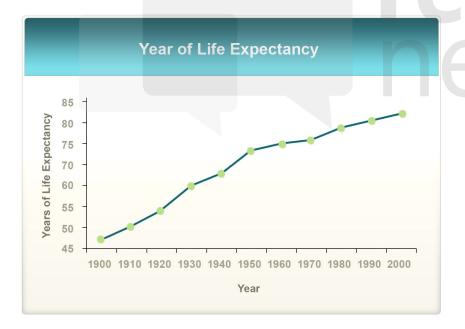
## How The World Got Lost On The Road To An Anti-Aging Pill

by Bill Sardi

#### Part 1

# Anti-aging pills: the public may not want them

One should have guessed that the pursuit of Ponce de Leon, that long sought-after fountain of youth, would be a poisoned spring before the world would find it.



American adults living today have a unique perspective, having lived through an era when their parents and grandparents survived, on average, only about four or five decades, to a life expectancy of nearly eight decades today.

In this era of increased longevity they have viewed what modern medicine often delivers – more years of living in a state of overmedicated senility and chronic physical debilitation. What senior Americans see are their peers living out their final years in futility, kept happy with endless drugs and circuses. The long-sought after fountain of youth has never materialized and they now fear death less than longevity. At a time when biologists say an anti-aging pill may become a reality, the demand for such a breakthrough can no longer be assumed.

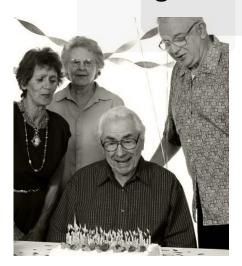
Death is the curse of life and in centuries past, most illiterate people would have swallowed a promised anti-aging pill straight away, no questions asked, just as Ponce de Leon would have unhesitatingly slurped the water from a spring that promised eternal youthfulness.

Not today – most senior Americans say they are wary of such a pill. In an online AARP poll conducted a few years back, senior Americans were asked if they would take such a pill. Most signaled a "thumbs down," saying they would not wish to live more years in a state of imagined senility and debilitation. They only heard about prolonged quantity of life, not the heightened quality of life that must obviously

accompany such a pill. Furthermore, many of those polled said they didn't want to outlive their retirement money, and still others that they didn't want to contribute to the overpopulation of the world.

Good god, they had might as well get in line for processing into <u>Soylent Green</u> after living an apportioned number of decades on the planet. Insurance actuaries would love this. Senior adults would unwittingly cooperate with the idea of dying on time.

### I wouldn't ever want to live that long



Show anyone a photograph of a man on his 100th birthday blowing out the candles on his birthday cake and the predictable response you will receive is "I wouldn't ever want to live that long!" The benefits of anti-aging pill could never be successfully marketed with this visual image.

#### Slow adoption period

Regardless of how miraculous a new technology may be, its public adoption takes time. Yet in these exponential times, the slow pace at which anti-aging pills are being embraced is bewildering. For comparison, it took 38 years for radio to reach a market audience of 50 million, but only 13 years for television to reach the same size audience, the internet 4 years and the I-pod 3 years.

After seven years (2004-2009) of marketing red wine resveratrol (rez-vair-ah-trawl) anti-aging pills in the US, Nutrition Business Journal estimates annual retail sales around \$30 million, or less than 1 million users compared against a population of 154 million adults over age 18 years of age, 35 million being over age 65. The retail market for resveratrol pills is divided into tiny slices. There are 218 resveratrol-based dietary supplements in the Natural Medicines Comprehensive Database (2010). Compare this to the sales of Viagra, a popular erectile dysfunction pill first introduced in 1998 which soared to sales exceeding \$1 billion in its first year.

Electric light bulbs only began to be widely adopted by the public when Thomas Edison put them on display at the Del Coronado Hotel in San Diego. But the longevity benefit derived from anti-aging pills cannot be experienced till the end of life. It can't be demonstrated as easily as an electric

light bulb. Which poses a question: will consumers opt to take a pill for years not knowing for certain if it will work?

The desktop computer took time to become user friendly, a problem that only Apple Computers addressed initially. Adoption of cell phones broadened when service areas expanded and fees become affordable. When entire countries have adopted cell phones to the point where hard-wired telephones have almost ceased to exist, then it certainly can be said that the long-dreamed of idea of Dick Tracy wrist phones has reached full market penetration as much as the Kodak snap camera did in the 1950s. Yet in seven years since a report in Nature magazine heralded the possibility of an anti-aging pill, acceptance of such a pill is still poor.

In the face of encroaching death, one would think more retirees would jump at the idea of an anti-aging pill, even if the evidence for such a technology is still a work in progress. But there have been so many failed elixirs of youth thrust upon the public before.

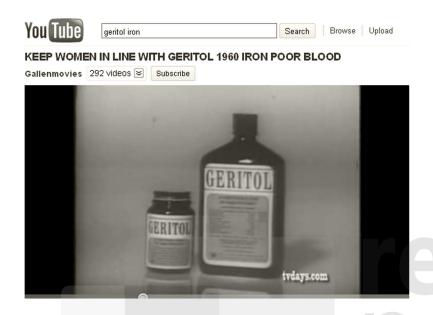
For most people, adoption of such a technology takes time, ironically maybe longer than the remaining years they have left to live.

#### **Remember Geritol?**

Senior Americans may remember Geritol, a liquid vitamin and mineral tonic that was widely promoted on television game shows such as *Twenty-One* and *The \$64,000 Question* (audience size 50 million) and the *Lawrence Welk Show* in the 1950s and 60s to their target audience of senior Americans. The introduction of this elixir came at a midpoint on the longevity timeline, when Americans were just beginning to routinely live beyond the age of 70.

Geritol was advertised to provide "twice the iron in a pound of calf's liver" – a daily dose provided 50-100 milligrams of highly absorbable iron along with an array of B vitamins and a swig of alcohol (12% alcohol content; wine is 2% alcohol by comparison). Alcohol greatly increases iron absorption. Millions of American adults naively took Geritol (also facetiously known as "iron dust"), which produced iron overload and fatty liver disease. Senior Americans were unwittingly getting sloshed with alcohol and in fact taking a product that might was well have been labeled as a pre-graveyard embalming agent. Geritol actually accelerated aging and led to the early demise of its consumers. Advertisements for Geritol in an era of black and white television are revealing; http://www.veutube.com/watch?v=pni97aPXP=w

ing: <a href="http://www.youtube.com/watch?v=pni9ZePXR-w">http://www.youtube.com/watch?v=pni9ZePXR-w</a>.



The University of California Berkeley Wellness Letter describes the problem well: <a href="http://www.wellnessletter.com/">http://www.wellnessletter.com/</a> <a href="http://www.wellnessletter.com/">http://www.wellnessletter.com/</a>

That the public would jump for Geritol and other false remedies for aging yet be slow to even sample red wine resveratrol (rez-vair-ah-trawl) pills, modern science's version of a Ponce de Leon pill, suggests that consumer desires and perceptions have changed. After all, resveratrol is the first youth molecule that has been widely heralded in prestigious scientific publications, such as Nature magazine, Science magazine, and Scientific American, rather than late-night TV infomercials.

We forget it took time for the public to widely embrace desktop computers and even cell phones. The internet spurred along adoption of both of these modern innovations. But anti-aging pills are freshly off of the drawing board stage. While public interest is growing, there are still more inquiries about hemorrhoids on Google than for resveratrol pills.

#### Not if it costs a dime

Oddly, while a red wine anti-aging molecule (resveratrol) was widely heralded on the front page of The New York Times and The Wall Street Journal in 2003 and 2006 and in 2009 was extolled on the CBS 60 Minutes television broadcast and the Oprah Winfrey Show, the sales of these pills did not rise significantly till online hucksters spammed the online world to falsely proclaim their brand of longevity pill was aired on television, tested at major universities and had already been proven to cure cancer, stop wrinkles, prevent Alzheimer's disease and trim waistlines.

When seniors heard they could purchase a trial-size bottle for free (just pay the cost of shipping), they had no idea they were being lured into a hidden online auto-ship plan to deliver monthly purchases of resveratrol pills and bill their credit card. They would take an anti-aging pill, as long as it was free! Whatever demand for red wine anti-aging pills has been created, it has been largely an online phenomenon fanned by outlaw advertisers.

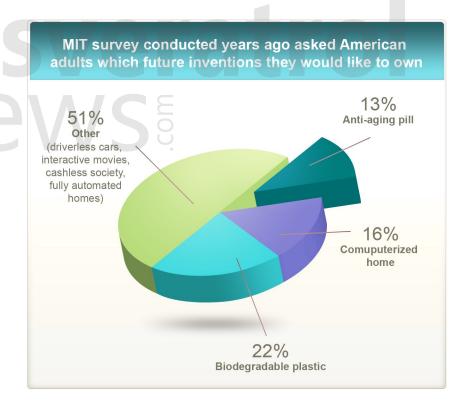
This confirms a survey conducted in Britain a few years back which showed modest acceptance for the idea of an anti-aging pill, but those polled said they would only take it if someone else paid for it. In other words, they would prefer their morning cup of coffee over a pill that would prolong life.

In marketing an anti-aging pill, a dilemma is that those who are closest to death's door – seniors — are the least likely to embrace the idea of such a development. Most would only consider it if their doctor prescribes it, if it wouldn't interfere with their hallowed prescription medications (they have no clue that they wouldn't need most drugs if the pill really worked), and it would have to be completely paid for by their health insurance plan. One man asked, "What happened to my mom and dad? I told them about resveratrol and they said they would take the topic up with the doctor. But they didn't say that about Geritol." People are now reluctant to drink from Ponce de Leon's spring.

## Convenience preferred today rather than longevity tomorrow

It would have been a good guess the road to super-longevity was going to be relegated to a lesser priority when an <u>MIT survey conducted years ago asked American adults which future inventions they would like to own</u>. Participants were

asked to pick from a list that included biodegradable plastics, driverless cars, interactive movies, a cashless society, a fully automated home or an anti-aging pill. Biodegradable plastic was the most preferred invention (22% of respondents) followed by a computerized home (16%) and then an anti-aging pill (just 13%). Maybe survey participants simply thought an anti-aging pill is a total impossibility and crossed it off their list.



This survey signaled a major change. Modern humans preferred to save the planet from pollution or increase their convenience over living more years. For them, the fountain of youth would deliver on its promise at some nebulous time in the future, whereas modern conveniences could be experienced immediately.

#### **Anti-Aging Pill Budgeted**

The Rand Institute, a think-tank for government, did issue a report about the cost of upcoming medical technologies and penciled in an anti-aging pill into future Medicare budgets. But the medical profession doesn't appear to be ready to address the idea of slowing aging instead of treating every age-related disease as they occur. The system is largely built around making money off of aging, not delaying it. Yet, say aging researchers, if the onset of agerelated disorders were postponed for about 7 years, this would spare in inevitable insolvency of Medicare. But any proposed technology to accomplish this remains nebulous in doctor's minds.

Many decades ago the first anti-aging pill did come into existence --- **penicillin**. At the time of its inception, there was debate whether such a pill should ever be unleashed upon society as it would surely bring with it the problems of overpopulation and hunger. However, the world learned

to efficiently produce more food, and the planet swelled to over 6 billion humans.

Penicillin may have added years to life, but also there were advances in public hygiene (chlorinated water that eliminated cholera, typhoid and dysentery) and fortified foods that largely eradicated diseases like pellagra, rickets and scurvy. So penicillin doesn't get all the credit. But none the less, it was demonstrated that a single pill could prolong the length of the human lifespan and have a profound effect upon humanity. For the first time a drug was referred to as a "magic bullet."

Few would question that the discovery and widespread use of penicillin, as first demonstrated by Alexander Fleming in 1929, was one of the greatest modern discoveries. But exactly where will resveratrol pills be placed in the public's mind? Anti-aging pills are an unexpected and sometimes unwelcome prospect. There is currently no category for such an invention in the public's mind. If there is, it is currently a negative one.

#### Adding years to the end of life

What modern medicine did was dramatically reduce infant mortality, increase survival at the beginning of life, and add to the pool of humans who would make it to age 70 and beyond. But now the challenge is to add more quality years to the end of life.

The problem is there is no conclusive way of proving a pill will add years to life without a decades-long study, which would be entirely impractical. There will be no "FDA-approved anti-aging pill." Markers of aging must be relied upon and some valid markers appear to be <u>red blood cell width</u>, <u>labile iron</u>, and <u>lipofuscin</u> formation (the accumulation of cellular debris over a lifetime). Red blood cell width is an off-the-shelf test that the public can begin to inquire about when they visit their doctors.

However, it appears there is a great deal of obfuscation going on when it comes to whether there is an anti-aging pill that is already available. Pharmaceutical companies want consumers to hold their breath for their pharmaceutically-made molecules to produce an anti-aging pill, bio-gerontologists are still arguing over what causes aging so they can continue to receive research grants, and online fraudsters are hawking all manner of pills that they falsely claim are proven to add years to your life. Just what is the public to conclude?

### Youthfulness preferred over longevity

Another daunting task is determining what the public really wants. As stated previously, the public doesn't necessarily want to live more years. What the public wants is precisely

what Ponce de Leon was searching for – not longevity but a fountain of youthful appearance and performance. For most adults, thick hair, smooth skin, and youthful sex drive and performance are preferred over longevity. The public spends more on looking young, buying contact lenses, plastic surgery, hair implants and skin treatments, than they do on a pill that would make them live longer. Vanity prevails.

### Genes have nothing to do with longevity

In this era when it has been said that "aging is optional," when humans have experienced unprecedented longevity only rivaled by the Biblical patriarchs, there are many reasons why most people living today won't likely achieve super-longevity even though it may be within their grasp.

Even for those retirees who do pursue a long life, it may come as a surprise to learn the absence of inherited longevity genes or failure to exercise regularly are not among the factors that would deprive a person from achieving optimal lifespan, currently believed to be around 120 years. Frankly, if an anti-aging pill is to be authenticated it should overcome the worst of diets and the absence of any inherited longevity.

If there were an existing anti-aging pill, and for the first time in the history of biology there certainly may be, it would largely be overlooked amidst the fear of longevity and confused desires of modern man, the decades-long suppression of anti-aging technology by the scientific and business community, and false notions about longevity left over from an era gone by.

### Factors that add/deduct years of life

Before this discussion about aging and longevity continues, it should be said that there are a number of reports which show that smoking, hard liquor, and other problematic health practices deduct years from your life. Habitual use of tobacco shaves about 10 years off life expectancy. Alcohol abusers who sober up add about 15 years to their lives. Abandonment of certain health habits may add years to a shortened life, but what we are talking about here is super-longevity, or what is called negligible senescence, something that has already been observed in selected animals.

So what actually does add years to human life? Most readers would be quick to say exercise and consumption of low-fat foods. But few centenarians ever took up aggres-

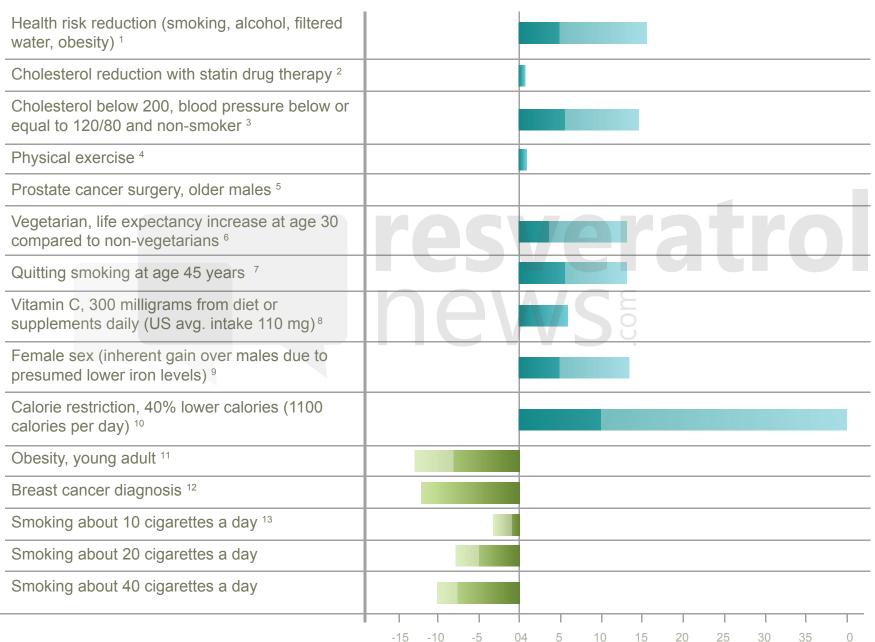
sive physical exercise programs, most ate less than ideal diets and few ever took a vitamin pill.

The list of life extenders is surprisingly disappointing. Cholesterol control only adds 0.5 years to life, regular exercise about 2 years. The greatest number of added years to human life would theoretically be produced by limited calorie intake--- around 30 years (see table on next page).

In every form of life including primates, a 50% calorie-restricted diet about doubles the lifespan. Food restriction is not considered to be a practice that most humans can adhere to, so with the mapping of the human genome and the advent of molecular medicine, it is thought that a pill could *mimic a calorie-restricted diet*, averting the need to deprive oneself of food to live longer. Whether the public will opt for such a shortcut is still in question.

Years

#### Added/Deducted years of life



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#### Part 2

# The hidden science of longevity

When did researchers first know an anti-aging pill might work?

It will come as a surprise to learn that the idea of an antiaging pill was on the drawing board decades ago but was tabled for a later date because it wasn't good for business and would interfere with the population control agenda in process.

A landmark document produced by insurance actuaries in 1979 is very telling. The report, entitled "Longevity and Genetic Engineering." published in the Record of Society of Actuaries (volume 5, No. 1, 1979), dealt with the possibility of extending human life up to 250 years via alteration of genetic machinery. An extended human lifespan would certainly pose problems for the life insurance industry which profits off of people dying on time.

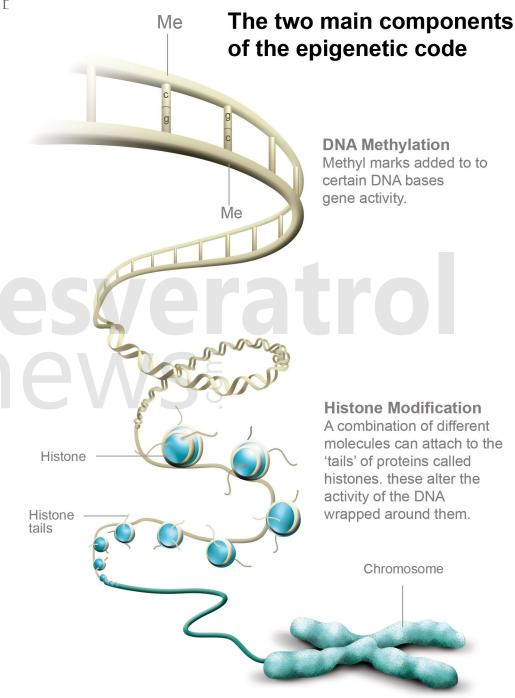
The 1979 report cited research which said: "Some breakthrough in the aging process itself will be necessary to extend the lifespan beyond 120 years." The report then went on to describe this breakthrough in remarkable detail, details which would only be revealed to the public 25-30 years later!

According to a 1974 Rand Corporation survey, 82 gerontologists believed new technologies would soon add 20 years of life to the American lifespan by 1991. During that time, <u>life expectancy only rose from 72 years to 75.5 years</u>, far short of what was predicted.

Did the medical industry drag its feet over introduction of anti-aging technologies that would have resulted in the Baby Boomers commonly living beyond their tenth decade of life?

Examination of details within the 1979 actuary report suggests this is so. Speaking in 1979 the actuaries said "some researchers report that elements called histine (histone bodies) act as covers to prevent certain genes from being accessed by the RNA. The controller of such histines (histone bodies) could then be the true leaders of cell function."

This is precisely what was announced in a report entitled "Unlocking The Secrets Of Longevity Genes" published in Scientific American in 2006 when professors at Harvard and MIT demonstrated that a red wine molecule is capable of switching genes on and off, what is called gene expression and gene silencing.



Histone bodies wrapped tightly or loosely around bundles of genes called chromatin facilitate the on-off gene switch. Imagine the prospect of cancer genes being switched in the "off" position.

In 1979, more than two decades before the human genome was mapped, it was already known that the number of genes in humans was unexpectedly low, only about 25,000. That small number, particularly because half of them are redundant or dysfunctional genes, means it may be possible to control biological processes.

But the public was left with the Darwinian model of genetics – that the genes they were born with cast their biological fate. People were misled to believe they were overweight, diabetic, or would live longer or shorter lives because of their father and mother's genes.

Why was there such a time lag in the delivery of this information to the public? The insurance actuary report went on to say: "To a large extent, genetic engineering is yet an experimental science and, as such, not one ready for widespread application in the field of medicine."

Not ready? When would it be a better time to employ genetic engineering to prolong human life than today? These actuaries were taking it upon themselves to decide it wasn't time to usher in such revolutionary technology. You will learn why below.

#### Molecular medicine in the 1970's

The 2006 report in Scientific American described small molecules, such as the red wine molecule resveratrol (rezvair-ah-trawl), which can enter the cell and influence genetic machinery in the cell nucleus. These small molecules were shown to prolong the life of primitive forms of life, such as yeast cell, fruit flies, roundworms, and finally high forms of life such as rodents. They were dubbed as molecular mimics of a calorie restricted diet. But this was all demonstrated and known in the 1970s!

A landmark report published in the Proceedings of the National Academy of Science in 1978 described a similar small molecule, <u>butyrate</u>, <u>which is produced as an end product of fiber digestion in the gut and is also provided directly in significant amounts in butter, as a molecule that alters the structure of bundles of DNA known as chromatin. It does this by inhibition of an enzyme known as histone deacetylase. Another report published in the same year confirmed this.</u>

Researchers knew they were switching genes on and off with a small molecule decades ago! It later became known that butyrate, a molecule that is likened to the red wine molecule resveratrol, is capable of prolonging the life of living cells in lab dishes via changes in gene expression.

Resveratrol is now widely panned as an anti-aging molecule and molecular mimic of a calorie restricted diet.

The actuary report hinted at the future discovery of biological aging clocks within the human body. The report said, "If these clocks were to be located and manipulated, conceivable the span of life could be extended to age 200 or even to age 250."

#### Age reversal already demonstrated

The report said: "If the genes hold the keys to the timing of natural death for an individual, then as we learn more about how to read that data, we may be able to read it for underwriting purposes. Perhaps a tissue sample taken from a prospect might show how much life he (as an individual) has left. This adds a whole new meaning to the term 'life expectancy'."

Researchers have recently demonstrated they can determine the biological age of tissues without a biopsy. Employing modern technology, they obtained digital images of the retina showing the accumulation of lipofuscin in the retina of the human eye of an 80-year old man who complained of poor night vision. After taking a resveratrol-based pill (Longevinex®) for 5 months, the lipofuscin in the patient's retina had diminished and his vision improved in five measurable parameters (night vision, side vision, acuity,

color vision and contrast vision). In this proof-of-principle study, for the first time in a human biological aging had been measurably reversed, accompanied by functional improvement! This suggests a day in the near future when adults can have a digital picture of their retina taken to determine their biological age with subsequent use of a cocktail of small molecules that could reverse the effects of aging!

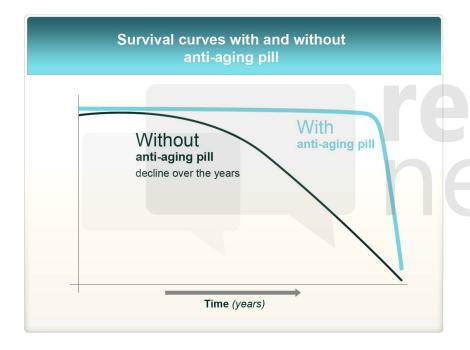
### Super-longevity is the ruination of the life insurance industry

The discussion continued as insurance actuaries mulled over the future of their profession in light of genetic engineering and super-longevity.

It became obvious that super-longevity would be bad for the life insurance industry. The insurance industry seemed to have inside knowledge of developments that would take place 25 years later. Were anti-aging breakthroughs intentionally delayed?

### More affordable life insurance, but who would buy it?

The insurance industry was already mulling over changes in their payout structure for life insurance policies. Their report said: "If life is extended, it is reasonable to expect that the period of healthy productive life will also be lengthened. Therefore, there could be very little need for an annuity with payments beginning at age 65. The continuing need in the annuity area would be for a short annuity to begin near the end of the healthy portion of the span of life."



The report went on to say: "Long life expectancies may call for long-term term insurance or many-times renewable term insurance. With a squaring of the mortality curve, so-called life expectancy term could become quite cheap and run to some fairly advanced ages. Single premium life insur-

ance could be offered at much lower rates than at present." Were life insurance companies truly ready to reduce their rates?

Gee, that would be great, life insurance companies wouldn't have to pay annuities for many, many years. However, their report went on to say:

"... if the probability of dying gets so small that perhaps, for all practical purposes, people would die from accidents alone, then maybe people would not be interested in buying life insurance at all. My view is who would buy life insurance when they did not perceive a need for it and who would sell it when they did."

The insurance companies figured out that a vastly prolonged human lifespan would put them out of business!

Do you find this difficult to believe? Well, it was also recently reported that eleven large life *insurance companies* own \$1.9 billion of stock in the top-five fast-food companies that deliver high-fat, empty-calorie meals to millions of Americans every day.

#### Misdirection: gene transplantation

What a 1980 Time Magazine report entitled "Moving Toward Designer Genes" focused on was gene transplantation, the injection of foreign genes into a mouse at its earliest stage

of development as a fertilized egg. The Time Magazine report said: "The experiment offers the possibility that by changing the genetic material in the human egg, doctors may one day be able to eliminate a host of inherited diseases." Yes, but it would only be the next generation that could benefit and inherited disorders only represent 2% of the spectrum of human disease. This appears to have been covered over to maintain funding for research. As an aside, it is possible to insert a gene into fertilized human eggs and restore the ability to synthesize vitamin C in the liver. A universal gene mutation that occurred many generations ago in human history halted the production of an enzyme (gulonolactone oxidase) that converts blood sugar (glucose) to ascorbate (vitamin C). Only humans, primates, fruit bats, guinea pigs and a teleost fish do not make vitamin C naturally as other animals do. It is surmised that if the natural synthesis of vitamin C could be restored, humans might live 200 years or more. Fish have had the gulonolactone oxidase gene inserted into their eggs and offspring naturally produced vitamin C. But the idea of doing this in humans is not a priority. This is another example of life-prolonging genetic technology that is not being applied.

#### Suppression of epigenetics

The suppression of epigenetics goes back a number of decades. While documented in the scientific literature, it was

not translated into language for the common man and disseminated to large public audiences via mass media.

When Austrian biologist <u>Paul Kammerer first noted what</u> are now known as epigenetic changes in toads in the early 1900's, other scientists denied this was possible and accused Kammerer of scientific fraud, which drove him to suicide. The whole sad story is told in the book entitled <u>The Case Of The Midwife Toad</u>. The misdirection of Darwinian biology would prevail for another ten decades.

In 1947 researchers demonstrated that vitamin A altered the expression of genes in mice who typically exhibit thick wrinkled skin and loss of hair coat due to having two copies of a gene for a single trait (known as a homozygous trait). The provision of vitamin A reversed these changes, producing less wrinkled skin. *This was an early example of epigenetics overriding an inherited trait.* Research like this was obviously overlooked in favor of the idea that inherited genetic traits were permanent.

In 1960 Francois Jacob, Jacques Monod and colleagues reported that there appears to be a double genetic determinism, one for gene structure and another for gene regulation, which they called "operator." The gene regulator would control gene expression (protein making). A "represser" would turn genes off. The "operator" or "operator" was later given the descriptor "epigenetics." In 1969

<u>Time Magazine refers to this discovery as one of the great</u> discoveries of that decade.

In 1963 <u>an article in Time Magazine</u> said: "Although geneticists agree that the giant molecules of DNA (deoxyribonucleic acid) contain the coded information that controls the development of living organisms, they have yet to decipher the message."

But as early as <u>1964 there was published science showing</u> that changes in histone proteins control gene expression (protein making). Researchers said: "A plausible functional relationship between histones and DNA's in the control of gene action seems to exist in some cases."

In 1977 Sydney Brenner, then director of the Medical Research Council laboratory in England, <u>made the first early attempt to explain "start and stop" signals in gene protein making</u>, what later became epigenetics. <u>Time Magazine briefly mentioned Brenner's discovery in a 1977 article.</u>

In 1983 researchers Lucio Luzzatto and Stanley M. Gartler, writing in Nature Magazine, explained that gene switching was also likely influenced by an alternate pathway which "probably involved methylation." Methylation, the donation of a methyl group to DNA via B vitamins was later proven to be an alternate method of switching genes in addition to the wrapping of histone strands around chromatin.

In 1995, the late Richard C Strohman, then emeritus professor of molecular and cell biology at the University of California, Berkeley, wrote of the impossibility of Darwinian biology in explaining human aging and disease. Strohman said the human genome only explains rar inherited diseases, which represent only about 2-percent of all maladies that afflict mankind. The genetic answer to chronic age-related disease, which predominates in long-living populations, is encoded in the epigenome involved in receiving signals from environmental factors such as food, food deprivation, solar radiation and temperature. A single mutation does not predict heart because there are duplicate genes. Nature has back-up systems. If one gene is mutated, a duplicate gene may function in its place.

Professor Strohman said: "Humans are well born, with genetic constitutions capable of supporting a life span of more than 100 years, with an average life expectancy of about 85 years, and an old age relatively free of morbidity (Freis & Crapol 1981; Tsai et al. 1978). In order for all of this to happen the human genome needs to find itself in an environment for which it has adequate representation-proper nutrition, housing, and sanitation, to name the obvious requirements... the natural history of our complex diseases shows that, in all probability, these are not genetic diseases, but are diseases of civilization."



Richard C. Strohman

Dept. of Molecular and
Cell Biology, University of
California, Berkeley

Professor Strohman went on to say: "Diseases tend to be place- (environment) specific and that, when people migrate, they tend to have those diseases common to their host population, not those that are common to the genes they brought with them, i.e., not common to their native population. These variations are reversible. Finally, these diseases are rare in populations that have

not been influenced by Western habits. Natural studies all indicate that our major premature killers are not genetic in any straightforward causal sense; they are diseases associated with changes in environment. That is the message from the past and present."

Professor Strohman was saying this in the face of tremendous hype over gene transplantation and the development of single-gene targeted drugs like Herceptin, Erbitux, Gleevec, Iressa, that have largely been disappointing and very costly. Age-related disease and aging itself involves multiple genes.

Strohman foresaw a rift between basic and applied biology coming. Epigenetics prevails but the drugs that were being developed were not fashioned around the control of the epigenome. With billions of biotechnology research dollars and drug profits involved, was the story about epigenetics hidden from public view for commercial gain and concerns about overpopulation? In other words, was scientific evidence for anti-aging pill being thrown back in the file cabinet, to be ignored for decades?

## A study of what Time Magazine reported about Longevity

A review of the historical archives at Time Magazine is very revealing.

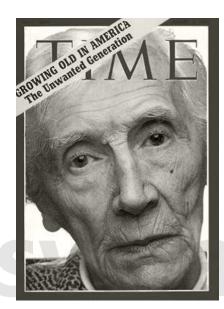
In 1971 Time Magazine was writing about the first successful transplant of genes into living tissues that might "some day be able to cure hereditary diseases." But Time didn't say inherited diseases represented less than 2-percent of all disease. The public was hanging onto the mistaken idea that their ancestors' genes predicted their health and longevity.

In 1970 Time Magazine quoted Dr. Alexander Comfort, then director of the Medical Research Council Group on Aging at University College in London, as saying <u>"some meth-</u>

od to reduce the rate of aging and to extend vigorous life by at least 15 years will be discovered within the next two decades."

The 1970 Time Magazine article said "there are giant molecules in human cells that eventually bind together... clog the cells, reduce their efficiency and eventually cause them to die." At the time researchers experimented with enzymes to clean up aged cells. The globs that clog aged cells were later characterized as cellular debris called lipofuscin. Lipofuscin accumulates when small bodies known as lysosomes within cells cannot adequately digest and eradicate cellular debris. The progressive accumulation of lipofuscin is a marker of aging. Time Magazine said the result of this research might add 30 years to the human life span. Time Magazine's editors said: "when the breakthrough comes in aging research, people in their 70s and 80s should have the energy of those in their 50s and 60s today."

But Time reporters then ventured into discussion of the outcome of such life-extending technology and the prospect it might destroy pension plans and the life insurance industry. "How could insurance and pension plans continue payments for decades longer? Will aging control become as vital an issue as birth control? In short, the changes resulting from a drastic extension of the lifespan, or even from a series of life-extending bonuses, may eventually exceed those brought about by splitting the atom or man's voyages to the moon."



For the first time, "aging control" rather than "birth control" was mentioned. By ignoring the discovery of epigenetics, the masses were to be kept in the dark about this discovery. It appears both the news media and the biology community were complicit in hiding this breakthrough.

Time Magazine's investi-

gators did not concede that a new frontier had emerged known as epigenetics until December of 2009.

And Time Magazine didn't really publish an expansive report that would draw the line between inevitable genetic fate and controllable epigenetic destiny until January of 2010 in a landmark article entitled "Why Your DNA Isn't Your Destiny." This article not only explained how epigenetic switches controlled aging and disease, but reported that epigenetic changes could also could be transferred to offspring in the next generation if there were strong epigenetic signals during conception, pregnancy and early childhood development.

Then strikingly, Time writers spoke of the work of <u>Randy</u> <u>Jirtle of Duke University who used simple B vitamins to re-</u>

<u>verse epigenetic changes in the next generation</u>. A rodent bred to eat all day long, which commonly results in diabetes and cancer, produced offspring that were normal when given B vitamins during pregnancy and early development. No gene transplantation was needed!

Time writers said: "The good news: scientists are learning to manipulate epigenetic marks in the lab, which means they are developing drugs that treat illness simply by silencing bad genes and jump-starting good ones."

But then Time's editors noted this striking admission: "The funny thing is, scientists have known about epigenetic marks since at least the 1970s. But until the late '90s, epigenetic phenomena were regarded as a sideshow to the main event, DNA." The research community is not taken to task by Time Magazine over its foot dragging and misdirection. And what influenced the epigenome were simple vitamin pills, not man-made drugs! The day the "age of epigenetics has arrived." Yes, but it was decades late. Had Time Magazine's reporters intentionally ignored what had been documented in the medical literature decades earlier? It appears so.

#### Time Magazine extols big pharma

Time Magazine seemed to play along with Big Pharma and its future promise to deliver more "magic bullet" drugs to

Americans. A 1957 article in Time Magazine said: "The reason for the astounding success of the ethical drug industry is the one that has increased U.S. life expectancy nine years in the last two decades: a steady stream of new and wonderful drugs designed to conquer, relieve or prevent almost every ailment from polio to ivy poisoning. Such recent newcomers as antibiotics, improved hormones, flu and polio vaccines and tranquilizers, have become as commonly accepted as vitamins and aspirin. Tranquilizers alone topped \$150 million in sales this year to vie with antibiotics as the industry's biggest seller. Some 70% of all prescriptions today are for drugs discovered in the past ten years."

Prescription drugs rather than vitamin-fortified foods, the Pure Food & Drug Act of 1906, the purification of drinking water that eradicated typhoid, dysentery and cholera, all played a stronger role than any pharmaceutically-designed drugs in advancing public health. But Time Magazine's editors extolled the drug industry for sale of hormones (estrogen replacement increased the risk for breast cancer), flu vaccines (which are largely ineffective, ignore innate immunity and actually deliver a weak form of the virus that causes the flu). Time's editors praised one drug company for screening over 8000 molecules to develop an anti-tuberculosis drug. But many natural molecules were overlooked in that quest – molecules that would work more effectively and less expensively like vitamin D.

<u>Time's editors went on to say</u>: "Having helped to raise the public's life expectancy (now 69.5 years at birth), (the pharmaceutical industry) is faced with a vast new market in the growing number of older people, (and) is working



eagerly on geriatric drugs designed to make aging easier. From its laboratories pour forth new wonder drugs with amazing rapidity." One drug company spokesperson said "You haven't seen anything yet." Fifty years later heart disease and cancer have yet to be conquered.

Only Sharon Begley, health writer for Newsweek, tells

the story accurately. Begley: "Roll over, Mendel. Watson and Crick? They are so your old man's version of DNA....
There's a revolution sweeping biology today—begrudged by a few, but accepted by more and more biologists—that is changing scientific thinking about the way genes work, the way diseases arise and the way some of the most dreadful among them, including cancer, might be diagnosed and treated. This revolution is called epigenetics, and it is not only beginning to explain some of the biological mysteries that deepened with the Human Genome Project. The emer-

gence of epigenetics represents a fundamental rethinking of how molecular biology works. The role of "misspelled" DNA (in the form of both classic mutations and genetic variation, first teased out in the 19th century by the monk Gregor Mendel) has turned out to explain... "only a small fraction of disease." "We were all raised on the Watson and Crick concept of DNA-driven inheritance."

But even Begley is lured towards drugs that would influence the epigenome, when the most powerful epigenetic agents are vitamins and small molecules found in grapes, berries, spices, olives and tea leaves.

If population control agents want to curb population growth then economic subjugation of the masses must be maintained. One wonders about the current worldwide economic crisis, which unfolded as if it were planned. *The gap between rich and poor is widening and with it a life expectancy gap as well*. In Britain researchers there have calculated for people under age 75 years, for very 100 people dying in the "best-off" areas there are 188 dying in the poorest areas. The poorest people in Britain are twice as likely to die before the age of 65 years, than the richest people. Poor diet, evoking epigenetic changes, produces an immediate effect. Genetic inheritance has little to do with this.

### What evidence would convince the masses?

Americans have been misled to believe their genes dictate their biological fate. In the minds of most Americans, their biological destiny is determined by their mother and father's genes. The Darwinian model of biology prevails. But in fact, genes are not cast in stone. They can be switched on and off, in a process called epigenetics, by small molecules that can be encapsulated into what constitutes an anti-aging pill.

Before any evidence involving the validity of an anti-aging pill can be fairly evaluated, Americans must shed this outdated notion that their genetic makeup is unchangeable. It is the foundation of what this new anti-aging technology is all about.

But even then, Americans are still searching for observable evidence that these youth pill work.

Assume for a moment there are strategies that can be employed to delay or reverse aging. For the moment, assume these have been scientifically validated. These strategies may include the consumption of red wine, or the use of a red wine pill. What would prompt the masses to begin using such a technology?

A guess is that it would be a pictographic form of evidence, not some data that an animal has x-percent less aging pigment. What the public is longing for is a picture of two laboratory animals of equal age, one that took an anti-aging pill and looks younger than the one who did not get the pill. The public is yearning for the wrong evidence. The anti-aging pill is not about wrinkles, it is about extra years of life.

#### Level of evidence

The problem for so many analytical critics is that there is a gap between what they deem to be scientific evidence and what consumers reckon to be subjective proof.

Scientists want to see controlled studies that are blinded, meaning one group takes an inactive placebo and another group takes the active therapy, and neither doctors or patients know who is getting the treatment. This is done to avoid bias in the selection of patients and to eliminate placebo effect. However, it should be noted here that there is no scientific evidence for the placebo effect and in fact, when researchers compared placebo with nothing, they produced the same result.

Scientists also want to see long-term (longitudinal) studies. This again is virtually impossible with humans as decades-

long studies would be the only way to produce conclusive studies of a longevity pill. Such studies are impractical and costly.

Modern medicine approves drugs that are statistically effective, not practically effective. If heart attacks occur in 1 in 500 people (2/10th of 1-percent) over a 5-year period and taking a pill will cut the heart attack rate in half, to one in 1000 (1/10th of 1 percent), it is deemed to be effective. On a relative basis it cut the heart attack rate by 50%, but in hard numbers only reduced heart attack risk by 1/10th of 1-percent; 999 people had to take the drug for one to benefit.

The classic example of this are statin cholesterol-lowering drugs, which effectively reduce circulating cholesterol numbers, but work only 1 in 71 users (3% effectiveness) to avert a mortal heart attack over a period of 3 to 5 years, says The Therapeutics Letter. The percentage of patients experiencing side effects from statin drugs exceeds its 3% efficacy. Patients only take statin drugs because their doctors tells them they might die of a sudden mortal heart attack if they don't.

However, if a consumer takes an anti-aging pill doesn't experience a benefit they can see in the mirror within a few weeks, they are far less likely to continue taking it. So the criteria used by science differ from that of the consumer.

### Restoring youth (erasing the visible signs of aging)

Even then, there are existing technologies that would erase wrinkles, cushion aging joints and thicken thinning hair. The blind spot of currently marketed anti-aging pills is that they are designed to produce cellular youthfulness, which leaves the gooey stuff called connective tissue out of the equation. A person may have youthful-functioning cells, but if they have decrepit connective tissue, which evidences itself as dried up, wrinkled skin, thinning hair, shrunken eyes and creaky joints, they will appear to be old.

The key molecule that holds moisture in connective tissue, and cushions nerves and joints as well as thickens hair and fills space in the skin is called hyaluronan (or hyaluronic acid). The body makes this Jello-like goo in cells called fibroblasts. A startling discovery was made recently where hyaluronan was injected into a knee joint and more hyaluronan was found in the joint than was injected. Hyaluronan stimulates fibroblasts to make more hyaluronan – restoring youthful levels.

Oral hyaluronan supplements can accomplish this too. The long sought-after fountain of youthfulness is at hand, and should be combined with cellular anti-aging strategies such as resveratrol. Such an invention has been postulated in a recent patent application.

The <u>oral consumption of a glucosamine-chondroitin supplement</u>, both which are precursors to hyaluronan synthesis, combined with quercetin, a molecule found in red apples which inhibits the enzyme (hyaluronidase) that breaks down hyaluronan, has been found to re-cushion joint spaces.

The <u>hyaluronan content of the face influences perceived</u> <u>age</u>. After hyaluronan injections judges assessed age downwards by 6 to 9 years. Dermatologists dominate this field of facial rejuvenation with hyaluronan injections and mistakenly claim oral hyaluronan is not orally absorbable. But the evidence says otherwise. The availability of a non-prescription anti-wrinkling pill has been obscured from public view by physicians who seek to dominate this field of regenerative medicine.

#### No guarantees

I've whimsically said that I will offer a guarantee to every person who takes an anti-aging pill. If they reach the age of 100 years, I will send them a birthday cake and 100 candles. If they don't reach the age of 100, I'll send them a full refund (③). I just don't know how they will collect.

The point is, in the back of the public's mind, a prospective buyer of anti-aging pills would like some guarantee it will work. There will never be any guarantees, and furthermore, most senior adults will have to rely upon the best available evidence since incontrovertible evidence is likely to be many years off into the future, beyond the remaining years of life of an individual.

#### Can super-longevity be achieved?

So, is super-longevity even biologically plausible? The naked mole says yes. Female naked mole rats live 30 years, ten times longer than other rodents. The naked mole rat simply does not get cancer. These rodents don't drink red wine or take anti-aging pills. Their arteries remain elastic and flexible throughout life. How do they accomplish this?

Female naked mole rats *make babies throughout life*. They experience no menopause. They are constantly menstruating and losing iron and copper, or donating iron, copper and calcium to make red blood cells, collagen and bones in their babies. Furthermore, in the burrowing of underground tunnels, naked mole rats wear away their front teeth, which is a "sink" for calcium. This is much like the way deer and moose avert calcification of their arteries by shedding their antlers. Female naked mole rats don't calcify and rust like their male counterparts, nor like most other animals including humans. The naked mole rat is the best example of super-longevity. That little rodent is teaching us how to live far longer than humans ever thought possible.

### Over-mineralization theory of life confirmed

Epidemiologists – disease investigators – confirm this overmineralization theory of aging and disease. The countries of the world that have wet grasslands, and cows and steers, consume the <u>most iron-rich red meat</u> and <u>calcium-rich dairy</u> <u>products</u> and have the highest mortality rates from heart disease and cancer.

#### Biological aging clocks

Since aging is a gradual process, which largely accelerates after age 40, any gradual changes in the human body over time might serve as a sort of biological clock to indicate how old we are from a physical standpoint.

A number of aging clocks have been discovered in the human body, that is, organs, tissues, hormones or blood factors that can be monitored for their gradual decline over the years of human life. Measures of activity in these biological clocks would distinguish biological age from chronological (calendar) age.

For example, the progressive shrinkage of glands with advancing age, such as the *thymus gland* which is involved in making T-cells to maintain immunity, or the *pineal gland* 

at the base of the brain that produces the sleep hormone melatonin, may be a marker of aging.

Another <u>aging clock is in the mitochondria</u>, about 300 small bodies within the cell which produce cellular energy. By the age of 80 only about 4% of these mitochondria are operational.

All of the aging clocks appear to be related to a process called <u>autophagy</u>, the <u>inability of cells to cleanse themselves of debris called lipofuscin</u> (li-poh-fuss-kin), which accumulates over time, generates free radicals, chronic inflammation, gene mutations, and eventually cellular dysfunction and cell death. <u>The inability of living cells to cleanse themselves of debris is considered to be central of the speed of aging. Autophagy can be manipulated by certain small molecules</u>, maintaining youthful cell function.

Organelles within cells called lysosomes, which produce cleansing enzymes, begin to calcify and rust over time, particularly after full physical growth is achieved around age 18 in males, and after menopause in females. Prior to that, calcium, iron and copper are directed toward the making of new red blood cells, collagen and bone. Once full growth is achieved, these minerals begin to overload human tissues, particularly the brain and liver.

By the time a male is 40 years of age he has twice as much stored iron, and four times as much accumulated calcium when compared to an equally-aged female, and has double the rate of diabetes, cancer and heart disease. <u>Women de-</u> <u>velop the same rates of disease once they cease menstrual</u> <u>control</u> of these minerals.

#### Three speeds of human aging

The human body ages at three different speeds in a lifetime. During the first two decades of life, when childhood growth is underway, there is no measurable accumulation of lipofuscin – no measurable biological aging. In childhood, all iron is being directed toward the production of new red blood cells. Copper is being shuttled to produce collagen and calcium to produce bones. Youngsters are having birthdays, but they aren't growing older.

Once full physical growth has been achieved the demand for these minerals subsides and these minerals begin to accumulate. Iron, copper and calcium overload result. During middle age the rate of aging progresses at an accelerated pace, which has been correlated with the formation of lipofuscin and the accumulation of minerals.

Late in life, probably around age 70 or so, the body reaches a steady-state of mineralization. The storage of iron reaches its peak. The rate of aging levels off.

Only the <u>over-mineralization theory of aging</u> explains these three speeds of human aging.

There is clear evidence that natural mineral chelators (key-lay-torz) can prolong life of living organisms. That <u>evidence</u> <u>goes back a few decades</u>. Only <u>modest doses</u> appear to produce a life-prolonging effect.

An example is green tea, which contains mineral chelating molecules. These molecules bind to metallic minerals such as iron, copper, lead and cadmium. An extract of green tea (EGCG) has been shown to lengthen the life of roundworms. Habitual green tea use has been shown to prolong life in humans. Female practitioners of the "Japanese tea ceremony" have been shown to have a mortality rate half that of other Japanese women.

#### Anti-aging, proof positive

While bio-gerontologists debate what causes aging, the red-wine drinking French have already discovered an antiaging pill. It's in a corked bottle. Red wine is loaded with an array of mineral-chelating molecules (resveratrol, catechin, quercetin, ferulic acid, malvidin, tyrosol, kaempferol, gallic acid).

The French are beginning to back away from smoking and their traditionally-made red wine is beginning to produce unprecedented longevity. The number of centenarians in France has risen from 8000 in 2000 to 20,000 in 2008. For a country of 62 million people who have a high-fat diet and

drink wine to the point of inebriation, this is remarkable. It equates to 100,000 centenarians if achieved in the U.S. population (~310 million). Wikipedia says the number of centenarians in the U.S., as of November 1, 2008, was estimated at 96,548. But that number is flawed. The U.S. doesn't have accurate birth data going back 100 years. Japan is second, with 36,276 in September 2008. The rate of centenarians in Japan is 1 per 3,522 people (but much higher in Okinawa), and reported as 1 per 3,300 in the United States. With a bad diet, and half inebriated, the French have one centenarian for every 3100 people!

The optimal health benefit of wine is achieved by drinking 3-5 glasses a day, which is the point of inebriation. The objective should be to remove the alcohol from the wine and offer a pill that delivers wine solids, called **polyphenols**.

#### Putting a red wine pill to the test

One such red wine pill (Longevinex®) was tested in the animal laboratory. It was compared against a calorie restricted diet and a single red wine molecule – resveratrol. Calorie restriction is the unequivocal intervention that produces longevity in all forms of life.

Life-long calorie restriction is required to differentiate 832 longevity genes in heart tissue of rodents. Short-term calorie restriction is only shown to activate 198 genes, whereas

the red wine pill delivering any array of red wine molecules in modest dose activated an unprecedented 1711 longevity genes over a short period of time. With a multiple small-molecule nutriceutical, <u>life-long adherence to a limited-calorie diet is not required to activate a large number of genes</u>. The calorie-restricted diet and the red wine pill activated 633 genes, all in the same direction. This study is presently the best available evidence that an anti-aging pill is at hand. Otherwise an adult would have to adhere to lifelong adherence to a calorie restricted diet or consumption of an anti-aging pill to obtain a longevity benefit.

This same pill has been <u>demonstrated in the animal lab to</u> <u>prevent cardiac death in the event of a heart attack</u> (working better than aspirin), and is the only resveratrol-based pill to exhibit an L-shaped safety curve – it was shown to protect the heart at all doses tested, without toxicity, ranging from 100-7000 milligrams of resveratrol (in press, Canadian Journal Physiology & Pharmacology) whereas a 3500-milligram dose of plain resveratrol kills the heart of a laboratory animal every time. The unique array of molecules in Longevinex® abolishes potential toxicity at any tested dose, whereas an over-dosage of resveratrol or red wine increases health risks.

#### Part 3:

# Productive and unproductive ways of thinking about living a long life

It appears that most of humanity may either inadvertently or intentionally pass up one of the greatest discoveries -- that long sought-after anti-aging pill. Oh, arguments will go on forever about their merits. But what if it is true this time?

The public, in search of eternal youth, is left with obsolete ideas ingrained in them from the past and present. The public is not about to shed false notions about longevity easily. These misconceptions distract from the personal discovery of an anti-aging pill.

If an anti-aging pill were to exist, the public would be unlikely to grasp it because so much faulty thinking stands in its way.

The following are some of the most common misconceptions about anti-aging pills interspersed with accounts of people who ventured out on their own unguided mission to achieve longevity.

#### Ten Ways Of Thinking That Will Keep You From Living A Super-Long And Productive Life

### 1. My parents lived long, and I will too; I have longevity genes

This faulty thinking goes both ways. Whether your family members lived long or short lives, your biological future is not predetermined. Your fate is not locked in your genes. Yes, you have been born with certain genetic predispositions, but genetic diseases represent a small portion of all disease, and not the common disease of aging per se.

First, gene mutations can be countered with dietary supplements. For example, virtually all humans have suffered a gene mutation in their distant ancestry that resulted in a loss of ability to naturally produce vitamin C. <u>Most other animals</u>, except guinea pigs, fruit bats, primates and humans, synthesize their own vitamin C in their liver or kidneys, and make more of this vitamin under stress. Vitamin C supplements counter this problem.

Asians have a problem producing haptoglobin, a protein that mops up iron. Loose iron degrades vitamin C. <u>So</u> Asians are more prone to atherosclerosis and need more vitamin C, again a problem that is countered with supplemental vitamin C.

Dark-skinned individuals genetically produce more melanin pigment in their skin and need to spend <u>10-times longer</u> in the sun to produce the same amount of vitamin <u>D</u> as Caucasians. They need vitamin <u>D</u> supplements.

Many people of East Indian descent cannot properly utilize folic acid (vitamin B9), which is required for repair of DNA and reduction of homocysteine, an undesirable blood protein. Again, folic acid supplements rectify the problem.

The lesson here is that even inherited health conditions can be reversed with dietary supplements!

Furthermore, the whole modern impetus for an anti-aging pill was generated by the mapping of the human genome and the discovery that genes can be switched on or off, what is called gene expression or silencing, by environmental factors such as temperature, radiation exposure, food provision or food deprivation. Then molecular biologists found certain natural small molecules can mimic these factors – for example the red wine molecule resveratrol is characterized as a molecular mimic of a limited-calorie diet.

It switches a similar number of genes in the same direction as a limited-calorie diet.

Don't think because your parents and grandparents lived long, that you will necessarily follow in their footsteps. The odds are you will, but that may be because you were exposed to the same environmental factors – drinking water, diet, sun exposure, chemicals, as your immediate ancestors. These are called familial rather than genetic factors.

The crossed-wires over locked-in genetic factors has caused many an adult to throw up their hands and think there is nothing that can be done to promote healthy aging. Your biological destiny is not locked in.

Consider the story of Opaline B, a 70-plus year old woman living in a Southern state, she had a health history that included a first heart attack at age 31 and many more over the following years. She began having difficulty breathing and couldn't even find the strength to walk out of her room. She called a friend on the telephone and asked for prayer. She struggled to the kitchen for a glass of water. When she returned to her bedroom she heard someone on the radio talking about a red wine pill. She instinctively hoped it would be what she needed. After four years of taking this pill (Longevinex®) she is completely off of heart medications. After 40 years of illness – no medicines! She says her doctors are so surprised. Resveratrol pills proved to be a godsend to her.

#### 2. I wouldn't want to live that long

Did you see Jean Calment, the world's oldest living human? She was riding a bicycle at age 100. She taped a few songs as a fund raiser at age 120. She lived 122 years. She had no visible wrinkles on her face at age 60 and she still had a full head of hair at age 113. The problem is, for most Americans, they are living into their eight and ninth decades with some level of senility and physical debilitation, placing a burden upon their loved ones and living in misery. Something can be done about this now. What has been demonstrated in the animal laboratory should not be confined just to animals. People can live vigorous and active lifestyles and achieve super-longevity.

Certainly the worst way to sell anti-aging pills is to suggest anything that prompts people to think about their mortality. Photos of a centenarian blowing out candles on their 100th birthday cake are often used to sell consumers on the benefits of cataract surgery, hearing aids and anti-aging pills. But these photos are counterproductive. People aren't happy about being older, they want to be younger. Most adults look at adds like that and say "I hope I never get that old." Can you blame them? The centenarian in the picture often looks they haven't the strength to even blow out the candles. Studies show older adults look in the mirror and see a younger image of themselves. Fortunately,

God arranged things so the cloudy cataracts in their eyes often hide their wrinkles.

### 3. I am too old to benefit; there is nothing that can be done for me

Tell that to Molly M., an 85- year old California woman who was bed-bound due to chronic pain for 5 years. Without her awareness, her son began adding the powdered ingredients of a red wine pill to her liquid multivitamin. Within weeks she was walking around the house doing chores. Puzzlingly, her vision declined, but her son reached for a pair of 7-year old spectacles and put them on her nose. Her vision had dramatically improved and her visual decline actually reversed by 7 years! With the aid of the local library service, which delivers books to her home, she began devouring a book a day. She even took a two-week vacation to Montana.

Another man, Jerry H, age 85-years, didn't think he was too old to benefit from resveratrol pills. Even though he was a retired genetic professor, he had no time to examine all the science behind these pills. He was in the end-stage of chronic lymphocytic leukemia, cancer of the blood. He was receiving blood transfusions. He was so anemic he had lost his side vision and couldn't bend over or walk up stairs without getting dizzy. He swallowed down 8 to 10

resveratrol (Longevinex®) pills at a time. He began to feel better. His doctor said he could pass up his next blood transfusion, his blood count looked so good. He regained his lost sight and began to drive an automobile again. His doctor has never observed such a reversal before. It is now six years later, and Jerry H is still alive and active. He has outlived the odds posed by a life-threatening disease. Resveratrol not only spared his life, it allowed him to remain active and independent.

You are never too old to benefit from this technology. This type of thinking has been refuted by the latest studies. Aging in animals has been reversed with the use of natural molecules. Brain function has been restored in lab animals to more youthful levels. Your doctor may be waiting for similar evidence in human trials that are still years from even being conceived or may be impossible complete.

### 4. I want to look young, not necessarily live long (vanity)

With advancing age it certainly becomes more difficult to look in the mirror and visualize the wrinkles and graying hair. Yet many Americans are finding something can be done about this. Connective tissue must be supported and even rejuvenated to maintain a more youthful appearance. Many Americans have discovered that taking oral hyal-

uronic acid, a natural Jello-like molecule in joint spaces, skin, hair and eyes, stimulates cells known as fibroblasts to make youthful levels of this molecule once again.

Lisa J., a middle-aged woman, who had recently began to experience after-symptoms from early hysterectomy-induced menopause, such as hair loss, dry wrinkled skin, joint aches, mood and sleep problems, began taking an anti-aging pill (Longevinex®) that promoted both cellular and connective tissue renewal. She was elated to find her body began to age in reverse – her hair thickened, her joint pain subsided, her skin began to glow and her mood improved. She serves as an example of what accelerates aging in women with the change of life.

The loss of estrogen removes the signal to produce hyaluronan, the "molecule of youth" that gives younger women radiant smooth skin, luscious thick hair and unparalleled joint flexibility. Due to heightened hormone levels during pregnancy, women experience these benefits to a heightened degree. Women who decided to receive estrogen replacement therapy will retain some of their youthfulness and avert the loss of calcium from bone. But there is a safer alternative, like Lisa J. discovered – the use of an estrogen-like molecule such as resveratrol, which does not increase risk for breast or other cancers, and which sends signals to retain calcium in bone via the osteocalcin hormone, combined with oral hyaluronan, which activates fibroblast cells to produce youthful levels hyaluronan again.

### 5. I'll take this information back to my doctor and see what he says

This is a way of saying, "this topic is over my head, I can't think for myself and sort all this information out, so I'll rely upon my doctor to make the decision for me." Too many millions of Americans employ this decision-making process.

It is of no matter that their doctor is brain-washed by pharmaceutical companies. It is of no matter that doctors know so little about alternatives to prescription drugs. What calls patients back to the doctor's office are requests for prescription refills. What generates income are drug consults added to the doctor's insurance claim form. The patient has no idea of these inherent conflicts of interest that exist in the practice of medicine today.

Just exactly how eager will modern medicine be to embrace anti-aging pills when they would eliminate the need for most medications taken by senior adults today? Yes, all the statin anti-cholesterol drugs, all the blood thinners, beta blockers, ACE inhibitors, anti-inflammatories, antibiotics, anti-virals, even anti-depressants, could theoretically be replaced by a resveratrol pill, that exhibits the same biological action as a pharmacy full of prescription medicines.

A 70-year old man in Hawaii ventured to find out just exactly what resveratrol pills could do for him. He didn't consult

his doctor. While he prided himself in reading scientific journals regularly, he first read about the promise of resveratrol in that paragon of scientific journals -- a throw-away newspaper, the Honolulu Advertiser. Suffering with angina and not wanting to undergo angioplasty, he opted for a resveratrol pill (Longevinex®) on the first day it became available. He purchased 100 boxes and paid for overnight delivery.

He swallowed the resveratrol pills down like candy in the beginning. What he experienced caused him to be dubbed "resveratrol man." His angina disappeared. His blood pressure fell into a range typically seen by a 13-year old. His cholesterol and triglyceride numbers remarkably fell into a desirable range.

There were other health benefits experienced beyond cardiac health too. A long-standing toenail fungal infection disappeared. His enlarged prostate gland, which caused him to make frequent trips to the bathroom during the night, subsided and he slept through the night for the first time in years.

Finally, suffering with skin cancers from exposure to the tropical sun, he took the powder from the resveratrol pills and mixed it in with red wine and coconut oil, and rubbed it on his skin and scalp. His skin cancers crusted up and disappeared. He provided pictures to prove it. Surprisingly, his white hair turned back to its youthful Aryan blonde! This

man wasn't going to wait for experiments with lab rats – he was what some call an early adaptor.

#### 6. I'd rather drink wine

Wine is medicine, maybe the best of medicines. What has kept it from receiving a blessing from modern medicine is that any endorsement would likely give over-imbibers a license to continue in alcohol abuse. To achieve optimal health, 3 to 5 glasses of red wine would be required, at a cost ranging from \$3-5 a day. For comparison, an antiaging pill would cost less than \$1 a day. Furthermore, that much wine suggests some level of inebriation every day.

## 7. I wouldn't want to outlive my retirement money

This is a definite concern of retirees. But the sad fact is, most Americans are living into their 80s and 90s and facing premature admission to a nursing home that will end up depleting most savings and retirement checks. Nursing home costs range from \$3000 to \$5000 a month. This poses real challenges to families of loved ones. There isn't a nursing home that truly wants its residents to regain their youthfulness and go back home. Most institutionalized seniors are over-medicated, ensuring they will never regain a non-demented state. Ask Larry M. who began taking a red

wine pill. He found he didn't need diapering any longer for his incontinence, which forces many older Americans into nursing homes.

### 8. I don't want to contribute to the overpopulation of the earth

Why wait, you are contributing to the problem now. What can we do to help you jump off a cliff now? Of course, this is faulty thinking.

### 9. It will never be proven; chasing longevity is akin to buying snake oil

Unproven youth potions have existed since time immemorial. Another variety of this thinking is verbalized as "they are making guinea pigs out of us." It hasn't stopped people from using them. In fact, a survey conducted in England found that people who used ineffective skin creams tended to use them more than brands that are truly effective. It behooves makers of these products to offer inferior products to boost their sales. Products that do work are not needed as often.

The "unproven" tag on resveratrol pills didn't hold back Fred H., a 78-year old retired professor, from taking a red wine pill (Longevinex®) every morning. His mental faculties improved greatly. He says he manages his money better now. He even developed a software program he had in his desk drawer for years that a large company just purchased. He attributes his achievements as a "late bloomer" to his anti-aging pill.

Howard C., a Southern California 60-year old film producer, says he used to have to take his Palmcorder into the shower with him because he couldn't recall his thoughts while having a solitary moment to think about challenging business issues. No longer – Howard even ditched taking a baby aspirin pill when he learned a red wine pill thins the blood more safely than aspirin and prevents damage to the heart should a heart attack occur.

Bob Q. says his doctor informed him his body was making too many red blood cells. There is no treatment except blood letting. He serendipitously began taking a red wine pill (Longevinex®). His red blood cell count normalized.

Marlin K. experienced progressive loss of his color vision. He had difficulty distinguishing traffic lights. He frequently wore mismatched suits and ties. It all became a thing of the past when he began taking a red wine pill.

Kathy V. works at the United Nations Building in New York. Her girl friends at work want to know what she is doing. She has undergone a facial rejuvenation, taking years off of her appearance.

David G. has struggled ten years with low back pain. Prescription pain relievers were of little help. A pill containing hyaluronan resolved his decade-long pain almost overnight.

In each of the above instances, the experienced benefits were not the initial reason for taking the pills. Consumers had no expectations. They were completely surprised by these events.

Consumers may not have to wait till the end of life to benefit from an anti-aging pill.

There ARE immediate benefits that some, but not all users of these pills commonly report. Benefits like profound mental focus and clarity, viagra-like effects, unexpected stamina and endurance, less need for medications, better sugar control, better blood pressure control, reduced infections.

You may experience no changes after taking an anti-aging pill. But according to researchers at the University of Connecticut, if you take 175 to 350 milligrams of resveratrol per day you will pre-condition your heart, so if you happen to experience a heart attack, resveratrol will have already triggered defenses in your heart and you will not succumb to a heart attack. Also, any damage to your heart will be limited and repaired faster. It is believed red wine-drinkers in France, who have a much lower rate of mortality due

to heart disease (90 per 100,000 versus 240 per 100,000 in North America), experience small heart attacks, just not mortal ones.

# 10. Don't interfere with God's timing. God dictates how long we will live. God is the giver and taker of life.

Who is to interfere with God? However, we must recall that the Bible offers the greatest example of longevity – the patriarchs, who lived up to 969 years – and it was the Apostle Paul who said: "That it may be well with thee, and thou mayest live long on the earth." (Letter to the Ephesians 6:3) It is a striking fact that some people who believe in God are reticent to accept anything that might add years to their life, claiming it might interfere with God's timing. But it is completely acceptable to do things that shorten the human lifespan, such as smoking tobacco or eating unhealthy foods. And, lest we forget, the wine in the time of Noah and Jesus was unfiltered. One glass of Bible-era wine provided 25-times more anti-aging molecules than wines produced today. We must also recall Biblical instruction to imbibe in moderation.

#### **Conclusions**

There are many mental roadblocks to cast aside and reams of scientific data to wade through in making an earnest decision to take an anti-aging pill. A person can only go so far before they decide to take the plunge and opt to try a resveratrol pill. The science behind these pills has been intentionally obscured for decades. The many online hucksters only further confuse the issue, using borrowed science and never having put their pills to the test. My god, the masses may be falling for Geritol all over again.

While resveratrol is a magical molecule in itself, the greater body of evidence for longevity comes from red wine where an array of molecules in modest dose (180-300 milligrams) produces the unusual longevity seen in the French, overcoming their high-fat, high-calorie diet. Controlled scientific studies confirm that resveratrol by itself does not fully equate with the near-magical properties of red wine. The synergism of an array of small molecules added to resveratrol facilitates effectiveness at lower and safer doses.

Evidence revealed in this report suggests American adults often have poorly founded fears of longevity. Americans are living longer despite themselves and are suffering with years of chronic mental and physical debilitation. Aging can not only be slowed, but reversed. The high cost of caring for aging parents, particularly nursing home care, which

typically exceeds \$3000 a month, suggests any technology that would delay the onset of age-related disease would be a money saver.

Experience with anti-aging pills suggests even wider applications. Their ability to <u>stimulate the production of stem</u> <u>cells</u> – a type of cell from which all other specialized cells in the heart, muscles, eyes, brain originate – is just now being reported.

As an example, Eric G, a 24-year old couldn't have guessed how desperately he would need to employ newly recognized anti-aging technologies to put his body back together. An off-road three-wheeler accident produced such trauma he was not expected to survive beyond a few hours after the accident. Every bone in his head was broken, jaw, orbits, nose, chin, cranium. He spent six weeks in a coma. Swelling was horrendous. Given the severity of his injuries, if he survived, he probably would not be able to see, hear, walk, talk or reason again. Somehow he did survive, but he had lost his sight and speech.

Eye doctors had to wait for inflammation to subside to even get a look inside his eyes. When they were able to utilize an ophthalmoscope to examine the back of his eyes, they found the optic nerve in both eyes was pale – indicative of no circulation to the back of the eyes. The eye doctor delivered the grim news to Eric's father. His condition is irreversible. Eric was referred to a retinal specialist and

follow-up care. The retinal doctor game gave the same prognosis – Eric's sight would not be expected to return.

But, following Eric's eye examination, the doctor wanted to give some hope to his family. So he gave his father a box of resveratrol pills. What followed would make history. Within a few short weeks, Eric began to experience perception of light. His rush exam at the eye doctor's office revealed his optic nerves were pink in both eyes – circulation had returned. Soon Eric was able to count fingers on the eye doctor's hand from a distance of 10-feet. He began tying his shoes and his speech returned. All this was indicative of unprecedented renewal of tissues --- possibly stem cells were being generated to become new nerve cells. It can be said that Eric is at the forefront of those who will benefit from this technology. It is not just for the old, it is for any body in need of repair.

While individual cases like Eric's are not scientific evidence, they do serve to point people suffering with otherwise irreversible conditions in a hopeful direction.

In another case, a physician writes that her 77-year old mother experiences severe curving of the spine and movement disorders --- uncontrolled head and hand shaking, symptoms that are not responsive to medications. Her mother was being monitored every six months at Stanford Medical Center in San Jose, California. Symptoms had continually progressed with each visit to the doctor. After careful

investigation, her daughter suggested she try a resveratrol pill (Longevinex®). Her daughter reports that doctors were shocked when her mother went in for a scheduled check-up and her condition had actually improved. She was told this had never been seen before. Her mother was able to walk now with the aid of a cane. She is back driving her car for the first time in years.

Another woman writes of the experience of his father:

"I want to thank you and your research team for this wonder drug. I read about the anti-aging research in Fortune (I think April 2007) and immediately started trying Longevinex® on my dad who is 69 years old, who has had 4 heart attacks, a stroke, a bypass surgery and a vascular surgery to replace his clogged carotid. So essentially he was counting his last days having lived through a post operative phase that includes 30 pills a day, weak memory, constant influenza and other respiratory ailments that kept plaguing him for the last 9 years (he was operated in 1999), to a point, where he and many of us in the family had given up on him having a nice retired life And then a miracle happened. Along came a drug called Longevinex® and changed the way his life was shaping. He has been taking L for the last 12 months and the improvements in him are astounding, unbelievable, miraculous and whatever other adjective you can use to describe a stunning transformation.

Today, after a year of taking Longevinex®, he is one of the most healthy 70 years olds, his memory is back to being razor sharp, he is healthy, can walk 5 miles a day (prior to L, he would barely walk a mile), has not had a single flu/respiratory ailment for the last 12 months and his doctors cannot believe this. His doctors are some of the leading heart surgeons in Bangalore, India (that's where he lives) and are astounded by his transformation. His recent blood and other tests have shown such a remarkable improvement that the doctors thought there was something wrong with the machines, or his sample was switched etc and got it done again.

Longevinex® has given my dad a second lease of life, I really don't care too much about what the critics of Longevine or resveratrol have to say, it has worked for me dad, he is a living example of a transformation that happened in front of my eyes and I cannot thank you and your team enough!!!" Madan Nagaldinne

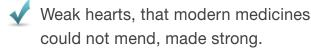
Naysayers may attribute these accounts to the placebo effect, or say they offer no objective proof. But so-called FDA-approved medications don't work in every instance either. Consider statin cholesterol-lowering pills that avert a non-mortal heart attack in just 1 in 70 users yet are FDA approved.

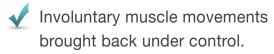
If anyone thinks all of what they have read herein is new, they might be enlightened by reading the life of Luigi Corrnaro, who lived 102 years, from 1464 to 1566 AD in Padua, Italy, and who was declared a glutton and a drunkard at age 40. Thereafter Cornaro religiously lived a life of temperance. His daily diet was comprised of 12-ounces of food and 14-ounces of red wine a day (only an Italian would call three glasses of wine a day "temperance."). He adhered to a limited calorie diet and consumed what would later would become a red wine pill. Wine in those days was unfiltered and provided about 25 times more wine solids than today's processed wines. Cornaro wrote a whole book about his wonderful long life, which has been translated into English. At age 90 he was jumping up on horses, singing songs and writing his book. You can find his translated online book here.

#### What is going on?



Irretrievably lost vision restored





Color vision regained.

Smooth skin recaptured.

Empty memory banks refilled.

These aren't everyday occurrences. Something very big is underway. Longevity seekers need to hear this.

#### Getting younger, not older

It is said that people don't desire to know how many years of life they have left to live. But what if you could undergo a brief assessment of your biological age, then take an antiaging pill and return months later for a non-invasive test that would tell you how many years you just have added to your life? In other words, how much younger rather than older you have become, from a biological standpoint?

#### 2

### A woman puts an anti-aging pill to the test





Ready to try it, but not believing, Cheryl had her husband snap a facial photo before she began taking an oral dietary supplement that claimed to rejuvenate her skin. Within 90 days these photos record the result of her personal test.

#### Blind spots (scotomas) disappear



Louis, a retired physician in Virginia, reports a bout of chicken pox at the age of 8, and a recurrence of the pox around 30 years later, had left him with blind spots (scotomas) in both eyes. About 30 years later, after taking a red wine resveratrol pill (Longevinex®) his scotomas disappeared in less than 23 months use.

#### **BEFORE**

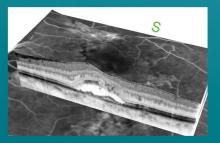
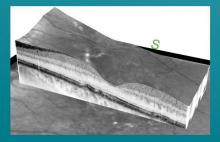


Image of scarred, bleeding, swollen retina with loss of central vision

#### **AFTER**



Retinal architecture has been restored to near normal, swelling is almost absent, vision restored to 20/20 acuity 45 days after taking anti-aging pill (Longevinex®)

The accumulation of lipofuscin (cellular debris) in human tissues is known as an aging clock. Lipofuscin can now be measured non-invasively via a brief procedure that captures a digital image of the back of your eyes (retina). The greater the amount of lipofuscin, the older one's biological age.

Imagine a day in the near future when people obtain a measurement of their ocular lipofuscin levels. Then they take an anti-aging pill for a specified time, and return for a follow-up picture. A reduction in lipofuscin levels would indicate reversal of biological age – literally turning back the biological hands of time. *This has already been demonstrated in a human*.

#### Elitists made a decision for all

It is one thing for people to shun an anti-aging pill because they errantly believe it will prolong years of misery and chronic debilitation. But it is another thing that elitists chose to take the decision-making out of their hands. Not only have elitists decided to take it upon themselves to make a covert decision about the development of an antiaging pill, but they have done so within a society which claims to be open, free and transparent.

Even more disconcerting, these elitists, working with insider knowledge, made a decision to delay introduction of an

anti-aging pill out of their own self interest, not necessarily out of interest to save society from the consequences of overpopulation.

Just how much medical research would be conducted if aging were conquered? Medical research budgets would be cut by billions of dollars as all age-related diseases would be vanquished with the implementation of such a technology. How many life insurance policies would be written if death lay 150 years into the future? How much doctoring would be avoided without age-related disease to diagnose and treat? How much would health insurance premiums cost with a youthful and robust adult population?

#### **Should humanity proceed?**

In 1976 Joel Kurtzman, a writer, and Phillip Gordon, a geneticist, wrote a book entitled "No More Dying." The title was obviously written for effect. At that time they wrote that "the prospect of living 150 years is not a fantasy."

They quoted Alex Comfort, a famous gerontologist, who said: "Unless we are slothful or overcome by disaster, it's probably going to happen within our lifetimes."

But then these authors agonized over the decision to proceed ahead, to produce unprecedented longevity and risk the social consequences. They said it could be done, but asked, should it be done?

They said, if the world reached a population of 7 billion by the year 2000 maybe 3 billion people would die of starvation and the Gross Domestic Product of the U.S. would have to reach \$4 trillion to avert financial disaster.

The U.S. GDP exceeded \$9 trillion by that year and there were 6 billion people on the planet without massive death by starvation. Countries of the world that are developed have much lower birth rates. Improve the economies of the world and population size will control itself. In developed lands women decide to have about two children, which is

population neutral. That is the current experience in Japan, Italy, North America and Western Europe.

#### The current predicament

What elitists did was place advanced countries in the predicament they are in today – a growing population of retirees whose healthcare bills cannot possibly be paid and the cost of healthcare so burdensome on society that it threatens insolvency.

### Health care expenditures over lifetime with and without anti-aging pill

Health care expenditures over lifetime WITHOUT anti-aging pill (1996 dollars)	Die at age 65	\$31,181	30% spent on last year of life
	Die at age 90	\$200,000	
Health care expenditures over lifetime WITH anti-aging pill (1996 dollars)	Die at age 90; 7 more healthy years of independent life; no nursing home	\$104,000	Less than 1% spent on last year of life

<sup>\*</sup> Calculated at \$60,000 less for last year of life costs and \$26,000 less for nursing home costs. The Effect of Longevity on Spending for Acute and Long-Term Care

New England Journal Medicine Volume 342: pages 1409-14, May 11, 2000.

In the U.S., there is a \$60 trillion shortfall for Medicare. Had an anti-aging pill been implemented in the 1970's, and 7 more years added to the human healthspan, the collapse of Medicare would have been averted. This is called the *longevity dividend*.

The seven-year healthspan extension was chosen because the negative aspects of aging tend to double every seven years. The idea is to produce a human population at the chronological age of 60 years that functions at the biological age of 53 years.

Imagine the consequences if society waits even longer to adopt an anti-aging pill. By the year 2050 Alzheimer's disease is expected to cost \$1 trillion. That is just a single age-related disease. While the U.S. Gross Domestic Product is expected to rise from \$14 trillion today to \$35 trillion by 2050, that is still a huge portion of a societies economic output for a single disease.

### Only lab rats will achieve super-longevity?

S. Jay Olshansky, Professor of Epidemiology and Biostatistics at the University of Illinois in Chicago, a proponent of the longevity dividend movement, says <u>"the belief that aging is an immutable process, programmed by evolution, is now known to be wrong."</u>

An extension of <u>disease-free lifespan of approximately 40%</u> has already been achieved repeatedly in experiments with mice and rats. Shall humanity confine longevity to laboratory animals? Shall the naked mole rat, who exhibits flexible arteries throughout life and never gets cancer, be the sole inheritor of super-longevity? Haven't the elitists made lab rats out of humans, and bred them to die early rather than live long?

We are putting epigenetics to use, but unwittingly. Obesity appears to emanate from early age in America, and not from overeating. Obesity now appears to be programmed into the population.

The insidious use of a synthetic chemical in food packaging (bisphenol A) since the 1950's appears to have <u>produced a breed of obese and disease-prone humans who have passed on this trait via epigenetic imprinting to their offspring</u>.

We know that prenatal exposure to endocrine gland disruptors, such as bisophenol A, may doom children to life-long obesity. An <u>American adult consumes ~7 pounds of bisphenol A annually</u>.

#### Mental obstacles to life extension

Richard A. Miller, M.D., Ph.D., Professor of Pathology and Associate Director of the Geriatrics Center at the University of Michigan, in his 2002 treatise entitled <u>"Extending Life:</u>

<u>Scientific Prospects and Political Obstacles</u>," bemoans the lack of public funding for anti-aging research. It is a pit-tance compared to health research budgets.

Miller calls this **gerontologiphobia** – "an irrational disposition to regard research on specific late-life diseases as marvelous but to regard research on aging, and thus on all late-life diseases together, as a public menace bound to produce a world filled with nonproductive, chronically disabled, unhappy senior citizens consuming more resources than they produce. No one who speaks in public about longevity research goes very far before encountering the widespread belief that research on extending the life span is unethical, because it will create a world with too many old people and not enough room for young folks."

At the writing of this report, there are only 7 reports on the topic of an anti-aging pill published in scientific journals listed by the National Library of Medicine. It is obvious, an anti-aging pill would put modern medicine out of business, and the research community is only giving lip service to the idea. A pharmaceutical company that touts an anti-aging hasn't the resolve to reach their objective. They say they will punt and conduct clinical trials for diabetes.

Professor Miller asks why don't we stop all current research on heart disease and cancer today, knowing such endeavors may allow people to live longer? Shall we remove seat belts from automobiles, insulin and antibiotics from pharmacies, and antismoking campaigns from schools? Of course all of this thinking is absurd, but it is where collective human thinking stands in regard to longevity.

Are we only to be allowed 40 healthy years? Maybe less due to bisphenol A exposure? Abortion and birth control limit the supply of new people. As for the adding of healthy years at the end of life, shall we proceed with covert euthanasia, which is the current road? The existing objective, to end life without pain, being totally numbed by multiple medications, is what we have settled for.