brain". In just 15 months, brain researchers had already reached or made significant progress toward more than half of their major goals, such as identifying the genes responsible for Huntington's Disease, Alzheimer's Disease, and a form of Lou Gehrig's disease, and finding new drugs to help in the recovery of stroke and spinal cord injury.

The fruits of this research cannot come a moment too soon, either for those struck with these diseases, or for our economy as a whole.

As we will hear today, the potential for savings through brain research is enormous. The Alliance for Aging Research, for example, recently estimated that:

a five year delay in the onset of Alzheimer's Disease could cut health care spending by as much as $50 billion annually;

a five year delay in the onset of stroke could save $15 billion annually; and

a five year delay in the onset of Parkinson's Disease could save as much as $3 billion each year in health care costs.

With savings like this within our grasp, we cannot afford to put the brakes on research spending. Instead, we must accelerate our investment in research that will pay for itself many times over in health care and long-term care savings for years to come.

We also, I believe, have a moral commitment to support research vigorously in order to alleviate the personal pain and suffering experienced by families who witness their loved ones deteriorating daily from Alzheimer's Disease, or being imprisoned by the progress of Parkinson's or Lou Gehrig's disease.

In addition to exploring breakthroughs in brain research, today the Committee will consider other means of reducing health care costs brought on by our aging population. We will hear testimony describing the findings of a major report of the Task Force on Aging Research, that I am releasing today, setting forth a blueprint on how to prioritize and fund aging-related research. This report reflects the work of over two dozen Federal agencies and scores of experts in the field of aging research on

how aging research should be allocated, and the Committee looks forward to pursuing these recommendations.

In these times of fiscal restraint, finding adequate dollars to fund research is not an easy task, and it is only part of the solution. We must also find better ways to promote private sector research initiatives and to disseminate information about the latest, most cost-effective techniques in treating chronic diseases. We must develop a strong national strategy if we are to have any hope of waging a successful war against the crushing health care costs that are facing us in the next two decades.

We are pleased to have a most distinguished list of witnesses here with us today. First, we are honored to have with us my distinguished colleague from Oregon, Senator Mark Hatfield, Chairman of the Senate Appropriations Committee, who has for many years been a leader in the fight for research funding.

We will then hear the personal experiences of persons whose lives have been touched by brain related disorders. Frances Powers, a young mother of two children, is herself in the early stages of Alzheimer's Disease. Millicent Kondracke, accompanied by her husband, Morton Kondracke, will provide us with a personal glimpse of her battle with Parkinson's Disease. We will also hear from Benjamin Reeve, who will talk to us about his brother Christopher Reeve's devastating spinal cord injury, and from Arthur Ullian, a Boston businessman who, following his own spinal cord injury, has committed himself to advancing treatments in neurological disorders.

We are also very honored to have before us today some of the nation's—and indeed the world's—leading neuroscientists to tell us how close we are to finding cures or treatments for these major diseases of aging, and experts in aging and research to testify on the savings we could achieve in this area.

Perhaps the best tribute we can pay to Dr. Salk and other scientific heros like him is to recognize the importance of investing in research. Undoubtedly, we will reap its benefits in human and economic terms millions of times over.

I thank the witnesses for taking time to be with us today and look forward to hearing their testimony.

Estimated Chance A Person
Over 65 Has Alzheimer's Disease
Age 75-84
Age 85+
%
1 in 33
1 in 5
1 in 2

Estimated Cost: $191 Billion

Alzheimer's = $160 billion

NIH Research (FY 94) = $379.3 million

Alzheimer's = $298 million

Stroke = $112 million

Parkinson's = $69.5 million

Stroke = $25 billion

Parkinson's = $6 billion

Billions of Taxpayer Dollars Saved By Delaying Major Brain Diseases of The Aged
Savings to health care system by delaying the onset of diseases by five years:
Alzheimer's Disease
$50 billion
$15 billion
$5 billion

Senator PRYOR. Thank you.

Mr. Chairman, would you like for Senator Hatfield to go ahead and make his statement, and then I could open with my statement after his? Would that be appropriate?

The CHAIRMAN. Any objection?

Senator JEFFORDS. No. I just have a statement I'd like placed in the record.

The CHAIRMAN. Okay.

Senator Hatfield, we yield to you.

STATEMENT OF SENATOR MARK HATFIELD

Senator HATFIELD. Thank you, Mr. Chairman.

I am very grateful to you and the members of this Committee for your courtesy, which assists me to keep my schedule, too, as we all have a problem in doing so.

Mr. Chairman, I want to commend you and the members of this Committee for having this hearing. As you know, we had planned to put a focus on this subject field in our Appropriations Committee, and we find it very comfortable in joining you in this Committee and consolidating our hearings to achieve the same goals.

I believe that this focus today on the brain and neurological diseases is very, very fundamental to our whole medical research field. I think that medical research, in the first place, is what we might call the engine that drives the train for a better quality of life for all Americans, and the advancement in medical research certainly represents the sole hope to millions of Americans today who suffer from disease and debilitating disorders.

You have gathered a very distinguished group of witnesses today—patients, scientists, advocates—a whole array of people who are concerned about America's future.

I need not tell you that, from my perspective—and I think most generally accepted throughout the world—that the National Institutes of Health represent the cornerstone of our premier biomedical research enterprise, and that enterprise, the greatest ever created in human history, is in deep peril.

Just a few weeks ago, the Senate rectified one of those disastrous courses that might have led to not just a reduction in funding for the NIH, but the actual abolition of the NIH. When you consider the Senate's Budget Committee had come forward with a $7.7 billion reduction in the next 5 years, your realize that is not merely a fiscal reduction. Yet, the Senate listened to the arguments and, by a vote of 85 to 14, took the needed action to reverse this freight train that was headed for the brink.

Since that time, in the Budget Committee that met between the House and the Senate to resolve their differences, they have come up with a Senate position of a 1 percent reduction in 1996, and then a 3 percent per year reduction for the next 5 years as against the House proposal of 5 percent.

Mr. Chairman, let me say as emphatically as I can that this is still totally unsatisfactory. This is not a victory. It is just a slower death to many of those projects that depend upon our continuing support. But we do have some breathing time, and that means we can handle and absorb the 1 percent from 1996 through the budget operation, but we have to mobilize even further the voices of people

heard here today and those they represent across this country in order to renegotiate, possibly with the Budget Committee, funding for 1997.

I would remind everyone to keep in mind this budget resolution is advisory—advisory. I can assure you that I am open to advice. I listen to advice every day, as we all do, from many constituents and others. But it doesn't necessarily mean that we have to take all of the advice that we hear.

I want to be a part of this overall effort of this Congress to reduce spending and to achieve a balanced budget, but, by the same token, I think we have to be careful not only about the dollar amounts we spend, but the way we spend those dollars.

I need not remind this Committee and others who are concerned about matters of the aging that, when we look at the way we allocate our funds today, we are not maximizing those funds. I say that in reference to the fact that when the President offered a comprehensive health care plan, and when the Republicans came out with their comprehensive health care plan, neither identified biomedical research as a relevant part of comprehensive health care—neither. Yet, we were committed to the proposition, both Democrats and Republicans, that we were going to get control of the spiraling health costs. We wanted cost-effectiveness and cost control.

My friends, I think we can all say that without biomedical research leading to cure and to better treatment there is no control, there is no cornerstone laid. How can you expect any structure then to survive?

I want to say, too, that when we look at the matter of the people, so oftentimes I have found in my political life the people are ahead of the politicians. The people often have a deeper understanding of issues than we give them credit, and certainly even at times a deeper understanding than we, who are their elected representatives.

Just last Friday, to illustrate my point, Research America released new data on polls that they had taken about the American people's attitude regarding support for medical research. The Harris Poll shows that—briefly, I shall outline—65 percent of Americans oppose cuts in medical research dollars, and 73 percent would pay higher taxes to support more medical research. In 1993 a similar poll indicated that about the same figure would support—listen to this—higher taxes to support more medical research. It showed that 61 percent urged Congress to provide tax incentives for private industry to conduct more medical research, and 60 percent are willing to designate tax refund dollars for medical research, which averages out to about $23 per person. Over 90 percent endorsed maintaining the United States' position as a leader in medical research, and 61 percent would like more information on medical research in the print and broadcast media.

The CHAIRMAN. Is that the kind of advice you are seeking and listening to?

Senator HATFIELD. I'll let you pursue that.

Mr. Chairman and members, I don't know of very many federally-supported programs that can claim the depth of support from the public that these figures indicate biomedical research enjoys.

And in even fewer instances, I believe, can one cite the public willing to pay more taxes for a specific identified program.

Last year, as the health care reform debate began, as I said, we did get an elevation of an issue that I think is very helpful, and I don't think it was a loss in that year merely because we did not come up with a final solution or bill, but I do think we have to take advantage now of the public awareness—growing awareness—and stabilize the biomedical research infrastructure because it cannot be stabilized merely through the appropriations process. I want to emphasize that this morning as the Chairman of the Committee.

A dedicated funding source must augment the annual appropriations that we depend upon to sustain our biomedical infrastructure and the hopes of millions of Americans, as well. I think that, in order to do that, we have to find supplementary money. It is not here in the budget this year. It will not be in next year's budget either.

I think we must wage an offensive against diseases—and let me assure you, Mr. Chairman and members of this Committee, that we have an array and a host of new viruses about which we have little or no understanding. As I said on the floor recently, when we used to hear the battle cry to get increased military spending, all that individuals had to do was shout, "The Russians are coming," and then it would be a contest to see who could add the supplement or who could add more to the military budget.

I say there is a comparative call today, and that is, "The viruses are coming," and we'd better be prepared for them. I hope we can get the same results with that battle cry that we used to always get—although not with my vote—to provide money for the military.

Two years ago Senator Harkin and I introduced a trust fund proposal which we will soon be introducing again on a modified basis. For $0.25 tax per pack of cigarettes, we can build about $4 billion a year in a specified earmarked medical research trust fund. I do say that, if we are going to ask for more money, I think it is a good way to raise it. I know where I am. I am in an environment that says, "No new taxes," and that says "we must reduce taxes." Well, I have been in a minority position before; nevertheless, I enter this whole battle to try to get more tax money on cigarettes to do more research.

Some people may call that tainted money. All I can say is that "'t'aint enough." [Laughter.]

Mr. Chairman, you will also hear today the promising results of research on Alzheimer's, Parkinson's, stroke, and other diseases. I think you begin to understand the importance of this, when you realize that today more and more of our dollars are spent for the sick and elderly in nursing homes and other forms of sick care. I think a more cost-effective plan would invest in medical research to delay dysfunctions in later life, as well as to cure costly diseases.

In 1992, Americans over 65 accounted for nearly 38 percent of the national health care bill of $800 billion; however, the NIH will spend only 7 percent of its budget on research in human aging in 1995. In 1995, the Federal Government invested $807 million in biomedical research on aging diseases. Of that amount, $117 million is invested in stroke, $304 million in Alzheimer's, and $71 million in Parkinson's and related neurological disorders.

Without new knowledge to develop new strategies to prevent diseases, new treatments to delay the progression of disease, and the new interventions to cure disease, health care costs will continue to spiral out of control.

Just to give you one brief point of reference, in contrast to $117 million to stroke and $304 million for Alzheimer's, this year we will have spent $2.4 billion for cancer, $897 million for heart, and $1.3 billion for AIDS. Every one of those diseases needs every one of those dollars.

But I think it is very obvious that we have to find new sources of revenue.

Mr. Chairman, I would close and ask that my entire statement be included in the record.

I'd like to go back to that fundamental issue that confronts us all the time, and that is, "What is our national security?"

I think too often we have had Presidents and Congresses of both parties see our national security exclusively in our arsenals in the form of bombs and other life-destroying capability. I think they missed the point that only one President got—President Dwight David Eisenhower, who understood that national security was composed of many parts beyond our arsenal. That's why he called it the "national interstate defense highway system." That's why he called his bill the "Defense Education Act," because he said it is made up of many, many things, and today many miss the point.

If we cannot protect our citizens from disease and disability, then the true enemy lies within our borders rather than outside our borders.

Thank you.

[The prepared statement of Senator Hatfield follows:]

THE PREPARED STATEMENT OF SENATOR MARK O. HATFIELD

Mr. Chairman and Members of the Committee:

I would like to begin by thanking Senator Cohen for his leadership in convening this hearing on biomedical research in relation to brain and neurological diseases. Medical research is the engine which drives the train for better quality of life for all Americans. Advancements in medical research offer the sole hope to millions who suffer from disease and debilitating disorders. I would also like to commend those who are participating in the panels today—whether patient, scientist or advocate—your leadership in advancing this issue is the key to America's future. I am pleased to join you to continue to shine the spotlight on what is one of the best investments made by the federal government today.

In these days of budget-cutting, the time could not be more critical for examination of biomedical research. As the Chairman of the Appropriations Committee, I know all too well the difficulties we face in dividing an increasingly strained financial pie among our domestic priorities. Yet I also know that if we do not place a priority on those tools within our arsenal which are true "investment" opportunities, we will have done less than our best to maximize the use of federal dollars. The National Institutes of Health—the cornerstone of our premiere biomedical research enterprise—is in deep peril.

Just a few weeks ago the Senate rectified a dangerous reduction in the Senate Budget Resolution. By a vote of 85–14, the Senate restored the majority of a seven-year, 10 percent cut to the National Institutes of Health by taking an across-the-board reduction from most of the other federal budget accounts. Although many regard the budget resolution process as symbolic, it does serve as a guide to the Appropriations Committee. I could not stand by and watch the Senate gut the biomedical sciences without trying to reverse the damage. But the news is not cause for celebration. The conferees on the Budget Committee have now reached an agreement and it is my understanding that the Senate position has been maintained only in the first year—for 1996, the Budget Resolution would cut NIH by 1 percent from the FY95 level of $11.3 billion. Beginning in 1997 and each year until 2002, the

Budget Resolution will cut NIH by 3 percent from FY95—a compromise between the House's cut of 5 percent and the Senate's cut of 1 percent. It is clear that we must recommit ourselves to our common task of keeping the promise and results of biomedical research in the forefront of policymakers' minds—particularly in the House.

We have an arsenal of tools to depend upon in this battle. The overwhelming strength of the budget vote was a surprise to me and I am convinced it is due to the political awakening of the biomedical research community. For too long, scientists and researchers have remained in their laboratories without entering the policy debate. Now that they have arrived, I have no doubt that their powerful message will take hold across Capitol Hill. In addition, the public is far ahead of Congress on this issue.

Just last Friday, Research America! released new poll data showing the strength of the American people's support for medical research. The Harris poll showed that:

65% of Americans oppose cuts in medical research dollars;

73% would pay higher taxes to support more medical research (this compares with 74% in the 1993 poll—holding steady!);

61% urge Congress to provide tax incentives for private industry to conduct medical research;

60% are willing to designate tax refund dollars for medical research (average amount was $23 dollars!);

Over 90% endorse maintaining the U.S.' position as a leader in medical research;

61% would like more information on medical research in the print and broadcast media.

There are few federally-supported programs that can claim this depth of support from the public. And, of course, there are even fewer instances in which the public is willing to pay higher taxes.

Last year, as the health care reform debate began to heighten, it became increasingly evident to me that a critical piece was missing, biomedical research. This was bipartisan neglect—from the President to the Republicans, none of the original bills proved for the growth of biomedical research. Despite the enormous cost of disease, none of the major health care reform bills addressed the role of medical research in conquering disease. There was no recognition that the ultimate in cost containment is a cure. Therefore, last year I joined Senator Tom Harkin in endorsing the establishment of a National Fund for Health Research as part of any package billed as comprehensive health care reform.

I am convinced that a stable biomedical research infrastructure cannot be maintained solely through the appropriations process. A dedicated funding source to augment annual appropriations is essential if we are to fulfill the hopes of millions of Americans suffering from disease and disability and achieve effective long-term health care cost control. This would of course be supplementary money, not replacement dollars. We must again mount the offensive for biomedical research by committing a funding increase, above appropriations levels, of several billion a year to the National Institutes of Health. I intend to soon introduce a modified version of the Hatfield-Harkin Trust Fund which will raise $4 billion per year for the NIH through a small increase in the tobacco tax—25 cents additional per pack.

Mr. Chairman, I know you will hear at length today about the future demographics which dramatically support our need for a continued investment in biomedical research. You will also hear about the promising research in Alzheimer's, Parkinson's, Stroke and other diseases. Currently, our present health care system responds to the increasing numbers of the sick and elderly by spending more money on nursing homes and other forms of "sick care". A more cost-effective plan would invest in medical research to delay dysfunctions in later life as well as cure and prevent costly diseases. In 1992, Americans over 65 accounted for nearly 38 percent of the national health care bill of $800 billion. However, the NIH will spend only 7% of its budget on research in human aging in 1995. In 1995, the federal government invested $807.3 million in biomedical research on aging diseases. of that amount, $117.2 million is invested in stroke, $304.6 in Alzheimer's and $71.6 million in Parkinson's and related neurological disorders. Without new knowledge to develop new strategies to prevent disease, new treatments to delay the progression of disease and new interventions to cure disease, health care costs will continue to spiral out of control.

The facts are irrefutable, Mr. Chairman. Biomedical research has succeeded in lessening the hold of disease. We must nurture its development and continue to place it among our fiscal priorities. Due to improved control of high blood pressure, stroke mortality has declined by almost 60% since 1970. Also due to risk reduction, the heart disease death rate has declined 40% since 1970. These are two of the

major causes of death in this country and because of biomedical research advances, both are declining.

Many in this country believe that our national defense lies in our arsenals in the form of bombs and life-destroying capacity. They may well be missing the point—if we cannot protect our citizens from disease and disability, the true enemy lies within our borders.

The CHAIRMAN. Senator Hatfield, thank you very much for a very powerful statement. It will be included in its entirety.

I might say, on behalf of the members of this Committee, that no one can doubt, looking at your entire record of service, both in the military and since that time, that you are, indeed, a man of great courage and conviction. We appreciate your appearance here this morning.

Senator Pryor, do you have an opening statement?

STATEMENT OF SENATOR DAVID PRYOR

Senator PRYOR. Mr. Chairman, I'm going to ask you to put my full statement in the record. I was so impressed with Senator Hatfield's statement, and also with his commitment. He is also a person of great vision, Mr. Chairman, and we all know that as his colleagues in the Senate. We are very fortunate.

The research community of this Nation—of this world, actually—is also very fortunate to have a friend like Senator Hatfield; someone who understands that community and that community's mission.

All of us in this country are going to eventually benefit from all of those research dollars mentioned by Senator Hatfield. We are benefitting from those research dollars now, as we sit here in this room. Not only the aging community, but everyone in this country and, indeed, the world are going to benefit from each of these dollars.

Senator Cohen and I joined with Senator Hatfield in helping to restore at least some semblance of balance for the NIH in research funding. I was proud to have joined with him, and I think that was a vote that we will look back on as a milestone in this ongoing debate. I hope that Chairman Hatfield can also be very persuasive with his colleagues in the budget process as to the importance and critical nature of each and every one of these dollars going to medical research.

Mr. Chairman, I hold in my hand 3 pennies, and those 3 pennies represent our medical research spending. Of all the health care dollars we expend, about $0.03 of each of those dollars goes into research. I think somehow or another we've got to reorder our priorities, even though we are in a time of great budget peril. There is no question about that. But this is truly a true investment in our Nation's health and, as you say, in our Nation's defense.

I salute you, sir.

Mr. Chairman, I thank you very much for calling this very timely hearing.

[The prepared statement of Senator Pryor follows:]

PREPARED STATEMENT OF SENATOR DAVID PRYOR

Mr. Chairman, I am pleased to join you at this morning's hearing and I commend you for calling it at such a critical time for biomedical research in this country. I am also glad to welcome our colleague, Senator Hatfield, who has played such a

leadership role in sustaining public support for medical research. I look forward to his testimony.

The disorders which are the focus of this hearing are familiar to all Americans: stroke, Alzheimer's, Parkinson's, Lou Gehrig's or ALS, multiple sclerosis and many others. These are diverse diseases, with different causes and complications. But years of progress made by committed researchers have bound them together with a bright line of hope. Today, there are hopes that effective treatments and even cures are within our reach for the first time.

Yet today, at the midpoint of the Decade of the Brain, we find that the medical research which holds the promise of future treatments and cures is threatened as never before by short-sighted budget cuts. I recently read an article in the New York Times which described the exciting potential of gene therapy as "the stuff of dreams". These treatments may be in use by the end of the decade, yet much of the research which will allow us to fulfill those dreams was done years ago at NIH or through NIH funding.

The potential for dramatic breakthroughs cuts across other areas of medical research and other terminal diseases. But the danger to progress in all these areas is acute. Today, there may be more enthusiasm in the Congress for cutting the budget of the National Institutes of Health than for pursuing cures and innovative treatments at the frontiers of medicine.

When we examine the tremendous potential that medical research holds, it is staggering that only three cents out of every dollar goes to medical research. At a time when the American public consistently expresses support for increasing the funds for biomedical research, we should listen to what the public says and give this research the full measure of our support.

These are the reasons both the Chairman and I joined Senator Hatfield in restoring funding for the National Institutes of Health during this year's Senate budget deliberations. When we were faced with a proposal which would have cut the NIH budget by 10 percent—or almost a billion dollars—and frozen all research funding at that level for seven years, Senator Hatfield successfully put forth an amendment which sent our conferees to the table with a strong message that we must preserve our commitment to medical research.

Mr. Chairman, I am glad you mentioned the report of the Task Force on Aging Research. I had the honor of serving on the Task Force and it is my hope that the full report, which is forthcoming, will unify the many agencies and institutions involved in aging research and help them pursue a comprehensive research agenda into the next century.

We must get our priorities straight. By some estimates, the costs of neurological and psychiatric disorders to our society may exceed half a trillion dollars every year. But even if the potential savings of biomedical research were not so dramatic, it would still be the right—the humane—course of action.

This is what makes these issues so vital. They affect millions, but those millions include our families, our friends, our children. They cost our society billions of dollars, it is true, but who could place a monetary value on saving a life when it is that of a loved one? I say this because these are not abstract issues to me: my own family has had to contend both with ALS and with Alzheimer's.

Mr. Chairman, I look forward to hearing today's discussion on these issues. I welcome the witnesses who have joined us today to share their experiences and I look forward to their testimony.

The CHAIRMAN. Thank you, Senator Pryor.

Senator Burns?

STATEMENT OF SENATOR CONRAD BURNS

Senator BURNS. First of all, thank you, Mr. Chairman, for holding this hearing. I'll submit my statement for the record.

I thought it was ironic, anyone that wanted to object to the Chairman of the Appropriations Committee for making his statement first. I thought that was going to take quite a lot of nerve around here to do that.

I serve with Senator Hatfield on Appropriations and know of his conviction, and I think his message this morning was a very simple one: we don't have a budget problem, we have got a priority problem.

I chair the Science, Technology and Space Subcommittee of the Commerce Committee. It is the same thing there. No matter what area we go into—the amount of dollars we spend on energy, on medical, or whatever, we don't spend enough in our research and our development of new technologies.

This morning I notice Mr. Reeve will be before us, and these people will come up and tell their stories. Under the best of circumstances it is hard to come before this Committee. We appreciate that.

Mr. Reeve, what happened to your brother is a tragedy. I have had some experience with those unpredictable creatures they call horses. We will listen to what you have to say and the rest of this panel—but I'm really looking forward to the panel to follow that, because I think it is time that we really take a look at that.

I thank you, Mr. Chairman and the ranking member, for holding this hearing this morning.

[The prepared statement of Senator Burns follows:]

PREPARED STATEMENT OF SENATOR CONRAD BURNS

Mr. Chairman, I want to thank you for holding this hearing this morning. At this point, I think most people have had some experience with Alzheimers or Parkinson's disease—either having a loved one afflicted or knowing someone who's loved one is afflicted. I have experienced it within my own family and it is not a pleasant experience.

I am truly thankful for the folks on our first panel. You don't come before us under the best of circumstances, and the courage it takes to tell your story is commendable.

Mr. Reeve, what happened to your brother is a tragedy. And though research couldn't prevent the accident from happening, it could sure impact his recovery. I'll be interested in hearing your perspective on what more can be done.

But what I most look forward to is hearing our outlook. Research is vital to finding out the causes and treatments for brain diseases and spinal cord injuries . . . and it is expensive. As we've seen, scientists can work diligently for years and still not discover the magic bullet. But they've got to keep working.

And when discoveries are made, the result is not only life-saving it is a money saver. Here we are looking at ways to control the budget, looking at ways to reduce health care costs and, though, in the short-term research may not seem to pay off, in the long term its a big money save.

Our population is getting older—we know that. And with the aging comes disease like Alzheimers and Parkinsons. Efforts are usually made to live as long as possible and as healthy as possible. Finding treatments for these diseases allows us to live with dignity into what should be our golden years.

Mr. Chairman, I am well aware of the impact these diseases and injuries have on families and on pocketbooks. I hope the witnesses we have in our second and third panels will have good news for us—if not the answer, at least a road map to get us where we need to go.

Thank you again for holding this important hearing and a special thanks to those folks who have come to share their experiences with us. God bless you.

The CHAIRMAN. Thank you, Senator Burns.

Senator JEFFORDS.

STATEMENT OF SENATOR JAMES M. JEFFORDS

Senator JEFFORDS. Thank you, Mr. Chairman.

I want to join in accolades for a very powerful statement. I think you are quite correct in pointing out we've got to be mindful of mindless cuts, that they can be counterproductive. Our goal is to reduce the deficit, but if we cut things which would help us reduce the deficit we're just not going to get there. Nutrition is another

one. Education is another one. I think that's a message we've got to make loud and clear—that we've got to be very careful.

As the Senator from Montana stated, it is a question of priority, so thank you for a very powerful statement.

[The prepared statement of Senator Jeffords along with the Statement of Senator Alan K. Simpson follows:]

PREPARED STATEMENT OF SENATOR JEFFORDS

Thank you, Mr. Chairman for holding this important hearing about the benefits of investing in medical research on the brain and spinal cord injuries. As we enter a much more austere budgeting and appropriation process than we have ever faced, it will be even more critical to spend out few federal dollars wisely.

As today's testimony demonstrates, we would do well to invest in brain disorder research. We all know that health care costs have been sky-rocketing and the costs of diseases like Alzheimer's, Huntington's and Parkinson's as well as head injuries, are important contributors, costing us up to $600 billion each year. With figures like that even incremental progress toward a cure or effective treatment could save billions.

We also can afford to ignore the people—the four million Americans affected by Alzheimer's alone, losing memory, personality and eventually the ability to function. We must also remember that each Alzheimer's patient has family and friends who have to helplessly watch the deterioration of a loved one.

But as we all understand, sometimes Congress needs dollars and cents evidence to do the right thing for people. And it is to that end that I am glad we are holding this hearing to show that even disregarding the potential of preventing human suffering, the monetary benefits that could be realized through effective prevention and treatment of these disorders would be tremendous. We have both a fiscal and humanitarian obligation to be sure that adequate research efforts, both public and private, continue to be funded.

PREPARED STATEMENT BY SENATOR ALAN K. SIMPSON

I thank my good friend Senator Bill Cohen for chairing this hearing regarding breakthroughs in brain research. I am a member of the "Parkinson's Action Network" and a strong supporter of research in this area. I have firsthand knowledge of how important it is. I personally watched my dear father battle Parkinson's Disease for over 30 years until he died in 1993 at the age of 95. He had many productive years after he was diagnosed with Parkinson's, but he also had a dramatic series of "Ups and Downs" throughout those years.

I am especially pleased that my old friend Senator Mark Hatfield will be testifying before the committee today. I am a cosponsor of his legislation, the "Morris K. Udall Parkinson's Research, Education and Assistance Act." Senator Hatfield has done such a great deal to advance this cause.

During the Senate's consideration of the budget resolution last month, Senator Hatfield was the one who offered an amendment to restore $7 billion in funding for the National Institutes of Health over the next seven years. His leadership was critical to the passage of this amendment. Senator Hatfield helped the Senate to understand that if we are to succeed in balancing the budget, we have to exercise some common sense ad recognize that research on Parkinson's, Alzheimer's and related disease will eventually yield significant costs savings in Medicare, Medicaid and other Federal health programs when medical "Breakthroughs" occur.

I am most intrigued by reports that significant new medical "Breakthroughs" may now be within our reach. This makes it even more important for Congress to give adequate support to the National Institutes of Health. To neglect medical research at this time would be a very costly mistake. I am convinced that there are many compelling reasons to continue this important work. I trust today's hearing will help to highlight the tremendous potential for critically needed progress in this area.

The CHAIRMAN. Thank you, Senator Jeffords.

Senator Feingold.

STATEMENT OF SENATOR RUSSELL D. FEINGOLD

Senator FEINGOLD. I expected others to be ahead of me. Mr. Chairman, I can only stay a moment, so let me just commend you and the ranking member, Senator Pryor, for holding this hearing.

I have to go briefly to a Judiciary Committee hearing where the Attorney General is coming for an oversight hearing.

I think this is the right time for an effort on this research—especially brain research. And I think it is especially appropriate that the senior Senator from Oregon, Senator Hatfield, led off this hearing.

[The prepared statement of Senator Feingold follows:]

STATEMENT BY SENATOR RUSS FEINGOLD

Mr. Chairman, I commend you and the Ranking Member, Senator Pryor, for holding this hearing. With the conference report of the concurrent budget resolution expected later this week, a review of brain research, especially in the context of our national budget priorities could not be more timely.

I think it is especially appropriate that the senior Senator from Oregon, Senator Hatfield, shared his thoughts on this today. He has been one of the most important advocates for research into Alzheimer's and other brain disorders, and I was proud to support his amendment to restore most of the proposed cuts to NIH when we debated the budget resolution in the Senate last month.

Senator Hatfield's leadership in this area was well known to me when I was a State Senator in Wisconsin working to create a program for those with Alzheimer's and related disorders. Maybe the single piece of legislation of which I am most proud from my service in the Wisconsin State Senate was writing our State's Alzheimer's program, which provides home and community-based services for those afflicted by the disease and their family members—a program that I feel strongly can only reach its full potential as part of a national long-term care program.

Though we were able to make a good start on long-term care services at the State level, the one aspect of addressing the problems of dementia that we simply could not address in any adequate way was research. The commitment to research really requires a national strategy, as the title of this hearing suggests.

I also want to pay tribute to those witnesses today who are here either because they themselves are in the public eye, or because they have a well-known family member.

Your willingness to come forward and share your stories really does have a significant impact.

My own interest in Alzheimer's Disease really stated because of an article I read about Rita Hayworth. More recently, I think former President Reagan and former First Lady Nancy Reagan deserve enormous credit for their willingness to be open about the former President's condition. Their courageous work will certainly help the drive for additional research support, as well as highlighting the plight that 4 million American families face.

Again, I congratulate the Chair and Ranking Member for this excellent hearing, and I look forward to hearing from our witnesses.

I remember when I was a State Senator working on the Alzheimer's Disease issue in Wisconsin. When Senator Hatfield came forward, that was the turning point on the national level for progress on a bipartisan basis with regard to research on Alzheimer's Disease, and so I was proud to support his amendment to restore most of the proposed cuts to NIH when we debated it during the budget resolution. I say that as a person who voted for very few amendments to restore funding. I appreciate his leadership in this area.

I want to particularly mention my experience on the Alzheimer's Disease issue in Wisconsin. I was able to craft a program to help families get the help they need to relieve what is often called in the Alzheimer's area "the 36-hour day." We could establish and fund a modest program to provide some services at the State level, at least to a degree, although I think that a serious effort to provide long-term care must come from the national level.

But at the State level we really couldn't begin to get off the dime with respect to research dollars. It is at this level, at the Federal

level, where that has to happen, as the Chairman of the Appropriations Committee has pointed out. And so, although I cannot stay, Mr. Chairman, I am strongly interested in this subject and have been for many years, and I appreciate your holding this hearing.

The CHAIRMAN. Thank you very much, Senator Feingold.

Senator Hatfield, the hour of 10 has now arrived, and we won't indulge in any more expressions of gratitude to you. We are grateful for your being here.

Senator HATFIELD. Thank you.

The CHAIRMAN. Our first panel of witnesses will provide us with the personal side of the numbers that we are going to be discussing this morning.

First we have Frances Powers of Lebanon, Pennsylvania, who will share with us her personal story of her battle with Alzheimer's Disease. We then will hear from Millicent Kondracke, accompanied by her husband, Morton Kondracke, who is, of course, no stranger to Capitol Hill. Mrs. Kondracke will share her story of dealing with Parkinson's Disease. And then we are going to hear from two individuals who have first-hand knowledge of the tragedy of sudden spinal cord injury, Benjamin Reeve, the brother of Christopher Reeve, and Arthur D. Ullian, who is the chairman of the National Campaign to End Neurological Disorders.

Please come forward.

I should indicate to the panel that I am advised that there is a vote scheduled to begin at 10:15, with two back-to-back votes to take place. What I plan to do is to try to run this panel, at least, and your opening statements until 10:25 or possibly 10:30, and then we'll take the 10- or 15-minute break.

Mrs. Powers.

STATEMENT OF FRANCES POWERS, LEBANON, PA

Mrs. POWERS. Thank you for this opportunity to speak as one who knows Alzheimer's not just now, but in my past.

When I was just a teenager my mother was diagnosed with early-onset Alzheimer's. I am 1 of 10 children. There were five younger than me. She had just given birth to my youngest brother.

Her twin sister also had early-onset Alzheimer's; therefore, the number of people—because early-onset is 50 percent hereditary, the number of people just on my mother's side from my siblings is 23 of us have the potential of having early-onset Alzheimer's. My two children—Jessica is 15 and Philip is 13—are at risk. The thought of them going through what I am going through is absolutely horrendous to me. As long as I can speak, I would like to continue to ask for research funds to stop this devastating illness.

Until a couple of years ago, I was the "rememberer" in my family. That's what they called me because I knew all the schedules, I knew all the places, I knew all the people we'd get to take care of everything in the house. I did a lot of work in the house in terms of woodworking and electricity, plumbing—just about everything—very mechanical aptitude.

If schedules needed to be taken care of, I was the one who always got it right. My two children and my husband both have attention deficit disorder, so it was just one forgetting after another. Now we all forget together.

That's when I started noticing that I had what I called—this is not to be crude, but I called it "brain farts" where my brain would simply become empty. It would be like a blank, and it would be always embarrassing. There was no way to tell when it was going to happen. I could be talking to somebody, and all of the sudden I didn't know what I was saying and couldn't get that thought back.

It is a very unusual thing to start with. I thought maybe I was more relaxed or easier going. I certainly didn't want to look at the possibility of Alzheimer's. Sometimes a thought would return. It doesn't return now. It is gone. If somebody else has heard my thought they can help me, but it doesn't come back on its own.

The first year that I knew was probably the hardest. The thing that I felt most was shame. I realized I felt shame because it is just not good to forget doctor's appointments, dentist's appointments, school appointments, bringing the kids where they are supposed to go. It hurt the kids a lot, but I just felt so inadequate.

I ended up speaking. It helped a lot to tell people. I spoke to the school secretaries, physicians, my automobile mechanic. I talked to everybody—my bank—so that I wouldn't let them think that they weren't worthy of being informed and worthy of keeping appointments with.

On a practical level, we've learned to compensate for some of this by living our life on dry erase boards. I buy big, huge ones and cut them up so we have them in just about every room in the house. The kids are required to tell me what they need to have done, then it is up to me to look at the board. That doesn't always happen.

I also carry a dry erase with me in the car so that if I'm driving along and all of the sudden I realize I was supposed to get Philip or I have to do that in 20 minutes, I can just pull over and write on the window real quick, "Get Phil, 2:20."

My children are really having a very hard time dealing with this. They also know that each of them has a 50 percent chance of getting this. I actually believed very securely that they wouldn't have to because of the research that was going on.

I really appreciated what Senator Hatfield said, because it gives me hope that there are people out there who understand. This is not going to stop with me, and it is not going to stop with other of my siblings. The only hope we have is for continued research.

I watched my mother die of Alzheimer's Disease. Actually, she got to the final stages and, by the time she died, she died of pneumonia. But she was already blind and very incapable of speaking. She weighed 72 pounds and was in a fetus position.

Because we are young getting this disease, it means that we don't have the opportunity to die of something like heart disease or lung cancer or such as that because we are all very healthy.

I want to let you know that my husband had the foresight years ago—he is a psychiatrist—to go ahead and purchase long-term care and already had our life insurance—so that we wouldn't hit the total devastation that you can get with Alzheimer's to wipe out the whole family. My father ended up divorcing my mother so that the State could take over her care because he couldn't do any more.

As an American history major in college, I have read of the continued perseverance of the people of this country when Federal and State and local governments have worked together when all odds

seemed against us. Alzheimer's to me is odds, and it is facing this Nation, as Senator Hatfield outlined.

Congress in this area—I think it is amazing they think they can do something different than continue research funding. It is like trying to potty train a child. It is as elementary as that. You can do more afterwards.

It is devastating to my family. My husband and myself have been helped a great deal by the Alzheimer's Association, and their support at all levels has been amazing. The thing that I have appreciated most for myself that gives me comfort is reading their newsletter to find out what little thing is coming up now, who is doing what for the research. I look at that and I find a great deal of comfort knowing that at least somebody is out there doing something very deliberately to help research funding continue.

I just want to let you know that living with Alzheimer's is, for me, a horrible way to die. I don't want to pass on to my kids that kind of reality that they have to follow if this Congress doesn't do something to turn the tables and allow research to go on in a very fast way.

Thank you.

[The prepared statement of Mrs. Powers follows:]

STATEMENT OF FRANCES POWERS
Lebanon, Pennsylvania

Before the

UNITED STATES SENATE SPECIAL COMMITTEE ON AGING
The Honorable William S. Cohen, Chairman

JUNE 27, 1995

THE LONG WALK HOME

My name is Frances Powers and I have Early Onset Alzheimer's. Some people think that only old people get Alzheimer's disease, but that is not true in my family. I am 45 years old, and my mother was the same age when she had Early Onset Alzheimer's. Her twin sister also had Alzheimer's, though she died of lung cancer. As I look back, I've probably had this disease for more than three years.

My two children, Jessica, age 15, and Philip, age 13, are at risk of developing Alzheimer's. My nine siblings and their children are all at risk of developing Alzheimer's. There are many other families out there who are also affected by the ravaging effects of this disease.

Until a couple of years ago, I was the "rememberer" in my family. If details or schedules were important, I was the one who always got it right. I was the memory for the whole household. Then I started having what I called "Brain Blipps". That is, in the middle of a thought or sentence, my mind would simply go blank. The thought would just disappear, maybe to return within a few seconds, or not at all. If you have ever lived near the ocean, it's like when the fog rolls in. You can feel the emptiness inside.

At first, I thought that this was because I was more relaxed in my life due to some emotional recovery work. However, my husband kept trying to tell me that he thought something might be wrong. This caused great conflict between us. I knew what he was implying, and I didn't want to look at it. As the months passed, the division between us grew. Finally, he asked me to call my closest sister Julie. We just cried. We knew without words. It's the worst feeling I ever had in my life. It meant the beginning of the end. The formal diagnosis only confirmed what my heart knew with certainty.

The first year of knowing was the hardest. I felt a great deal of shame. I knew firsthand, how incredibly lost I would end up being. My person would disappear. As time went on, we learned to adjust to the everyday changes. I kept forgetting appointments and details of people I was involved with. This made me very sad because I did not want them to feel unimportant. So I spoke to the school secretaries, physicians, dentist, my auto mechanic, my local bank friends and most especially my church. I found care and concern at all levels, and an affirmation of my relationship with them. This decreased the shame.

On the practical level, our home is run on dry erase boards. The main board now carries the daily schedules for the week, since the desk calendar became easy to miss. We also have cut up larger boards into pieces to place in the bathroom, car, bedroom, etc. To make larger visual reminders, I also write with markers on windows and mirrors. We have installed a car phone so my kids can reach me when they need to, especially when I forget to pick them up. In the future the car phone can be used if I get lost or confused.

I know alot about what I am walking into because I took care of my mother and I watched her vanish as a person. My children are now watching me. When I told them I had Alzheimer's disease, each cried and said, "You won't know who I am!" My children experience constant grief. If I had cancer I would probably die within a few years with my mind intact but with Alzheimer's, they will watch me drift away day by day. They will also watch a personality change that will be filled with frustration, anger and rage.

The only hope that I have is that my children, my family and millions of others will never have to face this themselves. This depends upon continued research funding by this government so that a cure or prevention of this disease can be found. The government is attempting to cut back in all areas. If Capital Hill cuts back in this area, they will pay much more later for what they could be taking care of now.

I watched my father spend all of his savings for my mother's care until he had nothing left. He saw his only recourse to be to divorce her so that the state would take over her care. She died in a despicable state hospital where the conditions were deplorable.

My husband Steve had the foresight to buy long-term care insurance long before I was diagnosed. Hopefully, enough was purchased to prevent what happened to my parents. We can afford the insurance and we bought it in time. Most people aren't so fortunate. They don't have the money to buy the insurance especially with the expenses one has at our age like house payments, braces, savings for college, etc.. We pay $208 for a policy that will provide three years of coverage. This probably won't be enough to cover it all but it will help. We have good friends and good family who hopefully will be there to help us through.

I would like to ask the people in Congress...please don't scale back the research funds for a cure for this disease. I have told my children that I do not believe they will have to suffer through Alzheimer's disease again. If Congress cuts back support for research, they are dooming my children and my nieces and nephews and the generations to come to continued suffering from this disease that could be cured with government support.

As an American History major in college, I have read of the continued perserverence of the people of this country when the federal, state and local governments have worked together when all odds seem against us. Now we face the odds of Alzheimer's and I ask each individual of Congress to please open your eyes and take the leadership to make policies that will guarantee health for our children.

My husband, myself and my entire family have been helped immensely by the Alzheimer's Association. This help has come in continual national and local newsletters reporting the latest developments politically and scientifically. My husband has received a great deal of support and encouragement in the groups sponsored by the local chapters. Through the local newsletters, we have been kept up to date regarding the latest developments in research and have been given hope and vision for the future. Through the Baltimore Chapter, I found support for myself meeting others with Early Onset Alzheimer's. Within a few weeks I am joining the Lemoyne, PA chapter for early stage A.D. This offers me an opportunity for encouragement, for new creative ideas to make it through a day and for a channel outside my home to grieve with others.

I again want to say how much I appreciate the Alzheimer's Association. Their sensitivity and care has encouraged me greatly and has increased my hope that Alzheimer's disease will some day be a disease of the past. Thank you for listening and thank you for caring.

The CHAIRMAN. Thank you very much, Mrs. Powers.

To your left there is a chart—a so-called "pie chart" [1] —that talks about the prospects of those who are between 65 and 74, that roughly one out of every three will develop Alzheimer's. At the age of 75 to 84, about one out of every five, and for those 85 and above it is one out of every two. Those numbers are truly staggering if you contemplate what is happening in terms of us living much longer, but they don't tell the kind of human story that you have just related to us in terms of what you go through day in and day out and the kind of apprehension and anxiety that your children now suffer, as well.

We will come back in a moment, after we have heard some of the other panelists, and we'll ask you a few questions at that time.

Ms. Kondracke.

STATEMENT OF MILLICENT AND MORTON KONDRACKE, WASHINGTON, DC

Mrs. KONDRACKE. Thank you, Chairman. I am grateful for the opportunity to tell you what Parkinson's means to me and to all of those who have suffered from it.

First, let me tell you that I live in fear every day that I won't be able to talk, that I won't be able to walk, that I'll fall, that I'll be unable to move. I fear that my face will be frozen, that I won't be able to swallow, that I'll be a living dead person, that I will end up like Representative Mo Udall, who now lives like a vegetable.

Let me first start out by telling you that I was never sick. I was always healthy. I didn't drink or smoke or eat too much. I exercised. All of the sudden one day I noticed that I was writing my last name, Kondracke, and I made the "K" wrong, and my handwriting was getting funny. I used to have pretty handwriting. This was 8 years ago.

Then I noticed also that my fingers shook when I put them on the table. I thought maybe I wasn't eating right, but then I went to a neurologist and he diagnosed me as having Parkinson's. I hated that neurologist. I didn't go back to him ever again. I went for a year to other doctors and was diagnosed with many different diseases, but then I went to the Mayo Clinic. First they said I had a tremor and then they said that I had Parkinson's because I couldn't wash my hair, I couldn't move my hand up and down.

I have been living with this for 8 years now, and I live in fear every single day of my life. I fear that I will lose my husband, who is very nice to me and treats me wonderfully. He is very good. But I still fear that I will be a burden. I am already somewhat of a burden. I wake him up in the middle of the night to take me to the bathroom because I can't get out of bed because I'm frozen, because I can't turn. And then sometimes, when I can slide down and crawl out to the bathroom, I fall. I fall every single day, and I am bruised all up and down my body because I can't walk sometimes. I don't know when it is going to happen.

The other day I was in the store buying some sheets and I stood up and I fell. Luckily, I have to now have somebody with me all of the time. I was really an independent person. I didn't need to

[1] See Senator Cohen's prepared statement for charts.

have people with me. I grew up in the slums and made it and went to college and went to graduate school. Now suddenly I have to be dependent on people. I can't even drive my car.

I am a social worker, and I had a private practice. Now I have to see a few clients in my house, and most of the time I have to cancel because I don't know if I will feel well.

I think that I'm going to cost the country a lot of money because I am going to be an invalid and a good-for-nothing. I'll be no good to society. I'll be a burden on society. I don't want to be a burden.

The CHAIRMAN. Before you continue, Mrs. Kondracke, I want to say your husband, no doubt, is a very nice man to you. He is less nice to us up here on the Hill.

We do respect him a great deal.

Mr. KONDRACKE. My wife is a woman of great courage and strength, and I am here for the duration, lest you have any doubts.

We had a happy life. We were both productive. We were both working hard. Eight years ago somebody arrived in our house, and it has been just eating away at our life. It is an unwelcome visitor in the house. It is Parkinson's Disease. There is not a day that goes by that we are not involved with it. Hardly a minute goes by that we're not discussing it, that we are not worrying about it, that we're not considering it, we're not plotting strategies for it, that we are not suffering over it.

This falling business is terrifying. People who go out to see Mo Udall at a veterans' hospital out by St. Elizabeth's say that he is totally disabled, totally unable to respond to people. Mo Udall was supposed to have an operation, and right before—one of the many surgical techniques are said to be promising. A couple of weeks before he was to have the operation he fell down a staircase and suffered brain damage and went downhill from there, and now he is totally disabled.

Because Milly's balance is affected by Parkinson's, that's the terror that we live in. She falls.

We were on vacation one time and she was off with a couple of other people and all of the sudden there was an emergency and Milly had fallen down and bruised her face and her lip was torn up and she had to have stitches and so on. Something like this happens all the time.

We can afford to have somebody live with us, which we eventually will. There are millions of people in America who don't have that option. Somehow they have to cope. The spouse involved in all of this is known as the "caregiver." Fortunately, we reached the stage in our sensitivity training as a people where caregivers get some attention and people know enough to say, "Gee, you must have it tough." Well, I don't have it anywhere near as tough as Milly does or the people who are actually suffering from this.

As a result of Milly's disease, I've gotten involved with the Parkinson's Action Network, which is the best lobby on behalf of Parkinson's Disease that there is. I have learned a great deal about this. Some of it, frankly, makes me furious.

Part of it is that the way medical research funding in the Government is structured is that what money you get does not have any relationship to the science, the promising quality of the science, the prospects for a cure. It largely has to do with how

much television time you get, how sexy your disease is, how big a star you have working on your behalf.

For example, AIDS funding—and AIDS has the entire Hollywood establishment with their red buttons on, red ribbons on—gets more than $1,000 from NIH—$1,069 per year per AIDS victim. It goes down from there, depending on how much publicity you can get. Cancer gets $295. Multiple Sclerosis gets $158. Heart disease, which you'd think would get the most because it kills the most, gets $93. Alzheimer's gets $54. Parkinson's Disease gets $26. Yet, everyone says that a Parkinson's cure is 5 years away if we could only get there.

Of the qualified funding for Parkinson's Disease, 10 percent can be given money at NIH because of this disparity in funding because there isn't enough. There are neural growth factors, there are fetal transplants, there are pallidotomies, there are thalamotomies, and so on. All of it is promising stuff. There is promising medicine. But it can't be funded because there isn't enough money, and the funding system is skewed and there is not enough of it.

Thank you.

The CHAIRMAN. Thank you, Mort.

Mrs. KONDRACKE. I would just like to finish and say something.

The CHAIRMAN. Yes.

Mrs. KONDRACKE. Parkinson's affects not only the old, but also the young. Of the population, 30 percent is under 50.

Mr. KONDRACKE. Which means that hundreds and thousands of productive citizens will not be able to fulfill their potential to pay their taxes, to make their contribution to the society that they otherwise would.

Mrs. KONDRACKE. Also, everybody thinks that Parkinson's is just that you have medicine and you are cured, but the fact is that medicine masks the illness and it only is productive for a certain limited time. It has bad side effects, and after a certain amount of years it doesn't work.

[The prepared statement of Mrs. Kondracke follows:]

Statement of Millicent R. Kondracke
To Senate Committee on Aging
June 27, 1995

I am grateful to the committee for inviting me to testify about Parkinson's Disease and its terrible impact on my life.

Parkinson's Disease is a degenerative neurological disorder that afflicts approximately one million Americans and is conservatively estimated to cost society $6 billion per year. This money could be saved, along with the terrible cost that Parkinson's inflicts on individual lives, if an investment were made in several very promising lines of research. I hope that Congress will take steps to accelerate this research.

Let me tell you what all this means to me personally. Eight years ago, I noticed that my handwriting was changing. Also, when I put my right hand on a table, there was slight shaking in the fingers. I was diagnosed with Parkinson's seven years ago. Like other Parkinson's patients, I take Sinemet, a medicine that replaces some of the dopamine that my brain no longer produces. In the beginning, L-dopa worked pretty well to control the tremor and stiffness that I experienced on my right side.

However, over time the medicine ceases to be effective and has its own terrible side-effects. I experience so-called "on-off" syndrome. There are times when the medicine unaccounably ceases to work. I will be sitting in a chair, try to get up and find that I am imprisoned. If I wake up at night to go to the bathroom, sometimes I cannot get out of bed and I have to wake up my husband to help me. Many nights I cannot turn over in bed by myself. If my husband is out of town, I have to crawl out of bed. Sometimes I fall on the floor and have to crawl to the bathroom. After I take my medicine, I have to sit on the floor for half an hour waiting for it to work. I can't stand up until it does.

The worst thing that happens is that I fall. I have black and blue marks all over me. Once on vacation, I stumbled over a curb and fell flat on my face, requiring stitches in my lip. I also fell on my face on my front sidewalk, scraping my cheek and forehead. I stumble or fall nearly every day in the house somewhere. I never know when this is going to happen because I don't feel any difference when Parkinson's is affecting my balance from when it isn't.

What I fear most is that I could end up like Morris Udall, the former Member of Congress and presidential candidate, who is now totally disabled, unable to move or communicate. Mo Udall fell down a stairway at home because of Parkinson's and suffered brain damage. It is my nightmare to be rendered totally disabled, totally dependent upon others.

Depression is a side-effect of Parkinson's. I also have trouble talking. Sometimes I feel incoherent, like my personality has changed. I feel diminished, embarrassed, and humiliated. Most of all, I'm afraid of what I may become--unable to swallow, bed-ridden, dependent, a burden on others.

I have described what it means that Parkinson's is a degenerative disease.

Let me tell you about the fiscal costs. I am a clinical social worker with an MSW from Catholic University. I had a thriving private practice in Bethesda, Md., with about 20 patients. Now, I am able to see only a few per week at my home, and often I have to cancel because I feel terrible. Now, I am a consumer of therapy to help me cope with this awful illness. I need physical therapy, medicine, and people coming in to help me move around the house. Eventually, I may need fulltime, live-in assistance.

I got Parkinson's at the age of 47. About 20 years of my professional life will have been affected. The average age of onset is 57, although 30 percent of patients are under 50. There is anecdotal evidence that more and more young people are being afflicted. This, of course, will raise the cost to society. In any event, Parkinson's is not a quick-killing disease. Its victims live for decades and the disease inhibits not only their lives, but those of their spouses, who are burdened by having to be constantly on call and worried about some disaster.

I have hope. Parkinson's literature and the newspapers contain reports of dramatic potential new treatments and cures. An operation called pallidotomy, the destruction of some brain tissue, significantly reduces tremor and rigidity in many patients. Of course, in some others, it leads to blindness and hemorrhages. And, the operation costs $20,000 to $40,000. Transplant into the brain of tissue from aborted fetuses is another promising operation, but it was blocked for years by federal regulation and there are reports that some in Congress want to block it again. At present, about one-third of fetal transplant surgeries produce no improvement, and it

also is an expensive operation. Scientists are working on genetic fixes for Parkinson's and also on so-called neural growth factors to help the brain regenerate lost cells.

All of this costs money, and Parkinson's research has been woefully underfunded at the National Institutes of Health. For Fiscal 1994, Parkinson's research recieved only $26 million in federal funding. Per victim, Parkinson's research is funded at a rate of $30 per year. AIDS receives more than $1,000, cancer, $259; heart disease, $95, and multiple sclerosis, $168.

I would strongly urge Congress to pass the Morris K. Udall Parkinson's Research, Assistance and Education Act introduced by Sen. Mark Hatfield, which calls for NIH to elevate the priority it gives Parkinson's to that now devoted to AIDS and cancer, and authorizing $100 million per year. The NIH budget needs to be increased, not reduced as a part of budget-balancing.

I am biased, of course. My life and future depend upon finding a cure for Parkinson's in the next five years or so. But if I can be objective, I would say that federal expenditures for Parkinson's research are also a good investment. Over five years, $50 million could well save $30 billion. A million people whose lives are wasting away would be rendered productive again.

The CHAIRMAN. Mr. Reeve.

STATEMENT OF BENJAMIN REEVE, BOSTON, MA

Mr. REEVE. Thank you, Mr. Chairman.

I have prepared a written statement. I ask that it be included in the record rather than read from it now, because I'd like the greatest opportunity to answer your questions. I thought I would just talk for a moment and say a couple of things.

Even in the case in which you might be a star, neuro injury is not a sexy disease. What happened to my brother is pretty well-known by accounts in the press. He was riding a horse with as much protective gear as anybody rides a horse with and was thrown from the horse. His spinal cord was injured. He is in the circumstances of every other spinal cord patient, which are very like the circumstances of every other patient who has a neurological disorder or disease. That is to say, you'd walk into his ICU room in Charlottesville, Virginia, and you would be impressed by all of the wires and tubes, all of the machinery that is there. It is all very modern. In fact, the ICU room looks like something out of a movie set about body transplants in the next century.

But it is all there merely to keep him alive. None of it is there to restore him to the person that he was or to accomplish anything that might be fairly described as a cure.

In his case, the reality is predictably stark, mostly because it happened suddenly and mostly because the circumstances around it articulate the reality very closely. But the reality is no different than it is for my grandfather, who died of Alzheimer's Disease; my uncle, who has Parkinson's; or any of the other family members of friends of all the people in the United States—and there are many—who have written us letters talking about their experience with neurodisease and disorder and what they are trying to do to live with it, particularly because there is nothing they can do to cure it.

The good news is that the science in this area has come a long way, and it has come a very long way particularly in the last 5 or 10 years. I would sincerely try to convince you that we have the opportunity scientifically to make great progress in this area.

Exactly what we can accomplish is hard to say because if we knew that then we wouldn't have to learn it, so it is a matter of taking risks, it is a matter of funding research that genuinely is designed to increase our knowledge of neuroscience, to increase our appreciation of neurology. We need to have the faith that it will provide improvement in the condition of everybody who has any kind of a neurodisease or disorder.

I tell you that we have received a flood of mail in Charlottesville. The American public knows very well that this is an area of medicine in which we have not done the research that we are able to do at this time, knows that we have not achieved the level of understanding that we owe ourselves, and recognizes that it is time to do so.

I otherwise thank you for the opportunity to be here, and I look forward to your questions.

[The prepared statement of Mr. Reeve follows:]

WRITTEN STATEMENT OF BENJAMIN REEVE BEFORE THE SENATE SPECIAL COMMITTEE ON AGING, WILLIAM S. COHEN, CHAIRMAN ON JUNE 27TH, 1995

Mr. Chairman, Members of the Committee, Senator Hatfield, thank you for your invitation to be here today.

Before you, and before the Congress as a whole, lies the matter of funding basic research concerning the structure and function of the central nervous system, by which we mean the brain and spinal cord. I am given the chance to speak here today because my brother has recently suffered a bad accident, but I say to you what I would have said in any event. I have learned a lot in the last three weeks about neurons, myelin, and glial cells, and for that I am thankful to all the many people who have educated and counselled me recently. Yet I was not a doctor before my brother's accident, and certainly have not become one since. The technical information I have gathered has only reinforced basic beliefs our family has long shared with many other people. My testimony today, summed up in a thought, is that although as a nation, we will need to do the housekeeping involved in protecting our borders or administering our currency, our most important business is to learn about ourselves and use what we learn to improve our lives.

In no area of medical research can effort be better spent than on the neurology of the central nervous system. Other areas of work certainly merit the attention we give to them, and more: while we are here in this room, millions of Americans are suffering the ravages of cancer. Nevertheless, work on the central nervous system rightfully should be our highest priority for basic medical research.

First, most of the potentially treatable disease in this country now is related to the condition of the central nervous system. Our successes against many infectious diseases and other illnesses have left us with those diseases and disorders against which we have not made the same kind of progress. Our population is aging. Older people experience more neurological ailments. Greater understandings in neuroscience will only continue to increase in value to the patient population.

To the need is coupled opportunity. Even those injuries to the nervous system we conceive to be sudden are, in fact, progressive. The secondary and tertiary effects of spinal cord trauma continue for weeks after the damaging event. We have in every instance, therefore, the chance to accomplish medical intervention.

Second, in no other area can incremental medical advances provide such a major alleviation of human suffering. I do not say that a "ten-percent cure" would not be valued by a person suffering from AIDS or antibiotic-resistant tuberculosis, but a ten-percent cure in the instance of many of the neural disorders can make much more than a ten percent improvement in a patient's condition. We have substantial laboratory evidence, for example, to indicate that even a five percent improvement in neural functionality in the spinal cord can make nearly a one hundred percent improvement in muscular function below the site of the lesion.

As will be described by economists who will testify in the next panel, leveraged cost savings accompany the human benefits. In no other medical field can the price of cure be so well repaid by a reduction in the costs of care.

Third, in no other area can a single advance in science potentially answer so many different questions and solve so many problems. Scientists in panels later to come in the course of this hearing will tell you that neural damage and neural aging appear to be very similar processes. The same research realistically can hope to benefit people suffering conditions as diverse as spinal cord trauma, Parkinson's disease, and Multiple Sclerosis.

Fourth, the central nervous system remains probably the least well understood of any of the major components of human physiology. Were we to gain an understanding of neural mechanisms as relatively good as our understanding of cardiology, what could be accomplished clinically would astound us all. Additionally, an improved understanding of the human brain and spinal cord is uniquely likely to provide us with non-medical knowledge -- with insight, for example, about the behavior of complex systems, structures that learn, adapt, and have language and memory -- among all of the fields of medical research.

Fifth, our nation is now in the lead in this area of research. It has taken us a great deal of effort and time, but we have built a research infrastructure which no other country can claim to match. We can make use of that framework and maintain and improve upon our scientific advantage by continuing our research. We have before made the mistake of abandoning the value of our work and forsaken the opportunities provided by other technologies we have developed, but need not repeat the error.

Sixth, no other area of work is as likely to provide marketable results. Basic research in this area is not only likely to produce useful results, but economically valuable useful results.

Seventh, finally, and most importantly, the central nervous system is the organ of the mind, of personality, individuality, consciousness, and knowledge. The qualities by which we are distinguished as human beings arise more from this physical part of us than from any other. People without a kidney miss having it, no doubt, but there is something fundamental, intimate, and absolute about our dependency upon neural function not duplicated by any other physical requirement we have as living humans. The liver, the pancreas, or the heart may all be transplanted, but, correctly, we have no thought to transplant, as an organ, the central nervous system. To work on central neural function is to work on our ability to be ourselves in a very primary way.

I recognize that this is the Special Committee on Aging, that for reasons of legislative convenience and necessity we have created a structure to focus on particular areas of concern, and that the issues particular to older Americans properly are one such area. I also recognize that many of the problems of the old are the problems of us who are not yet old, merely raised in a different context. Mr. Arthur Ullian of this panel will soon tell you that, when his spinal cord was injured, he became older quicker than he had before thought possible.

Let us be simple about it, we have a large population of aging people for the same reason we have a large population of people who have survived injury: advances in medical care have enabled us to keep alive those who otherwise would have died. We are now challenged to provide medically sound treatment truly to improve the lives of those with and for whom we have shunned death.

Mr brother Christopher has had the bad luck to sustain a severe injury for which there is not, and really can't be, complete protective equipment. Riding horses in a suit of armor has been tried; perhaps it satisfied the purposes of that time, but armor did not then and cannot now relieve all risk. At issue, necessarily, is our common courage in a sometimes dangerous and unforgiving world.

During his stay in the hospital in Charlottesville, Christopher and the family have received quite a bit of mail, tens of thousands of cards and letters, and, therefore, a certain amount of our time as a family has been spent reading messages from people in this country, almost all of them people we did not know, people from all walks of life. Many of them have suffered a neurological injury or disease, or have a relative or friend who has. We have received letters suggesting unusual courses of therapy or treatment, but we have not received a single piece of mail anything less than thoughtful, compassionate, and supportive. I can tell you with some assurance that the will of the people of this country is to transcend the limitations of our present knowledge and circumstances and to achieve real improvement both in the lives of individuals and in our common life together.

Certainly it is no secret that these are the days of budget cuts in Washington. The national debt is too large and growing too rapidly, and we truly need to think hard about what we are to spend money on. We are all aware that asking to spend money on one purpose is to say we should deny funding to another purpose, also good. Making the choice takes courage.

Again and again in the notes and letters we have received in Charlottesville we are reminded that at the moment we experience great fear, our courage is most required, and it will be most rewarded. Every person has a central nervous system, a brain and spinal cord. I have come here to say to you, to the extent I can persuade you to listen, that your decision to further the common commitment to understanding ourselves and improving our lives that we make by doing neuroscience will, no doubt, be the right one.

Thank you. I will, of course, be pleased to answer any questions you may have.

The CHAIRMAN. Thank you, Mr. Reeve.
Mr. Ullian.

STATEMENT OF ARTHUR ULLIAN, CHAIRMAN, NATIONAL CAMPAIGN TO END NEUROLOGICAL DISORDERS, BOSTON, MA

Mr. ULLIAN. Thank you very much, Mr. Chairman, for holding this hearing. I also want to thank your super staff for putting this together.

I am the president of the National Council on Spinal Cord Injury, and the chairman of the National Campaign to End Neurological Disorders. Both organizations are wide coalitions of the large patient organizations in the country—stroke, MS, ALS, head injury, spinal cord injury, epilepsy, and other groups that literally represent millions of Americans in this country who suffer in one form or another from a neurological disorder.

Many of these people are represented here today. I notice that Doctor Murray Goldstein is here, the past director of the National Institutes of Neurological Strokes and Disorders, and now the research director for cerebral palsy.

In addition to the time that I spend in this campaign, I also run my real estate office in Boston. We are in development of multifamily housing and maintain commercial properties in five States, from Delaware to New Hampshire.

This is a particularly difficult time for me because 4 years ago next week I fell off my bicycle and landed on the ground. My neck went back and I bruised my spinal cord. I didn't break a thing, yet I ended up in a wheelchair. I had no knowledge that these things can happen in one split second. Four years ago today I would only have a week more to walk around and to do the things that we all do everyday and don't even think about.

A lot of things I had to give up. I had played the violin since I was 7 years old, it was very important to me and it took me 2 or 3 years actually to sell my instrument. I had a tremendous amount of denial. I thought maybe I would be able to play it again, but in the end, I did have to sell it.

The main thing about spinal cord injury, however, is that it makes you old before you are actually, chronologically old in one particular way, and that is that it makes you dependent. I never used the health care system very much before my accident. None of who aren't sick use the health care system. What we know intuitively is that as long as people continue to get sick, health care costs will continue to rise.

What we need to do is to begin to curb that kind of long-term debilitating illness of which neurological disorders form a major part.

People often argue that technology increases the cost of health care, and they always come up with some kind of anecdote, having to do with an MRI their cousin had for a headache, and it cost $1,000. But, in fact, research, technology, has kept us healthier longer. People live very active lives until very late ages. My father worked every single day until he was 85, until he got sick. It is really an issue of when an illness hits you that you become dependent and begin to use the system.

A major part of Medicare and Medicaid and all of the other Federal costs, including SSI, is long-term care. In fact, when you look at Medicaid alone, 40 percent of Medicaid goes to the benefit of only 7 percent of the recipients, and those are for long-term care individuals who have basically spent down their assets and ended up on the Medicaid rolls. Half of those resources go for people who have Alzheimer's and other dementias, and the other half are for stroke and other problems.

As you mentioned, Senator, the baby boomers are really the major problem. These people are rushing toward retirement which they'll reach in 15 years, and 15 years is not a very long time. It was 15 years ago that Ronald Reagan became President. That's not a very long time ago.

When these people reach retirement, as you correctly pointed out, the retirement age population doubles in the next two decades. We know that people over 65 spend 155 percent more for health care per capita than people under 65. We would think that intuitively.

Obviously, even in today's dollars, if you double the number of people over 65, even if you were able to maintain the per capita cost, you would have to double the cost. In today's dollars that would add $200 billion to the Federal tax right off the bat.

Anyone in business knows that what you need to do to remain silent is not only cut—that's just the first line—but you also have to look for innovation. Fortunately, we have the innovation. That is what Americans do best. If you were holding this hearing 5 years ago, and you brought scientists here and you said, "We have a serious problem with all these baby boomers coming forward over-burdening the system," and the scientists responded "We have no solutions. We don't know what to do." Then we would have a very, very serious problem.

But, in fact, the reverse is true. What you are going to hear today is that there is a tremendous amount of hope. I must say, in an atmosphere in this country where we have a lot of despair, surrounded by Oklahoma and crime and budget cuts, we have an opportunity to look forward to tremendous hope, which the scientists are going to outline for you today. Because we can, in fact, relieve Parkinson's. We can delay the onset of Alzheimer's. We can prevent 20 percent of all strokes. We can do a number of other dramatic things that these scientists will explain.

This is really not a miracle. This is not a dream. It is a reality. We have the technological ability to do it, we have the tools, the intrastructure of laboratories and we have the manpower to do it. What we lack is the funding.

We know that every single week 500 people are going to be diagnosed with Alzheimer's. We know that 200 people are going to suffer a head injury. And we know that 10,000 people are going to suffer a stroke.

The CHAIRMAN. Mr. Ullian, I'm going to have to cut you off here because we are out of time as far as the vote is concerned.

We'll take about a 10- or 15-minute break until we get to the other vote, and then we'll come immediately back and pick up with the conclusion of your statement.

Mr. ULLIAN. Thank you.

The CHAIRMAN. The Committee will stand in recess for about 15 minutes.

[Recess.]

The CHAIRMAN. The Committee will come to order.

Mr. Ullian, we cut you off as part of your statement. I apologize. There is going to be a consistent pattern of voting throughout the day, so we will be interrupted from time to time, but why don't you complete it and then we'll ask a few questions and go on. We have two more panels following this one. We'll try to complete it as quickly as we can.

Mr. ULLIAN. Absolutely. Thank you.

I think, just to end up my statement, I think, if we look at funding research from a business point of view, one would have to make that investment because you have to stop these costs. If we don't make this investment now, 15 years from now, or even 5 to 10 years from now, when things really begin to multiply and the baby boomer population does hit us, I would be afraid there would be an awful lot of these books around called, "In Retrospect," and a lot of people would be saying, "We were wrong. We were terribly wrong."

We have the opportunity right now not to be wrong, to put that money in. It is not a lot of money that we are talking about. As Senator Pryor said, it is really only 3 pennies of every dollar that we spend for health care. That's very, very much less than every single business in the country spends on research and development. We all spend money—probably between 7 and 10 percent—on research. The military spends 15 percent, the pharmaceutical industry spends 15 to 20 percent.

I want to conclude. Last week I went to visit two young boys, 16- and 17-year-old brothers, who were driving home from a church supper. They are Mormons—nephews of California Congressman Ron Packard. I visited them in the rehabilitation hospital just outside of Boston. They were coming home and what we all, as parents, fear has happened. Their car went out of control and the two of them—Robert, who is 16, and Reid, who is 17, were both in the front seat of the van with a seatbelt on. They both sustained serious spinal cord injuries. The 17-year-old has a very, very high injury similar to Christopher Reeve's, and the younger one, who is 16 years old, has an injury which is slightly higher than mine.

I asked their mother if I could talk about them and mention them here, and she actually gave me a picture of them. These are just super, wonderful boys. Their youth is just taken away. It doesn't need to happen. We have the cures in our laboratories. You are going to hear from the scientists that the future is promising. We just have to nourish and support the science. I must say I thank you again for your work here in putting this hearing together.

[The prepared statement of Mr. Ullian follows:]

Testimony of Arthur D. Ullian
Chairman, National Campaign to End Neurological Disorders
before the Senate Committee on Aging
June 27, 1995

Mr. Chairman, Members of the Committee, my name is Arthur Ullian. I am the President of the National Council on Spinal Cord Injuries and Chairman of the National Campaign to End Neurological Disorders. Both are coalitions of national organizations representing the entire spectrum of neurologically-related diseases, all committed to the goal of finding cures and treatment advances in this area. Some of our members include the National Multiple Sclerosis Society, the National Stroke Association, the United Cerebral Palsy Association, the Epilepsy Foundation of America, the Parkinson's Disease Foundation, the National Head Injury Association, the Paralyzed Veterans of America -- and too many more to mention. On behalf of all these groups, I would like to say how much I appreciate the invitation to appear before you today, and the hard work of Senator Cohen's staff in organizing this very important hearing.

This week four years ago, my perspective, my goals, indeed my whole life, were quite different from what they are today. I was running a Boston real estate development company that includes hotels and apartment complexes in five states. I was sailing and skiing and biking and playing my violin as part of a chamber quartet. I generally followed a hectic and physically demanding schedule.

Then, on July 5, 1991, while I was riding my bicycle down a quiet country road near my summer home, the bike hit some small obstacle in the road, and I was thrown over the handlebars, bruising my spinal cord at the 6th cervical vertebra. In that moment, I was paralyzed from the chest down, and left with very limited use of my hands.

Since that day, though I still spend a small amount of time on my business, most of my energies are devoted to the coalition organizations, advocating for other people with disorders of the brain and central nervous system. It turns out there is plenty of work to do.

This is the hardest time of the year for me, the few weeks approaching the "anniversary" of my accident, which of course formed the demarcation line of my life. One of the strange things about having an accident like mine, or like Christopher Reeve's, is that unlike a disease, where there is a gradual convergence of genetic, environmental and other factors - and a slow onset of symptoms leading to a diagnosis - with an accident, your life is perfect, even blessed, one minute, and shattered the next. All the rules change completely. Your old ways of relating to your wife and your children, your friends and your colleagues all have to be re-negotiated. You have to relearn every simple task. Most difficult of all, you have to adjust to a life of dependency on others. In some ways, you experience an important aspect of aging before you are old chronologically. It is that concept of dependency that is at the heart of what we are here to talk about today.

Because it's not the number of years a person has lived that creates makes them old , but the *level of dependence* they live with. I can't help but think about my father, who still went to his office every day until he was 85. But if a senior, because they have had a stroke, or have Alzheimer's Disease or Parkinson's, or ALS (Lou Gehrig's Disease) - if that individual cannot get out of bed unassisted, or take care of their own personal hygiene needs, or remember how to take their medication properly, or prepare their own food - then that person is going to cost the government tens of thousands of dollars every year.

It's appropriate that this Committee is looking at Medicare and Medicaid cost containment now, because the demographics of the older, dependent population tell us that we can't start planning soon enough. Today, people over 65 consume one third of the total amount spent on health care services in America -- and that total is over one trillion dollars for the first time this year. And right behind this current group of seniors is the largest single generation in our history - the baby boomers, who will become "senior boomers" by 2010. Where there are 33-1/2 million people 65 and older today, there will be 40 million by 2010 and 70 million by 2030!

We know intuitively, and statistically, that people over 65 consume more health care than their younger counterparts. Those over 65 spend approximately $4000 per capita on health care every year, as opposed to $2600 for those under 65, an increase of 155%. When we acknowledge that the elderly population will increase by 25% over the next fifteen years, and by 115% over the next thirty years, we can't help but conclude that the total number of beneficiaries of Medicaid and Medicare will overwhelm the system even if we could maintain the per capita usage at the present rate.

More alarming if the fact that the single fastest growing segment of the population in the future will be the oldest old – those defined as 85 and up. This group will triple their numbers from 3 million today to 9 million in 2030 to 19 million by the middle of the next century. It's obvious that we have to take action now if we are to meet the health care needs of this population without bankrupting the federal programs that insure them. It's not enough to look seven years down the road: we have to be thinking in terms of at least fifteen years (when the demographic realities begin to apply) if our planning is to succeed.

Today, we're here to look at a very important strategy for controlling the skyrocketing demand on Medicaid and Medicare – the potential of sustained, long-term investment in medical research to result in delaying, controlling and preventing the costly illness that drives costs up. And of these illnesses, neurological are among the most costly, because of the chronic impairment and long-term dependency they often entail. For example, at least 40% of Medicaid payments go to cover long-term nursing care (for only 7% of the recipients) – and half that amount is allocated for people with Alzheimer's and other dementias. Alzheimer's Disease alone is costing this nation nearly $100 billion a year in direct and indirect costs. It won't do any good to decide that we're going to reduce reimbursements for these people's care – their disease will not go away. If Medicaid is cut, the cost will inevitably shift to other payers. The only solution is to work towards eliminating Alzheimer's. Or towards finding ways to delay the onset of its symptoms, which is clearly achievable in the next few years, and which would have the effect of saving billions of dollars annually by keeping people living independently at home a few years longer.

Another example of the way in which research can hold the line on costs, which you will be hearing about later, is stroke. Every year, more than half a million Americans suffer a stroke – and so much of this is preventable, especially the dependency-causing disabilities that so often come with stroke – the inability to walk, or speak, or retain memory. It was very interesting to me to learn how similar the cascade of events that takes place in the brain after stroke is to what happens in a head injury or to what happens in the spinal cord after an injury like my own.

Those similarities constitute a key feature of neuroscience, and neurological research. The discoveries that scientists are making every day in this field have application and importance for such a wide range of diseases: Alzheimer's, Parkinson's, Huntington's, Lou Gehrig's Disease, Multiple Sclerosis, Cerebral Palsy, stroke and head and spinal cord injuries. Breakthroughs in neuroprotective therapies and neuroregeneration techniques mean so much to the quality of life for people with all these disorders. That is why I am committed to the concept of one Neurological community - all speaking with one voice to convince you of the importance of finding additional funds for neurological research.

You can easily see the results of the "cross fertilization" of research efforts in the recently-released mid-decade report of the Dana Alliance for Brain Initiatives. The Dana Alliance is a consortium of 135 of the country's leading neuroscientists, led by Nobel laureate James Watson, who identified the structure of DNA. In this incredible report, the scientists summarize the progress made in a wide range of specialties over the past five years, and estimate what further advances can be delivered by the year 2000. Among their predictions are the following examples:

1) For mental disorders such as Schizophrenia, there will be a better generation of drugs with fewer and less severe side effects. It will be possible to chemically alter the brain to alleviate symptoms of the disorder;

2) In the areas of alcohol and drug addiction, scientists will be able to block the destructive effects of these substances on the brain, and in some cases, will be able to modify or extinguish their action within the brain;

3) In the area of blindness, the transplantation of cells into the retina will save the vision of those with age-related degeneration of retinal structures. Cataract development will be delayed, and treatments for diabetes-related blindness in development;

4) In Multiple Sclerosis, at least two agents will be available with better efficacy than Betaseron. Specific drugs will eliminate immune cells and possibly prevent all future attacks of the disease;

5) In spinal cord injury, clinical trials of an agent known as GM1 will enable the first treatment to enhance cord repair. Much more will be known about the mechanics of nerve regeneration, allowing new molecular and cellular therapies to promote reconnection of nerve fibers in the spinal cord;

6) For Alzheimer's Disease, new drugs will be available to delay the disabling symptoms for up to five years. Other therapies to replenish lost brain cells will begin to be developed;

7) In Parkinson's Disease, at least one and possible several new drugs will be in clinical trials, and gene therapy will be available. It will be possible to screen for the disease;

8) In stroke, risk-free, low-cost and relatively painless diagnostic techniques will be available to examine cerebral arteries. Prevention and treatment will be enormously improved, including drugs to protect brain tissue from ischemia and dissolve clots in artery walls;

9) In the area of chronic pain, safer and more potent pain relievers and more diverse delivery methods will be available, that so closely target the specific site of pain that side effects are very minimal and potential for abuse will be eliminated.

It is easy to conclude from these few examples of the Dana scientists' work that people with neurological disorders are not a small special interest group. Taken together, we may represent half the population of this country. Anyone present in this room today, or your parents, or your children, could easily acquire a neurological disease or disability at any time. Ben Reeve, who has left his brother's hospital room to join us today, knows this to be true. And Sheryl Nixon, who happens to be the niece of Congressman Ron Packard of California, also knows this to be true.

Mrs. Nixon has six children. One month ago, four of her children were involved in a serious automobile accident on the way home from a church youth group meeting. Her two younger children sustained only minor injuries, but the two older boys - Reed, 17, and Robert. 16, suffered paralyzing spinal cord injuries. I met Mrs. Nixon and Robert last week at the West Roxbury, Massachusetts VA Hospital. And I couldn't help but be struck by the faith and courage she showed in spite of the overwhelming care-taking task she and her husband now face. If it weren't for the incredible, ongoing fund-raising efforts of the Nixon's community, the cost of the boys' injuries would very soon bankrupt this family.

The good news for the Nixon brothers lies in the advances you will hear about from the neuroscientists here today -- advances in our understanding of the mysteries of neuronal pathways, how they work, and why they stop working properly in certain diseases or accidents. Driven by new understanding in genetics and molecular science, by advances in brain imaging techniques and computer modeling capability, brain research has been following a dramatic trajectory over the past several years. If there is to be a future for Robert and Reed, the path of that trajectory has to continue on an upward path -- and at an accelerated pace. We know it's the humanitarian thing to do, but just as important, it's also the economically farsighted thing to do.

During the hearing this morning, you will hear an important statistic. You will hear that between 1970 and 1980, while the elderly population increased by 15%, Medicare rose by 4.3%. In the previous decade, 1960-1970, the elderly population rose by only 6%, while Medicare costs increased by 9%. You would think that the rise in costs would be commensurate with the rise in numbers of elderly, but that was not the case. Why? The answer lies in the variable of technology, in the fruits of medical research. The 1970's saw an explosion of new therapies and diagnostic devices that kept older people healthier, more independent and out of hospitals and nursing homes.

Medical research has given us so many gifts in such a short time period, has improved our lives in so many ways, and is so integrated into contemporary life that we take it for granted, much as we take radio, television and computers for granted in 1995. Nowhere outside of America do people enjoy such good health or such a long life expectancy. In Russia, for example, the average citizen lives 15 years less than we do here, and in poorer health, and the chief difference is the availability of cutting edge medical treatments widely available to our citizens and unavailable to theirs.

The health care picture is not perfect. Disease obviously still exists and it exacts an enormous cost, both human and economic. The chronic, disabling illnesses that require long-term care are of particular concern, because they are the chief culprits in driving up costs. But, as our colleagues from the neuroscience community will tell you today, we can now say with authority that within a few short years -- with adequate funding -- we will be able to delay, control or prevent these costly diseases. And when we can do this, we will save billions of dollars in Medicare and Medicaid each year, while creating an even better quality of life for millions of our citizens.

Respectfully submitted to the Senate Committee on Aging, June 27, 1995.

The CHAIRMAN. Thank you, Mr. Ullian.

I just have a few questions. I'd like to perhaps start with you, Ms. Powers.

One of the things that caught my attention among the many that you had to say was the use of the word—you said you felt a sense of shame.

Mrs. POWERS. Yes.

The CHAIRMAN. And that you would go into memory lapses. You'd be in the middle of a sentence and forget something. And then you went on to talk about your children having a 50 percent chance of acquiring this disease, as well.

Are they aware of the percentages that you have talked about?

Mrs. POWERS. Yes.

The CHAIRMAN. Have you made them aware of this?

Mrs. POWERS. Yes.

The CHAIRMAN. Or is this something they picked up on their own?

Mrs. POWERS. No. Because it is in our family, when they even were very young, because they didn't have a grandmother on my side, all of that was explained to them.

The CHAIRMAN. What is their reaction to the things that they read about? You mentioned you get a good deal of comfort from the newsletters you receive——

Mrs. POWERS. Yes.

The CHAIRMAN [continuing]. In which day after day, week after week, or month after month there appears to be a promise of scientific breakthroughs. Does that give them a sense of hope?

Mrs. POWERS. It gives them hope. That's what I tell them they have. We have a big God, and we also have a country that has committed itself to research funding. That's what got me about this—thinking about cutting these areas. They know that research is going on. My family, my siblings, all of my nieces and nephews, they know that research is going on and that the possibility of them having to have it 20 years from now is not high if research funding continues. If it doesn't—and I've told them this. "That's why I'm going down here for, guys. I have to do this because I need to tell them that I have two children and I have some nieces and nephews that are directly impacted by this and the lack of funding will cloud their future."

So they know it. And, as youth has a way of doing, they walk on each day.

The CHAIRMAN. Mrs. Kondracke, you talked about how you live in fear, and you went through the various fears that you go to bed with every night—of being unable to talk and walk and swallow and ending up like Mo Udall, and fear, I guess, of being a burden on society, itself, which is a terrible fear and a burden to carry.

I was wondering, when we talk about breakthroughs being just around the corner or 5 or 10 years away, does that seem like a lifetime to you in terms of, "It is 10 years away. I've got to wait 10 more years"? Are there ups and downs you have in terms of having hopes and false hopes? You read one report one day, and a different report another day. Is it sort of a ping-pong effect that you get caught on?

Mrs. KONDRACKE. Right. I have hope for 1 year. Ten years is awfully—it's too long to wait. But there is the pallidotomy and there is fetal research and cell research. I hear about all the research, and so I have some hope. It gives me some hope, but it doesn't last very long—especially when I hear about what is happening in Congress about all the cuts.

The CHAIRMAN. Your husband mentioned some of the techniques that can be utilized today. I think he mentioned fetal tissue transplant, surgery, pallidotomy. Those are pretty costly, and none of them carry any guarantees.

Mrs. KONDRACKE. Right.

The CHAIRMAN. Is this something that you would consider undergoing?

Mrs. KONDRACKE. Yes, I would. A pallidotomy I'm considering, even though it cuts into your brain. I just want to have—even if I have 5 more years with Morton and my children I think it is worth it.

The CHAIRMAN. So even though there are great risks associated with any operation—particularly any kind of a brain operation——

Mrs. KONDRACKE. Yes.

The CHAIRMAN [continuing]. You feel that the risks are outweighed by the benefits you might receive?

Mrs. KONDRACKE. Yes.

The CHAIRMAN. You touched upon this, Morton, and that is the politicization of research. Women's groups we know lobby for increased funding for breast cancer, and osteoporosis. There are calls daily, as we know, for AIDS research. How do we avoid pitting one group against the other? How do we go about doing this, kind of balkanizing the whole research field and saying we've got one group here, one group here, and one group here? Is there anything that you have determined would prevent this kind of bidding contest going on between each group lobbying for its research funding?

Mr. KONDRACKE. Clearly, the answer is to increase the whole pie and to pass a bill like the Hatfield-Harkin bill to expand the funding for NIH research in general, and then each group can get some increase.

Frankly, in the environment that we now have where we are talking about whether we are going to have 5 percent cuts or whether we are going to stay flat, which is a net cut because of inflation, anyway, to be more realistic you'd have to say that somehow there needs to be a rationalization of the process whereby the priorities are determined on the basis of which investment will pay the most dividends in the short run.

That's a cruel choice that somebody is going to have to make unless Congress can be persuaded to expand the entire research budget, which it ought to do not only in the interest of the victims, but in the interest of the national economy. After all, medical research is one of our great investment industries. It is what we sell to the world. It creates jobs.

It strikes me as totally mindless, when you've got a wonderful industry like this that is dependent on basic research that the Government funds, to cut it back. It is—what are all of the examples? Selling your seed corn. Eating your seed corn—all of that stuff.

The CHAIRMAN. Who do you think should make these choices? Should it be Congress, the scientists? Who should make the determination of where the allocation goes, and which case is more important in the short run or long run?

Mr. KONDRACKE. I would think that a directive from Congress to rationalize the system would be the wisest, and then let the scientists do it. I assume that they'll have a fight over it, but that's what agencies are for.

The CHAIRMAN. Mr. Ullian, you are a successful businessman, and you have indicated that you would apply your business knowledge to that of medical research, as well. Basically, you need to make an investment in order to get a good return, short-term or long-term.

One of the difficulties that we have in Congress is something called "scoring." For example, we know that there is roughly $100 billion being lost every year through health care fraud and abuse. There is legislation pending—that I happen to be the author of—here in the Senate that would try to deal with fraud and abuse in a very aggressive, law enforcement way. The estimates are that we could save a substantial amount of money by combatting fraud and abuse.

The difficulty, of course, is that CBO cannot score the savings, cannot calculate the savings out; therefore, all that is scored are the costs of what it takes to make the investment to get more law enforcement, but you don't get any financial benefit on the books. That's what makes it difficult, as we are now trying to work our way through the balanced budget approach by the year 2002.

I take it from your business background you would, nonetheless, say, whether you can score the savings or not, it is worth making the investment, even though it runs the risk of increasing the size of the deficit in the short-term in order to get a major reduction in the long-term?

Mr. ULLIAN. Absolutely. That's what we do all the time. Every business does that. You make an investment and you would expect a return.

I must say that if I had the experts that you are going to hear from now telling me as positively as they will how far along we are in the research, you'd have to make that investment. You'd make it even with less authority than they are going to give you.

They already have proof from their own laboratories that the treatment advances resulting from their work will actually provide us with enormous returns. The costs are so huge.

For example, if I had even a partial increase in function so that I had my triceps back, I could transfer in and out of this chair myself. I might not need a caretaker. That would save me $35,000 a year. When you multiply that by all the people with spinal cord injury, even if you went down just a little bit of a level you're talking about saving hundreds of millions of dollars. If you extended or delayed the onset of Alzheimer's by even a year, you're saving billions of dollars.

Investment is the only way to go, and that's what we would do. I agree with you.

The CHAIRMAN. Mr. Reeve, can you tell us, based on your experience—I assume that you had no prior interest in spinal cord injuries?

Mr. REEVE. As such, no I did not, Mr. Chairman.

The CHAIRMAN. And you've become not necessarily an expert, but you've become more knowledgeable about spinal cord injury since your brother's tragedy?

Mr. REEVE. We all learn of necessity. It is the same experience that everyone else in whose family there has been an incident of neural disease or disorder goes through. It comes with the territory.

The CHAIRMAN. What kind of advice would you pass on, based on your experience, to other families who suddenly find themselves confronted with tragedy. For example, Mr. Ullian talked about the two young boys who were injured in an automobile accident. What kind of advice do you give to families who now have to confront this? Is there something the medical community is doing or can be doing to give more hopeful information out as far as the future is concerned? What kind of advice would you pass on to families who have suddenly been visited with tragedy?

Mr. REEVE. Senator, if you'll forgive me, I think there is a considerable extent to which they know and they learn as part of the process. I cannot tell you how greatly I am impressed by all of the people who have gotten in contact with us who have had the experience and who have learned not just the technical details from having had it, but learned an enormous amount about our condition in life as people and our life together as a community.

I am here today because I do think it is all about courage. I think the patients have the courage. I have known Parkinson's patients who have said literally that they would like to donate their brain to science as a way of redeeming their own circumstances.

I don't think the issue actually lies with the people who have suffered the neurological condition. I think it requires that we, in whatever way we need to administer it, make the decision that it is our common purpose to do this kind of medical research, that we engage in it, and that we do basic research as well as research that we hope secures immediate results.

Just as eating your seed corn doesn't work well after a series of years, if we focus too heavily on research for which we hope to get immediate results, we will not even be able to guide that research well or measure its benefits unless we also do the basic research.

I'm asking the Committee, to the extent possible, to also support basic research in neuroscience.

The CHAIRMAN. Thank you very much.

Senator Burns.

Senator BURNS. I have just a comment. I want to thank all of you for coming today. That's number one. It takes a lot of courage to do this.

I was talking to Benjamin over the break a while ago. It seems like we do a fairly good job in prevention, but we don't do a very good job as far as a cure or finding out things about Parkinson's. I lost my father-in-law to Alzheimer's a couple of years ago, and we lost a 16-year-old daughter in an accident, so we have seen our share. But what I was talking to Benjamin about the accident with

horses—and, of course, coming from Montana, like I said, I've had some experience with those unpredictable creatures, and we can't prevent that.

But I also served on a rural committee for the National High School Football Federation. I've got about 20 years officiating football. We were going through this thing with the helmets, with neck injuries and this type thing. I went to a national meeting and I made a recommendation and they thought I was the worst person in the whole world. I said, "If you want to quit having head injuries from football, take the mask off," because our coaching techniques were—they were using the helmet as a weapon. They have less debilitating injuries in Australian rules football than we do in American football and we wear all the armor.

If you get your nose broken once from sticking your face in there, you aren't going to stick it in there any more.

Sometimes we have to be a little bit practical, and maybe a little bit of common sense will tell us some things that we have to do.

I voted for and supported more money to the NIH, and I will continue to support that.

Morton, I want to ask you a question. At what point—who judges, when we get to the point of diminishing returns, how many dollars can we throw at it—not throw at it. That's a bad term. How many dollars can we invest before we're just up against the wall and there is a point of diminishing returns?

Mr. KONDRACKE. Senator, it seems to me that we are miles from that point. When only 10 percent of the qualified projects at NIH—this is with good science behind them—can be funded, we are 90 percent short of that wall. In arguing with your colleagues, I would say if that's one of their arguments it seems to me that it is an empty argument.

There is no money being thrown at useless projects——

Senator BURNS. That was a bad term. I'm sorry.

Mr. KONDRACKE. But there is no money being—these projects, the projects that do get funded, are the projects that, by and large, the scientists think are the most promising. Of projects that they think are promising, 90 percent are not getting funded. So it really is not an issue.

As they decide out there what projects get funded or not, they decide partly because Congress tells them. Congress has directed that money be spent on certain diseases, based on the amount of political oomph that they have behind them.

For example, we all, taking an example from other diseases, are now pushing a bill called the "Morris K. Udall Parkinson's bill," which would expand the funding to $100 million a year from—I think it is $26 million now. This would still put us way lower than many of the other diseases, but it would also direct NIH to give to Parkinson's research the same attention that it now gives to AIDS and to cancer and heart disease and so on by establishing a specific center.

That is us. That is what we want. But we are only doing what other diseases have done. Congress is involved in this process, and it presumably is going to stay involved in the process because it is the people's representatives, and when they hear from various constituencies they respond.

I don't know how to get around this situation. All I know is that the net, the bottom line of all of this is that there is nowhere near enough money that there is any worry that we are spending money on unqualified projects.

Senator BURNS. I have the same concerns that the Chairman does. How do we get away from this tug-of-war? We've only got so many dollars, and the next movie star or whatever comes to town and that heightens the demand—but what you have done this morning with this panel is I think you brought an awareness. You've elevated the awareness again. We need that. We have to have that in order to take the argument forward.

By the way, I just read "Too Funny to be President." He is one of my favorite people—Mo Udall. If anybody wants to read a very funny book, it is a very funny book. By the way, he still had a tremendous sense of humor up until when he could still remember you.

Thank you, Mr. Chairman, for this. I thank this panel for coming today, too. Thank you very much.

The CHAIRMAN. Mr. Reeve, did you want to comment?

Mr. REEVE. If I could just briefly say, Senator Burns, I've got the same answer that Mr. Kondracke had.

We need to trust ourselves. It is true that there are problems with fraud in administration, but we will know when we are doing the right thing.

The biggest feature of the circumstance of someone who has a neurological injury is the sense of helplessness—lying flat on your back, strapped to a bed in an ICU—helplessness. It really, for me, is all about making the decision as a society that we are going to do something about that helplessness—whatever we can, whatever lies next before us to be done. And we'll know when it makes no sense. That's not the biggest problem. We can administer grants. We can tell people we want to spend money thoughtfully and not waste it. I think that's all to be accomplished.

Thank you.

The CHAIRMAN. On behalf of the Aging Committee in its entirety, let me thank each of you for coming. Again, we have a lot of charts on the walls here. They don't tell the story really. Unless we put a human face on these statistics and talk about the human suffering that is involved, we tend to get lost in numbers. We start talking about reaching certain deadlines and goals by certain years, and what is lost in that entire sweep of debate is the human factor.

We can talk about the Three Penny Opera, but not the 3 pennies going for research. That was a very excellent case of demonstrative evidence being presented—$0.03 of $1 going for research is not nearly enough, as you indicated, Mort.

To all of you who have come forward, it does take courage to talk about what you experience on a day-in, day-out, hour-by-hour, minute-by-minute process.

We thank each of you for coming and for the effort you have all been leading to persuade us that we have to do more. I think, based upon your testimony, we will, in fact, do more.

Thank you very much.

We'll now call the second panel.

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Our next panel is going to discuss the enormous cost that brain-related disorders have on society and is going to explain why investing in medical research today is going to save us billions of dollars in the future.

First we are going to hear from Doctor Richard Besdine, who is the Director of the Travelers Center on Aging at the University of Connecticut Health Center. He is here representing the Alliance for Aging Research and is going to discuss a report by the task force that I am going to release today.

The report is entitled, "The Threshold of Discovery: Future Directions for Aging Research." It reflects the work of over two dozen Federal agencies and experts in the field of aging and provides us with a road map on how we can better allocate resources toward aging research.

Our next witness is Doctor Guy McKhann, who is the Director of the Zanvyl Krieger Mind/Brain Institute of the Johns Hopkins University. He is here representing the Dana Alliance, which is responsible for bringing some of the best minds in medicine together and agreeing on goals that can be achieved in the area of neuroscience by the year 2000.

Next we are going to hear from Doctor Jerry Avorn, who is an associate professor of medicine at Harvard Medical School and director of the Program for the Analysis of Clinical Strategies, Brigham and Women's Hospital. Doctor Avorn will discuss the need to encourage new technologies for diseases and will explain how we can better transfer information on new technologies and treatments in order to bring health costs down.

Finally we are going to hear testimony from Robert Goldberg, who is a senior research fellow at the Gordon Public Policy Center at Brandeis University. He will discuss why research in diseases such as Alzheimer's, Parkinson's, and stroke will ultimately lower health care costs for American families and Government health programs.

I want to thank each of you for coming forward. Before you begin, I might point out that we also have in the audience Joss Javitz, who is the son of Jacob Javitz. He is here representing ALS, Lou Gehrig's Disease. As you know, Senator Javitz had that disease. I want to recognize him. I might point out that Senator Pryor's older brother also died of Alzheimer's, so he has a direct interest in this, as well.

Gentlemen, why don't we begin? Doctor Besdine.

STATEMENT OF RICHARD W. BESDINE, M.D., DIRECTOR OF THE TRAVELERS CENTER ON AGING, UNIVERSITY OF CONNECTICUT HEALTH CENTER, REPRESENTING THE ALLIANCE FOR AGING RESEARCH, FARMINGTON, CT

Dr. BESDINE. Thank you, Senator Cohen.

Members of the press, guests, friends, and colleagues, it is a privilege for me to be here this morning. I speak to you as an academic geriatrician. I am a professor of medicine and sit in an endowed chair, the Travelers Chair in Geriatrics and Gerontology. For almost 25 years I have been an advocate for enriching health care of older persons with science. I have taken care of patients,

I have taught what I thought to be the best care of those patients, and done research to try to improve that care.

I, like all of us in this room, have been tremendously moved and encouraged by the bravery and the experiences recounted by the previous testifiers.

I know these hearings today are focused on the brain, but we have to remember that central nervous system disorders are only one of the land mines that older persons must avoid as they, and we, try to march successfully and independently into old age.

Chronic diseases of all sorts generate the astoundingly high costs of care and the loss of function that spoils the lives of too many older Americans. Of course, I am personally deeply disturbed by the spiraling costs of care for older persons, but I am even more disturbed by short-term chainsaw approaches to controlling those costs.

Although cost of care for older persons will exceed $350 billion this year—and I think that's a lot of money—the fact is that much of that cost could have been avoided had we pursued the kinds of investment in science and the translation of that science into clinical practice that has already become a theme of our discussions here this morning.

I would like to emphasize that, although saving money is in all of our interests, it is the life quality for older Americans—and the older Americans the young and middle-aged persons in this room hope to become—that is really at stake.

I do have the privilege of being spokesperson today, as a member of the Scientific Advisory Board for the Alliance for Aging Research, of the Task Force on Aging Research (TFAR) report. As you have already said, Senator Cohen, this is the product of nearly 3 years of work mandated by the Congress to lay out a blueprint as to how we could prioritize and select the projects, as well as strategies for funding those projects, that can make a profound difference to all of us as we age.

As I say when I talk to younger physicians to get their attention, "These are the interventions that will keep you out of the nursing home." The TFAR report contains prioritized recommendations to the Secretary of Health and Human Services that will allow us to prevent the escalation of disease and disability that currently marches in lock step with population growth of older Americans.

Identifying the resources to get this agenda accomplished is absolutely essential. I shudder to think that the profile of America in the 21st century will simply be the multiplied rates of disease, disability, infirmity, nursing home admissions, giant burdens of home care cost, and family suffering that we see today with only 33 million people over the age of 65 and less than 4 million over the age of 85. When those numbers of the oldest old are tripled early in the 21st century, "You ain't seen nothing yet." I truly do not want to see America dominated by care of a vast population of frail elders; I think none of us do. The alternative is sensible prioritized investment now in a research agenda like that detailed in TFAR.

I fear that absent from most of the current debate on health care cost is any strategy to shut down the engine that is driving those costs, which is age-associated disease and the disability—whatever the disease—that we find in far too many older persons.

There are three overarching themes of this TFAR report that are articulated before entering into the 192 recommendations gleaned from almost 3,000 suggestions from scientists and experts in the field of aging, as well as from agencies with an interest in aging research, over the past 3 years.

The first is that past research has produced enormous benefit to the well-being of older persons by sparking innovation in health care and prevention strategies. You've heard about some of that already.

The second theme is that the avalanche of aging boomers absolutely demands additional investment in research on aging to prevent disabilities in that now middle-aged population.

Third, and most important of all—and I think you'll hear emphasis on this from the members of the third panel—we stand right now on the threshold of major scientific advances that will improve the quality of life and independence for older Americans with appropriate investment in specific research projects on aging.

Examples include identifying and perhaps intervening in genetic risks for diseases and for loss of function—again, regardless of the disease driving that loss of function. Understanding of how cell growth is regulated, both up and down—up in the sense of tumor or hyperplasia of tissues, and down in the sense of atrophy and loss of function in organ systems.

We have heard a lot but not nearly enough about Alzheimer's Disease—cognitive function, both in normal aging as well as disease-driven, and many other specific areas of research where there is enormous good information already.

The cost to implement TFAR, the Task Force on Aging Research report, is an additional $1.1 billion investment in aging research over a 5-year period. That has been divided into about half of immediate priority, meaning that money needs to be invested within the next year, and then high priority, which can be invested in a 2- to 5-year period.

I would close simply by pointing out that a 5-year delay in the onset of disability from the leading 10 causes of disability in the United States this year, could save in 1 year more than $250 billion.

If we could delay the onset of disabling conditions in older Americans for 1 month, whatever the cause, that 1-month delay would generate a net savings of $4 billion, and that $4 billion would accrue each month as long as that delay were prolonged.

Thank you for this opportunity. We stand on a threshold of opportunity, not only to save money but also to improve lives of those Americans now in youth and middle-age—the old of the 21st century. Please don't slam the door in the face of older persons and the older persons yet to come.

Thank you.

[The prepared statement of Dr. Besdine follows:]

Alliance for Aging Research

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OPENING STATEMENT OF RICHARD W. BESDINE, M.D., SCIENTIFIC ADVISOR, ALLIANCE FOR AGING RESEARCH

Senator Cohen, Committee Members, Members of the press, Ladies and gentlemen. I am Dr. Richard Besdine; I am Professor of Medicine, Travelers Professor of Geriatrics and Gerontology, and Director of the Travelers Center on Aging at the University of Connecticut Health Center in Farmington, Connecticut. Today I speak not only for myself and the field of aging, but also for the Alliance for Aging Research -- a not-for-profit organization; I serve on its Scientific Advisory Board. The Alliance for Aging Research wants to commend Chairman William Cohen for convening this timely hearing on breakthroughs in neurological research and for releasing the report of the congressionally-mandated Task Force on Aging Research which underscores our belief that research on aging will be a critical element in the nation's efforts to curb rising health care costs.

The report, entitled ***The Threshold of Discovery: Future Directions for Research on Aging,*** was authorized in 1990 by Congress with the strong support of the Alliance. Its goal was to bring together the country's leading scientists in aging research as well as directors of the nation's many federal agencies and departments involved in aging research to assess the scientific understanding of aging in America and to point to the brightest prospects from research and science for answers to many of the debilitating diseases and conditions of our time.

This report is extremely timely -- it comes as the Congress begins its debate on the future of the Medicare program. The National Institutes of Health may well sustain cuts of 10 percent or more in the current budget cycle, while Medicare and Medicaid look like they will face chain-saw cuts unprecedented in their history. Noticeably absent from the current debate over Medicare is any strategy to shut down the engine driving these rising health care costs -- age-related diseases and loss of independence in our rapidly enlarging aging population.

We are now experiencing an unprecedented and dramatic growth in the oldest age groups, thanks largely to the successful application of the fruits of past research. In 1900, only four percent of the population was 65 and above. Today, those over 65 years of age constitute about 13 percent of the population and by 2030, one in every five Americans will be over 65. The "oldest old," age 85 and older, is the fastest growing segment of the population and will rise from 3.3 million in 1994 to 9 million in 2030 and to 48 million by 2050. Soon the Baby Boom -- the largest generation in American history -- will turn into the senior boom. How will the country care for them?

Health experts in aging research see a force at work, which might be called the *force of morbidity*. It is the clock-like regularity by which risks of chronic aging-related disease double approximately every five years after middle age. Except for rare conditions such as Down's syndrome, most diseases such as Alzheimer's and Parkinson's disease, stroke and osteoporosis are nearly unheard of in people younger than 40. But beginning in middle age, the risks double every five to seven years for a wide variety of chronic illnesses. For example, the rate of Alzheimer's rises steeply with age. It seldom occurs in middle age, then the likelihood doubles exponentially every five years after about age 60. Alzheimer's strikes 2 percent of people aged 65, 4 percent by age 70, 8 percent by 75, 16 percent of those age 80, 32 percent by age 85, and astonishing 47 percent of people over 85.

The Task Force declares war on aging-related disability by adopting a determined *strategy of delay* against the rising risks to chronic disease as both plausible and highly effective. Delaying the diseases of aging is a relatively new idea, but one with great potential. Either by delaying the onset by five years or by effecting a five-year "time out" in the progression of these aging-related diseases, the exponential portion of the curve would have one less doubling near the end of life. This would eliminate half of all cases of the disease and half of the attendant costs and misery. Even a brief delay can translate into dramatic savings:

- a five-year delay in the onset of Alzheimer's disease could save $50 billion dollars annually;
- a five-year delay in the onset of cardiovascular disease and stroke could save an estimated $69 billion annually;
- a five-year delay in the onset of Parkinsonism would save approximately $3 billion a year;
- a one-month delay in the onset of severe loss of independence will save $4 billion each month.

The growing consensus of the authors of the Task Force report is that postponing the diseases of aging is realistic and achievable as a prevention strategy in this decade. This goal needs to be imbedded in public policy and the areas of priority research outlined in the Task Force report should be funded immediately. To fully implement the research initiatives recommended by the Task Force, the allocation of $841 million presently mandated by the Department of Health and Human Services and by Veterans Affairs on all forms of aging research needs to grow by approximately $1.1 billion over the next five years.

America faces enormous economic and social costs if we fail to improve health and functioning in old age. Either we continue paying for the "sick care" which this rapidly approaching army of aging Baby Boomers will require, or we adopt the more humane and cost-effective option of investing in first-rate research which can help to cure, prevent or delay dysfunction in later life.

We all want to see our government fiscally responsible. We want to hold down health care costs. I am convinced that medical research holds the ultimate hope of reducing those costs and improving life quality for older persons.

The CHAIRMAN. Thank you, Doctor Besdine.
Doctor McKhann.

STATEMENT OF GUY M. McKHANN, M.D., DIRECTOR OF THE ZANVYL KRIEGER MIND/BRAIN INSTITUTE, JOHNS HOPKINS UNIVERSITY, REPRESENTING THE DANA ALLIANCE FOR BRAIN INITIATIVES, BALTIMORE, MD

Dr. MCKHANN. Thank you, Senator Cohen, for the opportunity to come here today.

I am a professor of neurology at Johns Hopkins and have been for about 25 years, but I am here today representing the Dana Alliance for Brain Initiatives. That's a group of 138 brain scientists, some of the leading scientists in the United States. Our goal is to bring to the attention of the American people the advances in brain research—what we have accomplished, what we think we can get done and, most importantly, what impact this will have, not only on the people, like we have heard earlier this morning, but also in areas of health policy—both ends of this spectrum.

We have a report that is essentially reporting on what has occurred halfway through the Decade of the Brain. I'd like to enter that into the record. It has things broken down by age periods, and it has a section on the aging brain where we talk about the accomplishments that have taken place in Alzheimer's Disease; the memory loss that's part of normal aging, Parkinson's Disease, stroke; and the problem of pain.

I'll let my colleagues on the next panel talk more specifically about some of those advances, but I would like to make just several points about that.

You people in policymaking can diddle around with the health care system all you want, but that's not the way you are going to really cut costs. You are going to cut costs by preventing these problems, coming up with better cures, and mitigating them. We are very confident that we can achieve those goals.

You, in your opening remarks, talked about Jonas Salk. Albert Sabin was a patient of mine, and I knew Jonas Salk, as well. I think it is worth going back to say: How did they create their individual polio vaccines? First they had to get that virus. Then they had to identify that there wasn't one virus, there were three. If they had never made that step, there never would have been a vaccine.

Doctor Enderis group at Harvard had to figure out how to grow that virus in a dish, and then they could alter the virus, and then they could make a vaccine. The vaccine had to be tested in animals, and finally in humans. If any one of those steps had been interrupted, we'd still be talking about how to finance more iron lungs.

That's where we are in brain research. We are really halfway down those steps. This is not the time to stop.

I would just finish with an analogy that I like to use about football. If you were the San Francisco 49ers, you spent all that time in planning, all that time in recruiting players, and you were marching down the field in the Super Bowl for the winning touchdown, you don't walk off the field when you are on the 10-yard line. That's the danger that could happen to brain research.

I would leave it again to my colleagues to talk about specific advances, but we are very confident that we can meet these goals.

Thank you.

The CHAIRMAN. Especially if you have a Joe Montana and Jerry Rice at the 10-yard line.

Dr. MCKHANN. We do.

The CHAIRMAN. You do. All right.

Doctor Avorn.

STATEMENT OF JERRY AVORN, M.D., ASSOCIATE PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL DIRECTOR, PROGRAM FOR THE ANALYSIS OF CLINICAL STRATEGIES, BRIGHAM AND WOMEN'S HOSPITAL, BOSTON, MA

Dr. AVORN. Thank you, Senator Cohen.

My name is Jerry Avorn. I'm an internist, a geriatrician, and a health services researcher. I'm an associate professor at Harvard Medical School and director of the Program for the Analysis of Clinical Strategies at the Brigham and Women's Hospital in Boston.

The main area of work of our group is to study how health care technology, including drugs and other technologies, is used in practice. In that sense my comments will be somewhat different from some of the thoughts you have heard earlier, but I think in many ways complementary to them.

What are the ways that doctors use the technologies currently available, particularly for the elderly but in all aspects of the health care system? And how might we do a better job of getting the available science that has been developed through research over the years into the hands of the practicing doctor, so that he or she can do a better job of taking care of patients? Increasingly, a better job also means a more cost-effective job.

In addition, we are concerned with learning about the outcomes of what doctors do. The Nation, for many years, has not paid as much attention as we might to the question of what shape the patient is in X months or years after we doctors make an intervention. If we are talking about providing the best and the most cost-effective care, we've got to get a handle on that, as well.

The hearings today are focusing on three main ways out of the current crisis that we are facing—and it is a crisis—in terms of both cost and access. Access is the frequently-forgotten other side of the coin of our cost problems in health care.

We have heard and will be hearing much more about basic science. I'd like to talk about two other issues, how we can apply what we know. One of them is the issue of technology transfer. How do we get the information from the lab, from the clinical trial, into the hands of the practicing doctor? The second is: How do we really know what is the best thing for the doctor to be doing?

Right now we need to admit that the technology transfer, the application of currently available knowledge, is suboptimal, at best, at the bedside. We need to do a much better job of making sure that doctors are practicing 1995 medicine and not 1985 or 1975 medicine.

We are also not doing a very good job of keeping doctors educated once they leave training, about what is the current best way of

treating problems. This is particularly true in a very rapidly moving field such as neuroscience, as well as in the care of the elderly, in which many physicians have never had even a day of formal training.

Unfortunately, it is no one's job to make sure that a given doctor is really current or is practicing the most fiscally responsible kind of care. It is not the responsibility of any group or of any entity. While we physicians are being asked to practice more cost-effective medicine, nobody is telling us how. Nobody is identifying for us what the most cost-effective choices are.

The belief—which I think is somewhat naive—is that "marketplace forces" are going to somehow get us all to be more efficient and more cutting-edge. But marketplace forces alone are not going to do that. We need to know what is the best course of treatment, what are important advances that may have come out of the laboratories or the studies that you'll be hearing about later, and we don't have that.

Let me give you two brief examples from some of our own research that illustrate this. They are in the area of brain disease and neuroscience at the applied level.

One is a paper that we published in the "New England Journal of Medicine" in 1992 looking at how psychoactive drugs are used in the nursing home setting. If ever there were a setting of frail, vulnerable patients collected together and receiving a great deal of medical care at great cost without much physician input, it is the nursing home.

We found, as other observers have found, that the utilization of psychoactive drugs in this setting is often haphazard, and sometimes quite inappropriate clinically from the points of view of geriatrics and psychopharmacology.

We put together an innovative program in which we sent people out from Harvard Medical School to go to the nursing homes to teach the doctors—where we could find them—and the nurses and the aides about the optimal use of these drugs. These were potent psychoactive drugs, sometimes quite useful, sometimes quite dangerous.

To summarize our findings in just a few words, we discovered that this kind of educational outreach could dramatically improve the intelligence of the use of those drugs, just by educating doctors, nurses, and aides about what the right thing to do was.

We also found that when we un-over-medicated—if there is such a word—the elderly patients in these settings simply by teaching their doctors and nurses how not to over-sedate people and use these drugs more intelligently, in this randomized control trial the patients in the experimental homes experienced an improvement in their memory this was not because we had discovered the cure to Alzheimer's—you'll hear about that in the next panel—but because we managed to get doctors to not over-tranquilize patients. As if by magic, they began to function more normally.

This is not an astonishing breakthrough from the point of view of basic science, but it is critically important to those patients who could remember things who couldn't remember them before.

I often think that if I had discovered a drug that could do that and was able to go public with a company to produce it, we would

be able to make it onto the New York Stock Exchange and see a tidy profit.

What we did do instead of that was just to educate people. It ended up having a very useful clinical effect, all the same.

Another example is a paper coming out from our group this month in the American Journal of Medicine. In it, we studied the rate at which older patients were being mistakenly treated for Parkinson's Disease when, in fact, what they had was a side effect of medications that had been prescribed to them, particularly major tranquilizers.

This is a particularly important problem in the elderly, and we heard very eloquently this morning about the tragedy of Parkinson's Disease. It is a major tragedy when it happens on its own, or idiopathically, as we say in medicine; it is even more tragic when what is thought to be Parkinson's Disease is, in fact, a side effect of a medication that has been prescribed to the patient for some other purpose.

We have a number of medications like that. Many of them are quite useful when used intelligently, but our research has shown that there is a two- to three-fold increase in the rate at which patients are mistakenly thought to have "come down with Parkinson's" and are given drugs like L-dopa. This is usually not effective treatment when what is being treated is a side effect of another drug.

Drug-induced Parkinson's is a condition we can fix tomorrow, unlike the idiopathic kind that Mrs. Kondracke talked about. That is going to take several more years. But it would be tragic to add to the Mrs. Kondracke's of the world people who are experiencing drug side effects mistaken for Parkinson's Disease.

So what can be done? One rapid and potentially very practical approach is to make better technology transfer in health care a national priority. Make it the responsibility of a number of groups. I'm not talking about the Federal Government taking this over. But I am proposing that we encourage the development of a plurality of groups whose business it would be to get information from the clinical trial, from the lab, into the hands of the practicing doctor. While we are at it, we should also make sure that what is communicated includes information about the most cost-effective as well as the most current means of treating disease.

We need to do that. Consider the example of Standard and Poor's, or Moody's, in which we have independent, free-standing, private sector groups that rate bonds, that rate companies, that essentially say, "This is a company that is solvent; this is a company that is not." We need to be doing that in multiple ways for medical treatments, as well. This could be done through medical schools, it could be done through professional societies, it could be done through free-standing companies designed for this purpose.

I'm not advocating that the Government decide what's right and what's wrong, but the Government could lubricate the process with a very modest amount of funding, perhaps through some public/private collaborations. Within a couple of years, this kind of activity could well be self-sustaining and would not be a drain on the public till, because this information is valuable. We just need a mechanism of greasing the wheels a bit.

There is one final area I don't want to omit mentioning. We need for doctors to be able to have better information on the best way to use available technologies. What is the most appropriate workup to diognose a given condition like Alzheimer's Disease? Of the dozens of drugs available to treat a given problem, which are the most appropriate and cost-effective? That is the kind of research that we must pursue to get at the root of our health care cost crisis.

The Nation is now spending about $1 trillion, as you have heard, in health care. A fair amount of the care delivered is outmoded and inappropriate. I would much rather see us contain our health care costs by getting rid of that inappropriate or wasteful care rather than by rationing or cutting budgets of the research activities you have heard about today.

The question has come up as to whether this is something we can afford. On the contrary—It would be fiscally irresponsible for the Nation to fail to do this.

Thank you.

[The prepared statement of Dr. Avorn follows:]

Harvard Medical School

Program for the Analysis
of Clinical Strategies

AN IMMEDIATE AND PRACTICAL APPROACH TO THE MEDICARE AND MEDICAID COST EMERGENCY

Testimony before the Committee on Aging
United States Senate
July, 1995

Jerry Avorn, M.D.
Associate Professor of Medicine, Harvard Medical School
Director, Program for the Analysis of Clinical Strategies
Brigham and Women's Hospital
Boston, MA

Research currently underway at the NIH and in university laboratories holds the key to generating enormous long-term savings to Medicaid and Medicare. *But more immediate savings -- achievable within 1-3 years -- could be realized through consistently appropriate utilization of currently-available therapies. To achieve this, we must be able to disseminate current, cost-effective treatment information to practicing physicians as efficiently as possible.* Today, this "technology transfer" is spotty at best, with much current practice driven by less-than-current data, personal bias, anecdotal experience and the promotional efforts of vendors. A very high proportion of physicians do not have easy access to the information that could guide them to the most efficient and up-to-date diagnostic or therapeutic interventions in a wide variety of clinical areas.

Part of the problem has been that neither the public or private sector has been responsible for making new information available to clinicians on an ongoing basis, once a doctor's training is completed. In general, no meaningful competency requirements exist for either medical license renewal or reimbursement by insurers. *Enabling practitioners to get access to the best treatment information would be one of the most painless routes to controlling health care expenditures.*

One type of information-sharing system already documented to be effective is "*academic detailing*," in which outreach educators meet with physicians and offer information on managing a variety of clinical problems (much as drug company representatives do every day to increase sales of their products). Formal cost-benefit analysis of such programs has demonstrated savings amounting to twice the administrative costs.

We are now proposing a more technology-based solution to the problem of disseminating information to physicians at low cost and great speed. This would entail delivery of targeted information on cost-effective care which would be *updated on a regular basis*, made available on diskette or through an on-line service, as well as in hard copy. Such a program would focus on recent clinically relevant findings and on cost-effective care; its content would be generated and updated by committees of academics and practitioners independent of commercial interests and working outside the sphere of any governmental agency, to avoid the appearance of creating a massive "Federal Cookbook of Medicine."

The appropriate federal role in launching such a program would be two-fold. First, the government could *inject seed money* necessary to encourage development of this decision-support data by private-sector groups. (Within a year or two, the marketplace will insure that the best of such programs prevail and become self-supporting.) Federal support in the initial stages would insure that the program, and its resulting savings, would become a reality much sooner than would otherwise be possible.

The second role for the federal government would be to *provide incentives for physicians* to utilize the program. These might include revenue-neutral differential payment rates for participants, or encouraging malpractice insurers to offer such doctors lower premium rates.

Although small-scale computer-based projects of this type have been initiated in several hospitals and universities, development of a broad-based effort such as this has been hampered by two factors. Until now, physicians have had little incentive to practice medicine on the basis of cost-effectiveness. Secondly, powerful personal computers as well as a variety of software and on-line technology have never been as widespread, user-friendly, or inexpensive as at present.

It is not enough in 1995 to tell physicians we must change our practice patterns to reduce health costs. To do this, we must have access to the best available clinical information on effectiveness as well as cost. In the absence of such knowledge, forcing doctors to utilize less health care resources is likely to result in rationing, shortcuts, and worse outcomes...much of which would prove more costly. Cost-consciousness is not adequately addressed in medical schools, and is too rarely discussed in the research literature. We are proposing a tool that can make cutting edge information on diagnostic and therapeutic advances, as well as cost-effective decisionmaking, available to every physician, throughout his or her career and regardless of geographic location, resulting in less "trial and error" medicine, less duplication of effort, fewer adverse effects, hospitalizations, and preventable disability. Not only is the potential for savings apparent, but the positive impact on quality of care could be considerable.

The final piece of the puzzle lies in promoting the kind of *outcomes research* that will allow us to evaluate common treatments in order to determine which therapies are truly the "best buys" for our patients. The FDA requires only that new drugs or devices demonstrate better efficacy not how they compare to existing therapies, and explicitly rejects cost-effectiveness as a standard of evaluation. If we are serious about reducing costs while maintaining a high standard of care, basic research must be augmented by comparative studies to discover which of several ways of managing common clinical problems are the best *and* the most cost-effective over the long-term.

The CHAIRMAN. Thank you, Doctor.
Doctor Goldberg.

STATEMENT OF ROBERT M. GOLDBERG, SENIOR RESEARCH FELLOW, GORDON PUBLIC POLICY CENTER, BRANDEIS UNIVERSITY, WALTHAM, MA

Mr. GOLDBERG. Thank you, Mr. Chairman.

Just to follow on Senator Burns' comment, I would agree that they should take the mask off of football. When I played football in high school in college I started out at 6 feet, 7 inches. You can see the results of the increasingly more rigorous play. [Laughter.]

Mr. Chairman, I'm sort of a lone wolf in the policy community because most of my colleagues go around the country saying that medical progress is the source of, not the solution to, rising health care costs. It is easy to see why. We have all these anecdotes of the 90-year-old person hooked up to monitors and tubes going through a bypass. Those are examples of, "Gee, maybe we should just sort of draw a line at a certain end of life."

It is true in some cases new technologies do add to costs. In other cases, new drugs—such as new drugs for AIDS or cystic fibrosis—allow people to live longer instead of dying earlier and more cheaply.

But I believe in this case we should apply a Marxist principle—not Karl Marx but Groucho Marks—and that is: who do you believe, me or your eyes? I think, after looking at the analysis, my feeling is that if you look at the mix and incidence of serious diseases today as opposed to yesterday, treating yesterday's diseases, as Doctor McKhann mentioned, in today's dollars would be enormously expensive. From that perspective, medical progress has allowed us to avoid some of the most expensive and costliest forms of care.

We are concerned about the 33 million people and more that may be dealing with long-term care costs. Imagine if 50 percent of the population had to face that prospect.

Lewis Thomas was sort of my mentor, so to speak, several months removed on this. He said the cost of treating disease is never as high as the cost of managing the same diseases without any technology or half-way technology whatsoever.

I brought here a couple of charts [1] to show that it is not just in the past—eliminating tuberculosis or eliminating polio or eliminating the hospitalization of mental illness—that allows us to save money, but even in Medicare in the last 25 years I believe the cost of medical progress has been maybe subtle but as significant.

Now, the scenario that most of my colleagues would project is you've got this huge surge of the baby boomers, of which I am one, despite my youthful appearance, and that this larger population——

The CHAIRMAN. I am not, despite my youthful appearance. [Laughter.]

Mr. GOLDBERG. Touche—and that, as this older population begins to live longer, we are going to have to have this financial Armageddon.

[1] Charts are included in Mr. Goldberg's prepared statement.

It would probably surprise you if I told you that the rate of increase in Medicare spending was slowest in the decade where the elderly population was increasing the fastest in this century. Let me just take you through this.

Between 1960 and 1970, the number of elderly as a percent of the population rose by 6 percent. During that time, per capita Medicare costs, adjusted for inflation, went up 9 percent a year.

Between 1970 and 1980, the elderly population increased 15 percent, but the Medicare inflation adjusted spending per person went up only about 4 percent a year.

I have a little chart here to show you the power of medical progress in controlling health care costs. These will be on display after this hearing, obviously.

You can see here that—this is 1970 to 1982. Then I picked 1983 to 1994, because that's when the prospective payment system took effect. You can see the mushrooming costs under the command and control structure, where as here the increase without the significant controls were slight. That's not to dismiss PPS as a form of cost control, but to suggest that the more powerful tool is really medical progress. I'll tell you why.

As people have said before, people don't get sick as much and they don't die as much. Here is what has happened over the last 30 years to death rates among people 65 and over. In all diseases—heart disease, and one of the most important brain diseases, stroke—65 percent decline since 1960. That's also a good marker for the fact that there are fewer people having that disease, going to the hospital, and then going to nursing homes.

We have never scored that savings, so we always sort of either take it for granted or talk about it anecdotally. What I'm trying to do is, in my research, quantify it.

What does that mean for the future? What it means for the future is—as you can see here, I just took hospital costs. The per patient hospital cost for elderly for selected diseases—heart disease, brain disease, and cancer—you see that brain disease, because of the length of stay involved—and this is just hospital cost, not long-care cost—is the most expensive for hospital cost, which is Medicare cost, of any disease.

So, in terms of prioritizing our efforts to control costs now and in the future, I think that brain disease is a place where we can have a tremendous effect on the bottom line.

As Doctor Avorn, who is probably too modest—he is really a pioneer in this stuff. We don't have to wait for breakthroughs to control costs. If we move medicine in the information age, we can do things like find out, for example, that we can save billions of dollars treating people with new anticoagulants for stroke. We find that only 2 percent of Medicare patients that suffer from schizophrenia receive clozapine, which we know saves $23,000 per patient annually for hospital costs.

There are estimates—conservative estimates—that 10 to 50 percent of people who are treatment-resistant should be on this drug. Why is only 2 percent of all Medicare patients on it? I don't know the answer, but it is something we should pursue.

There are other examples of what I would call clinical practice improvements—just doing it better, doing is smarter—because quality care doesn't cost more. It usually costs less.

Medicine is the only industry I know where doing it right the first time is not the guiding principle of those people that are controlling the bucks in the system. Medicare has got to get on board in that respect.

Finally, I just want to say that, while clinical practice improvements will control costs in the future, the only way to control the cost of these diseases is to control disease, itself.

As you see, it is no coincidence that there has been a rising tide of progress over the last half century. This is a very young industry. This is one of the youngest professions that we have—medical progress. When you look at this chart here to see all the things that are coming down the pike, you have to—I cannot help but feel very optimistic that if we just stay the course, investing smartly in clinical practices now and in future breakthroughs in the future, we are going to come back here 5 to 10 years from now. I may not be as youthful-looking as I am today, but I think I'll be able to say quite happily that I told you so.

Thank you very much.

[The prepared statement of Mr. Goldberg follows:]

Testimony of Robert M. Goldberg, Ph.D.
Senior Research Fellow, Gordon Public Policy Center,
Brandeis University
Before the Senate Special Committee on Aging
June 27, 1995

Mr. Chairman, thank you for the opportunity to testify today. My name is Dr. Robert Goldberg and I am Senior Research Fellow at the Gordon Public Policy Center at Brandeis University. As I have discussed with your staff, I am working on a report that examines the total cost of mental illness to Medicare and Medicaid and identifies clinical practices and biomedical innovations that could reduce future expenditures. When that report is complete, I would be more than happy to discuss the findings with you. Today I would like to discuss some of my preliminary observations about the role of medical progress as a cost containment tool.

Mr. Chairman, most policy analysts believe that medical progress is the source of, not the solution to, rising health care costs. It is easy to see why. Relative to doing nothing, innovations such as noninvasive imaging, invasive cardiology, transplants, kidney dialysis make up a larger and larger part of health care costs. And it it is true that in some cases new technologies or procedures turn out to be useless or overused. In other cases – such as AIDS – new treatments keep people alive and in hospitals who would have died quickly and less expensively than before.

But the more accurate way of evaluating the cost-benefit of medical progress is to see whether the mix and incidence of serious diseases, as well as the methods by which we treat them today, is less expensive than treating yesterday's diseases in today's dollars. From that perspective, medical progress has allowed us to avoid a significant amount of the most expensive forms of care such as nursing homes, hospitals and rehabilitation. In the main, there are few diseases for which medicine possesses the outright capacity to prevent or cure where the cost of the technology used is itself a major problem. As Lewis Thomas, the late medical writer and physician once noted: "The cost is never as high as the cost of managed the same diseases with no technology or halfway technology."[1]

Prior to the introduction of antibiotics and vaccines, treatment for infectious diseases consisted largely of keeping people comfortable until they died or recovered. The cost of managing If polio, tuberculosis, mental illness and heart disease by the best methods of 1955 or even 1965 would be astounding. It would require the most demanding kind of nursing care, with the obsessive concern for details of diet that characterized the therapy of that time, the daily monitoring, surgical intervention." Most of us cannot remember that in the 1950's expensive plans were being made for new and expensive installations for the surgical removal of infected lung tissue before streptomycin came along and the hospitals themselves were closed up.[2] Hospital care for TB alone would cost $25 billion a year. The cost of hospitalizing people with all forms of mental illness could be equally as expensive. And the expense of care for thousands of polio-stricken children, with iron lungs would run into the billions as well.

In the past 25 years, the cost-benefit of medical progress has been more subtle but equally as significant. We would expect Medicare costs to skyrocket if the elderly population increased rapidly and if seniors suddenly began to live longer. Yet, the rate of Medicare growth was slowest precisely during the decade that the elderly population was growing larger and older than at any other time in this century.

Between 1960-1970 the number of elderly as a percent of the population rose 6 percent. During the same time period, Medicare costs increased about 9% per cent a year after inflation. Between 1970-80 the elderly population increased nearly 15 percent between 1970-1980. Medicare enrollment jumped 40 percent, the fastest ever. Yet, per capita inflation-adjusted Medicare spending went up by only 4.34 percent a year during that time period. And between 1983 and 1994, per capita inflation adjusted Medicare spending went up about 5.5 percent, higher than the previous decade but still slower than at the program's start. [3]

The credit for the relatively slower rate of growth goes not to government control of entitlements but medical control of disease and disability. Since 1960 there has been a 50 percent decline in the incidence of death due to heart disease and a 65 percent decline in the incidence of death due to stroke. Morbidity -- measured in terms of quality of life years lost -- from liver and kidney, disease also declined by up to 100 percent.[4] Since, 1981, the average number of medical conditions per person per year for people aged 65 and over dropped has dropped by 11 percent, which means more elderly are remaining independent and healthy for longer periods of time.[5]

Hence, the cause of rising Medicare costs is disease and today, the most expensive diseases -- schizophrenia, Alzheimer's and other brain disease in particular -- are the one's we are still unable to do a lot about. The average hospital cost of brain disease is nearly twice that of heart disease and cancer. As a result, brain diseases compound the difficultly of dealing with other ailments and themselves contribute to longer hospital stays, intense constant monitoring at home, a large number of readmissions to the hospital and long term care.

But we don't have to wait for the next biomedical breakthrough to control costs. First, we must move medicine into the Information Age. There is a growing body of research -- much of it done in treating mental illness -- that shows that using information technology to define what does and does not work in medicine, improves the quality of care how it is provided. And in turn, this patient-centered approach reduces the large variations in medical practice that are at the heart of wasteful spending. This technology for controlling -- called clinical practice improvement will also insure that the goal in using future innovation is not newness for newness sake but increasingly superior care for every patient. For example:

- Stroke can be prevented by better control of hypertension. Nearly 650,000 elderly are hospitalized due to strokes each year at a hospital cost of $7 billion each year.[6] More consistent use of new anticoagulants and aspirin can reduce the rate of incidence of stroke by between 25%-64%.

- Currently only 2 percent of Medicare patients suffering from schizophrenia receive clozapine. At present, clozapine maintenance treatment for schizophrenia saves an average of $23,000 per patient annually, for an annual total savings of approximately $1.4 billion for the estimated 60,000 patients receiving clozapine.[7] Since up to 50 percent percent of all treatment resistant schizophrenics should be receiving clozapine, a program that evaluates Medicare use of clozapine could be used to improve patient care and reduce costs.

- Treatment of pressure ulcers (or infected bed sores) for people with spinal cord injury is a major expense in hospitals. Improvements in clinical practice have eliminated the reliance on expensive equipment require to prevent the formation of such ulcers and promote their healing. Hospitals using these clinical practice improvements have saved $250,000 a year. If every hospital adopted these pressure ulcer protocols, over $250 million a year could be saved.[8]

- A program designed to detect and treat reversible delirium, depression and other mental disorders in elderly patients hospitalized with hip fractures reduce their average hospital stays by 2 days and produced savings of five to eight times the extra cost of their psychiatric evaluation and treatment. Elderly patients admitted to the hospital for other physical ailments could also benefit from such programs, leading to similar cost reductions.[9]

- Improved preventive treatment of post operative wound infections reduced the number of infections by 400 percent, saving $14,000 for every case avoided. [10]

Clinical practice improvements could generate billions in savings in the use of current medical knowledge. Only research-based innovations will enable us us to prevent and control brain diseases and their costs. Let me conclude by briefly describing the cost-saving potential of what will scientifically achievable in the next decade.

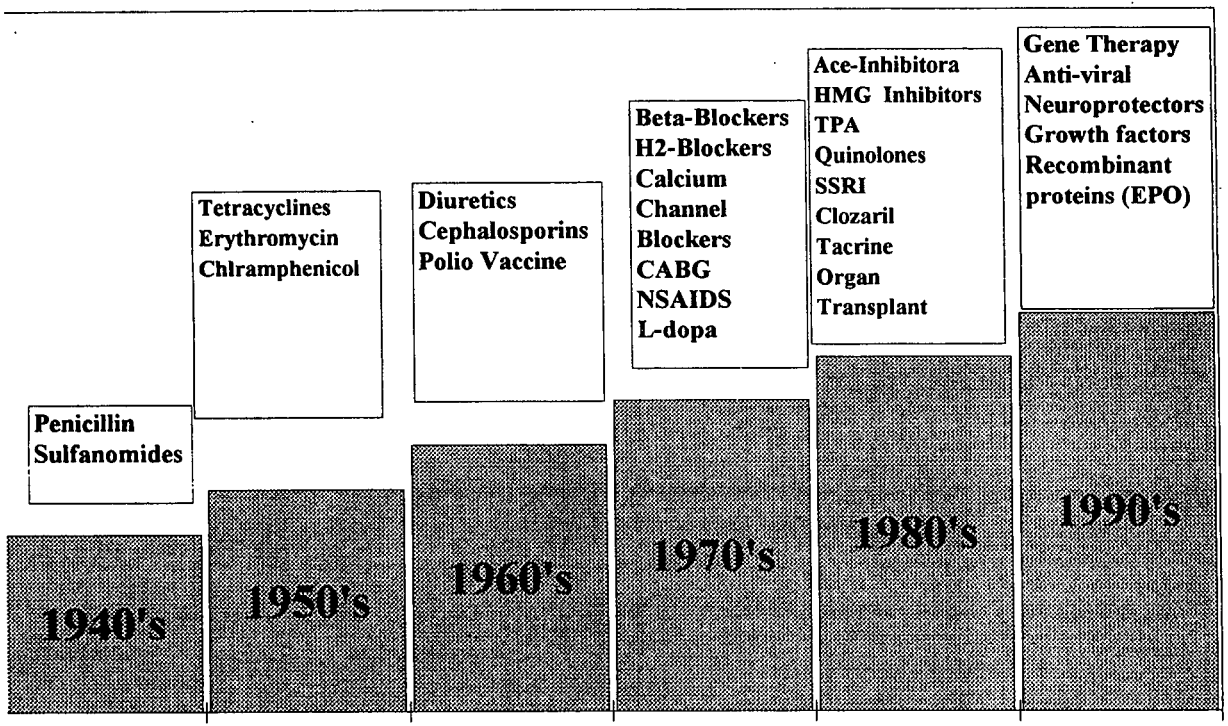
Within five years, it will be possible to delay the progress of such diseases as Alzheimer's and Parkinson, reduce the incidence of stroke and schizophrenia and cut the recovery time of people

with spinal cord injury by 20 percent. In turn, such advances will help reduce the cost of Medicare and Medicaid. For example, future treatments for spinal cord injuries could yield 10-20 percent reductions in the projected economic costs of SCI by the year 2000 and 30-40 percent reductions by the year 2005.[11] Since nearly 70 percent of all spinal cord patients are covered by Medicare or Medicaid, such advances would be a significant value to the government. And a Battelle Institute study concluded that reducing the incidence and progression of Alzheimer's alone would $40 billion in long term care costs and $20 billion in Medicare costs between now and 2010.[12,13]

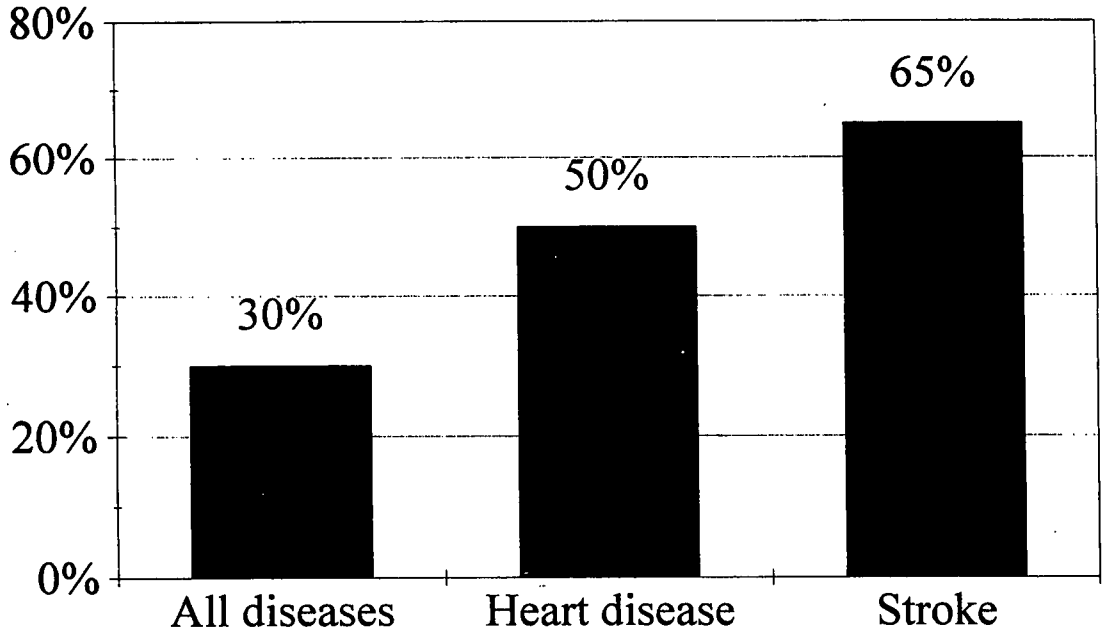
There are many other examples for how medical progress can control health care costs now and in the future. Medical progress can help us reduce the cost of Medicare without resorting to an arbitrary set of cuts and a command and control approach to medicine. Advances in treating mental illness and other brain diseases are a central part of that vision. Data is needed to both evaluate the role of medical progress in reducing Medicare costs and to develop better approaches for maximizing its cost benefit. I look forward to assisting you in any way possible in that endeavor.

1 Lewis Thomas, The Lives of a Cell.
2 Lives of a Cell page 41.
3 Per capita Medicare spending increased by 57% between 1970-1982. At the same time, Medicare enrollment increased 40 percent. In 1983 the Prospective Payment System was instituted to control Medicare spending. Yet, between 1983 and 1995 per capita Medicare spending rose 109 percent while Medicare enrollment increased by 14 percent.
4 ibid.
5 Judy Foreman, "Illness Rate Dropping for US Elderly Population." The Boston Globe, Monday, June 19, 1995.
6 National Hospital Discharge Survey: Annual Summary, 1992, National Center for Health Statistics.
7 Meltzer, et al., **American Journal of Psychiatry** 1993; 150:1630-1638.
8 Brent C. James, MD, Susan D. Horn, Ph.D., Robert A. "Management by Fact: What Is CPI and How Is It Used?." In Clinical Practice Improvement: A New Technology for Developing Cost-Effective Quality Health Care, Faulkner and Gray, New York, 1995.
9 Strain, et. al, American Journal of Psychiatry, 148, 1991, pages 1044-1049.
10 Susan Horn, Ph.D., Department of Medical Informatics, University of Utah, Personal Communication, May 1, 1995.
11 Dr. Wise Young, Ph.D., M.D., Department of Neurosurgery, New York University, Personal Communication, May 9, 1995.
12 Lewin-ICF update of Huang L., Cartwright WS and Hu T. "The Economic Cost of Senile Dementia in the United States, 1985". **Public Health Reports**, 1988; 103 (1): 3-7.Alzheimer's direct costs currently are about $21 billion a year. Most of this expense is due to hospitalization ($ 6 billion) and long term care services ($ 9 billion)
13 Brown R, Elixhauser A, Sheingold S, Luce , et al., **The Value of Pharmaceuticals: An Assessment of Future Costs For Selected Conditions**. Battelle Human Affairs Research Centers, Washington, DC, 1991, page 73.

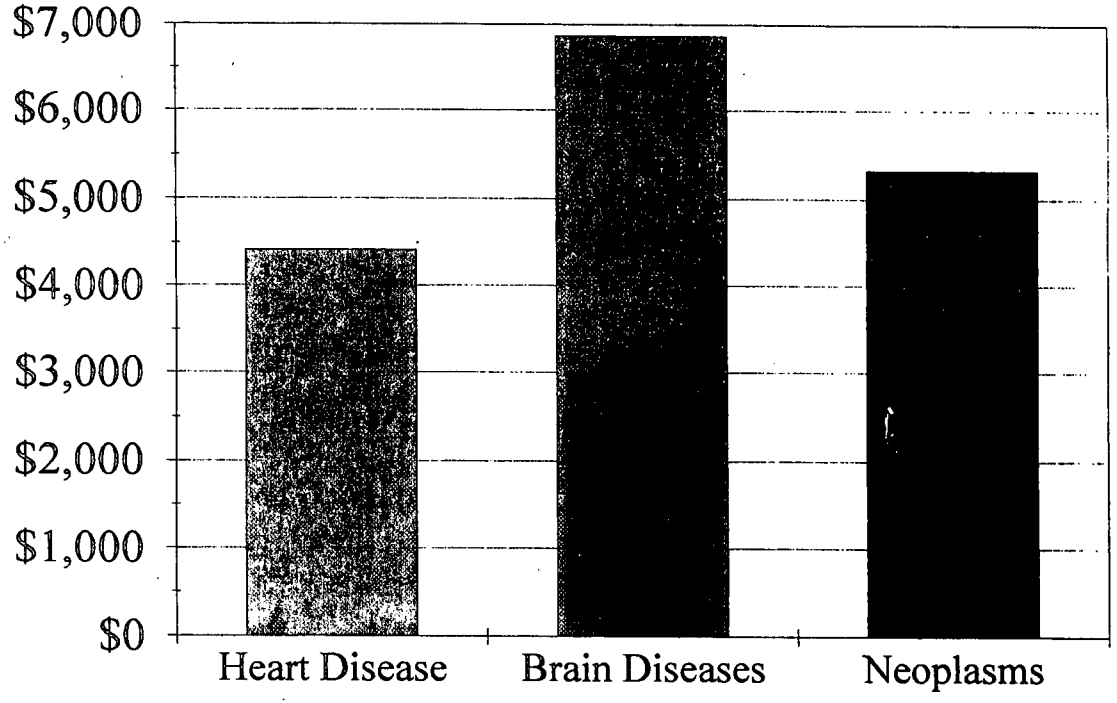
Medical Progress Past, Present, Future



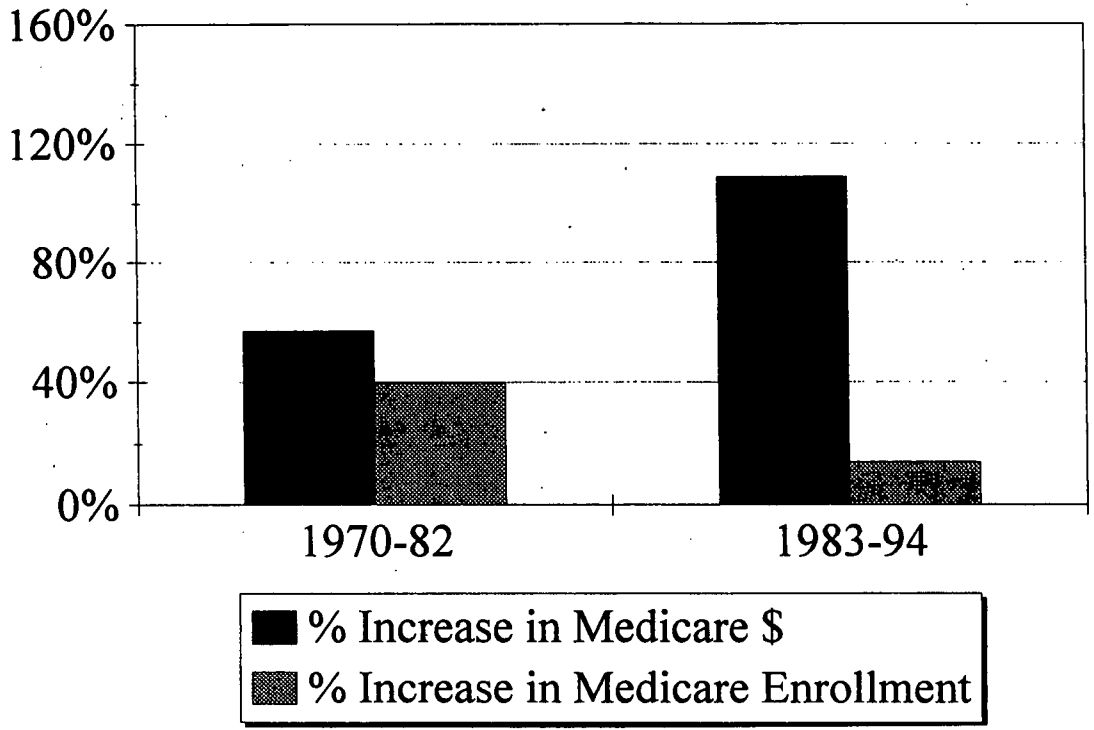
Percent Decline in Death Rates Among People 65 and Over:1960-90



Estimated Hospital Cost Per Elderly Patient For Selected Diseases



Medicare Growth Compared to Rise in Medicare Enrollment



The CHAIRMAN. Thank you very much. You may want to display those flash cards of yours to the audience because that was too quick a turn for them to catch. Maybe you can set those up over there where they can see those.

Mr. GOLDBERG. All right. I'd be delighted to.

The CHAIRMAN. Gentlemen, first let me thank you for coming and say that you are practically pushing on an open door up here. I have been on the Aging Committee since it was originally conceived in the House in 1975. There was an Aging Committee in the Senate long before that in which there was very important work done by Senator Percy way back in the early 1970s.

Senator Percy was ahead of his time when he held hearings dealing with nursing homes, which he labeled as "warehouses for the dying" because they were simply putting people in nursing homes and keeping them drugged up with no real attempt at rehabilitation, or restoration of dignity and activity. Since that time a great deal of change has taken place.

Back in 1978 I introduced a measure which I thought had some real promise. It was called, as I recall, the Annual Physical Checkup Act of 1978. What I was trying to do was to encourage people to visit their physician once a year.

I have never received more negative mail since the time I served on the Judiciary Committee concerning the impeachment of Richard Nixon. The negative mail came from all sides. It came from doctors who said, "Wait a minute. An annual physical checkup? It is not like sending your car in here where we are going to go through a checklist and change the oil or look for spark plugs and other types of things each time in order to diagnose what might be wrong."

I had many constituents who also wrote in and said, "This is a giveaway to the doctors. You're just trying to get us to go to those doctors more often than we currently do. They thought it was a ripoff from both sides. The bill died a very quiet death very early in 1978.

I was not deterred. In 1981 I introduced another measure called the Wellness Act of 1981. I was convinced that we have to do more to take better care of ourselves, that we bring a lot of the medical problems onto ourselves by overeating, smoking too much, eating too much, drinking too much, not exercising enough, and then, of course, getting sick, going to hospitals, and incurring huge costs in order to get us back on the right track.

I felt there were things we could and should do to take better care of ourselves, because if we continued on the path of simply gorging ourselves or feeding our appetites without regard to the consequences, there was no health care system in this country or elsewhere that could afford the problems that we were generating.

The answer was—and what I wanted to do was to give a tax incentive to companies to institute wellness programs at their place of employment, and the notion, of course, was if you institute programs such as encouraging nonsmoking, if you have perhaps either workout equipment and facilities on your premises or give memberships to health clubs, that you might thereby encourage people to engage in much healthier practices. You would reduce absenteeism. Hopefully you would reduce alcoholism. You would reduce the level

of smoking. You would have a much more productive work force, which would benefit everyone. You'd have a better product, a better work force. You'd have lower insurance costs because the insurance company wouldn't be paying as much, and on and on.

Of course, the answer was if it was such a great idea then the private sector will take care of it, so that went nowhere.

So here we are now in 1995, and we have seen some progress as a result of education, as a result of programs we have seen in the private sector—not any at the Federal level that I am aware of.

Doctor McKhann, I think you used the word "you can gild around the medical system all you want." Is that the phrase that I picked up?

Dr. MCKHANN. I think I said "diddle."

The CHAIRMAN. Diddle? All right. Thank you for that clarification.

But ultimately it comes back to those in the profession who are going to provide the kind of relief that we are all looking for.

Wellness will only carry us so far. We do have an obligation to take better care of ourselves. A lot of it has to do with the level of poverty in our society. I find in my own State that in the more impoverished areas you have less wellness habits. You have the eating of a lot of starchy foods, a lot of rich foods, a lot of sweet foods, a lot of drinking of alcohol. The more progress you see in the way of economic ability, the more you see people adopting different habits. I think perhaps this is true in many other States, as well.

But that doesn't deal with the genetic problems we've been discussing today, and surely that doesn't deal with the traumatic injuries that Mr. Ullian was also talking about today. It seems to me that all of you really have zeroed in on the basic problem.

I don't know, Doctor McKhann, if we are at the 10-yard line or the 40-yard line, or if there is any real consensus on that within the medical community. But it seems to me that we have made enormous progress in the last few years. Frankly, I have been astonished to find there was an agreement within the medical community, for example, to say that we are going to reach some kind of a consensus here, we're going to develop a consensus within the medical community. That's not easy to do. I was interested in how that was brought about.

Dr. MCKHANN. I think it has taken time. It has taken the time to recognize each other's progress because people are compartmentalized in their work. I think one of the things that the Dana Alliance has been able to do is break down some of these barriers between, for example, neurologists and psychiatrists, and realize we are all working on the brain. We're all trying to figure out how the brain works and what can go wrong with it. That has been a big step in being able to forge this kind of consensus.

The CHAIRMAN. As I look at that chart, it is almost a medical version of the Contract With America, right? You have 130 of the top people and organizations in the country saying we have a time frame that we are going to try to meet. We are halfway there, or 90 percent there—whatever it is—but we are going to reach that particular goal.

I think it is truly a credit within the neurological community, as such, to try to put aside differences and say , "We have a goal to achieve."

There was one question I had for all of you, and that is: The American Medical Association recently issued a rather scathing report condemning the increasingly popular practice of patenting new surgical procedures and medical procedures, saying that it was unethical, it would severely inhibit medical progress.

Doctor Besdine, do you have——

Dr. BESDINE. Yes. I just noticed that last week. I don't know more about it than you do, other than having read about it. I think it was in the "New York Times."

My take on that is that they are exactly right. Any ownership and patenting, and therefore restriction of application of new medical technologies will delay use and increase costs for patents. We think of medical technology as multimillion-dollar machines, but ways to tie surgical knots and approaches to parts of the anatomy have now been included, that going far beyond what patent laws were designed to protect. The result will reduce availability of these innovations, most of which are ultimately Government-funded at least in the R&D phase, and restrain their application to the population.

The CHAIRMAN. My understanding is there are some 80 countries which prohibit such patenting activities, including Great Britain, France, Japan, and others. The question is: Should Congress diddle around—if I can use that expression—by saying you can't do it and we are going to prohibit that because it is going to impede medical progress?

What do you think, Doctor McKhann?

Dr. MCKHANN. I think that almost every innovation is based on previous information. Very seldom does something come out of the blue. Just because someone says, "I did this little part of it. I have an exclusive right to that," I think is absolutely wrong. I feel very strongly that the AMA is right in this act, and I think Congress probably will have to take some action.

Dr. AVORN. The rationale that is sometimes offered for patenting either procedures or devices or drugs is that this is how you generate the capital to fund the research. That brings us back to what we are talking about today.

If the capital to pay for the research comes out of the public sector, then it really is something that belongs to the public in that case, the researcher doesn't have to worry about having a lock on the product to get the capital to do the work.

The CHAIRMAN. So basically you wouldn't confine it, then? If Congress is providing funding in whole or part, then obviously the public has an interest, and in those circumstances you would advocate we prevent patenting?

Dr. AVORN. Right. But the bargain that Congress has to hold to is to keep the flow of capital available so that there will be the next set of innovations.

The CHAIRMAN. Doctor Goldberg.

Mr. GOLDBERG. I would take slight exception to that, because I think the experience with the reasonable pricing clause showed that trying to regulate the nature of the intellectual property can

sometimes have a stifling effect on innovation. But there is one way to make—and I think there is a legal difference between inventing new technologies and improving upon a better mousetrap, so to speak. There is one way to flesh these people out, and that is to let him submit his new surgical procedure to the FDA for clinical efficacy, and I'm sure he will be more than happy to withdraw his patent because anyone who has to—anything that is new medically that has to be defined as "safe and efficacious" costs a lot of money, and I don't think an individual surgeon is going to want to put up with that.

The CHAIRMAN. I have a couple of quick questions. One of the problems we have is, as I mentioned before, about scoring something. You have discrepancies within the medical community, as such, in terms of how much is spent and how much will be saved. The Dana Alliance, for example, says that Alzheimer's Disease costs more than $60 billion a year. The Alzheimer's Disease Association says it costs $100 billion a year. How do we——

Dr. BESDINE. I think 100 is more than 60.

The CHAIRMAN. So 100 is more than 60? Is there any real need to try to get a fix on the savings, or is that something that's not quantifiable? Is this something we should just understand is a general proposition—if you invest the money, you are going to save a great deal more—without trying to be too specific about it?

Dr. MCKHANN. I think it depends upon what you count. The $60 billion is a very strictly accounted cost of care figure. The $100 billion is the cost not only of medical care, but of custodial loss of productivity, family time, diseases and caregivers. I think that the summer of 1995 figure is $100 billion for Alzheimer's.

The CHAIRMAN. Doctor McKhann.

Dr. MCKHANN. I'm just a poor country doctor from Baltimore. You're talking about big money. I would think of it more as a denominator. The point is that the amount of that denominator we spend for research is way, way too small, and it doesn't make any difference whether you make it $60 billion or $100 billion. We haven't increased that numerator. That's what the real problem is.

The CHAIRMAN. What did you think of Doctor Avorn's suggestion that perhaps the Federal Government has to get involved in terms of creating some kind of a pilot program whereby you would create some incentive to have greater dissemination of medical information? Is this something the Federal Government should do, or should they leave to the private organizations?

Doctor Besdine.

Dr. BESDINE. I think we have to be cautious about what we mandate. The AHCPR clinical guidelines—that is, guidelines to physicians about how to manage some very big-ticket diseases and problems often clustering in older persons—are a good blueprint for bringing documented affective evaluation and management strategies to practitioners. Now, how far we want to go down the Government regulatory process to say that if a physician does or does not do something that is outside the guidelines that will then not be reimbursed for that episode of care, or in a capitation system will be penalized, is discussion that requires a great deal more time and expertise to join. I would be hesitant to make any decisions with the information we now have on the table.

The CHAIRMAN. Doctor McKhann.

Dr. MCKHANN. I'm concerned about central guidelines because they become too rigid and inflexible. I would like to see, in this particular area—there probably are other, more flexible ways to handle this problem. It is an education problem, really. I'm not sure that a regulation is a good way to handle an education problem.

Dr. AVORN. Let me say that I fully agree with everything that was just said by Doctor McKhann and Doctor Besdine. My written testimony indicated that the last thing we need is a Federal cookbook of medicine. I think the Federal Government should encourage outside of Government the development of recommendations and the provision of information. This is quite different from regulation, which is not at all how I think of this.

Mr. GOLDBERG. I'd like to go back to that scoring issue for a second, because I think it is possible to score it. Private companies are already doing it. They are taking a look at the cost/benefit of a mental health benefit in terms of the wages paid out, lost productivity, days off, and so on.

Ken Wells at the Rand Corporation and others have done studies that would show that you can link outcomes to process steps to productivity.

We now have the data sets and information to do it, and I think, as a matter of corporate policy, every company, including the Federal Government, should start beginning to sort of link those dollars and activities together, very definitely.

The CHAIRMAN. I'm going to have to cease my inquisition here. We have one final panel that I want to make sure gets on before too much more time passes.

I want to thank each of you for the contributions made. You have been very, very helpful. Thank you.

Our last panel of witnesses includes four of the top scientists in the field of neurology. Each of them is involved in the cutting edge research aimed at eradicating or treating brain-related disorders which plague our aging community. They are going to share with us the latest information on neurological research and discuss how far we have come in the last decade into discovering the secrets of the brain.

First, we are going to hear from Doctor Allen Roses, Jefferson Pilot Professor and Chief of Neurology at Duke University Medical Center, who is going to discuss his recent discovery of the Alzheimer's gene and his theory on how he may be able to cure the disease.

Next we will have Doctor Dennis Selkoe, professor of neurology and neuroscience at Harvard Medical School and Co-Director of the Center for Neurological Diseases at Brigham and Women's Hospital. Doctor Selkoe has also done extensive work on Alzheimer's Disease and will describe a different hypothesis about the disease and why he believes we'll soon be able to produce drugs to slow or block the progression of Alzheimer's Disease.

Our next panelist is Doctor Ole Isacson, director of the Neurogeneration Laboratory at McLean Hospital and associate professor in the Program of Neuroscience at Harvard Medical School. He is currently leading a research team that is involved in a very

promising surgical procedure to help patients with Parkinson's Disease gain independence.

Finally, we will hear from Doctor Dennis Choi, the Jones Professor and Head of Neurology at Washington University School of Medicine, who will describe some of the recent breakthroughs in treating and preventing brain damage, and his current work on rendering the brain resistant to stroke.

We are extremely honored to have each of you with us today. We understand how much time this is taking from your own very important medical professions. Your effort to help the Committee understand this problem is going to be very, very valuable indeed.

Why don't we begin? Doctor Roses, perhaps you could begin the testimony.

STATEMENT OF ALLEN D. ROSES, M.D., JEFFERSON PILOT PROFESSOR OF NEUROBIOLOGY AND NEUROLOGY, CHIEF OF NEUROLOGY, DUKE UNIVERSITY MEDICAL CENTER, DURHAM, NC

Dr. ROSES. Thank you, Mr. Chairman.

I also represent the Medical and Scientific Advisory Board of the Alzheimer's Association. I have been chairman of the Wakeman Award Committee for Research and the Recovery of Spinal Cord Injury. And I'm currently involved in genetic studies in both Parkinson's Disease and ALS.

My friends say I do too many things, so what I'm going to do today is just talk about Alzheimer's Disease. But some of the things I have to say about Alzheimer's Disease applies to these other diseases, and you can judge for yourself what yard line we are at.

I am going to discard what I thought I was going to say because most of the numbers have been given, and basically bring you up to date on where we are in the genetics of Alzheimer's Disease.

Alzheimer's Disease of late onset, which constitutes more than 90 percent of the people with Alzheimer's Disease, is the first prevalent, common disease to have the susceptibility genes for it defined by positional cloning or reverse genetics. The methods that have been used for Alzheimer's Disease are now proposed to be used for many other late onset diseases, not just neurological, as we have been doing in our laboratory, but for diabetes, osteoarthritis, nonlipid heart disease, hypertension, glaucoma, cataracts.

The genetic susceptibility to all of these diseases as a function of age is now being recognized, and Alzheimer's Disease is now a model for molecular gerontology.

Now, where are we in terms of score-keeping and inflation? Tomorrow there will be inflation. At 6 tomorrow an embargo will be lifted to talk about a new gene that is the major gene for early onset Alzheimer's Disease. On Thursday it will be published in the journal Nature. With that gene, the APOE gene, the APP gene, we cover the genetic field of Alzheimer's Disease by about 95 percent of the prevalent cases.

This country has glorified the search for the gene. I can tell you the name of that gene will be S–182, and you now know as much about it as you did before I told you.

It isn't the finding of the gene that is the end point. And it isn't the tools of the genome project that are the end points. The important activity is what we do with those genes with the knowledge of what is relevant to the pathogenesis of the diseases. Much of this work is nonglorious, labor-intensive, and argumentative—in the best sense of argumentative, with scientists disagreeing on hypotheses—to get to what produces the disease and at what steps can it be interdicted.

I frequently get asked by the press: How does it feel to have led the group that found the Alzheimer's gene? It doesn't feel any differently than it did before. What we need to be glorifying is getting the mechanisms of the disease and getting the drugs, procedures, or other initiatives that will stop these diseases.

I don't need to go into what the inflation is on a year-by-year basis in terms of the numbers of dollars available. What has happened in science, and particularly in neurological disease, is that we have had a tremendous explosion in the inflation of the knowledge base. We do not have the resources to take it to the next steps because what is invested in research that has been done is there. What is coming and what we should do after tomorrow, for instance, after this new gene is published—there is no new money or insufficient new money to be able to take it further.

We have the tools. We are on these yard lines, and we are racing down. If you want to keep score—you started the hearings, Mr. Chairman, talking about polio. We all know what the cost now would be if we had iron lungs for all our children. I look at these dire predictions for Alzheimer's Disease as a doubling of the number of people with Alzheimer's Disease every 20 years. In another 40 years we will have 16 million people.

There are going to be two types of people in this world when my children and my grandchildren and I get to the age of risk for Alzheimer's Disease. They are not going to be Republicans and Democrats. They are going to be people with Alzheimer's Disease and the rest of us taking care of them.

This is a multi-multi-billion dollar problem that exceeds our ability to keep score. The terror of it is that we are leading the pack in Alzheimer's Disease now, not following. We are at the point where we can make major, major contributions and the spigot of support has run dry. Unless that is changed, the scorekeeping is all in the negative.

The beginning of this inflation is underway now in Parkinson's Disease. The beginning of this inflation of knowledge is underway in a whole wealth of neurological diseases, including stroke. It won't be very, very long before the demands will be made for progress in that area.

I just brought one chart with me. Basically, it is the APOE genotypes of 99.5 percent of the people in the population. What you see there in the different color lines are the age of onset of Alzheimer's Disease as a function of your genotype. Of the people in this room and in this country, 30 percent have at least one APOE–4 genotype.

If you have the best genotype, 2–3, by the time you are 140 years of age you will get Alzheimer's Disease.

We are all moving toward Alzheimer's Disease, but at different rates. One of the things that the pharmaceutical industry can do superbly, if it is given the right targets, is to change the rate so that we push the age of the people at risk, particularly the people who will develop it earlier, to the later forms. We delay the onset by up to 20 years.

So if you want to do month-by-month accounting, that's one thing, but the science today promises that we can delay the onset of Alzheimer's Disease by 10 to 20 years, not 1 or 2 months.

Thank you.

[The prepared statement of Dr. Roses follows:]

Prepared statement of:

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ON THE RELATIONSHIP BETWEEN GENE IDENTIFICATION AND DISEASE MECHANISMS

The construction of detailed maps of the human genome proceeds at a bewildering pace with the daily addition of details of gene location and sequence. The discovery and linkage of previously unknown, novel disease genes using positional cloning strategies has become almost commonplace. During the course of virtually every disease-related positional cloning project, many previously identified candidate genes spawned fantastic tales of relevance, usually based on prior hypotheses or prejudices of pathogenesis. Once linkage is established, occasional candidate genes associated with known phenotypic abnormalities become immediately obvious. Candidates for diseases characterized by neurophysiological alterations such as ion transport abnormalities, like sodium channel abnormalities in the periodic paralyses and myotonias, or sodium and chloride transport functions of the cystic fibrosis gene, have been successfully identified. However, for the majority of disease genes identified by positional cloning, the excitement (measured in press releases and 15 minute sound-bites) has been the discovery itself rather than clarifification of the mechanisms of pathogenesis. The hype has been focused on the technical accomplishment of identifying the inheritable locus. The physiology and the therapeutic implications, other than the inevitable discussions of gene therapy for every disease, have lagged far behind - mostly because the financial support for research has not kept up with the inflation of new, highly relevant data. Funds to develop the leads for research in a timely manner are virtually absent.

By comparison to the glamorous and organized resources for each nation's genome project, support for investigating the morbid pathophysiology triggered by each newly identified disease gene locus has been wanting. The gene cloners have provided the tools that were successfully used by genetic epidemiologists to identify relevant genes. Investigators with experience in biochemistry, physiology, cell biology, or pharmacology are attempting to use these new molecular biology tools, except without new finacial resources to keep up with scientific inflation. In many instances, the discovery of the mutated gene was the end-point, with little or no continued inquiry into the processes leading to disease expression. In most of the gene searches in which I have personally participated, most of the successful cloning teams are trained in nucleotide technologies and have gone on to look for the next gene for the next disease.

My own research began with myotonic muscular dystrophy (DM) in 1970. In 1992, seven competing teams of gene hunters announced with much fanfare- and no fewer than six papers in Science, Nature, and Cell - that they had nabbed the defective gene that causes myotonic dystrophy, a devastating muscle wasting disease. Yet almost four years later, the number of people working on phenotypic expression of DM-related phenomena fills a cozy corner in a pub. There were more investigators as authors on any one of the gene reports than are currently working on the pathogenesis of DM. Most of the subsequently published works have been quick descriptions of the complete genomic structure or inaccurate efforts to examine gene expression. Functional studies of the myotonic dystrophy protein kinase (DMPK) gene and its relationship to disease are rare, and certainly not greeted with the "fanfare" in the learned news journals, defined by weekly press releases of "important" new discoveries. With DM, as with other diseases associated with increased variable trinucleotide repeats, the mutation may be the mode of inheritance. However, studies of the morbidity in affected tissues or cell types and the relevant metabolic pathophysiologies take longer and have little new support. Each mechanism may be quite different, so that no organized technology can take the lead in orchestrating excitement.

If one accepts that the major contributions of the genomic revolution are the discoveries of disease-relevant genetic loci, then it follows that the newly crowned genes must be the starting point for the discovery of relevant processes leading to disease. Usually missense mutations in late-onset diseases are expressed as proteins; unfortunately, studies of protein interactions are more difficult and time consuming than gene identification. The genetic locus defines relevance - and whatever pathogenic mechanism is uncovered derives from the effect of the relevant mutation or polymorphism associated with the disease.

When does a genetic trait become a disease?

There are several important insights that have become evident from the genetic riches now available. The first is the notion of time and disease. In diseases inherited as autosomal recessive traits, where both alleles are mutated, the disease is most likely to become symptomatic in the infantile or childhood years. In autosomal dominant diseases, a later age of onset distribution extends over decades, frequently observed as variable phenotypic manifestations of disease. In late-onset diseases, the genetic mutations provide no flash of insight into the symptomatology, but the mutated genes provide a relevant entry into metabolic processes that have gone wrong. The challenge for the future is to translate the pertinent genetic information into discoveries of the mechanisms of pathogenesis. It is interesting that the term applied to proteins coded by expressed genes (mRNA) is "translation." The English word for translation implies a version or interpretation, rendering, or digestion of information. This translation also directs the secondary, tertiary and quartenary structure of the proteins, providing immense diversity to potential functional interactions in many cellular sites.

It is appropriate that neurodegenerative diseases lead the way in interpreting pathogenic processes since neurologists have long had a bad reputation for categorizing diseases without effective treatments. The heterogeneity of the brain far exceeds that of any other organ and provides the landscape to observe subtle differences in protein structure providing a recognized morbid set of signs and symptoms that

differentiate a specific clinical disease. When a liver or kidney gets sick, there is little comparative cultural diversity among cell types. However, each time a defined group of neurons is preferentially affected with earlier pathology, a remarkably different clinical syndrome can be expressed. Processes affecting motor neurons produce weakness, spasticity and atrophy; basal ganglion cells, movement disorders; hippocampal cells, memory disturbances; ad infinitum.

To understand the late-onset of specific involvement of defined motor neuron subsets, for example, the processes that normally govern cell durability and their relationship to time of survival must be uncovered. The modifications, structure and functional diversity of proteins and their interactive effects on physiology over long periods of time involves a higher order of magnitude complexity than the genome project.

The Alzheimer diseases

Alzheimer disease is a devastating memory disorder that affects more than four million Americans. An individual with memory problems can be diagnosed in the clinic as having probable or possible Alzheimer disease following a series of psychological, physical and biochemical tests that rule out other causes of dementia. The disease progresses over a four to twelve year period, ending with the victim in a debilitated, vegetative state. A physician cannot make the diagnosis of definite Alzheimer disease until an autopsy is done: brains of victims become much smaller than normal, suggesting that many brain cells have died, and microscopic examination of the brain tissue reveals senile amyloid plaques and neurofibrillary tangles, two neuropathological hallmarks of the disease. The plaques are primarily composed of an insoluble, sticky substance called amyloid β-peptide; they lie near and around nerve cells of AD brains. Neurofibrillary tangles are nests of twisted protein filaments that appear initially within the nerve cells and remain as the cells wither and die.

There are three identified genes known to be associated with the clinical and neuropathological syndrome of Alzheimer disease. It is still unknown whether the mechanisms of pathogenesis leading to the different forms of the Alzheimer diseases are distinct or related. The amyloid precursor protein locus (APP, *AD1)* was the first gene to be identified with a rare form of early-onset (mean age in families of 40-60 years) Alzheimer disease. Missense mutations of this gene are found in affected members of less than twenty families in the world, but are definitely associated with the etiology of this form of Alzheimer disease. The second gene to be identified was apolipoprotein E (APOE, *AD2*) found on chromosome 19. This was the first susceptibility gene for a common disease discovered using the technology of positional cloning. As with blood types, the presence or absence of three major alleles (versions of a gene) determines the specific composition of apoE protein in the body. These expressed alleles of the APOE gene also determine the age of onset and risk for late-onset Alzheimer disease. The third locus, called S182 (*AD3*), involves missense mutations of a newly discovered gene on chromosome 14 that is the etiology, or cause, of a comparatively very early-onset Alzheimer disease. Individuals with this form of Alzheimer disease are usually symptomatic by 50 years of age. S182 codes for a protein with the predicted structure of a membrane-spanning molecule that may be similar known receptor and ion transport channel molecules. There are other families with the genes for early-onset Alzheimer disease that are coded at undiscovered loci, and there are undoubtedly other susceptibility genes for late-onset Alzheimer disease.

Alzheimer disease: etiology versus pathogenesis

Several terms should be defined briefly in order to understand where we are today in the field of Alzheimer disease. Etiology refers to the triggering causes, while pathogenesis refers to the mechanisms by which the morbid process of disease takes place. Each different gene mutation that leads to clinical Alzheimer disease is a different etiology.

In AD1, there is no doubt that missense mutations of APP are uniquely associated with early-onset Alzheimer disease in certain families. There are no cases of early-onset Alzheimer disease in these families without a missense mutation unique to that family. There are, however, several individuals with APP missense mutations who are two standard deviations older than the average age of onset in these families and who do not yet have the symptoms or signs of Alzheimer disease. It should be noted that this situation is no different than many other classical autosomal dominant diseases, for example Huntington disease, where a few individuals carry the genetic trait but do not become sick until very late in life, if at all. In late-onset diseases, especially those inherited as autosomal dominant traits, the age onset can be quite variable as can the progression of different signs and symptoms. It is of extreme importance that, in the case of missense mutations of APP, an epistatic effect of APOE alleles has already been demonstrated.

If APP mutations are the etiology of one form of Alzheimer disease, then what is the pathogenesis over the period of time until the signs and symptoms become clinically apparent? The flow of disease production is from the starting point of etiology through the pathogenesis to the end point markers of disease. Unfortunately, genetic disease-related research often gets stuck on correlations of the late-stage manifestations of disease rather than starting with the relevant genetic variation that triggered the disease. For infectious diseases in which genetic susceptibility was well-established, the environmental etiologic agent (i.e., bacteria and viruses) provided a powerful experimental tool. Without the epidemiology of polio virus epidemics, we might still be trying to explain the acute motor neuropathy by examining the end point pathology of the brain stem and spinal cord.

The etiologic effects of APP, S182, and the various APOE genotypes are on the distribution of age of onset of the Alzheimer diseases. If we view missense mutations of APP and S182, and apoE genotype-specific combinations as variable triggers for the pathogenesis, the wealth of apparently conflicting hypotheses may become less disagreeable. Some of the experimental facts may actually begin to make some sense. By analyzing the Alzheimer diseases as a function of genotype and time, two independent variables, the cascade of interacting dependent variables such as clinical symptoms, signs, laboratory test findings, and neuropathology may be pieced together without the preconception that one dependent variable is the causative agent.

Conclusion

Alzheimer disease research is poised for the development of preventative and symptomatic therapies. Tens of billions of dollars per year can be recovered from health care costs. It does not need to be an entitlement to have Alzheimer disease in old age. The exciting possibilities in Alzheimer disease cannot be carried forward to new therapies unless the basic science of the brain is also supported. This involves many laboratories, many of them new to Alzheimer disease research. Without adequate funding for new ideas, we cannot make the rapid progress necessary to present and treat Alzheimer disease.

Our political leaders can cap expenditures for Medicare and health care and only accomplish leaner care for increasing numbers of elderly. Only by preventing the diseases that chew up 50-80% of the costs can the problem be solved. Investment in Alzheimer research alone could save $100 billion per year. The basic sciences are a necessary part of support because, as detailed above, we could not predict where the genetic breakthroughs would lead.

We hear politicians talk about our grandchildren and what they will inherit. If we do not stop Alzheimer disease, we will have two types of people in this country for our grandchildren to deal with - and not Democrats or Republicans - but victims of Alzheimer disease and the armies of people who care for them.

The CHAIRMAN. Thank you, Doctor Roses.
Doctor Selkoe.

STATEMENT OF DENNIS J. SELKOE, M.D., PROFESSOR OF NEUROLOGY AND NEUROSCIENCE, HARVARD MEDICAL SCHOOL, CODIRECTOR, CENTER FOR NEUROLOGIC DISEASES, BRIGHAM AND WOMEN'S HOSPITAL, BOSTON, MA

Dr. SELKOE. Thank you, Senator Cohen. I'm delighted to be here and very grateful to you and the Committee for focusing this much attention on brain research and brain diseases.

I'll speak also, as Doctor Roses did, about Alzheimer's Disease, but it is important to say that this is one primary example of the burden of brain diseases. There are many other diseases, and I think it is admirable that you and the staff members of the panel chose not to focus only on one disease but to talk about several of them.

Alzheimer's is one that the public knows well. It is very common. Our former President, Ronald Reagan, suffers the disease now. Indeed, his public disclosure I think has been an important milestone in reducing the shame for the disease that we heard discussed by the first panel.

I would make one point about Doctor Salk. If you read his obituary closely in the "New York Times" you noticed that, just 2 or 3 years prior to the declaration that his vaccine and then ultimately the Sabin vaccine really worked, there was great gloom and doom. There was a real sense that early trials and vaccines had not worked and that there actually had been some patients who came down with the disease.

There was a sense in the medical community in 1952 or so that perhaps this kind of research wouldn't pay off. Clearly it did pay off, and we are all the beneficiaries.

I think it is an important message to make to your colleagues that there are times when it looks like things aren't working so well, and then just within months or a year or so there is major progress.

In the case of Alzheimer's Disease, that rate of progress that occurred between 1952 and 1955 with polio has been achieved, I think, between 1991 and 1995. As Doctor Roses referred to, we can't say any longer we don't know the cause of Alzheimer's. You often hear this in the press, at a cocktail party. People throw up their hands and say, "No one really has any idea what causes the disease."

We do have specific genetic factors that almost certainly are the cause of the disease in those particular families. Now comes the hard work, as Doctor Roses pointed out, of saying how these genes do their dirty work. That is something that is being addressed by scientists around the country.

There are a couple of points that I think would be helpful to you and to other members of the Committee when you make the argument that biomedical research funding should not be cut or, if it is cut at all, as Mark Hatfield addressed, only minimally.

One is that this is an enterprise that does not cost an enormous amount of money. As you know, scientists who study this disease very rarely get rich from doing this science. The actual Federal

guidelines for post-doctoral fellowships call for very low salaries in the $20,000, $30,000, and $40,000 range. So it is important to emphasize to the public and to other Members of Congress that this is an enterprise that is rather inexpensive in terms of resources, particularly in terms of human resources.

The scientists do this because they love the science. That's something that is wonderful about scientific accomplishment in America—that there are enough people who really care about this, regardless of the financial reward.

Another point is that neuroscience is probably the great frontier now in biomedical science. It might have been cancer and cardiovascular disease a few years ago, and before that infectious disease. Almost everything that you read about in science now that is really the most exciting development relates to figuring out how the brain works.

So funding more research, in general, and neuroscience research, in particular, plays to the future. This is the area that has caught the attention of the scientific community.

I also think that increased research funding is a great way to stimulate public/private partnerships. Academic scientists, such as some of the people on the panel today, discover causes for diseases and work out the mechanisms, but the actual development of drugs is done in the private sector.

If one needs to make a further hard sell about not cutting neuroscience research or biomedical research in general, one can certainly make the point to one's colleagues that here is a way of enabling entrepreneurs—biotechnology companies and pharmaceutical companies—to do much more, to make much faster progress. Without the NIH, the taxpayers' funding of basic research, biotech and pharmaceutical companies are not going to achieve near the degree of progress.

So, to me, this is really an easy sell. The scientists are very eager. The genes, in the case of Alzheimer's Disease, the cause in a large fraction of cases, have been discovered. We need to work out the mechanism of those genes. It is a relatively modest investment that also pays off in major gain for the private sector and in jobs to the private sector.

I leave you with three points. First is that this business of finding a treatment for Alzheimer's is underway. Drug screening is being done, and it is based on achievements brought about by NIH funding. There have been discoveries, such as the one we made in our lab that a particular protein in the brain builds up, and there are ways now of screening for drugs that block that protein.

So the work is well underway. Just as Doctor McKhann said, I don't know if we can say we are at the 10-yard line or the 30-yard line, but we are very far along in finding small molecules that pass the blood/brain barrier that could block one or another step in the disease.

The second is that even a partial treatment will clearly save an enormous amount of money. You have heard that many times. My own projections suggest that if we could delay by 2 or 3 years the entry into nursing homes of many of our Alzheimer's patients, we could save several tens of billions of dollars in a short term.

By delaying that nursing home entry, we're not just delaying the inevitable. Some of those patients who don't enter nursing homes will never enter them, because treatments will become more and more effective and they will be able eventually to stay at home. Perhaps in the early years of therapeutic research they will still die from the disease, but later they will die with more dignity at home. Eventually, at least some of the cases will be prevented all together.

The third major point I would close with is this recurring theme that basic research needs to be funded by the Government, because it is very early, but reduction to practice is something that comes from the private sector.

All of us who are concerned about stimulating the economy—particularly a Congress that is looking at ways to cut the budget and enhance private sector productivity would want to sign up not for a decrease but actually for a modest increase in biomedical research.

The only thing that I heard today that really concerned me was Senator Hatfield's own statement that perhaps compromise would be reached that would reduce the NIH budget by 1 percent the first year and 3 percent in successive years in the next 5. Of course, that isn't, in my view, the right direction to move the NIH budget. It may be the kind of compromise that is necessary in the current political climate, but I would still encourage you and your colleagues to consider not a reduction but at least a level funding or modest increase in NIH spending.

[The prepared statement of Dr. Selkoe follows:]

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"Breakthroughs in Brain Research:
A National Strategy to Save Billions in Health Care Costs"
Senate Special Committee on Aging
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Alzheimer's Disease: The Economic Benefits of a Breakthrough

Dennis J. Selkoe, M.D.

Professor of Neurology and Neuroscience
Harvard Medical School and
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Alzheimer's disease is the most common cause of senile dementia (age-related mental failure) in the United States. It has an estimated prevalence of approximately 600-900 persons per 100,000 population, and its prevalence is steadily rising with increasing longevity of the population. The disease is rare prior to the age of 60 and is infrequent prior to the age of 70. However, its incidence (number of new cases per 100,000 population) rises sharply with increasing age, so that many patients come to medical attention with initial AD symptoms between the ages of 70 and 85. As there is no leveling off of the incidence very late in life, new cases of Alzheimer's disease continue to be diagnosed from the population that survives beyond age 85. It is estimated that approximately 3-4 million Americans are suffering with the symptoms of Alzheimer's disease at this time.

Biomedical research has made major progress during the last 5 years in understanding the causes and fundamental mechanism of Alzheimer's disease (AD). The causes relate to specific genetic factors that markedly increase the likelihood of getting AD. Because the three different genes implicated to date in AD (additional genes are likely to be identified in the future) all appear to work via a common mechanism (build up of amyloid plaques and widespread secondary neuronal damage), it is likely that drugs which interfere with this common "cascade" in one genetic form of AD will also have some benefit for other genetic forms. The goal of current therapeutically oriented research on AD is not a, "miracle drug" that would cure the disease, but rather to identify a number of drugs that will slow one or another step in this cascade. Ultimately, there will likely be numerous drugs to treat different stages and features of AD, rather than just one or a few drugs. The situation is analogous to the treatment of other chronic, common age-related pathologies, such as atherosclerotic cardiovascular disease and hypertension.

If research on drug discovery for AD were significantly accelerated, it is highly probable that drugs that slow the progress of the pathological cascade or, in some patients, fully inhibit it would be found much sooner than if we continue research at the current pace. The discovery of one or several drugs that would slow the AD process would mean that patients would be able to live at home longer before requiring the services of a nursing home or similar facility. Currently, the large majority of AD patients end up in nursing homes, because the requirements for their daily care are so intensive. Indeed, it is estimated that perhaps as many as 50% of America's nursing home residents have AD.

With the rapid increase in the segment of the population over age 65, a delay initially of 1-2 years and later of as much as 5 or more years in the time of entry into nursing homes would save a considerable fraction of current total nursing home expenditures for AD patients. In this regard, it is important to emphasize that the drug therapies which are now scientifically close would not simply slow the course of the disease and delay nursing home entry, but would sufficiently retard the disease in some AD patients that they might not need nursing home admission at any time. Thus, perspective AD therapies are not simply delaying the inevitable but are *eliminating* it in a percentage of patients while *delaying* it in a further, larger percentage.

At this time, patients newly diagnosed with AD can survive anywhere from 3 to 15 years before they die of the disease. (AD is considered the 4th or 5th most common medical cause of death in the U.S.) Patients tend to enter nursing homes approximately one-half to two thirds of the way through their course of illness from earliest diagnosis to death. Therefore, delaying the date of entry of patients into nursing homes by one or two years initially and perhaps by five or more years within the next decade can be expected to substantially decrease the number of new nursing home admissions for AD and decrease the total time a treated AD patient spends in the nursing home. If, to use a general example, we believe that an average AD patient might spend half of his/her ~ 10 year course of illness in a nursing home (i.e., 5 years), drugs that are now in the process of being developed might be expected to decrease this number to the range of 3 to 4 years, and later to less than 3 years. Because AD is a disease of late-life and there is a high probability of contracting other fatal illnesses, slowing the progression of AD would lead to a certain number of deaths from competing causes prior to the time an AD patient would otherwise have entered a nursing home. This point is one of the considerations when one discusses the impact of therapy for a disease occurring very late in life. Of course, this argument does not deal with the most important reason for accelerating research on AD therapeutics: relieving the enormous suffering of patients and their families.

Based on my knowledge of the clinical problem and the current pace of research, I believe that a significant (for example 25-50%) increase in total AD research funding would accelerate the discovery of drugs, particularly if the additional money could be applied in part to therapeutically oriented drug screening programs in both academic and pharmaceutical labs. It is my opinion that such an increase in funding and subsequent acceleration of drug discovery would lead to earlier clinical trials, improvements in the initial (first generation) drugs and earlier arrival of more effective (second and third generation) drugs. Given the detailed knowledge about AD therapeutic targets already in the pipeline in both academia and the biopharmaceutical industry, a 25-50% increase in effort would, I believe, lead to drugs that retard disease progression by 1-2 years within the next 3 to 5 years, rather than within the next 5 to 8 years. If this increase in funding and effort is maintained, then retarding the rate of disease progression by more than 2 years could be achieved within 5 to 8 years, rather than in the 8 to 12 year period I would predict based on our current rate of progress.

If the above estimates are applied to current figures for the number of new nursing home admissions per year with a diagnosis of AD and the total number of dollars paid by all payers for AD-based nursing home expenses, one should be able to derive rough estimates of the potential cost savings that could come by slowing the course of the disease initially by 2 years and later by 3-5 years or more. Of one point I am certain: the interest in AD research is intense in both the academic and pharmaceutical sectors, and many good or even excellent ideas regarding the mechanism and treatment of AD currently go unfunded. Therefore, an increase in funding for AD of the magnitude I suggest above is very likely to lead to smarter, more efficient experiments addressing the several pharmacological targets that have already been identified by AD researchers. The alternative, leaving AD research at its current rate of progress, will produce effective drugs considerably later than will be possible with such an increase in effort, with attendant personal and societal costs.

The CHAIRMAN. Doctor Isacson.

STATEMENT OF OLE ISACSON, M.B.-Ph.D, DIRECTOR, NEUROGENERATION LABORATORY, McLEAN HOSPITAL, ASSOCIATE PROFESSOR IN THE PROGRAM IN NEUROSCIENCE, HARVARD MEDICAL SCHOOL, BOSTON, MA

Dr. ISACSON. Thank you. First I would like to thank you for inviting me here and for your wisdom and strength which you share with Senator Hatfield in bringing this issue on board right now.

I also want to acknowledge the help of Joan Samuelson and Arthur Ullian in preparing my testimony, and inspiring testimony by Milly Kondracke.

I find this time particularly exciting in Parkinson's Disease research because I really, truly feel that we are at the threshold of finding new treatments. I would like to first introduce some of the knowledge we have now and the current research strategies, and then end with some ideas about what more funding could do for brain research.

On the chart [1] on the side there you see that with increasing age you are more likely to acquire Parkinson's Disease. In fact, it has been calculated that we each normally lose about 3,000 to 4,000 cells per year, and I have calculated that during this hearing we will lose about 2 each.

If you just have a slightly accelerated rate of cell loss, you are very likely to develop Parkinson's Disease during a normal life span.

We know quite a lot about Parkinson's Disease. As Arthur Ullian indicated, we already have some basic science foundation about how we would go about treating the disease. We know, for instance, that there are a half million cells on each side of the brain, and about 95 percent of these cells die if you get Parkinson's Disease.

Now, historically—as you can see on the second chart there, the "Health Science" article on Monday, June 19, by Judy Foreman, for which I provided some facts—initially, people didn't know what the cause of Parkinson's Disease was, but they found out that when there were some lesions of the brain in specific regions the symptoms almost miraculously disappeared.

Out of that came pallidotomy and thalamotomy, which is described here in point one and two. But at the end of the 1950's they found that dopamine was a neurotransmitter in the brain and that the cause of the disease was the loss of the neurons. So on came L-dopa, which revolutionized the treatment for Parkinson's Disease. These surgical treatments got abandoned fairly quickly because they thought that they had a solution.

However, as you know, there is a phenomenon called on/off in Parkinson's Disease in which, as Milly Kondracke described, the drugs don't work. There is an off period when it doesn't work, or on when you get excess movements.

So about 10 years ago people started thinking about the surgical treatments again—the pallidotomies—and at the same time the idea emerged that if L-dopa doesn't work, if you could replace the cells that are dead through neurotransplantation, which has a lot

[1] Charts are included in Dr. Isacson's prepared statement.

of controversy for other reasons. The idea that you can replace the cells that are dead emerged. That is known as neurotransplantation. That is point three on that chart.

I have participated in the neurotransplantation procedure development, and we are quite hopeful that will provide a reasonable treatment in some form if appropriate resources are dedicated to it.

Those are the treatments that are on the verge of becoming clinical reality. Some of them are already clinical reality but they are not available to many patients yet.

The CHAIRMAN. Are you going to talk about your own experimentation?

Dr. ISACSON. If you'd like me to.

The CHAIRMAN. Yes.

Dr. ISACSON. What we did was, facing the issue of the dopaminergic unavailability of fetal dopaminergic cells, we tried to find other cell sources. One of them was pig cells, which is a fairly easy source to obtain fetal cells from. As it happens, as Jay Leno puts it, human brains and pig brains are quite interchangeable.

We found that in animal experiments such dopaminergic cells could reverse an animal version of Parkinson's Disease.

We have actually brought this technology to the FDA and they have approved us trying this in five patients for safety, so-called "phase one" trial. So far the two patients we have done are doing quite well, but obviously it is the very beginning of something that may become useful in the future. We may use genetically engineered cells or progenitor cells, but the basic science is driving new clinical initiatives, and that's what I think is important.

That's what we did. That's ongoing work. That grew out of basic research funds in the order of maybe $150,000 a year over a 4- or 5-year period, which is not a lot of money. This funding burden was shared about equally between Federal funds and private funds, which is typical for science in the United States.

Just to add to the list of emerging treatments, there are about three more. One is called neuroprotection, in which you try to protect the cells from dying. There are a number of new factors being discovered that could aid in such work. They haven't yet reached the clinic, but it is quite likely that they will if research is directed toward that.

The susceptibility genes for Parkinson's Disease are being studied very intensely now. They haven't, I think, come as far as in Alzheimer's Disease. It may be a different ball game. But it is useful work.

Finally, gene therapy may emerge in some form to aid in new treatments, or even cures.

So finally, then, I'd just like to note on the——

The CHAIRMAN. All of your full statements will be included in the record. I notice you are skipping quite a bit. It will be in the record, itself.

Dr. ISACSON. I would perhaps just like to make two points about funding, which I can see from my own work. Frequently people think that with more medical research we increase the cost of health care but, as indicated previously, if we could just prevent or delay a disease by 10 years we would save billions.

Moreover, for instance, neurotransplantation or pallidotomy is seen by many of our scientists as a one-time procedure. For instance, if the cost of L-dopa per year is around $5,000 and you have to take this for 10 to 15 years, the cost is between $50,000 and $75,000 per patient. One surgery would not be more than around $20,000. So you would actually save money that way.

Indeed, developing countries of the world—China, Brazil, and so on—have adopted neurotransplantation research programs for that reason, because they don't have L–dopa available to them. Like with the polio vaccine, you actually save a lot of money by new treatment.

As a recent immigrant to the country, I have previously seen research in other countries, and I think there is a very fine tradition in the United States in brain research and very fine infrastructure and talent that may go wasted unless appropriately funded.

I'm sure I'm preaching to the people who already know this here, but I'd like to mention it as part of my testimony.

Thank you.

[The prepared statement of Dr. Isacson follows:]

Testimony of Dr. Ole Isacson, Director
Neuroregeneration Laboratory-
Harvard Medical School/McLean Hospital
Before the
Senate Special Committee on Aging
Senator Bill Cohen, Chairman

June 27, 1995
Hart Senate Office Building, Washington, D.C.

Senator Cohen and members of the committee, I am Ole Isacson, Director of the Neuroregeneration Laboratory at McLean Hospital and Harvard Medical School. My research laboratory is dedicated to basic research on prevention and treatment of neurodegenerative diseases, with particular emphasis on Parkinson's, Huntington's and Alzheimer's disease. Using animal models of aspects of these diseases, our research team studies the nerve cells that die or show damage in these diseases. For Parkinson's disease, we have recently developed and used an alternative cell source to human fetal cells for neural transplantation. Embryonic pig dopaminergic cells can reduce parkinsonism when implanted in experimental models. A few months ago, human clinical trials were initiated using this methodology developed in the research laboratory. My research is directed towards fully utilizing the inherent plasticity of the brain in brain repair.

My testimony on Parkinson's disease in this hearing entitled "Breakthroughs in Brain Research, a National Strategy to Save Billions in Health Care Costs" will outline what happens in Parkinson's disease and how we may deal with this disease. I find this time particularly exciting in research on Parkinson's disease because we are really at a threshold for providing an acceptable treatment or even conquering this disease. I will provide you with data to show that we are developing new and useful clinical methods to deal with the disease. With new treatments, we will be able to save not only the patients, but also a considerable amount of money and resources that this disease drains from society. With a comparatively small investment into research, we could save billions of dollars on Parkinson's disease alone if it was conquered at this time.

WHAT'S THE MATTER IN PARKINSON'S DISEASE AND WHAT CAN WE DO ABOUT IT?

You have probably seen a Parkinson patient. Typically, without any pharmacological treatment, a person afflicted with Parkinson's has a hunched position and slightly unstable gait, with the arms trembling in a fairly stiff posture. The typical motor signs involve lack of movement, slowness of movement, rigidity and tremor. In addition, many with Parkinson's disease experience emotional difficulties in dealing with the disease, but are normally alert and do not feel that their minds are affected. The instability in their posture, the masked face, the gait disturbance, the speech disturbance and the poor dexterity are very incapacitating. This type of patient was first described coherently by James Parkinson (1755-1824) in an essay "On the Shaking Palsy" (1817, Sherwood, Heely and Jones, London, England). In the United States alone, there are now at least a million Parkinson patients, and approximately 1-2% of persons above age 65 will get the disease. Nationwide, drug therapy alone costs about 6 billion dollars per year and the costs of hospital care and other consequences associated with a person having Parkinson's disease are estimated at 25-50 billion dollars per year.

Like Alzheimer's disease, Parkinson's is a disease that may happen in younger people, but the risk increases dramatically with age. This is probably because many of the cellular systems in the brain are difficult to renew or regenerate by themselves. When nerve cells start degenerating as we get older, it becomes harder and harder for the brain to compensate for the loss of these cells. For instance, in Parkinson's disease the symptoms are caused by the loss of a small population in the brain consisting of 500,000 dopaminergic cells in each hemisphere. They are situated deep in the midbrain in a place called the substantia nigra, which means the black substance. In any brain that grows older, some of these dopaminergic neurons will die over time. The rate at which they die is individual. For certain people, whose rate of dopaminergic cell death is slightly higher than normal, the likelihood that they will eventually lose the critical 85-90% of the cells that are needed for normal function is high. The brain somehow manages to compensate for a loss of almost 85% of these cells, but when only 50,000 dopamine cell or less remain on each side of the brain, the symptoms of Parkinson's disease appear. Thus, the neurotransmission that takes place at the nerve terminals that produce dopamine is necessary for all of us to initiate movements. Without it, we freeze up and become unable to move.

The incidence of Parkinson's disease increases with age. As part of the normal aging process, dopamine cells in the substantia nigra die. In most people, by the age of 65 the number of dopamine neurons is 50% of the number at birth. The dopamine-synaptic density and the dopamine levels concurrently are reduced to half of their original level. This phenomenon of dopaminergic cell death seems not to be exclusive to humans. When we study other animals such as rats or mice, we see that over time they also lose nerve cells in the analog region of the substantia nigra. In fact, animals that are older sometimes display a similar movement disability to that seen in Parkinson's disease. And if we give to aged rats that show such deficits the equivalent pharmacological substitution for the lost dopamine, they markedly improve their movement capacity. It is likely that Parkinson's disease has existed on earth and in humans for a very long time, but as the average life span has increased in later civilizations, the prevalence of Parkinson's disease has also increased. I will not discuss the theories explaining Parkinson's disease preceding the 1950s and 1960s; although they were based on the notion that there was something wrong with the brain, they did not present a plausible explanation for this disorder. But along with a number of serendipitous findings during strokes and surgeries, there were the occasional anecdotal reports of patients that markedly improved in their Parkinsonism following some type of surgical procedure or small brain injury. This, of course, gave reason to believe that possibly there were some "bad" cells in the brain that caused the disease. This type of idea was therefore explored further by neurosurgeons who followed observations made by other clinicians to suggest that if damage was done to some cells in the pallidal region of the brain, which is a region adjacent to the caudate and putamen where the dopamine terminals are, then possibly one could relieve some of the symptoms. Indeed, one of the first explorations of this method, called pallidotomy, was done by a group in Sweden, and they reported their finding in *Acta Psychiatrica Neurologica Scandinavica* in 1960. This clinical evaluation of 81 cases showed that a number of them—not all, but certainly a significant number—showed some improvements following heat-induced damage to the pallidal regions. These findings were significant and illustrated the possibility that Parkinson's disease could be alleviated to a degree by some kind of interference with the regions and circuitry involved in motor regulation.

However, the discovery from basic research in the late 1950's that reductions of a neurotransmitter, dopamine, could create catalepsy (total lack of movement) in rats (Carlson, 1959, Pharmacol. Rev. 11, 490-493) prompted further studies that showed that Parkinson's disease is due to a lack of this neurotransmitter, dopamine, rather than some "bad" cells in the brain. This realization carried a fundamental neurological message: that when cells die in the brain, the resulting neurochemical deficit related to the loss of the cell and the synapses they carry, create a specific syndrome of the neurodegenerative disease. Similar discoveries followed about losses of specific subsets of neurons in Huntington's disease and Alzheimer's disease, creating specific neurochemical deficits. Likewise, in amyotrophic lateral sclerosis (Lou Gehrig's disease) and other syndromes, small subsets of damaged or dead neurons were responsible for the symptoms observed.

The pharmacological substitution therapy provided by L-dopa revolutionized the treatment of Parkinson's disease. The neurosurgical treatment (pallidotomy) now became uninteresting to many clinicians, as it was hoped that L-dopa was a sufficient treatment for Parkinson's disease, and moreover, that this type of pharmacological substitution would be possible for all of the other neurodegenerative diseases. It turned out that the solution wasn't so simple. After 5 to 10 to even 15 years of treatment, the L-dopa became less effective, and not in the manner of normal drug-induced tolerance. The patient experienced severe fluctuations in the drug effect, despite relatively constant levels of the drug in the blood and the brain. The so-called "OFF" phenomenon describes a time when the drug somehow becomes ineffective for the patient. At such times, the patient freezes up momentarily and loses mobility. The "ON" times are when the drug works and the patient gains mobility. However, both the "ON" and" OFF"times may be adverse. Symptoms can fluctuate wildly with L-dopa treatment or analog drugs. During "OFF", freezing and rigidity and inability to initiate movement is then further compounded by side effects during "ON", such as extra, involuntary movements generated by the drug. These hyperactive movements and dystonia (abnormal muscle tension and postures) are debilitating. Given that these "ON-OFF" phenomena appear earlier and more prominently in patients with chemically induced Parkinsonism (such as due to MPTP drug abuse), it seems probable that the more severe the damage to the dopamine system, the less likely it is that systemic drug delivery (oral administration of drugs, for instance) will be effective. Moreover, it is reasonable to assume that one of the reasons L-dopa becomes less effective is that it cannot be taken up by the decreased number of surviving dopaminergic neurons to create some form of regulated release of the transmitter.

This has led a number of scientists to question whether pharmacological drug substitution therapy will be effective for the age-related neurodegenerative diseases. If synaptic control and regulated release of a single substance is needed, then we may have to deal with the more complex issue of trying to re-create synaptic networks and/or preserve them from degeneration. Since the "ON-OFF" phenomena in Parkinson's disease are so debilitating, some neurosurgeons and neurologists found it worthwhile to explore pallidotomy once again in the 1990s. Recent work suggests that a localized lesion of the ventral globus pallidus (the internal segment) can alleviate some of the movement disorder of Parkinson's disease. Another procedure, "thalamotomy", surgically removes a subset of neurons in the thalamus (see insert figure) that participates in the parkinsonian tremor. Like all experimental methods, there is the need for an extensive evaluation of the effects, particularly the long-term effects, but based on the early trials in the 1960s, and the not so dissimilar trials of 1995, this is a way of dealing with the motor-associated circuitry that takes in to account the physiology of the brain, and how various regions of the brain interact.

To many of my colleagues, however, the idea of further damaging circuitry to remove a problem due to the loss of cells, is counter-intuitive. We have, instead, explored the possibility that the very adaptive mammalian brain can integrate new cells into places where they have died. This type of reintegration of neuronal elements is also known as neural transplantation. For Parkinson's disease this means that the dopaminergic cells that have died will be replaced by new neurons capable of integrating with the patient's own cells. The brain is a mesh of cells that communicate and signal over long distances and that fire in response to various stimuli. As previously mentioned, nerve cells die in Parkinson's disease. If we start out with slightly more than one million dopaminergic nerve cells per human brain, when we have lost 90% (or 900,000) of those cells, the brain cannot cope anymore and we get symptoms that are consistent with the loss of these dopaminergic neurons. These dopaminergic cells form synapses in the front of the brain, in the corpus striatum, or caudate and putamen. In order to reimplant and repopulate the caudate and putamen with new dopaminergic synapses, the technique was developed for neural transplantation of embryonic cells that have the capacity to send out new processes and form such synaptic contacts. The brain region is seeded with new cells capable of sending fibers throughout a large volume of that brain region. In transplanted patients over time (between 1 and 3 years), the implanted cells manage to recover the dopaminergic transmission signal, while a nonimplanted brain further deteriorates, typical of the disease process for Parkinson's disease. Some patients actually do not require any more L-dopa treatment after transplant. To the best of my knowledge, this is the first time that Parkinsonism has been reversed without L-dopa treatment. Many patients, although not free from all of the symptoms of Parkinson's disease, have reduced the "ON-OFF" phenomena almost completely and are having substantial benefits from these implanted cells. These new data suggest that implanted embryonic cells can continue to grow like in a normal developing brain, and since it takes about 60 years for most of the dopaminergic cellular elements to die in a Parkinson brain, we hope that a similar time frame will be available to the implanted embryonic cells.

In addition to the L-dopa or dopamine agonist drugs previously mentioned, and the neurosurgical treatment methods, there are a number of research efforts to prevent or treat Parkinson's disease. Some centers are involved in locating so-called susceptibility genes for Parkinson's disease. Although there seems to only be a small proportion of Parkinson's patients with a genetic component, certain genes may make it more likely to develop Parkinson's disease. If the disease is multifactorial, susceptibility genes may lower the threshold for developing the disease. Some scientists also indicate that there may be a heterogeneity among susceptibility genes, such that different genotypes may develop the same Parkinsonism. And as we have previously discussed, the disease is age-linked and therefore a number of biochemical changes occurring naturally by age may interact with the genes at various times. Such genetic research, in combination with new methods in molecular biology, may give us tools to develop preventive treatments.

As previously discussed, when dopamine is so severely reduced in the caudate putamen that Parkinsonism appears, we can give patients a precursor of

dopamine, L-dopa, to reverse some of the loss of dopamine in the brain. This was first reported by Birkmayer and Hornykiewicz (Wien Klin. Wochenschr. 73, 787-788, 1961). Along with the discovery that L-dopa substitution worked in the early phases of Parkinsonism, the last 35 years of neurological research has provided us with a number of drugs that can either mimic the action of dopamine (analogs/agonists), block its uptake from the synapse (re-uptake blockers) and stimulate its release or inhibit its metabolic removal. In addition, other neurotransmitter-related drugs that interact with dopamine in the caudate and putamen have been used. The outstanding discovery that the precursor to dopamine (L-dopa) will provide symptomatic relief for patients with Parkinsonism still remains with some minor modifications, the major drug treatment for patients. However, the fact that this drug and other similar drugs lose their effectiveness over time still remains the major problem with Parkinson's disease. It is unclear at this time whether optimization of the dopamine agonist effects can provide an effective long term treatment for Parkinsonism, even if new receptor agonists are developed. The question therefore remains whether it will be necessary with synaptic replacement in the striatum to reverse the course of advanced Parkinsonism.

Most preferable would be intervention against Parkinsonism before the disease develops. Current initiatives in this direction are based on cell biology and physiology studies of dopaminergic neurons. Scientists have studied what substances are toxic to such cells. These studies indicate that toxins either produced within the body or introduced from outside may be involved. A few years ago, it was suggested that the initiation of L-dopa therapy could be delayed for a year or so if the patients were treated with Deprenyl, the inhibitor of an enzyme called Mono-Amine-Oxidase B (MAO-B). The idea for this treatment came from observations of people who developed a form of Parkinson's after the illicit use of a drug called MPTP. MPTP had caused selective degeneration of dopaminergic neurons in the midbrain, almost identical to that seen in the Parkinson's disease that develops with age. Because MAO-B inhibitors can sometimes prevent formation of toxic compounds from MPTP in the brain, it was reasoned that if similar substances were responsible for injuring nerve cells in the more common form of Parkinson's disease, then MAO-B inhibition could be beneficial. Initial highly publicized clinical trials suggested that MAO-B inhibition could slow down the progression of the disease, but more extensive clinical trials suggest that these changes are probably due to effects other than the prevention of nerve cell death. Since MAO-B can block the breakdown of dopamine, the initial effect is most likely derived from elevation of dopamine in the brain, and therefore patients do not have to use L-dopa until somewhat later. While one can be hopeful about future treatments to prevent Parkinson's disease, the current neuroprotective methods are still in an experimental stage. However, there is intense research activity in the field of neuroprotection. Recent discoveries in neuroscience of the many neurotrophic factors, small proteins responsible for maintenance and growth in the nervous system, have given us new tools to prevent neuronal death. In cell culture and preliminary animal studies, it has been shown that brain-derived neurotrophic factor (BDNF) can help dopaminergic neurons against toxic insults. Similar effects have been obtained by infusions and the supply of glial-derived neurotrophic factors (GDNF) and transforming growth factor β (TGF-β). If research is directed towards appropriate delivery of such substances to patients at risk for developing Parkinsonism or patients with accelerated cell loss in the substantia nigra, it is likely that some benefits could be derived. Moreover, by this kind of research we may find other substances that could mimic the effect of trophic factors and therefore help prevent the degeneration in the substantia nigra and other vulnerable brain regions. It is my overall impression that basic neurobiological research towards understanding the mechanism involved in neuronal death, and of dopaminergic neuronal death in particular, are well-underway and very focused. It is likely that these studies will yield sufficient insight to develop clinical therapies within the next five years. A word of caution in this regard, though, is that while clinical trials may be initiated, it could be some time before they are refined so that they can be available to a large number of Parkinson's patients.

With improved understanding of the disease process, the rapid development of new methodologies in medicine from molecular biology will most likely provide additional methods to deal with Parkinson's disease. Using the existing techniques in molecular biology, we can insert genes into some types of cells (gene therapy). These novel methods can be employed to generate cell sources that release dopamine. A number of scientists are trying to genetically engineer cells that are non-neuronal and could be used as biological pumps in the striatum. Other scientists are focusing on the fact that the brain contains nerve cells that form synapses and that it may be necessary to obtain fetal cells from non-human fetuses or other biotechnology-derived cells to treat Parkinsonism. If gene therapy develops over the next 5-10 years, the insertion of specific genes into cells of the brain could be useful. If we find susceptibility genes that are active in the development of Parkinson's disease, gene delivery may provide a tool to block such genes. Moreover, as an alternative to drug treatment, genes that could produce dopamine-like substances could be inserted into patients. Scientists are currently trying to insert the gene that produces L-dopa (a gene called tyrosine hydroxylase). By increasing the supply of the synthesizing enzyme in the caudate-putamen, they hope to provide help to Parkinson patients. If they also develop ways of controlling the release of dopamine and ways of feedback controlling the various genes involved, such strategies could become useful in the future. In the immediate future, I believe that the research directed towards finding neuroprotective agents, and the research directed towards finding cell replacements or surgical methods to deal with Parkinsonism, are effective strategies to provide a treatment for Parkinson's disease and save billions in health care costs.

THE CONSEQUENCES OF MORE RESEARCH FUNDS FOR AMERICAN NEUROSCIENTISTS

Finally, I would like to share with you my views on the potential of basic neuroscience and neurological research in saving billions of dollars in health care costs. It is clear that we are at a stage where we can find strategies to either block the development of some of the age-associated neurodegenerative diseases or treat them by new methods. It appears to me that we are on a collision course with the future in the sense that unless we deal with the large number of people that will be afflicted with age-related neurodegenerative disorders now, it will be an overwhelming burden to society within decades. Senator Hatfield has put it well: "To not increase neuroscience funding at this time is simply irresponsible."

The number of patients with age-related neurodegenerative brain disorders is already high (estimated at 5-6 million Americans). Moreover, a large base of young people is shifting towards an inverted demographic triangle, in which the baby boomers will move to the top. This shift may increase the number of people who are not engaged in economic activity and who will require some form of care. If an investment is made now into the considerable capacity and output of the neuroscience and the neurological research community in the United States, these costs can be reduced or totally averted. The economic marginal benefit is therefore enormous, and in human terms it is not even measurable. The demographic shift in the United States towards an older population suggests that in order to provide these people with an active life and not have approximately 10% of the population above 65 years of age afflicted by devastating neurodegenerative diseases, we need to find cures and effective treatments for these disorders. It is my view that these diseases can all be treated, and it is primarily now a matter of deciding how to fund the basic and clinical research communities to reach that goal. The threshold for discoveries that could lead to treatments is low. The cure, however, will not be on anyone's doorstep by chance, and therefore there has to be a clear commitment from research funding sources, whether they be federal or private, to solve this problem. A federal resource, such as extramural NIH funds, is a very cost-effective and complementary source to industrial research and development. In my experience, competitively awarded federal money spent on medical research is highly cost-effective. The relatively low salaries for academic research scientists compared to the length of their education, the low salaries of their assistants and technicians, and the time-commitment by personnel in research contributes to the low cost. This means that a lot of advanced research work gets done at a relatively low cost. A federal source of funding, such as the NIH, can provide an optimal way for research support through its peer-review system. The work funded is frequently non-overlapping between the pharmaceutical research and laboratories at universities in similar fields. This is because the research process takes complementary forms in industry and federally funded research programs. Development of potential clinical treatments and products by the pharmaceutical industry frequently grows from fundamental basic research done at academic institutions.

It is my view that industry and clinical medicine depend on the domain of university-based, fundamental research to develop effective treatments for neurodegenerative disorders. I'd like to give you an example of this. The development of neurotransplantation cells for a disease like Parkinson's and Huntington's, in which I have participated, has been made possible by funds from the NIH and the biotechnology industry. As for the nation as a whole, these research costs were shared equally by industry and federal sources. However, the competition for NIH neuroscience grants is currently brutal and many worthwhile projects and exceptional scientists are not funded. Many scientists spend more than 50% of their effort writing grants. Only about 10% of newly submitted proposals to the NIH are funded. I estimate that the cost for the most effective preclinical research programs directed towards basic research on Parkinson's disease to be in the order of $200,000-400,000 per laboratory group per year. I believe that if you could fund a hundred such projects/programs per year, new treatments could be available within a couple of years and an effective therapy or cure for Parkinson's disease within 5 years. That is at a cost of $20-40 million per year. For a total cost of $100-200 million over 5 years this could be achieved. Such fundamental discoveries usually have spin-offs to related disorders and we can therefore also expect benefits for other other similar diseases.

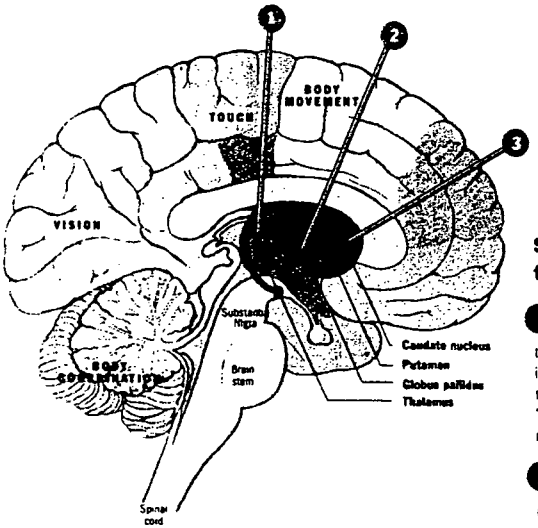
Over the next 5 years, the total cost to American society in health care costs for Parkinson's and Alzheimer's disease, some of which are going to be carried on the shoulders of individuals, and others costs of course through medicare and medicaid, is in the order of $100 billion per year. Now, if increased research funding of, say, $100 million is appropriated, it is one-thousandth of the cost if the problem is not solved. That means that for every $1.00 you add to the neuroscience research fund, you have the chance of immediately saving $1,000. And that is only an economical analysis, which I am not here primarily to speak about. If we consider this in a long-term perspective, the benefits in savings and reduced human suffering to the people of the United States would be enormous. It is my feeling that there is a large awareness in the American community of the risks of aging, and particularly, the risks of acquiring diseases like Alzheimer's and Parkinson's. Therefore, I believe that the American community at large would favor federal funding for medical neurological research at this time. The type of science we are considering has been carried out with excellence in the U.S. and brought respect from the rest of the world. In my opinion, having worked and seen research in Sweden, England and France, there is currently considerable outstanding, but underfunded talent in the American neurological/neuroscience research community. This asset would be wasted unless more resources are appropriated.

HEALTH|SCIENCE

THE BOSTON GLOBE • MONDAY, JUNE 19, 1995

What happens in Parkinson's Disease

For unknown reasons, cells die off in a part of the midbrain called the substantia nigra and stop producing the chemical messenger, dopamine. Normally, dopamine is released through long projections into two other areas, the caudate nucleus and putamen. With normal amounts of dopamine, cells in these areas fire normally and trigger the firing cells in two other areas, the globus pallidus and the thalamus, all of which results in the smooth initiation of muscular movement. But when there is too little dopamine, the process goes awry, causing cells in the globus pallidus and thalamus to fire abnormally, leading to the tremors and muscle rigidity typical of Parkinson's.



Surgical treatment for Parkinson's

1 Thalamotomy or thalamic stimulation
Neurosurgeons use electrodes to kill cells in the thalamus or a new technique - inserting a "pacemaker" into the patient's chest, which sends electric currents through wires connected to the thalamus in order to "jam" the overactive circuitry and restore normal movement.

2 Pallidotomy
Neurosurgeons insert thin electrodes into the globus pallidus and destroy the abnormally-firing cells.

3 Fetal cell transplants
Neurosurgeons can implant fetal cells - from humans or pigs - through thin needles into the caudate nucleus and putamen, where they then produce the missing dopamine.

SOURCE: DR. OLE ISACSON
GLOBE STAFF GRAPHIC/D. BUTLER

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Transplant success debated

In April, Tony Johnson, 67, a civil engineer from Taunton, became the first person in the world to have brain cells from fetal pigs implanted in his brain to combat Parkinson's disease, which he has had for 27 years.

Neurosurgeons have been experimenting since the early 1980s with implants of human fetal cells in Parkinson's patients. They have had considerable success but aroused moral and and legal opposition from abortion opponents, because the cells came from aborted fetuses.

The implanted fetal cells take up residence in the patient's brain and begin supplying the dopamine that Parkinson's patients lack.

Over time, the implants reduce by about half the rigidity and slowness of movement of Parkinson's and can reduce to nearly zero the "off" time that patients suffer when medication stops working, says Dr. Ole Isacson, director of the neuroregeneration lab at McLean Hospital. The implants appear less effective against tremors.

So far, about 25 fetal transplants have been reported in the medical literature, but neurosurgeons estimate that hundreds have actually been done, despite debate about the surgery's effectiveness. Some argue that because patients are desperate, any promising intervention could appear to make patients better through the placebo effect alone.

To settle that question, Dr. Curt Freed, director of neurotransplantation for Parkinson's at the University of Colorado School of Medicine, has embarked on a controversial study of 40 patients.

His team will make small holes in the skulls of all 40 patients. Twenty will have needles inserted through the holes and fetal tissue injected into their brains, but the other 20 will not – a kind of "sham" surgery.

Neither the patients nor a team of doctors who will evaluate them in New York will know who got which surgery. As of last week, the team had operated on four patients.

Though it will take time to get results from Freed's study, many neurosurgeons are optimistic about fetal tranplants, among them Dr. James Schumacher of the Lahey Hitchcock Clinic in Burlington. He has been working with Isacson to find ways to use fetal pig cells instead of fetal human tissue.

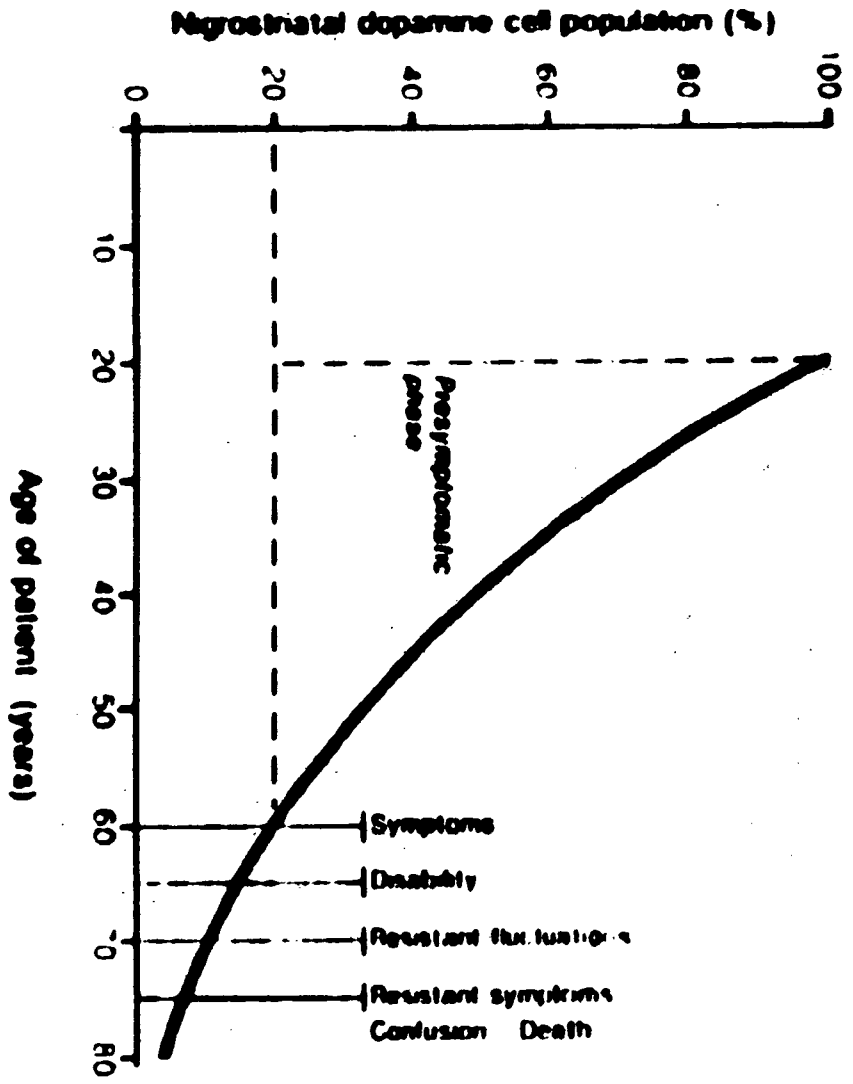
The advantages are clear, they say. To get enough human tissue for one transplant, surgeons must get fetal tissue from several dozen women undergoing abortions within a two-day period. Then testing must be done to be sure the tissue is free of viruses like HIV or Hepatitis B.

By contrast, says Schumacher, "Pigs don't have AIDS. These animals are raised in a strict environment. They are screened for every pathogen known, so they are cleaner and more plentiful."

It is too soon to tell how well the pig cells are working for Johnson, but Johnson's wife, Mildred, says they have "made the 'on' times much smoother and longer, his speech is much better, he can walk better and he's definitely turning around. You can see signs the cells are starting to work. . . .

"It's almost like miracle."

JUDY FOREMAN


Nigrostriatal dopamine cell population (%)
0
20
40
60
80
100
Age of patient (years)
10
20
30
40
50
60
70
80
Presymptomatic phase
Symptoms
Disability
Resistant fluctuations
Resistant symptoms
Confusion
Death

The CHAIRMAN. Thank you, Doctor Isacson.
Doctor Choi.

STATEMENT OF DENNIS W. CHOI, M.D., JONES PROFESSOR AND HEAD, DEPARTMENT OF NEUROLOGY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS, MO

Dr. CHOI. Mr. Chairman, I'm honored to testify today on the topic of research advances relevant to developing treatments for stroke. Our Nation needs these advances.

Each year about half a million Americans will have one or more strokes. These strokes will rob them of important abilities—in many cases, the ability to speak, to walk, to think, or to live independently. In some cases it will rob them of life, itself.

Stroke is the leading cause of adult disability, and although it doesn't usually kill, it occurs so commonly that it is the third leading cause of death in the Western world. The huge economic costs of stroke have already been covered this morning.

Despite its heavy impact, stroke remains today, as it has been since the beginning of recorded history, a common scourge beyond the reach of medical countermeasures.

Physicians are able to diagnose the condition with certainty, but there are, as of yet, no established treatments capable of preventing the process of stroke-induced brain damage once it has begun.

The good news is that the quickening pace of advancements in medical research—which several people today have articulated—has brought treatments for this age-old disease within our grasp. I believe in this case we are at the 10-yard line.

We know now that most stroke is caused by blood clots which block blood vessels, usually arteries, leading to the abrupt loss of blood flow to a portion of the brain. If you look at this diagram here,[1] it is a cartoon of a region of brain that has lost its blood flow, thereby losing needed oxygen and nutrients. A smaller number of strokes are caused by blood vessel rupture leading to brain hemorrhages.

This loss of oxygen and nutrients results, sadly, rapidly in brain cell death, which we call cerebral infarction.

Research has already led to progress toward stroke prevention through the control of risk factors such as hypertension, and through surgical intervention in subsets of patients with severe carotid artery plaques—that blocks a major artery supplying the brain.

Two fundamental strategies now promise to yield effective, acute interventions for stroke patients. The first is thrombolysis. Applied urgently, measures directed at breaking up the obstructing blood clot may be able to restore blood flow before maximal irreversible damage has been done. Agents to accomplish this, such as genetically engineered tissue plasminogen activator, reduce brain infarction in animals and are already in clinical trials.

The second strategy, which Doctor Isacson has referred to from the Parkinson's Disease standpoint, is neuroprotection. We know that the brain is much more vulnerable to damage induced by loss of blood flow than most other tissues in the body. Research over

[1] Charts are included in Dr. Choi's prepared statement.

the last decade has led to the identification of several key factors responsible for this heightened vulnerability.

In particular, over-release of the brain transmitter glutamate, which is a chemical normally released in small quantities from one nerve cell to signal a neighboring nerve cell, may contribute to stroke-induced brain damage. During a stroke, transmitter glutamate is dumped out in an uncontrolled fashion, leading to the lethal overstimulation of some nerve cells.

Together with a cohort of other investigators in this field, my colleagues and I have studied this process of glutamate-induced cell death, which we call "glutamate neurotoxicity." Collectively, and aided critically by "blue sky" neuroscience research conducted in many laboratories, investigators in this field have learned a lot about the nature of glutamate neurotoxicity—how it is initiated, how excess calcium enters nerve cells and damages cell metabolism, and what final events ultimately cause nerve cells to die.

This knowledge promises to facilitate the development of a set of rational countermeasures. One of the best ways so far to block glutamate neurotoxicity is to block the receptor proteins on the surface of nerve cells where glutamate docks, the key and lock. This docking is what initiates the toxic damage.

Glutamate antagonist drugs, which block these docking proteins, these receptor molecules, have proven effective in reducing brain damage in experimental animals. I refer you to this second panel here. What you see here is a rat brain. This is an experimental stroke. This experiment was conducted recently by Chung Hsu at Washington University, but it is typical of many similar experiments conducted over the last few years in several other laboratories.

What you see is a rat brain in the lower panel that has had an experimental stroke and has been stained with a stain called TTC. The area of brain infarction is, I think, intuitively appreciated as the white area on one part of the brain.

The brain has been cut like a slice of bread, so it has been laid out in a series of slices.

If you track with your eye across the lower row, you can see the large white area, the brain infarction, in a rat that has sustained a stroke much like a human would.

In the top row I think you can readily appreciate that there is less infarction. The difference is that the animal in the top row was treated with a glutamate antagonist drug.

As a member of the Dana Alliance for Brain Initiatives led by David Mahoney, Guy McKhann, and others, I have joined many fellow researchers in the specific prediction that brain research, if allowed to develop along its current trajectory, will produce the first effective acute interventions for stroke easily within the current decade.

Beyond this horizon lies the exciting prospect of combining several different treatment approaches to achieve additive benefits.

Furthermore, some of the basic mechanisms of nerve cell injury that occur in stroke such as glutamate neurotoxicity may be triggered by certain other insults to the nervous system such as trauma, seizures, or certain other neurodegenerative diseases.

Glutamate antagonist drugs, in fact, have already shown beneficial effects in animal models of spinal cord injury. I think it likely some day that the application of these drugs or other related strategies will help spare individuals the magnitude of tragedy that has sadly affected Mr. Ullian or Mr. Christopher Reeve.

The possibility, indeed, that the study of one neurological disease will generate insights useful in understanding other diseases, has grown enormously, and this synergy is accelerating our progress today.

Never have the gains been closer, more apparent. Senator Cohen, your support—past and present—for biomedical research is deeply appreciated.

[The prepared statement of Dr. Choi follows:]

Hearing: "Breakthroughs in Brain Research: A National Strategy to Save Billions in Health Care Costs."

June 27, 1995
Senate Special Committee on Aging

Testimony of Dennis W. Choi, MD, PhD (Jones Professor and Head of Neurology, Washington University School of Medicine, St. Louis, MO).

Mr. Chairman, ladies and gentlemen. I appreciate the invitation to testify before this distinguished Committee on the topic of research advances relevant to developing effective acute treatments for stroke. Our nation needs these advances. Each year, about a half a million Americans will have one or more strokes. These stroke will rob them of important abilities - in many cases, the ability to speak, to walk, to think, or to live independently. In some cases, it will rob them of life itself. Stroke is the leading cause of adult disability. Although stroke usually does not kill, it occurs so commonly that it is the third leading cause of death in the Western world. The economic costs of stroke to our country exceed 25 billion dollars annually.

Despite its heavy impact, stroke remains today as it has been since the beginning of recorded history, a common scourge beyond the reach of medical countermeasures. Physicians are able to diagnose the condition with certainty, to treat associated disorders, to attend to comfort, and to assist with subsequent rehabilitation, but there are as of yet no established treatments capable of preventing the process of stroke-induced brain damage, once it has begun. The good news is that a quickening pace of advancements in medical research has brought treatments for this age-old disease within our grasp.

We know now that most stroke is caused by blood clots which block blood vessels - usually arteries - leading to the abrupt loss of blood flow to a portion of the brain (**Fig. 1**). A smaller number of strokes is caused by blood vessel rupture, leading to brain hemorrhages. In either case, the loss of normal blood flow deprives the brain of needed oxygen and nutrients, resulting in brain cell death - which we call cerebral infarction. We have made progress towards stroke prevention, through control of risk factors such as hypertension, and through surgical intervention in a subset of patients with severe carotid artery plaques. Two fundamental strategies now promise to yield effective acute interventions in stroke:

1. Thrombolysis. Applied urgently, measures directed at breaking up an the obstructing blood clot may be able to restore blood flow before irreversible brain damage has occurred. Agents to accomplish this, such as tissue plasminogen activator, reduce brain damage infarction in animals and are presently in clinical trials.

2. Neuroprotection. The brain is much more vulnerable to damage induced by loss of blood flow, than most other tissues in the body. Research over the last decade has led to the identification of several key factors responsible for this heightened vulnerability. In particular, overrelease of the brain transmitter glutamate - a chemical which is normally released in small quantities from one nerve cell, to signal another nerve cell - may contribute to stroke-induced brain damage. During a stroke, transmitter glutamate is dumped out in an uncontrolled fashion, leading to the lethal overstimulation of nerve cells.

Together with a cohort of other investigators in this field, my colleagues and I have studied this process of glutamate-induced nerve cell death - "glutamate neurotoxicity". Collectively, we have learned a lot about its nature: how it is initiated, how excess calcium enters nerve cells and damages cell metabolism, and what final events ultimately cause nerve cells to die. This knowledge has facilitated the development of a set of countermeasures. One of the best ways to block glutamate neurotoxicity is to block the receptor proteins on the surface of neurons, where glutamate docks - key in lock - to initiate toxic damage. Such glutamate antagonist drugs have proven effective in reducing brain damage due to experimental stroke in animals (**Fig. 2**).

As a member of the Dana Alliance for Brain Initiatives, led by David Mahoney, Guy McKhann, and others, I have joined many fellow researchers in the specific prediction that brain research - if allowed to develop along its current trajectory - will produce the first effective acute interventions for stroke within the current decade. Beyond this horizon, lies the exciting prospect of combining several different treatment approaches to achieve additive benefits. Furthermore, some of the basic mechanisms of nerve cell injury occurring in stroke, such as glutamate neurotoxicity, may be triggered by certain other insults to the nervous system, such as trauma, sustained seizures, or neurodegenerative diseases. Glutamate antagonist drugs have already shown beneficial effects in animal models of spinal cord injury. I think it likely that someday the application of these drugs, or other related strategies, will help spare individuals the magnitude of tragedy that has sadly affected Mr. Ullian or Mr. Reeve. The possibility that the study of one neurological disease will generate insights useful in understanding other diseases, has grown enormously, and added to accelerating progress.

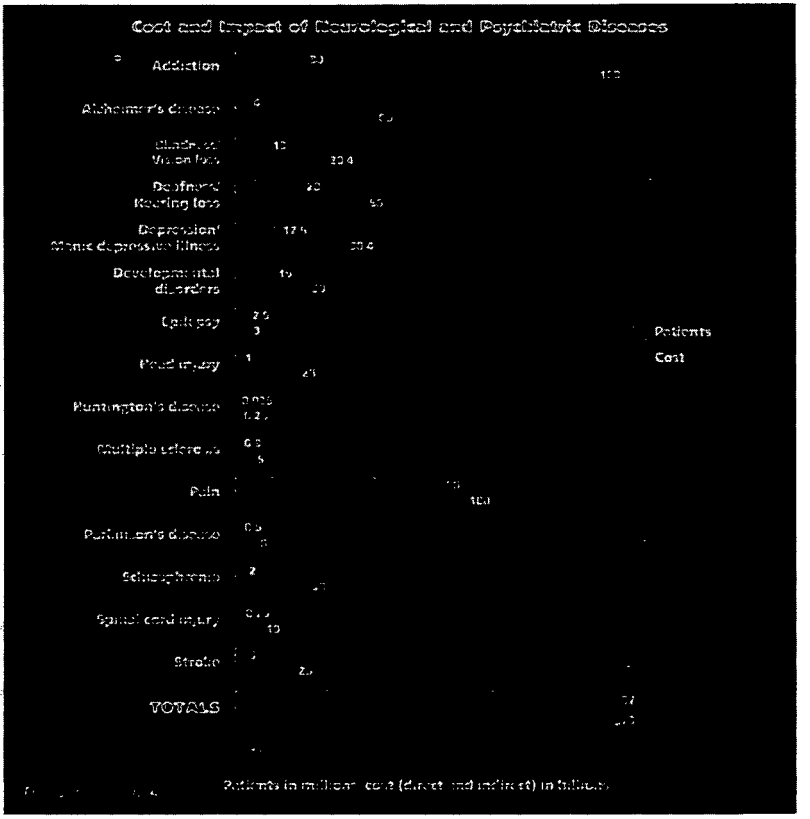
We must keep up our commitment to medical research. Never have the gains been closer, more apparent. What we would save by slashing federal funding for research does not compare - is only a fraction of a penny on the dollar - to the massive losses we truly sustain due to disease - real costs, drained out of our economy each year like heartbeats. Medical research represents our only hope for reducing both the costs of disease, and their associated burden of human sorrow, in our futures.

DELIVERING RESULTS: A PROGRESS REPORT ON BRAIN RESEARCH (May 1995)

Summary

The most important and productive medical research happening today is the study of the brain. Since the Federal government declared the Decade of the Brain in 1990, researchers have solved some of the most stubborn riddles of the brain, and have created and improved treatments for the disorders that afflict it. The stunning progress of the last five years gives future researchers a higher vantage point on which to stand while scanning the horizon for cures.

How does this affect you? One in five Americans is struggling with a brain-related problem at any given time; *each* of us will face such a struggle at some time in our lives. It may be pain, depression, memory loss, or one of the many problems like these that can be chronic and recurring. It may be swift, like head injury and stroke; or it could be degenerative and fatal, like Alzheimer's and Huntington's diseases. Or, a lifetime of anguish could result from a child or grandchild's battle with addiction or schizophrenia. Some of these afflictions are life-ending; all of them are life-*diminishing*. The cost in personal terms is beyond measure; in hard economic terms it is more than half a trillion dollars a year.



But now, the human brain is no longer a "black box" — the misunderstood and mysterious source of self, its maladies misdiagnosed and undertreated. Today, at the midpoint of the Decade of the Brain, it is clear that a new era has begun for individual health and vitality. For all three of the major stages of life that you and your family will experience — childhood, adulthood, and the later years — discoveries about the brain's mechanisms, how it forms, grows and ages, how to heal and strengthen it, are raising our expectations for dealing with brain-related difficulties, giving you the realistic chance to avoid suffering.

If your maternal grandmother died with dementia, the most common symptom of Alzheimer's, should you worry that your later years will be marred by this disease? Scientists are discovering ways to find out. Also, by the time you reach the average age of onset, these same scientists could be able to fend off the disease.

The causes of cerebral palsy, retardation and learning disabilities are being revealed, increasing the chances that it will be possible to prevent these horrible conditions in your own children.

The discovery of drug binding sites in the brain is enabling researchers to work towards potential treatments for addiction, so that the lure of drugs will be much less likely to steal the youth, or the life, of someone you love.

Most of the brain afflictions that can severely alter your life, by affecting you or someone close to you, are yielding to researchers. For all those who cry, "Why me?" when they are confronted with a brain disease, scientists are approaching the day when they will be able to answer. As the progress snowballs, and the discoveries come more quickly, the likelihood of your life being destroyed by a neurological ailment continues to shrink.

Beyond the personal aspects, our nation itself has a massive stake in brain research. Today, neurological and psychiatric disorders together account for more hospitalizations and more prolonged care than almost all other diseases combined. No surprise there: Over the last hundred years, we got better at keeping people alive and ambulatory as far as their respiratory, circulatory, digestive and reproductive systems were concerned, but we were stymied by the brain.

Now neuroscience is catching up. In the next five years, we will help brain and nervous system patients in large numbers, and because these patients number in the millions of people, developments in brain science will transform our assumptions in planning for the future. In particular, at the societal level, the view of crippling, chronic, long term, and mental illnesses will be much different.

When the expanding numbers of aging Americans have less to fear from the brain diseases of aging, and when disorders that begin at or before birth, and last a lifetime, are progressively fewer and less disabling, then the lost work days (by patients and those who care for them) will fall, and leisure activities will rise. Reduced social spending, decreased work absences and improved quality of life all give relief to a troubled economy.

The achievements outlined in our report, however, are just the vanguard of greater things to come. One of the most significant facts about the progress we have made in brain research is that more brain scientists today are working on questions of basic science. This accounts for the diversity of disorders we have been able to address in such a short time. Clinicians focusing on specific diseases now have better odds of finding the keys to the disorders they are researching because there is so much more information to draw upon.

That is precisely what makes brain research so exciting. We understand it better each day. And because of that, we will solve problems of affliction that have truncated our lives since the dawn of humankind. Everything lying ahead of us is opportunity and hope.

Here are some highlights of the progress report, and some predictions for the next five years. Join us in celebrating the hope offered for current and future victims of brain disorders:

CHILDHOOD

- Researchers believe that a major reduction of spasticity in cerebral palsy and prevention of one-third of all CP cases arising from low birthweight will occur within five years.
- New findings point to a family of drugs that may correct drug-induced developmental abnormalities in children.
- Thanks to recent public health studies, psychiatry now classifies schizophrenia as a developmental disorder, and promises more effective medications by the year 2000.
- Researchers identified genes that contribute to inherited forms of blindness and deafness and several forms of mental retardation, including the most common inherited form among males (Fragile X Syndrome). Growing evidence suggests that genes also play a role in learning disabilities and schizophrenia.

ADULTHOOD

- The first drug to block craving in alcohol addiction - Naltrexone - has recently been approved as an adjunct to psychotherapy.
- Success in treating depression now approaches 90% with more precise antidepressant drugs which avoid unwanted side effects.
- Obsessive-compulsive disorder has become treatable.
- For the first time ever, researchers have identified a treatment (and are testing another) which alters the natural course of multiple sclerosis.
- Researchers have identified the sites where drugs of abuse bind in the brain, and by 2000 hope to have effective cocaine-blocking agents.
- Recent refinements to treatments leave many more epileptics seizure-free.
- Discovering serotonin-responsive proteins led researchers to develop sumatriptan, an effective treatment for migraine headaches.
- Improved clinical care now returns some 94 percent of patients with spinal cord injuries to their communities. Researchers may have the first treatment to enhance spinal cord repair by 1996.
- Genetic research has identified specific genes that cause Huntington's disease and familial Lou Gehrig's disease. New findings show that genes may also play a role in addiction, manic-depressive illness, depression and epilepsy.

THE LATER YEARS

- Several genes have been found that lead to Alzheimer's disease. Cognex (tacrine), approved in 1994, is the first drug for treating Alzheimer's symptoms. A combination of genetic testing and positron emission tomography (PET) scanning may yield an early diagnostic test for Alzheimer's. Also possible: an eye-drop diagnostic test and a spinal fluid analysis test.
- The first animal model of Alzheimer's disease (a transgenic mouse) has recently been produced, and it is already being used to test drugs to slow the progression of Alzheimer's.
- An effective approach to gene therapy for Parkinson's disease will emerge before 2000. Relief from Parkinson-like symptoms has been achieved in monkeys using dopamine-enhancing drugs.
- A new bloodclot-dissolving drug can improve the outcome of stroke, if administered within two hours of onset.
- A chili pepper extract, capsaicin, now helps relieve chronic pain (even in cancer): Within five years, scientists expect to have developed non-addictive pain relievers.
- Recently discovered proteins that nourish, repair and promote the growth of nerve cells are leading to drugs (some already in trials) that increase resistance to stroke.

TECHNOLOGY

Imaging:

- Now, functional magnetic resonance imaging (fMRI) allows doctors to view the active brain, and at their desktops to interactively scan entire brain structures.
- Using charged Xenon gas, laboratory scientists improved MRI signal strength by a factor of 10,000, producing more clearly defined pictures in animals.

Disease models:

Scientists are working with living organisms in laboratory settings to test compounds and find new directions for investigation. Animal models available today include:

- Alzheimer's disease
- Developmental disorders
- Several different forms of epilepsy
- Multiple sclerosis
- Pain
- Traumatic brain injury

SOURCES FOR NUMBERS

The Developing Brain

Developmental Disorders (cost and patients): National Institute of Neurological Disorders and Stroke, 1993.
Schizophrenia (patients): National Institute on Mental Health, Update August 1993.
Schizophrenia (cost): NIMH, 1995.

The Mature Brain*

Blindness/vision loss (cost and patient numbers): National Eye Institute, 1994.
Deafness/hearing loss (patients): National Institute on Deafness and Other Communicative Disorders, 1992.
Deafness/hearing loss (cost): Hallworth, R, et al. "Hair Cells and Hearing" Press Conference, Society for Neuroscience Annual Meeting October 26 1992.
Depression (patients): National Institute on Mental Health, Update August 1993.
Depression (cost): Rice, Dp and Miller, LS. "The Economic Burden of Affective Disorders" Advances in Health Economics and Health Services Research 1993.

The Aging Brain*

Alzheimer's Disease (patient numbers): "News Notes." National Institute on Aging, 1989.
Alzheimer's Disease (costs): National Institute of Neurological Disorders and Stroke, 1993.

* All other patient and cost numbers (not listed here) are as of 1993, from the National Institute of Neurological Disorders and Stroke.

The Dana Alliance for Brain Initiatives is an independent, nonprofit organization of 138 leading neuroscientists, including five Nobel laureates, whose sole commitment is to advance education about the personal and public benefits of brain research.

If you wish to receive additional copies of this summary, a source list, or the full report entitled "Delivering Results: A Progress Report on Brain Research" please contact:

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The CHAIRMAN. Thank you.

Sitting here listening to you I feel a little bit as if—to stay with the football analogy—I were about to challenge either Steve Young or Joe Montana about the best way to carry out a 2-minute drill to get down the rest of the 10 yards to the goal post.

I don't purport to have the expertise that could permit me to intelligently cross examine any of you on your areas of specialty.

Doctor Roses, I will tell you yesterday I spoke with Senator Stevens, and I said, "You really should come to this hearing tomorrow," because he is someone who is very important in the U.S. Senate. He serves on the Appropriations Committee, but has a dedicated interest to the brain. He is always sending me articles pertaining to the brain. I said, "I've got some pretty important testimony tomorrow." He said, "Have you got Doctor Roses?" as if to say if I didn't have Doctor Roses he probably wouldn't be here. I said, "Indeed, he is going to be on the panel, along with other very distinguished guests.

Unfortunately, he is chairing a hearing at this time and couldn't be here, but I want to assure all of you that there is a growing number of people who, indeed, appreciate what is being done and the promise that you hold for dealing with these serious problems. It couldn't be put more starkly than you put it, Doctor Roses. It won't be Independents or Democrats or Republicans, just those who are suffering and those who are caring for the suffering. That's a prospect that I think is truly frightening if we don't help complete the task of getting the full 100 yards.

But, of course, we are never going to reach there, are we? There is always going to be another 100 yards. We are going to hit the first 100 yards and there will be other diseases we will have to contend with.

Doctor Choi, I think you touched upon this briefly in your final comments. We talk in other contexts in terms of cross-fertilization. I think in your context you would talk about serendipitous discoveries. Is that a phrase that you use? Namely, that you are proceeding down one line of inquiry and suddenly it opens up into another. That is what I think we are going to see more and more of.

As we reach the 100-yard limit for perhaps Alzheimer's or Parkinson's or other types of afflictions, we are going to find other things that we have to contend with, so there will always be another 100 yards to run.

But I do appreciate the fact that each of you have come here today to, I think, add a very important element to this entire debate.

We talk about saving money. Let me give you an example of something on a very practical level here.

Many of my colleagues on my side of the aisle would like to demonstrate to our constituents that we are, indeed, very concerned about excessive spending and we are going to set forth a demonstration that we are cost conscious, and one of the things they would like to eliminate is this Committee. As a matter of fact, I was successful in preventing the elimination of this Committee this time. Two years from now I expect that there will be another effort made to abolish this Committee, as well.

To me, it is very cost-inefficient. Very little is dedicated to the Aging Committee, as such, and we do work on this Committee that very few, if any, other Committees undertake. There is no other Committee in Congress that serves as a repository for examining issues which affect not only the elderly, but people who might suffer the same afflictions that the elderly suffer.

Art Ullian is not old, but he has been rendered old by virtue of his spinal injury. So this is an area that I think many of my colleagues fail to appreciate, but perhaps more did than I give credit for. We were able to save the Committee this time.

So we are fighting battles up here, as well, to say that this is very cost-effective. We are exploring regions now. Even though the Committee doesn't have "legislative jurisdiction," we accumulate evidence that we take to other Committees such as the Budget Committee or the Appropriations Committee in saying this is something that we need to look at very carefully.

Doctor Selkoe, I think you pointed out you were a little bit concerned about Senator Hatfield's statement. I think what Senator Hatfield was saying was that even though the budget will probably be approved this Thursday or Friday, that next year he intends to wage another battle to restore funding, not to cut it. I think you should take some measure of hope for the lengthy and I think very encouraging statement that he, as chairman of the Committee, gave this morning.

I just want all of you to know that the information in testimony that you have given this morning will be taken and presented to our colleagues, and that we will see to it as best we can that we emphasize the point that this really is a wise investment, and even though we can't calculate or calibrate what the ultimate savings may be, we do know that if we invest more than the three penny opera that we will likely see a real Shakespearean result, something quite extraordinary in terms of the return paid.

I don't think that we can afford our system as it currently is. There is no way that we can pay for the extraordinary costs that are coming. When we start talking about Medicare going broke in just 7 years—that's what the trustees have indicated. Seven years from now or 6½ years from now there will be no money left in Medicare, period. No money to pay any hospital or any doctor for reimbursement for any of the services. That gets our attention. When the trustees tell us that, it gets our attention.

What do we do? We have three choices. We can either increase the payroll tax across the board on every working family, or we can "try to slow the growth of Medicare" from 10 percent to 7.1 percent, or maybe a combination of the two. But we have to do something. We can't simply say the problem is coming, that there is a tidal wave out there but it is 7 years away and we'll just wait another 7 years until it hits and many of us will either be out of office or then writing retrospectives about how we should have taken action. We can't afford to do that. We've got to do things right now.

We can do things in trying to prevent fraud. For example, there is a lot of fraud that we know about and you know about. It is out there and it is so easy to steal from the current system, so we've got to change that.

But if we can, in fact, realize the kinds of savings that we saw on the boards before of $50 billion in dealing with Alzheimer's or $15 billion in stroke, and another $3 or $5 billion in Parkinson's, then we have saved some real money, and that's how we are going to deal with the problem of Medicare and Medicaid and long-term care. All of that has to be a combination of things.

I think your testimony is extraordinarily effective in this effort, and this Committee will take this information and present it to our authorizers and appropriators to see if we can persuade them this is a penny or 3 pennies or 5 pennies well-invested, and it will produce pounds of savings years from now.

So I thank all of you for coming. We appreciate what you are doing for the country and for humanity very much. Thank you.

The Committee will stand adjourned.

[Whereupon, at 12:55 p.m., the Committee was adjourned, to reconvene at the call of the Chair.]

Research America
AN ALLIANCE FOR DISCOVERIES IN HEALTH

PRESS RELEASE

CONTACT:	**Mary Woolley**
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DATE:	**June 23, 1995**

FOR IMMEDIATE RELEASE

NATIONAL POLL UNDERSCORES AMERICANS' SUPPORT OF MEDICAL RESEARCH

Dr. C. Everett Koop Issues Warning: Insufficient Medical Research Could Be Hazardous to Your Health

Washington, June 23--At a time when this nation is focusing on deficit reduction and budget cuts, spending on medical research has surfaced as a national priority that the American public values and warns should not be cut. This and other findings were part of a nationwide poll of 1,004 adults conducted by Louis Harris and Associates from June 8 through 10 for Research!America.

"Congress seems to be moving in a direction that is going to cut medical research substantially," former Surgeon General and Research!America board member Dr. C. Everett Koop says. "This new poll clearly tells Congress that Americans are counting on medical research to keep them healthy and don't want to cut spending in this area."

The results of the poll indicate:

--65 percent oppose cuts in medical research dollars;
--73 percent would pay higher taxes to support more medical research;
--61 percent urge Congress to provide tax incentives for private industry to conduct medical research;
--60 percent are willing to designate tax refund dollars for medical research;
--over 90 percent endorse maintaining the United States' position as a leader in medical research; and,
--61 percent would like more information on medical research in the print and broadcast media.

"It's time that elected officials reflect the public's confidence in medical research and the way these tax dollars are spent," says Research!America President Mary Woolley, speaking on behalf of the advocacy organization's 350-plus members, representing 20 million Americans. "The results of this Harris poll clearly indicate that Americans want medical research to be a higher national priority."

Serving also as chairman of the National Safe Kids Campaign, Koop points out that another important finding of the new Harris poll is that young people are even more willing to pay for medical research than are their elders. "All of us who are looking to a brighter future for our children and grandchildren should be speaking out now in support of medical research," says Koop.

Research!America is a national not-for-profit public education and advocacy group dedicated to increasing public awareness about the value of medical research and the importance of putting research to work to achieve a better quality of life.

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Public Attitudes About Medical Research

A nationwide public opinion poll of 1004 adults
(random-digit dialing)
June 8-11, 1995
margin of error +/- 3.1

Research!America Louis Harris & Assoc., June 1995

Support for Basic Research

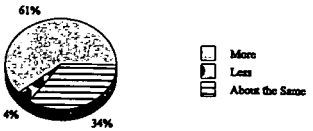
Even if it brings no immediate benefits, basic scientific research which advances the frontiers of knowledge is necessary and should be supported by the Federal Government.

(Question adapted from the National Science Board's *Science and Engineering Indicators*).

Research!America Louis Harris & Assoc., June 1995

Information on Medical Research From the Media

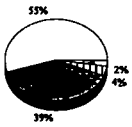
Would you like to see more, less, or about the same?



Research!America Louis Harris & Assoc., June 1995

World Leadership

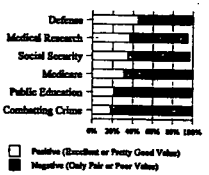
How important is it that the U.S. maintains its role as a world leader in medical research?



Research!America Louis Harris & Assoc., June 1995

Value of Selected Federal Programs

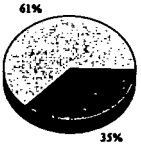
- Americans rank medical research among the top taxpayer supported programs.



Research!America Louis Harris & Assoc., June 1995

Willingness to Spend More

Should your Representative in Congress and Senators support or oppose legislation that would give tax credits to private industries to conduct medical research?



Research!America Louis Harris & Assoc., June 1995

Willingness to Spend More

If you could check off a box on your federal income tax return to have some of your tax refund be designated to medical research, do you think you would do this?

- When those who were willing to designate were asked the dollar amount they would check-off, the median response was $23.

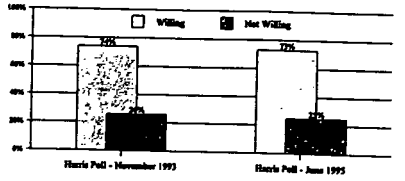
Research!America Louis Harris & Assoc., June 1995

Opinion on Proposed Cuts in Federal Support for Universities and Hospitals

Research!America Louis Harris & Assoc., June 1995

Willingness to Spend More

Would you be willing to pay a dollar more per week in taxes if you knew the money would be spent on medical research to better diagnose, prevent and treat disease or not?



Research!America Louis Harris & Assoc., June 1995

News

THE ALLIANCE FOR AGING RESEARCH

FOR IMMEDIATE RELEASE
JUNE 27, 1995 [6 AM]

CONTACT: MELANIE MODLIN
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RESEARCH ON AGING CALLED "CRITICAL" TO CURB RISING U.S. HEALTH COSTS

New Congressionally-Mandated Report Urges Additional Funds For Research To Prevent & Delay Costly Diseases of Old Age

WASHINGTON, DC -- The current aging of the American population and the coming tidal wave of aging Baby Boomers argue for immediate increased public investment in aging research, according to a new report to Congress released today by Senator **William S. Cohen** (R-ME) in a hearing on breakthroughs in neurological research by the Senate Special Committee on Aging.

The report, entitled ***The Threshold of Discovery: Future Directions for Research on Aging***, was authorized in 1990 by Congress to assess the scientific understanding of aging in America. The report also points to some of the best hopes from research and science for answers to many of the debilitating diseases and conditions of our time. At its inception, the Alliance for Aging Research, a national nonprofit advocacy organization, pressed for legislation adopted by Congress which mandated funding for the Task Force on Aging Research, which has now issued the report.

Following compelling testimony from **Benjamin Reeve**, brother of spinal cord injury victim **Christopher Reeve**, and from **Millie Kondracke**, wife of ***Roll Call*** editor Morton Kondracke and a sufferer of Parkinson's disease, the Committee heard testimony from a number of America's leading scientists and researchers about new breakthroughs that could save the nation billions of dollars by preventing, postponing or delaying major health problems that afflict many aging adult Americans.

"America faces enormous economic and social costs if we fail to improve health and functioning in old age," stated **Dr. Richard Besdine**, a scientific advisor to the Alliance for Aging Research. "Either we continue paying for the 'sick care' which this rapidly approaching army of aging Baby Boomers will require, or we adopt the more humane and cost-effective option of investing in first-rate research which can help to cure, prevent or delay dysfunction in later life."

In responding to Dr. Besdine and others who testified before the Committee, Senator Cohen was also emphatic in his support of aging research: "Delaying the onset and finding cures for Alzheimer's disease, Parkinson's disease and other diseases and conditions of aging will save billions of dollars for Medicare, Medicaid and the entire health care system. As we seek to preserve Medicare, we cannot afford to put the brakes on aging research. We must

develop a national strategy toward preventing, delaying and curing the diseases of aging, if we are to have any real hope of digging out from under the avalanche of aging health care costs."

Adding his support to Senator Cohen and Dr. Besdine was **Daniel Perry**, executive director of the Alliance for Aging Research and one of three public members of the Task Force on Aging Research. "This report could not come at a more critical time," Perry said. "The National Institutes of Health may well sustain cuts of 10 percent or more in the current budget cycle, while Medicare and Medicaid look like they will face the most draconian cuts in their history."

"At the same time, the number of aging Americans is escalating rapidly, thanks largely to the successful application of the fruits of past research. Soon the Baby Boom -- the largest generation in American history -- will turn into the senior boom. How will the country care for them?"

"We believe that the federal government should move aggressively to contain costs and mitigate the human suffering caused by the diseases and conditions of aging by funding a cost-effective strategic research and development program. The Task Force report lays out such a program in some detail, and it is aimed at delaying long-term illness and disabilities that affect the elderly."

To fully implement the research initiatives recommended by the Task Force, the current allocation of $841 million presently mandated by the Department of Health and Human Services and by the Department of Veterans' Affairs on all forms of aging research would need to be significantly increased to approximately $1.1 billion.

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PREVIEW SUMMARY

THE THRESHOLD OF DISCOVERY: FUTURE DIRECTIONS FOR RESEARCH ON AGING

MEDIA NOTE: Full copies of this report will be released by the Senate Special Committee on Aging on Tuesday, June 27 at 9:30 AM in Room 216 of the Hart Senate Office Building. For more information about the hearing, please contact Michael Townsend of Senator William S. Cohen's office at (202) 224-5364.

The report is entitled ***The Threshold of Discovery: Future Directions for Research on Aging***. It was authorized in 1990 by Congress to assess the scientific understanding of aging in America and to point to the brightest prospects from research and science for answers to many of the debilitating diseases and conditions of our time. At its inception, the Alliance for Aging Research pressed for legislation adopted by Congress which mandated funding for the Task Force on Aging Research, which issued the report.

The report was developed by the Task Force on Aging Research, whose 38 members included: four Members of Congress, six directors of Federal agencies, the Surgeon General, representatives from the National Institutes of Health, and the Department of Health and Human Services and Veterans Affairs. The Alliance for Aging Research was one of three public organizations that was asked to make contributions to the Task Force.

Over 75 of the nation's leading scientists in aging research also made contributions to the Task Force Report. The report's resulting 192 recommendations propose research initiatives that encompass a broad spectrum of issues -- biological, medical, health services, psychological, social, economic and demographic. Each recommended area of research offers real potential for preventing or delaying many of the chronic diseases that afflict middle-aged and older people.

As detailed in the report, some examples of emerging therapeutic interventions that may postpone or prevent chronic age-related diseases include:

- Testing individuals for genetic predispositions to a wide range of age-related diseases (including cancer, Alzheimer's disease, hypertension, osteoporosis, arthritis, and others), initiating early detection efforts, and even undertaking preventive strategies. Understanding the linkages between genetic predisposition and disease processes offers enormous potential for the development of improved treatments.

- Reducing the impact of coronary heart disease and stroke, the major causes of morbidity, mortality, and disability, particularly in older persons, is virtually at hand. Possible strategies range from primary prevention directed at modifying certain risk factors to improved detection, diagnosis, and treatment of clinical conditions.

- Identification of pre-symptomatic patients with Parkinson's disease and placing them on preventive therapy before significant symptoms appear.

Full copies of the report are available to the media by contacting either:

Jane Shure
Public Information Office
National Institutes on Aging
301-496-1752

or

Melanie Modlin
Communications Director
The Alliance for Aging Research
202-293-2856

# # # #

PARKINSON'S ACTION NETWORK

STATEMENT OF PARKINSON'S ACTION NETWORK
By Joan I. Samuelson, Esq., President

Submitted for Hearing of
Senate Special Committee on Aging
June 27, 1995

I am one of millions of Americans with Parkinson's disease. Our organization, the Parkinson's Action Network, was created to give a voice to our community in the effort to speed up the research effort delivering breakthroughs and cure of this dreadful disorder.

Parkinson's is an invisible, insidious disease which kills the brain cells that produce dopamine, a neurochemical that controls motor function. When at least 80% of those cells are dead, the symptoms -- of stiffness, tremor and slowness of movement -- begin to emerge. At that point, a person begins to show some combination of those symptoms, and they only increase as more cells degenerate.

Approximately one million Americans have Parkinsonism, the symptoms of Parkinson's disease. At least three times that number are losing dopamine cells from Parkinson's, but do not yet show symptoms and do not know they are at risk.

With the state of science now, we are fighting a losing battle to keep the basic movement that permits us to function. A drug commonly known as "L-dopa" replaces the missing dopamine and restores function, but it works inefficiently, it produces side-effects, and eventually it does not work at all. As Parkinson's-caused nerve cell degeneration advances, it strips away each automatic movement our systems need to walk, talk, swallow, even move at all.

The testimony today of Millicent and Morton Kondracke gives one example of the dreadful toll that Parkinson's takes on the people it strikes, and their loved ones. Their story is tragically common: my story and those of countless others in our Network files mirror theirs. As an example of the later devastation that awaits us, attached to this statement is that of Michael J. Strone, who tells of the life his parents now lead

after 18 years of Parkinson's. In addition to Mr. Strone's father, his grandfather and great-grandfather also suffered from Parkinson's. It is important that the Congress know of our suffering. It is equally important that it understand the financial devastation the disease inflicts on us and our country. Parkinson's is estimated to cost America $6 billion per year in medical costs, disability support and care, lost productivity, lost tax revenue and other social costs. Our estimates suggest that this figure greatly underestimates the true cost.

Attached to this statement is a compilation of profiles of the financial burden on people with Parkinson's. They range from people with limited disability to those completely incapacitated. In every case the cost is significant. Parkinson's medication is very expensive, and alone probably costs Americans in total well over a billion dollars. The battle against loss of function also involves ongoing physician's treatment, physical therapy and other social services. The disability that comes as the disease progresses, however, is financially devastating.

See the example of "Male IV": his assisted living costs $104,000, half of which is paid by Medicaid. This takes a huge toll on the American families hit by Parkinson's, but it also hits the taxpayer, in the form of higher Medicare, Medicaid, SSDI and other programs. See also "Male II," who was hit with symptoms at age 28, permanently disabled from employment at age 36, and will burden the society for the rest of his life.

Despite the common myth that Parkinson's only affects the oldest sector of the country, in fact the average age of symptom onset is 57, with a third of all victims' symptoms starting in their 20's, 30's and 40's. Since Parkinson's soon begins to disable its victims, most victims' work productivity is affected. The financial impact is enormous.

In a 1988 study, a group of researchers at the University of Rochester developing a pharmaceutical treatment that attempted to slow progression of Parkinson's calculated the cost savings that would result from just a small delay. They calculated that of the 44% of Parkinson's patients in the first stages of the disease, 31% would lose their jobs within one year as a result of Parkinson's. They further found that a mere 10% slowing of Parkinson's progression would translate into 16.9 additional weeks of employment per patient. This modest improvement would result,

they estimated, in a net return of $327 million annually in additional taxes paid, savings in disability payments and delaying costs of institutionalization.

In comparison, the federal government's research investment is only $26 million, which amounts to $26 per year per person presently suffering from Parkinson's symptoms. (This does not even count the millions who have pre-symptomatic Parkinson's.)

The science offers tremendous potential. Ole Isacson, M.D., who testifies today, and others across the country describe great progress in research using tissue transplants, gene therapy and other biotechnical and surgical approaches. Parkinson's is often described by researchers as the neurological disorder most likely to produce a cure. As a consequence the breakthroughs are coming, but they are in slow motion because of the minor federal investment.

In the meantime, we continue to suffer, and America sustains a huge, unnecessary financial burden. This cost will increase dramatically as the "baby boom" generation ages.

Better accounting of the true cost of Parkinson's should be a priority, and our community is collecting the data to provide one. In the meantime, though, the Congress should realize that each year it keeps Parkinson's research funding at such a low level, it is doing more than delaying the rescue of our suffering community. It also is increasing the huge federal health and human services burden by an amount manyfold greater than the amount we need for a cure.

PARKINSON'S ACTION NETWORK

THE COST OF PARKINSON'S:
PROFILES OF PEOPLE SUFFERING FROM PARKINSON'S DISEASE

Following are individual examples of the million Americans bearing the financial burden of Parkinson's disease. These examples illustrate that the current estimates of the cost of Parkinson's -- presently estimated as approximately $6 billion per year -- is a very conservative figure. That amount probably only includes basic medical care costs. It does not include the huge additional costs of related medical costs resulting from falls and other Parkinson's consequences; non-medical care such as physical therapy; disability benefits from private insurance and government programs such as SSDI or SSI; lost tax revenue due to early retirement or reduced employment; assisted living, respite care and nursing homes; and the lost tax revenue from lost employment opportunities of care-giving family members.

FEMALE I	Years with Parkinson's	9
	Age at onset:	36
	Current age:	45
Status:	Working full-time but disabled from previous employment as trial attorney.	
	Medication costs/year	$2,788.00
	Medical care/year	$650.00
	(plus travel to specialists)	
	Related care (physical therapy, etc.)	$ 2,340.00
	Lost taxes on earnings lost per year	$20,000.00
	TOTAL PER YEAR	**$25,778.00**

* * *

MALE I	Years with Parkinson's:	6
	Age at onset:	40
	Current age	46
Status:	Permanently disabled from full-time employment as CPA.	
	Medication costs/year:	$ 4,697.00
	Medical care/year:	$ 1,950.00
	Private disability insurance paid/year:	$72,000.00
	TOTAL PER YEAR	**$78,647.00**

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MALE II	Years with Parkinson's:	9
	Age at onset:	28
	Current age:	37
Status:	Permanently disabled from employment as city employee.	
	Medication costs/year:	$3,000.00
	Medical care above insurance/year:	$20.00*
	Related care (physical therapy, etc.):	$1,440.00
	Disability insurance/SSI payments:	$10,536.00
	Taxes previously paid on $31,500 salary, less taxes now paid on SSI/disability benefits:	$18,086.00
	TOTAL PER YEAR:	**$33,082.00**

* Care covered by Kaiser with $3,600/year premium.

* * *

MALE III	Years with Parkinson's:	18
	Age at onset:	37
	Current age:	55
Status:	Permanently disabled from employment from job earning $83,400/year.	
	Medication costs:	$3,924.00
	Medical care:	$200.00
	Related Care (physical therapy, etc.)	$3,200.00
	Disability payments by Aetna Insurance and SSDI:	$51,756.00
	TOTAL PER YEAR:	**$59,080.00**

* * *

MALE IV	Years with Parkinson's	18
	Age at onset:	53
	Current age:	71
Status:	Totally disabled; unable to care for self; needing round-the-clock care.	
	Medication costs:	$2,500.00
	Medical care:	$10,200.00
	Related care (hospitalization and care following a fall caused by Parkinson's symptoms):	$40,000.00
	Assisted living (in-home hired care to assist family; 50% paid by family, 50% paid by Medicaid):	$104,000.00
	TOTAL PER YEAR:	**$156,700.00**

STATEMENT OF MICHAEL J. STRONE, ESQ. TO THE SENATE SPECIAL COMMITTEE ON AGING
HONORABLE WILLIAM S. COHEN, CHAIRMAN

THANK YOU FOR THE OPPORTUNITY TO SUBMIT THIS STATEMENT ON BEHALF OF ALL THOSE IN THIS COUNTRY WHO ARE AFFLICTED WITH PARKINSON'S DISEASE. I BEG YOUR INDULGENCE TO TAKE A MOMENT OF YOUR TIME TO CONSIDER SOMEONE WHO CANNOT BE HERE WITH YOU TO TESTIFY IN PERSON.

THIS MAN IS EMBLEMATIC OF THE ONE MILLION PEOPLE AFFLICTED WITH PARKINSON'S DISEASE: HE WAS A PHYSICIAN -- A HEALER OF PEOPLE, FORCED TO RETIRE BECAUSE HIS HANDS AND BODY NO LONGER WOULD OBEY HIS COMMANDS. HE SITS NOW AT HOME, A PRISONER OF A CHAIR FROM WHICH HE NO LONGER CAN ARISE WITHOUT ASSISTANCE. IF HE STANDS UNAIDED, HE WILL FALL, UNABLE TO GET UP. EVENTUALLY, HE WILL BE UNABLE VOLUNTARILY TO MOVE AT ALL. HE IS COSTING THE GOVERNMENT OVER $150,000 ANNUALLY IN CARE. THIS ONCE VIBRANT MAN HAS SAID ON MORE THAN ONE OCCASION THAT IF HE COULD HOLD A GUN STEADY ENOUGH TO SHOOT HIMSELF, HE WOULD. **THIS IS THE REALITY OF PARKINSON'S DISEASE.**

LET ME TELL YOU ALSO ABOUT A WOMAN WHO SHOULD BE ENJOYING HER GOLDEN YEARS. INSTEAD, SHE STAYS AT HOME TO FEED, CLOTHE, CLEAN AND CARE FOR THAT ONCE VIBRANT MAN WHO SPENT HIS LIFE CARING FOR HER. SHE CANNOT SLEEP AS SHE AWAITS HIS CALLS FOR HELP IN THE MIDDLE OF THE NIGHT. HER PLIGHT IS IGNORED BY EVEN HER CLOSEST FRIENDS BECAUSE SHE IS NOT THE *SICK* ONE. SHE FEELS CHEATED, DEPRIVED OF HER LIFE AS WELL AS HIS. SHE BECOMES EMOTIONALLY BARREN AND PHYSICALLY ILL. SHE DESCRIBES HERSELF AS A *WIDOW WITH A HUSBAND*. SHE HAS CALLED THE SUICIDE HOT-LINE THREE TIMES THIS YEAR.

LEST YOU THINK THAT THIS IS MERELY SOME FIGMENT OF AN OVERACTIVE IMAGINATION, LET ME ASSURE YOU THAT THESE TWO PEOPLE ARE VERY REAL: THEY ARE MY PARENTS!

THE TRAGEDY OF PARKINSON'S DISEASE IS ONE THAT MANY OF US KNOW ALL TOO WELL. THE DISEASE DESTROYS NOT ONLY THE LIVES OF THE AFFLICTED BUT THE LIVES OF THOSE CLOSEST TO THEM, AS WELL. YET, PARKINSON'S DISEASE REMAINS IN THE SHADOWS OF THE PUBLIC'S CONSCIOUSNESS, ITS NATURAL ADVOCATES TOO SICK AND PREOCCUPIED TO ENSURE THAT THE DISEASE GETS EVEN ITS FAIR SHARE OF ATTENTION.

THE FEDERAL GOVERNMENT ANNUALLY SPENDS OVER $1000 ON EACH *AIDS* PATIENT; ON PARKINSON'S DISEASE: $26! THIS STARK STATISTIC IS NOT MEANT TO DIMINISH THE SIGNIFICANCE OF ANOTHER DISEASE, BUT SIMPLY TO POINT OUT HOW WOEFULLY INADEQUATE THE FUNDING IS FOR PD'S ONE MILLION SUFFERERS.

THIS COMMITTEE MUST TAKE INTO ACCOUNT THAT MY FATHER HAS BEEN DIAGNOSED WITH THIS DISEASE FOR EIGHTEEN YEARS. HE MAY BE EXPECTED TO SURVIVE (AS OPPOSED TO LIVE) FOR MANY YEARS TO COME IN AN INCREASINGLY DEBILITATED STATE. THE COST TO THE GOVERNMENT IN ECONOMIC AND HUMAN TERMS IS INCALCULABLE WHEN EXTENDED TO THE ONE MILLION PARKINSON'S DISEASE PATIENTS AND AN EQUAL NUMBER OF CAREGIVERS. THAT IS WHY ALLOCATING DOLLARS TO RESEARCH TODAY IS NOT ONLY COMPASSIONATE BUT FISCALLY COMPELLING. A CURE OBVIATES THE NEED FOR CARE AND TREATMENT, SAVING THE FEDERAL GOVERNMENT UNTOLD BILLIONS IN CARE AND MEDICAL COSTS.

PLEASE HEAR OUR PLEA. YOUR CONSTITUENTS AND COMMON SENSE DEMAND IT.

THANK YOU VERY MUCH.

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Morris K. Udall Parkinson's Research and Education Act S. 684 and H.R. 1462

I. The Strong Public Need for the Act

Parkinson's disease and related disorders afflict as many as 1.5 million Americans, approximately 40 percent of whom are under the age of 60. The cause of Parkinson's is not known at this time. What is known is the cells producing dopamine (a neurochemical) inexplicably degenerate.

Persons afflicted with Parkinson's suffer uncontrollable tremors, muscle stiffness and a loss of motor function. Eventually, Parkinson's renders its victims incapable of caring for themselves, placing a tremendous toll on the victims, their families and loved ones. It is estimated that the disease costs society nearly $6,000,000,000 annually.

Yet, the federal program for Parkinson's research is grossly underfunded. Parkinson's research receives far less support than most other disorders, totalling only $26 per patient in direct funding in 1994.

II. The Act's Proposal for Meeting the Strong Public Need

The Morris K. Udall Parkinson's Research and Education Act was re-introduced on April 6, 1995, by Senator Mark O. Hatfield (R-OR) and Congressman Henry Waxman (D-CA). The bill will:

- Authorize funding of $100 million to the National Intitutes of Health for Parkinson's research;
- Expand basic and clinical research into Parkinson's, and coordinate the research agenda;
- Establish Morris K. Udall Parkinson's research centers across the country;
- Establish Morris K. Udall Excellence Awards;
- Establish a Parkinson's databank and information clearinghouse; and
- Establish a National Parkinson's Disease Education Program.

III. Morris K. (Mo) Udall

The bill is named in honor of former Arizona Congressman Mo Udall who served in the House from 1961-1990. Diagnosed with Parkinson's in 1978, Mr. Udall was forced to retire due to Parkinson's complications and is now living in a long-term hospital facility in Washington. As chairman of the then-House Interior Committee, Mo was widely respected for the ability to steer such controversial legislation as the Alaska Lands bill and the Surface Mining bill through a contentious Congress by being able to charm, cajole and outwit his opposition. Congressman Udall contended for the Democratic nomination for President in 1976 and, although he finished second to Jimmy Carter, he gained widespread respect and affection for his grace and courage. His determination to live a full and vigorous life even though afflicted with Parkinson's has gained him further admiration.

IV. Contacts

- Sue Hildick, Legislative Director, Senator Mark Hatfield (R-OR), 202/ 224-3753.
- Karen Nelson, Staff Counsel, Congressman Henry Waxman (D-CA), 202/225-3976.
- Jeff Myers, Legislative Assistant, Congressman Fred Upton (R-MI), 202/225-3761.
- Joan Samuelson, Director, The Parkinson's Action Network, 707/ 544-1994.

Kenneth E. Judy
499 Leland Road
Fredericksburg, Virginia 22405
June 26, 1995

The Honorable William S. Cohen
Chairman, Special Committee on Aging
SD-G31 Dirksen Senate Office Building
Washington, DC 20510-6400

Dear Mr. Chairman:

I am writing to you today to testify about the very real life consequences of caring for and dealing with a loved one who has Alzheimer's disease.

I have been coming to the National Institute on Aging (NIA) ward at the National Institutes of Health's Clinical Center with my wife, Bernice, who has been a volunteer in a research study for close to five years. Bernice was diagnosed at the NIA as having Pick's disease, a rare disorder with symptoms similar to those of Alzheimer's disease. The NIA nurses' input and insights have helped me learn how to take care of Bernice's many daily needs and how to keep her comfortable at home. I have to dress her, bathe her. I still give her a kiss once in a while and tell her she's still the best smoocher, and she always gives me a smile.

Often the nurses will call on the physical and occupational therapists to make suggestions as well. I really value that kind of support, and I feel they have contributed to my ability to care successfully for Bernice at home. They do more here than just research. Compassion and support make the NIA program special.

Being a volunteer is like being a part of a big family. I always look forward to coming. The staff are genuinely concerned, not just about Bernice, but about me too, and how I'm coping. We have two kids and whatever researchers learn from Bernice today might help them and others in generations to come. That's how I feel and I know that's how Bernice would feel, even though she can't say so. No one can depend entirely on themselves when they're faced with something as devastating as this. You have to depend on others.

Sincerely,

Kenneth E. Judy

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