Let the Market Do It

Richard Whitten, MD

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From my title you probably expect me to solve the global financial problems; sorry to disappoint, but my goal is much more limited

> A few years ago, (it seems like only yesterday) Frank Powell made an eloquent and convincing case for the importance of embryonic stem cell research in an Academy presentation
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> Implicit in his talk was the assumption that if the federal government did not fund the research it would not get done, or at least not quickly enough
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> Indeed, virtually all public discussion on the stem cell issue to this day has failed to make the distinction between federal and private funding of that research
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> At the time I found Frank's case for the need for the federal government to fund that research to be less than convincing

This led me to consider the reasons for my doubts, and that led me further to examine the fundamental differences in how decisions are made in public versus private enterprises

> I have studied, practiced and taught in universities, government hospitals, private hospitals and public health clinics not only in the US, but also in England, Poland, Russia and throughout Latin America
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> I have seen many examples of what works, and what doesn't work in those places in health care innovation and delivery
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> The evolution of the practice of ophthalmology over my professional lifetime has also given me a clear view of the power of private markets to develop new medical treatments
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> I have come to the conclusion that the need for stem cell research is too great to rely on, or even to involve to a significant degree, tax payer funding of that research
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> And my conclusions are independent of any debate over the ethical or moral concerns that have dominated discussions of embryonic stem cell research

This will be unquestionably an opinion piece

> What is more, I will demonstrate my case purely by personal anecdotal evidence
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> My anecdotal approach will give those who do not agree with my conclusions ample opportunity to reject those conclusions without having to deal with messy facts, studies or expert opinions

But I hope to convince you that in the area of medical research the private capital market is the most effective place to achieve the desired outcome of useful therapies

While we as a nation plunge headlong into the nationalization of our health care delivery system, we need to be cognizant of the importance of at least protecting private funding of medical research

My talk will be decidedly contrarian, given the current state of affairs in Washington, but I hope you will not find it to be too curmudgeonly

In fact, I was beginning to think I was the only person in the country with this opinion

Fortunately, an op-ed piece appeared in the Wall Street Journal just two days ago, written by Dr. Scott Gottlieb, former Deputy Commissioner of the Food and Drug Administration, strongly supporting my position, and buoying my spirits

I will hand out a copy of his apt remarks at the end of my talk, for those who wish to gain extra credit

In my opinion, probably the most significant reason for the rapid increase in health care costs in this country is that the power of private enterprise to invent effective new medical technologies has sped well ahead of our ability to pay for those advances by producing goods and services in other areas of our economy

From my perspective I do not see doctors, hospitals, or pharmaceutical and other medical technology firms becoming wealthy out of proportion to other sectors of the economy

I only see enhanced longevity and improved lifestyle enabled by the increased availability and demand for new therapies

I doubt that any of you would publicly admit to favoring inhibition of the development of new therapies as a desirable approach to cost containment

However, we will necessarily end up with rationing of care, and indirectly, with limitation of research, under a government run health care system, but that is the subject for another day

That circumstance would necessarily result in inhibition of the development of new medical therapies, by making it less profitable to take the risks

Government has ample opportunity to encourage medical research in the realm of tax incentives and patent law for businesses, as well as to offer patient safety regulation and payment for new therapeutics under government health programs

But government should not be significantly involved in the innovation or risk taking phase of research

When government invades an area of private enterprise, it usually gobbles up the most important asset of that endeavor, human capital, in ways that I will demonstrate later

And when government uses taxpayer funds for a project, it must necessarily take those funds out of the private sector, and hamper the uninhibited use of those funds by the inevitable "political strings"

However, government certainly has the ability to inhibit research with over-regulation, as Dr. Gottlieb points out in his editorial

We have a tradition in Academy of presenting no more than one talk relating directly to our day jobs

I have carelessly not used up that allowance in my previous four talks, and I hope to graduate to Senior status in the not too distant future

Therefore I decided to use what I have experienced during my professional career in ophthalmology to explore the more general question of government involvement in medical research

I realize that I am sailing upwind against a hurricane of the political winds in Washington these days

However, I hope to demonstrate by concrete example that a free market approach can be the most efficient pathway for medical research in the long run

I will use the remarkable story of the development of the intraocular lens to illustrate my point

But first, let me back track and remind you of some basics of anatomy and physiology

The crystalline lens is a small button of tissue which sits behind the pupillary opening in the eye

In order for the eye to see objects in the surrounding environment, incoming nearly parallel light rays must be focused to a point approximately one inch from the eye's front surface in order to present a clear image on the retina at the back of the eye

Approximately one fourth of the needed focusing power is supplied by this lens, the remainder being provided by the transparent cornea at the front surface of the eye

In our youth, the lens is entirely transparent and quite flexible

The natural elasticity of the lens allows it to change its shape and thus shift its focus from far to near by virtue of the contraction and relaxation of the circular ciliary muscle

This muscle sits behind the iris and is attached to the lens by fine fibers known as the zonular ligament

Embryologically, the lens is derived from the surface ectoderm, which also forms our skin

Like skin, the lens continues to grow throughout our lifetime

But unlike skin, the old lens cells do not shed, but rather are compacted into the center of the lens, as new cells are added to the outer cortex in onion ring fashion

The older cells in the center of the lens gradually become more dense and dehydrated, and thus are less elastic

This results in the familiar loss of close focusing ability experienced by each of us as we age

These older cells also lose their pure clarity due both to the accumulation of pigments and to eventual death of cells

Over time the lens thus becomes progressively more opaque

When the opacity starts to interfere with clear vision we refer to this condition as cataract

The ancients assigned this name because the black pupil eventually turns white in advanced cataract, just as clear water becomes white when it is rendered turbulent by a waterfall, or cataract

When cataract causes impairment of normal activities, the only treatment is removal of the opaque lens

When I started my training in ophthalmology in 1970 the standard treatment for cataract was complete removal of the cataractous lens, followed by the fitting of spectacles which replaced the lost focal power

These thick glasses produced a highly magnified image with greatly reduced peripheral vision and a greatly distorted spatial sense

We were unable to perform the surgery if only one eye had a cataract, since the brain could not fuse two disparately sized images, so we had to wait for the better eye to also become impaired, thereby greatly prolonging the disability of poor vision

Contact lenses somewhat reduced these optical problems, but fitting and maintaining contact lenses in the elderly is often an insurmountable challenge

In addition, studies showed that cataract surgery resulted in a significant increase in serious and potentially fatal hip fractures in the elderly due to the impaired mobility caused by distortion from the thick glasses

The theoretical advantages of being able to replace within the eye the focal power of the natural lens following its removal had been the subject of speculation for many years

However, the delicate nature of the interior of the eye proved to be a barrier which prevented any progress along these lines

At the end of World War II an English eye surgeon, Sir Harold Ridley, noted that some downed RAF pilots had pieces of the fractured Plexiglas cockpit canopy imbedded in the interior of their eyes

Having no practical means of removing the particles, he chose to simply sew up the holes and observe the eyes

Even after several years, there was no detectable reaction to the bits of plastic within the eyes

As a side note, it is fortunate for us that he did not have current technology, with which he would have immediately removed those pieces

One can almost see the comic strip light bulb above his head as the idea struck him to fashion that apparently inert plastic material into the shape of a lens

Over the next two decades he, and others, tried various methods of making lenses out of Plexiglas, or polymethyl methacrylate, which would permanently replace the removed cataract

All of those attempts failed, often with disastrous effects on the operated eyes, due both to the mechanical difficulty of attaching the lens in the appropriate position within the eye, and to crude manufacturing techniques which left rough edges on the lens implants

Because of the obvious advantages a successful lens design would offer in terms of quality of life for a large segment of the elderly population, a number of doctors, working independently, continued to attack the problem during the 1970's

These surgeons were largely shunned by the academic establishment, in which I found myself at that time, but they labored on, mostly in informal labs in their office or garage

I recall one of the most respected members of the ophthalmology faculty at UCSF stating that intraocular lenses were going to become the thalidomide of ophthalmology, a gold mine for malpractice lawyers, as we removed all the "ticking time bombs" from these eyes down the road

As potential technical breakthroughs became evident, however, venture capitalists adopted the researchers, enabling them to fund much more sophisticated research facilities

Over the next two decades dozens of startup companies introduced many new intraocular lens styles, some of which were dramatically successful in bringing the desired outcome of safe sight restoration

As the marketplace of surgeons and their patients selected the most successful lens styles, the number of companies in operation was reduced to a handful within a few years, through mergers and acquisitions of the successful, and bankruptcies of the less successful

At the same time, the average cost of a lens dropped from over $1000 in the early 1980's to less than $100 today, all driven by market forces

Each company strove to increase its market share by offering incremental improvements in the lenses

Initially all the lenses were made of rigid plastic, like a hard contact lens, requiring an eight millimeter (1/3 inch) incision in the eye to introduce the lens into position

Recovery of good vision often took several months as the eye gradually resumed its normal shape

Surgical techniques were evolving which allowed removal of the cataract through much smaller incisions by liquefying and vacuuming out the opaque material

So lenses were designed in flexible materials which allowed them to be rolled into a tiny tube for implanting in the eye

And the soft, flexible nature of these lenses also makes them much better tolerated in the interior of the eye over the long term

It now requires only a three millimeter (less than 1/8 inch) incision to perform the entire operation of removal of the cataract and insertion of the intraocular lens

This results in so little distortion in the shape of the eye that visual recovery is nearly immediate

The point of this example is to emphasize that this sea change in improved quality of life for the 1.5 million patients operated annually in the US alone occurred in less than a generation without a dime of taxpayer expense

The role of government was vital, however, in accepting the new technology as a covered benefit in the Medicare program (although this approval occurred several years after private insurers paid for the procedure)

The vast majority of intraocular lens recipients are enrollees in Medicare

In other words, the taxpayer had the luxury of being able to let private investors assume the risk of failure and the cost of development, while we reaped the reward of the successful outcome

With very little effort, the list of medical advances over the past few decades funded entirely by private investors can be almost endless

At the beginning of my medical career radiologists were limited to simple x-rays taken from several angles to study the interior of the body while visualizing little other than bones and air

Very limited imaging of non-bony structures was restricted to what one could outline using often dangerous and painful introductions of air or other contrast materials into the body

Computerized tomography and magnetic resonance imaging have revolutionized diagnosis and treatment of a broad spectrum of disease, rendering visible every inch of our body structure

Terril Efird has told me that virtually all of the advances in his area of expertise have been made by private firms pursuing expected profit from new technical developments

Consider the many advances made by new drugs, and devices such as endoscopes and lasers in diagnosis and treatment as other examples of medical progress achieved virtually entirely by private capital

I would argue that insofar as technology such as stem cell research shows any promise as a potentially effective, and therefore profitable, treatment for many diseases, the venture capital market will find the funds to make it happen

I would also argue that the total cost of privately funded research would be far less than if it were funded by the federal government

I suspect that probably many in this room disagree with me on the latter point, and most likely also on the former point as well

Let me take you back through some life examples to illustrate my assertions

I have been involved with the University of California system in different capacities from undergraduate student to clinical faculty over many years

I think it would be not unkind to point out that passage of California's stem cell research bond measure probably led most medical grant writers within the UC system to try to find a way to implant the words "stem cell" into every grant request they wrote, unmindful, I am sure, of whether their children would be able to afford to redeem those bonds when they mature

In other words, their effort is to convince grant review committees, who are spending "other people's money", that their request is meritorious

For the committee members the main concern is to appear to be fair and objective while funding a project that has a reasonable chance of producing a positive outcome

While lip service is always paid to the ultimate goal of beneficial results, a positive outcome may be judged by grant committees as merely the ability to get an article published in a peer reviewed journal, whether or not any useful advance is produced

Dr. Gottlieb's editorial pointed out that in the 60 years of its existence, the NIH, the major government funder of medical research, was only able to discover or fund the discovery of 84 new drugs, many or most of which probably did not even ultimately make it to market; not a very good return on investment

Another anecdote points out the myopia of government agencies in deciding on fruitful areas of medical research

Eighteen years ago I visited several medical facilities in St. Petersburg, Russia, where the Director of the main health clinic proudly showed me the research work of the Chair of Ophthalmology

According to him, she was correct in her diagnoses 80% of the time using her wonderful new research tool

What she was doing is taking photographs of the patient's iris, and making diagnoses in other parts of the body

This is what we know as iridology, a pseudoscience which has a predictive accuracy and scientific validity somewhat below astrology

But she had convinced the establishment that this research justified both her job and the purchase of the only computer in the clinic at that time

In contrast let me relate my daughter's brief career at Microsoft

She was a program director in charge of projects in the planning stages for Microsoft Network

She would assemble teams from several different disciplines to brainstorm proposed new programs, the team often working seven twelve hour days a week

In two instances of which I am aware, her projects were canceled after several months before reaching their final state, not because their product was unworthy or because they were not doing their jobs well

But the management decision in a rapidly changing business environment was based on a determination that the projects were no longer likely to be relevant and profitable

This was extremely frustrating and demoralizing to the team, which had worked so hard on the project, and was a key factor in my daughter's decision to leave the firm

I cannot imagine a grant review committee acting with similar alacrity and objectivity when a stem cell project hit a dead end, as the majority probably will

If Microsoft's actions seem understandably distasteful to you, I ask you to compare the balance sheets of Microsoft and our federal government

In other words, government programs tend to be process oriented while business programs are necessarily outcome oriented

In a government program, as long as procedures are followed appropriately the program is virtually eternal

We are still subsidizing mohair producers because we were afraid we would not have enough of that wool for military uniforms during World War II, even though mohair has not been used for that purpose for years; no doubt the mohair producers are filling out their forms correctly

I predict that the subsidized labs that came to a dead end in their stem cell pursuit would retain lobbyists to ensure their annual inclusion in the federal budget for years afterward

In business, a failed outcome leads to demise of the program, and if large enough, to demise of the business

When government attempts to be an outcome operator it often fails

As an example, when racial inequalities were addressed by government, the initial stated goal of assuring equal opportunity, a process declaration, morphed into the goal of equal outcome

This necessarily resulted in quotas, which have had little effectiveness in correcting the initial problem, and in at least some cases are counter-productive, yet the process continues

On the other hand, an example of a potentially useful process operation of government was outlined for us in the talk by Paula Landis on bringing together all the various stakeholders to correct the environmental damage resulting from over allocation of San Joaquin River water

This was clearly not a problem which could be solved by private enterprise, but a successful outcome will necessarily be the result of both private and government input

I would like to take on one more aspect of government funded development programs based on another personal experience

Back in the late 1980's I was privileged to have spent a long day shadowing my friend Bruce Bronzan, who was then a member of the California State Assembly

My most memorable moment of that day was sitting in on the negotiations of the Assembly Ways and Means Committee

At that time the California Legislature was finalizing its bid for the federal contract to build the Superconducting Super Collider, which was planned to be built near Sacramento

During the day that I sat in the committee's closed session on the proposal, most of the discussion was by Assemblywoman Maxine Waters

She asserted that her caucus would not approve the proposed bid for the Super Collider unless it somehow included about one million dollars to be allocated for a child care center for unwed mothers attending a junior college in her Los Angeles district

Her rationale was that since Northern California would reap an economic benefit from locating the SSC there, it was only fair that Southern California should also get some payback

I was stunned that others on the committee were not even surprised by the inclusion of such a totally unrelated issue in a multibillion dollar federal grant proposal

But it was a dramatic illustration to me of why the political process can never be as efficient as private enterprise in attaining its stated goal

Needless to say, California's bid was thankfully unsuccessful

As you are possibly aware, the "successful" Texas bid came to naught, and the SSC now sits empty south of Dallas after having spent two billion federal dollars to build 14 miles of tunnels

It was never completed because cost estimates escalated from the approved 4.4 billion to more than 12 billion dollars after starting the project, and it is now used only for occasional military training exercises

Let us now return to my original position, that is, that government sponsorship of stem cell research is not needed

Just two months ago, Geron Corporation was given FDA approval to initiate human trials of embryonic stem cell implantation in patients suffering from acute spinal cord injuries

Geron is a publicly traded biotechnology firm located in Menlo Park, California (NASDAQ symbol GERN for those who want a piece of the action) which develops biopharmaceuticals for the treatment of cancer and degenerative diseases

The embryonic stem cell lines involved in this study were developed prior to 2001, and would thus have qualified for federal research funding under then-existing guidelines had such funding been sought

However, no federal funds were used either in the development of the product, or in support of the ongoing clinical trial

Investors in the company apparently felt that the potential for profitable products is great enough to risk their own capital in hopes of sharing in that return

They additionally have voted with their pocketbooks to eschew “free” taxpayer dollars, which they feel would slow the process of new product development

Geron is only one of many privately financed companies in the US alone which are pursuing new therapies using both adult and embryonic stem cells

In addition to private capital, a number of disease-based charities such as the American Cancer Society have devoted substantial research dollars to the stem cell effort focused on their particular disease

I am certain that they will demand that their limited resources go to projects which show great promise

Probably few of these companies would turn down federal dollars in support of their research if offered

However, it is my opinion that without the cold heartless discipline of the market, these dollars would not be put to their most efficient use

A massive infusion of “other people’s money” with all the usual federal guidelines and paper work would lead to these labs becoming increasingly process oriented

> The business of following the prescribed process to continue the flow of money, rather than focusing on the goal of a useful product, would assure the survival of many jobs in support of that process, but would not necessarily hasten the outcome of a successful therapy

I see this change of focus every day, as I suspect some of you also may in your work lives, while providing care to the substantial percentage of my patients who are “wards of the state” in medical matters; that is, they are “covered” by Medicare or other government programs

> At the facility where I operate, the California Eye Institute, Saint Agnes Medical Center was recently required to spend nearly one million dollars to buy redundant surgical instruments based on what I call a process declaration
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> The CEI has twenty years experience with approximately 100,000 operations with an incidence of post-operative infection well below the national average for this relatively safe type of surgery
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> However, the accrediting agency used by the federal government declared that the standard sterilization technique in use during all that time by us as well as by most similar facilities around the country was not sufficient to prevent infection
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> The agency required a much more labor intensive sterilization process taking several hours, in place of our established process, which takes only 15 minutes

Our previous process allowed the same set of instruments to be re-used several times a day, while under the new rules a given set can only be used once per day, thus the need for many new sets

> Not only did redundant, rapidly outdated, instruments have to be purchased, but also an additional full time person had to be hired to handle the increased processing of the instruments
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> The process mandated by this agency has the mathematically impossible task of further reducing negligible patient complications in order to justify these changes in procedure
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> I do not need to emphasize the effect that such process-oriented activity has on the cost of the desired outcome of successful surgical procedures
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> Nor do I need to point out the additional people who will be consigned to the medically uninsured category because of those increased costs
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> But the accrediting agency is spending other people’s money, and is focused only on their mandate, so those are not their concerns

Our federal government is a wonderful invention, which provides us all with a remarkable degree of security, and an unfortunately ever shrinking degree of freedom, to pursue our own paths to happiness

But when it comes to innovation and risk taking, the government seems capable only of offering roadblocks to that wonderful inventiveness of the American character

We cannot at this point be certain that, despite a lot of hope and hype, stem cells will ultimately prove to be of significant value in the treatment of human disease

I, for one, would rather let those who are willing to take that gamble foot the costs of finding out, and I am more than willing to let them reap whatever rewards come from that effort

So Frank, I am with you all the way on the desirability of uninhibited research in the area of stem cell therapy of human disease (and pet disease as well for that matter)

But we do have a fundamental difference of opinion on the optimal process for funding and carrying out that research

I will close with an abridged quote from Thomas Jefferson which has implications well beyond the topic of tonight's talk. "The same *prudence* which in *private* life would forbid our paying our own money for unexplained projects, *forbids* it in the dispensation of the *public* moneys…We must not let our rulers load us with perpetual debt...The principle of spending money to be paid by posterity, under the name of funding, is but swindling futurity on a large scale".