This is a Synopsis of the introductory information on the web-site, which includes the Home page, Forward, and Preface and also includes Background on Life-Extension Science.

FOUNDATION FOR INFINITE SURVIVAL, INC. (Est. 1972)
LIFE-EXTENSION & CONTROL OF AGEING PROGRAM

**WWW.FIS.ORG**

PRESENTING A SYSTEMATIC APPROACH TO LIFE-EXTENSION SCIENCE
WITHIN A BROADER, PHILOSOPHICAL FRAME-OF-REFERENCE

**T**his site is directed, primarily, to persons who are interested in the emerging science of life-extension, which brackets the subjects of health, disease prevention, curative medicine, and, in particular, regenerative medicine and the control of biological ageing. All of those are different aspects of the same condition - i.e., biological vitality.

**W**e present a systematic approach to this enterprise and will do so within a broader philosophical context. And there are important psychological, sociological, and ecological elements that are contingent to life-extension.

**T**o provide the essential background, you are asked to read the following Introduction and invited to Register so that we can send periodic notices as we build our program and this network of participants.

**T**hank you for your interest.

C.A. Everone, Trustee.

**REGISTER**

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## FORWARD

Life-Extension Science is about "Health", and it encompasses the well established, conventional areas of:

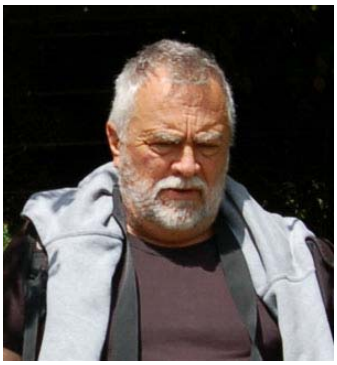
- **health maintenance**,
- **disease prevention**, and
- **curative medicine.**

However, Life-Extension Science does so from a unique and radically different perspective. Although health, prevention, and medicine are agreed to be good things and are desired by most people, those practices, by themselves, have serious contra-indications and adverse effects, unless we also focus on curing the underlying cause of modern diseases - i.e., **biological ageing**. Reversing and controlling ageing is the next barrier to advancing the quality of personal life and improving humanity in general; and without the control of ageing, there never will be any significant health maintenance or disease prevention; and conventional, curative medicine will be of only limited use. The current state-of-the-art is woefully inadequate.

I will be asserting, here, that there is one and really only one true approach to Health; and that is what will be presented as Life-Extension Science. Health and Life-Extension are interrelated, because if Health is really improved by some procedure, then the effect of that would be, naturally, some degree of Life-Extension. And the Control of Ageing is fundamental to the goal of Health and Life-Extension.

We know where this science presently stands, and we know where it needs to go, and most of the basic knowledge is already in place. So, the task is getting from where we are now to where we want to be. It is mostly a problem of engineering and the translation of scientific knowledge to technologies in a mission-oriented program under ethical and competent management. See the adjacent inset.

**The author at age 17**



**The author at age 67**

The difference here is "ageing" - i.e., a decline in biological vitality which is caused by a decline in cell number, rate, and quality. The ultimate goal of Life-Extension Science is the invention of technologies which will restore and maintain biological vitality (again: cell number, rate, quality) back to what one had between the ages of 20 ± 5. Keep that target model in mind. That is the optimal expression of each person's genotype, and that is where we need to go with our science. At such level of biological vitality, function would remain high, disease minimal and easy to cure if it did occur, and the potential lifespan greatly expanded. Such technologies reside in experimental, regeneration biology (e.g., stem cells, transcription factors, eumitogens, and such).

Biological ageing is a disease - caused by a universal,

First, however, there are a couple of notions from communication theory that are appropriate.

The process of "communication", is, most fundamentally, about getting what one wants. Communication is not just the transmission or exchange of messages. Rather, you only know if you have communicated if you get what you want. Obviously then, having a clear idea about what one wants is essential. And therefore, what this writer wants, here, is to identify people who are positively interested in the subject of life-extension and control of ageing (either for one-self or future generations or both) in order to build a network of participants and bringing this science to its full realization, as quickly as possible. That is the goal of this communication; and it begins by having interested parties **Register**.

Another notion is the 5 stages in making an effective communication, which are:

1) Attention,
↪ 2) Interest,
↪ 3) Conviction,
↪ 4) Desire, and
↪ 5) Close.

genetic defect in our specie. Beginning at about the age of 30, the natural down-regulation in cell number, rate, and quality progresses, at first slowly and then exponentially, causing the chronic diseases, and leading to senility and a limit on maximum life-span to under 100 - but for all practical purposes to about 85.

We do not need a grandiose, centralized, Manhattan or Apollo type of project to bring about the solution - rather the approach must be measured, incremental, and actionable.

If you have gotten this far in the message, then I have your "attention". The following Preface and Introduction should accomplish stages 2, 3, and 4; and the "close" is to have you **register** so that we might build your interest in becoming part of that international network of participants and, again, bring this technology forth as rapidly as possible.

Everyone, whether they know it yet or not, has a vested interest in this enterprise. Because the cure of biological ageing and the extension of a healthy and fully functioning life-span are an aspiration of virtually all people, it can be assumed that I (this "signal sender") and you (the "signal receiver") have an interest in common. In other words, it is in our best interest for us and as many others as possible to participate in this effort or at least to become properly informed about it.

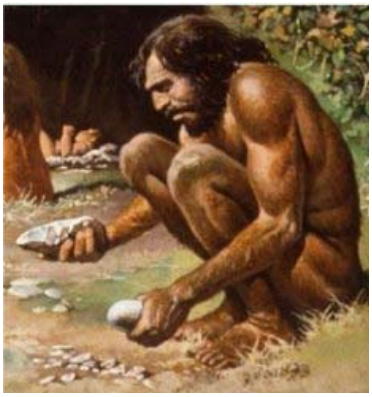
Your interest is appreciated,

*Chadd Everone*, Governing Trustee

## PREFACE

**Philosophy *vis a vis* the Science.** I became involved in Life-Extension Science in 1972 and published the first position papers soon thereafter. [1] Our current approach is essentially the same today as it was envisioned then, with the exception of the research strategy for the control of ageing, which now focuses on advancing *regeneration* biology rather than assuming that the answers are in *gerontology*. Having been in this field for some time, I can claim to speak with some authority not only about Life-Extension Science but also about the broader aspects and implications in psychology, sociology, ecology, and general philosophy. I have come to the conclusion that the major barrier to advancing Life-Extension Science is philosophical, much more than it is the science and the technology. In other words, the main problem is with our values, aspirations, psychological denial, and the level of consciousness and "spirit". Therefore, let us first cover some philosophical framing.

For the moment, try to disassociate yourself from the crowd and your usual identity - suspend your attachment to your nationality, your gender, religion, social values and position, and current historical setting. Ask yourself: "what is this thing called life and living - this arduous and apparently meaningless and ever-changing scene of fluctuations and illusions - the *Maya*?" And keep in mind that how *you* understand and define the purpose of Life will determine, in large measure, the processes which *you* take in living your particular life - the maxim, "purpose dictates process", applies. First, consider these indisputable, generic facts.



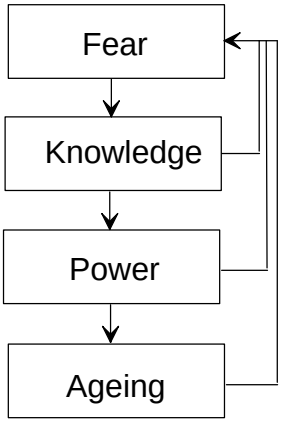
**Our Period in Evolution.** Obviously, you are, most fundamentally, your body; and your body was created by the bodies of your parents, whose bodies were created by their parents, and so on - in a ancient chain of biological entities going back to the murky, evolutionary past. Anthropologists calculate that we (Cro-Magnons or Homo Sapiens) were derived from a small cluster of about 12 inbred hominid mutants in East Africa (a cluster of 12 would be the minimum number who could sustain a mutation sufficiently to amplify their population and create a new specie). These Stone Age creatures (living by "nature, red in tooth and claw", as Hobbes characterized the primitive human condition) migrated throughout that African continent and over the Sinai landbridge, to inhabit all of the other continents (over a period of some 200,000 years), during most of which, they were barefoot and either naked or clothed in animal skins with their babies strapped to their backs. Burial mounds show that, until more recent history, none of those earlier people lived longer than about 35 years with half of their population dying in childbirth and early

[1] Everone CA, 1977; A Systematic Approach To Life-Extension And Control Of Ageing; Journal of Applied Nutrition, 29(3&4) p.32-47, 1977. Everone CA, 1978; A Uniform System For The Delivery Of Life-Extension Applications And The Advancement Of Ageing Research; Presented at XIth International Congress of Gerontology, Tokyo, Japan, August 1978.

infancy. As they radiated out of Africa, they diverged into different geographies, developing different languages and customs and becoming our present multi-racial, multi-ethnic, and multi-national groupings. For most of that history, we were dirt poor, surviving by scavenging, gathering, and hunting; and virtually everyone of us has mostly grunt peasants and slaves in our lineal heritage. Fire was captured, metallurgy invented, plants and animals domesticated, and farmers replaced the hunters and gathers. Then about 200 years ago, industrialism, the use of carbon-based fuels and other energy systems, and advanced technologies ensued, leading to our current situation. If 20 years is the period for a generation, then we are, now, some 10,000 generations from our earliest animal ancestors. The main struggle during that arduous process has been for survival and a struggle over resources, against both other human beings (our "relatives") and with Nature to control and amplify those resources. It is amazing to reflect on the fact that of all the species on Earth, we are the only one who knows that we are going to die, who has a sense of history and the future, who knows how we are made and can have magnificent conceptions like the "big-bang" as the origin of the Universe and that we come from star-dusk, and who is capable of intelligent self-design. The single most fundamental pursuit over the eons of our history has been Survival - survival of self and, by extension, survival of progeny. Survival is the single most fundamental purpose of life; it is the condition upon which all other conditions depend. The basic instinct is to survive in the present, near and more distant future, and, ultimately, indefinitely over time; and this is the central principle which forms the philosophy or Ideology of the Goal of Infinite Survival and which is promulgated in tandem with our effort in life-extension. Through most of our evolution, the sole enemy has been external circumstances. Now, in our epoch, the next struggle (the real struggle) is with the limits and detrimental aspects of our own nature. It is said that if we really wish to improve the human condition, then we must improve human nature, itself - *videlicit,* human, physical nature. And Life-Extension Science is the cutting edge of that transformation.

**Salvation Doctrine.** Virtually everyone adheres to some kind of a Salvation Doctrine. The religious, belief systems dominate; and even for those people who reject religion, they almost always hold some kind of a spiritualistic belief. Because life (as it is presently constructed) inevitably entails suffering and death, these beliefs all posit some kind of a dualistic paradigm of existence - a material realm which is NOT permanent and a non-material realm which IS permanent with a person's existence migrating from the former to the latter or oscillating between the two. Life-Extension and Control of Ageing will not yield immortality. However, it does offer the prospect of a greatly extended span of life, in optimal condition with an open potential and a transition out of our limited constraints of time and circumstances with their inevitable suffering. Death would result by accident or be voluntary rather than imposed by our Nature. Such an increase in freedom will also entail greatly expanded responsibilities. It has been said that *"the sins of the Fathers will be inherited by the generations which follow*"; but that was when the life-span was very short. With life-extension, we will long enough to inherit and have to correct our own sins - only simple justice!

**The Four Enemies.** An anthropologist and author by the name of Castenada (1968) presented the notion of there being Four Enemies to the individual who would be 'at cause' in the world rather than remaining a victim of circumstances and other people.



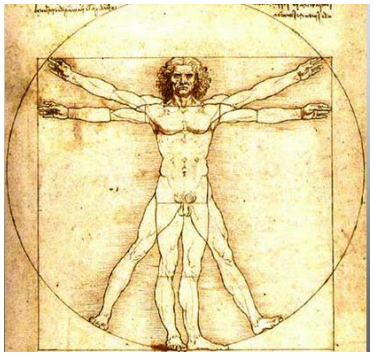

As Shakespeare put it:

> "To be, or not to be, that is the question.
> Whether it is Nobler ... to suffer
> The Slings and Arrows of outrageous Fortune,
> Or to take Arms against a Sea of troubles,
> And by opposing, end them:" [2]

And later, Thomas Jefferson paraphrased Shakespeare and noting:

> "... all experience hath shewn, that mankind are more disposed to suffer, while evils are sufferable, than to right themselves by abolishing the forms to which they are accustomed." [3]

The first Enemy, as Castenada saw it, was "**Fear**". Fear afflicts and tends to paralyze everyone and keeps most people in their place, which results in a person remaining a victim of circumstances and social oppression. However, if a person learns how to over-come one's Fear by persistence, trial-and-error, and challenging the restraints imposed by circumstances, then a person eventually obtains "**Knowledge**" - i.e., knowledge about how the world works. But then, Knowledge, itself, becomes the next Enemy because either one gets depressed and despondent by realizing the truth about reality or becomes arrogant in their knowledge, both of which lead to a down-fall. If a person can conquer the Enemy of Knowledge, then one gains "**Power**" or how to make the world work according to one's will and desire. But then, again, Power becomes the Enemy, because it easily leads to greed and tyranny and, consequently, defeat. Power needs to be controlled and is more of a trust than it is simply getting what one wants. Finally, the last Enemy is the inevitability of "**Ageing**" because when the body becomes frail, the person regresses backward, loosing one's Power and Knowledge, and eventually relapsing down to Fear, desperately trying to protect oneself by holding on to what one has. So, you see, under present constraints, the Four Enemies rule the human condition - both individual and social. But, if the Enemy of Ageing were to be conquered (as it seems inevitable in the foreseeable future), then one would have the time, the strength, and, indeed, the necessity to conquer the other 3 Enemies and become *at cause* in the world rather than remain *at effect,* so that you do not get stuck in your current circumstances.



**Save yourself.** You are routinely being asked to save someone else or something else - e.g., whales and endangered species, starving children with malaria, historic buildings, donate to a political candidate to "save" the county, etc. Here,

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[2] Hamlet by William Shakespeare,1623.

[3] Declaration of Independence, 1776; written by Thomas Jefferson and adopted by unanimous consent of the thirteen United States of America.

you are being asked to save yourself and kindred. Indeed, unless you are also working on saving yourself, it does not make much sense to devote your resources to saving others. Unless ageing is cured, we are all committed by our nature to a relatively short life-span and the tragic prospect of progressive senescence - something which is already becoming a major burden on the social fabric. These are blunt and impolite statements; but they are accurate and true; and like any problem, if we are to solve it, then we must confront it directly and not take soporific comfort in denial and politically correct euphemisms. See it as it is; say it as we see it; and move forward to solve it!

If you **Register**, we will forward a link to personal **Life-Expectancy Calculation**. It takes about 5-10 minutes and will give you a sense of yourself over time within the unfolding progress in Life-Extension Science. And the following Introduction provides the general principles and definition of key terms with respect mostly to the science of Life-Extension.

## BACKGROUND

The field of Life-Extension Science is laced with mis-conceptions - not only in the mind of the general public but also, more importantly, within the scientific and professional communities. So, let us ground ourselves in a common understanding of some of the history and basic principles because the approach which we take and eventual success are dictated by these fundamentals.

First, the term "science" refers to a particular way of thinking, knowing, and establishing truths, one that requires the verification of ideas by reference to physical evidence. Science is a body of knowledge that is based on reproducible, material facts. The purpose of scientific thinking is to accurately understand the world in order to create desired out-comes. While entailing aspiration, belief, intuition, hope, and all the other aspects of the human psyche, scientific thinking is grounded mostly on the faculty of Reason. It assumes that there is a cause for every effect and by proper analysis and reasoning one can derive objective methods to understand how *effects* are *caused* and how to *cause* desired *effects*. Science is distinct from the more common ways of knowing such as by tradition, by authority, rationalization of prejudices, conjecture, *et cetera*.

The history of Life-Extension Science can be divided into three stages (Ancient, Pre-modern, Modern), which parallels the more general history of human consciousness as it has migrated from the Superstitious toward the Rational.

### Ancient

Long before recorded history, different cultures held myths about physical Life-Extension and eternal youth. The earliest recorded story is of Gilgamesh (2,500 BCE), an ancient king of Mesopotamia (now Iraq), who received a sacred herb from God that would give eternal youth, only to abandon his vigilance by following asleep and allowing a snake eat it. In other words, we could have been immortal, if it had not been due to the negligence of our ancestor; and here we are today, groveling in the dirt as lowly mortals.

Gilgamesh

The Hebrew Bible or Torah (600 BCE) postulates that humans are a fallen specie being descendants of our original ancestors, who violated the mandate of God against eating the fruit of the Tree of Knowledge. When they disobeyed his commandment (again, due to a snake), God surmised that, now, being in possession of Knowledge, then they would certainly go for the second tree, the Tree of Life, and thereby become immortal, like God, himself. So, God (being a jealous god) expelled them from Paradise to live a miserable life on this Earth until Jesus (and later Mohammed) offered redemption and promised an ever-lasting life in a

Adam & Eve

transcendental realm. Also, the Torah refers to the original Patriarchs who had life-spans of up to 1,000 years, ostensibly because they were more perfect, being closer to the creation.

Lao Tzu (400 BCE) espoused a philosophy called Taoism, which means the "Path", which would lead to eternal life or immortality. Observing that life, itself, was immortal, being passed on from one generation of entities to the next by certain fundamental connections to Nature, a system of four practices for eternal life was developed - right movements, right breathing, right diet, and the sexual practices known as *coitus reservatus*, which was to retain the essential life energy. This system did not work, and Taoism eventually reverted to a mystical philosophy; but the practices are still popular today as offering health and longevity.

Lao Tzu

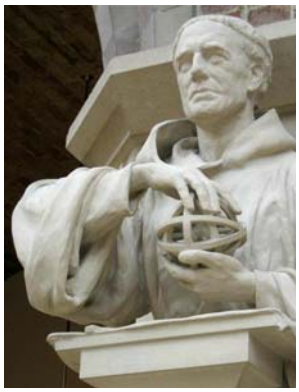
The first emperor of unified China, Qin Shi Huang (259 – 210 BCE) is reported to have died from ingesting mercury pills that were intended to give him eternal life; and to this day, his burial mound remains unexcavated because large pools of mercury are said to be still protecting him and to unearth that would create a ecological disaster.

Qin Shi Huang

Finally, the pursuit of Alchemy is one of the most ancient schools of life-extension (from the 2nd Century BCE all the way into the 17th Century). A chemical science and speculative philosophy that aimed to achieve the transmutation of the base metals into gold, to discover a universal cure for disease, and the discovery of a means of indefinitely prolonging life, Alchemy is best represented by Paracelsus (1493 – 1541). An educated physician, he pioneered the use of chemicals and minerals in medicine and, although failing in achieving his aims, he did contributed significantly to the foundations of modern chemistry and pharmaceutical medicine.

Paracelsus

## Pre-modern



**Roger Bacon**

Not satisfied with understanding life by reading the ancient philosophical and biblical texts, intellectuals started looking to the study of Nature, itself, to understand not only life and the world in general but also the mind of God - being that Nature was the ultimate creation of God. One of the earliest such thinkers was **Roger Bacon** (1214 - 1294), a Medieval, Franciscan friar who brought into Western civilization the scientific philosophies of Aristotle (384 - 322 BCE) and Alhazen (965 - 1040 CE). In one of Bacon's works, "The Cure of Old Age, and Preservation of Youth" he properly identifies ageing as a disease ("... you make every day a considerable step toward Old Age, which is it self a Disease."), and he advocates mostly a sparse diet for the prolongation of life.

**Luigi Cornaro**

Several centuries later, an Italian Renaissance nobleman by the name of **Luigi Cornaro** (1467 - 1566) advocated the same dietary practice in his work "Discourses on the Sober Life". Reaching a crisis in his debauched life-style, at about the age of 35, Cornaro was told by his physician to either stop his excessive practices or face imminent death. He took the advice to heart and began a strict life-style of diet control, moderate exercise, and, in general, temperate practices. He lived to the age of 99, which was rare in those times. Dietary restriction is still the single most effective "Phase I" Life-Extension practice and, today, is the subject of rather intense scientific study.

**Francis Bacon**

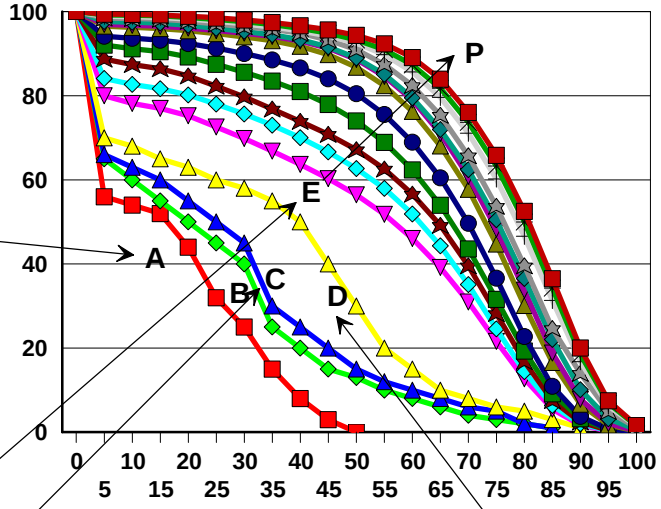
**Francis Bacon** (1561 - 1626), who is credited with propounding the philosophical basis of the modern scientific method and was perhaps a distant relation to Roger Bacon (*supra*), is said to have died by contracting pneumonia while studying the effects of freezing on the preservation of meat - this, ostensibly, relating to his research into life-extension.

## Modern Era

The modern or scientific era of Life-Extension Science begins with a mathematician by the name of Benjamin Gompertz (1779 - 1865). His mathematical discover is the basis for the "Survival Curve", which is probably the single most important concept in the history of Life-Extension Science. Tasked with how to calculate the actuarial basis for determining life-insurance policies, Gompertz visited countless English burial grounds, recording the birth and death dates on grave markers. From those data, he formulated how to calculate the probability of death at any particular age and discovered that, after the age of 30, the likelihood of dying increased exponentially. In his work "On The Nature Of The Functions Expressive Of The Law Of Human Mortality...." he spoke of the underlying cause of mortality as being the "force of mortality" (i.e., ageing) which is built into the system rather than being a consequence of environmental contingencies. This can be seen in the "Survival Curve", as explained in detail, below.

**Bejamin Gompertz**

In the adjacent graph, the percent surviving for a given population of humans, on the Vertical axis, is plotted against chronological age categories on the Horizontal axis. All groups begin with 100% surviving and end with 0% surviving. The survival curve **"A"** is for Stone Age people, as evaluated from their burial mounds. These were hunters and gathers. At age "0", 100% of the population is surviving, but almost 50% are dead by the age of 5 years and virtually all are dead by the age of 45. Effectively, ageing did not afflict Stone Age people. The environment was so harsh, that people did not survive long enough to age. The adults were sturdy and functional until they were killed or die early of natural causes. The survival curves **"B" and "C"** are for the classical Greek (300 BCE) and Roman periods (50 CE). Here again, about 50% of these groups were dead early in life - by the age of about 20. However, more people did survive into their 50's and a few rare ones survived to 80. These populations represent farming or agrarian cultures - still harsh but improving. Curve **"D"** represents the 1800's in England or early industrial civilization. Still there is a high mortality in infancy and early adulthood, but the survival begins to increase during the middle years. Curves **"E" through "P"** range from 1900 - 2012 and are accurate, coming from census data. What is demonstrated here is that, as industrialism advanced with the food supply being more constant, improvements in hygiene, heating, and people living off the dirt, clean water, then immunizations, and conventional medicine particularly during child birth and through early development,



more and more people have survived into old age, such that death during the early ages goes to almost zero and almost all of the population now survives into advanced age. 50% of the population is now living beyond 80 years, which is well into the period of senescence.

**Biology** is the study which is relevant to Life-Extension Science. Here is a review of some of the important steps forward.

For almost all of history, living matter was thought to be a condition in which material, non-living substance was imbued with a vital force or spark - usually equated with the idea of a soul. This was known as the doctrine of "vitalism". With the invention of the microscope in the 17th Century, the world of the invisible became accessible, and the sub-structures of life began opening to observation and understanding.

**Theodor Schwann**

Schwann (1810 - 1882), from his microscopic studies of tissues, demonstrated the doctrine that: "All living things are composed of cells and cell products".

**Robert Remak**

Building on that observation, Remak (1815 - 1865) discovered that the origin of cells was from the division of pre-existing cells.

And capping off the search for the fundamental living unit, Virchow (1821 - 1902) adopted the postulate of Remak with his famous motto: *Omnis cellula e cellula* ("every cell originates from another existing cell like it") or (where a cell arises, there a cell must previously have existed.)

**Rudolf Virchow**

The cell, then, is the basic unit of life and all new cells arise from prior cells. There is no spontaneous generation. Your body originated from a fusion of one cell from your mother and one from your father, which divided to creat new cells, tissues, organs, and the whole system. It is the cell which is the site of disease and the target of medicine; and regeneration or control of ageing must deal with the vitality of cells, meaning restoring their number, rate, and quality of components.

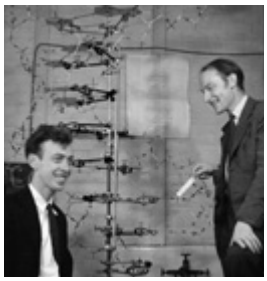
Friedrich Miescher (1844 - 1895**),** a physician and physiological chemist, was the first to isolated and identify nucleic acid or what eventually came to be called DNA. Prior to this discovery, the dogma was that all life forms were composed of only three types of chemicals: proteins, fats, and carbohydrates and there was no idea about the mechanism of how those components were assembled into cells.

**Friedrich Miescher**

Alfred Hershey (1908 - 1997) and Martha Chase (1927 - 2003) are given the credit for confirming that DNA is the genetic material. Their work built upon the prior experiments of Griffith and of Avery, MacLeod, and McCarty. Previously, biologists thought that proteins carried hereditary information. Once established as the hereditary molecule, an on-rush of work went into mapping and characterizing DNA.

**Chase & Hershey**

In 1953, James Watson (born 1928) and Francis Crick (1916 - 2004), relying on the X-ray diffraction images take by Franklin and Gosling (1952), demonstrated the structure of DNA. In biology, structure equals function; so, with the structure known, research could begin on deciphering how DNA works as the information repository for the construction of all other biological structures - mostly amino acids which are then used to build proteins, carbohydrates, and fats.



**Watson & Crick**

In 1962, Gurdon (born 1933) transferred the nuclear DNA of a body cell into an ovum, stimulated the ovum to develop, and created offspring that are identical to the parent (i.e., cloning). This demonstrated that all of the genetic information to create an entire entity was in the nuclear DNA of each and every cell of the body - i.e., the body is a hologram. That work was done originally in frogs but came to be done in sheep and, by now, has probably been done in humans.

**John Gurdon**

In 1990, the Human Genome Project was initiated as an international research project with the goal of determining the sequence of the chemical structures of DNA. This involved identifying and mapping about 25,000 genes in the human genome. It was completed in 2003 The team leaders were Francis Collins, who directed the US National Institutes of Health, and John Craig Venter, who left that government group to head a private venture capital firm - both shown here at a ceremony with President Clinton.

**Venter & Collins**

In 2002, Shinya Yamanaka (born 1962) demonstrated that a body cell could be stimulated by "transcription factors" (originally discovered here at Berkeley by Penhoet in 1974) to cause the cell to revert back to a stem cell type which could then be stimulated back into a completely new body cell - thus, laying the foundation for regeneration biology by "eumitogenic" agents or agents which stimulate body cells to divide properly. Every time a cell divides, it completely reconstructs or regenerates itself, *de novo*. The Human Genome Project (1990 - 2003) mapped the entire molecular structure of nuclear DNA, which is the basis for manipulating DNA directly or indirectly and which will be the key to Life-Extension Science via the regeneration of optimal cell functions (number, rate, and quality).

**Shinya Yamanaka**

**Early medical therapies.** Early efforts at rejuvenation had a rocky but paradoxical start.

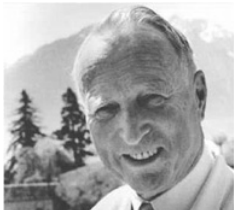
Brown-Séquard (1817 – 1894) attempted rejuvenation treatments by injecting hormone extracts into patients. Any reported effect was due to placebo; and he damaged many people, falling into disrepute. However, his work did give rise to the field of endocrinology which is now a standard part of conventional medicine.

**Charles Brown-Séquard**

Voronoff (1866 – 1951) transplanted organs from animals to humans, claiming rejuvenation, but similarly damaged patients. However, again, his work gave rise to organ transplantation which is now a standard part of conventional medicine.

**Serge Voronoff**

Paul Niehans (1882–1971) injected people with animal, embryonic cells as a rejuvenation treatment, which is still practiced today even though without major effect. However, now human embryonic stem cell therapy is the cutting edge of medical research.



**Paul Niehans**

So, while all of these early practitioners were wrong, *per se*, and were vilified in their time, they were right in concept, which frequently is the way science proceeds - good ideas, premature starts, eventually refined by advances in research. Events from 1950 forward, are sketched roughly as follows.

In the early 1940's, demographers noted the emerging shift in the survival curve as discussed previously and again represented in the adjacent graph. Due to multiple factors (e.g., mostly increased standard of living, public health measures such as maternal and infant care, occupational safety, vaccination and antibiotics, water sanitation) early death was being prevented with the majority of the population beginning to survive into old age. The demographers warned that society was becoming a "gerontocracy".

**The Era of Gerontology.**

Because of the mistakes such as **Brown-Séquard**, **Voronoff**, and **Niehans** (*supra*), the scientific community held the whole idea of rejuvenation as quackery, and they were phobic about the subject of life-extension, in general. For example, when the Journal of Gerontology was founded in 1947, the motto of the society was "To add life to years, not just years to life". This was meant to distance gerontology from life-extension. However, there is a fundamental misconception that is embedded in this motto because if you really do something to add "life to years" then the consequence of that would be to add "years to life" and, inversely, if you really do add, substantively, "years to life" then whatever you did would have had added "life to years". This misconception established a kind of antipathy in the field of gerontology to work on life-extension, which persists to this day. However, there was agreement that if rejuvenation therapies were to be invented, then the ageing process needed to be studied at the level of biological changes. Thus, arose the field of gerontology which has dominated Life-Extension Science until recent times.

Under the auspices of the Atomic Bomb Casualty Commission, **Hollingsworth** (1926 - 2008) studied the effects of high radiation on the survivors of the Hiroshima, atomic bomb blast, doing physiological measurements and medical examinations from 1948 to 1959. It appeared that exposure to radiation accelerated the ageing process.

**J.W. Hollingsworth**

**Shock** (1907 - 1989), in many ways the dean of the science of human ageing, carried forward the measurement of biological systems over time in the "Baltimore Longitudinal Study of Aging". Initiated in 1958, his work is still being conduced with the support of the National Institutes on Aging. (Incidentally, the American way of spelling ageing is "aging", but we prefer the traditional spelling - it representing more accurately the phonetics.) The work of Shock is the foundation for our Uniform Testing & Evaluation System, which will allow for both the application of differential diagnosis, preventive medicine, and experimental therapies and is a major component of our approach in the Life-Extension & Control of Ageing Program.

**Nathan Shock**

**Harman** (born 1916) picked-up on the work of Hollingsworth and the radiation biologists of the 1950's, formulating the "Free Radical Theory of Ageing", and espousing "Antioxidants" as the method for slowing ageing, which continues to have wide support among many scientists. Radiation, the exposure to toxins, and general metabolism cause cell damage by generating molecules with unpaired electrons or "free radicals". In extreme exposures, these free radicals can be mitigated by administration of antioxidant chemicals. However, after decades of attempts, no such chemical has every demonstrated efficacy in any of the many animal experiments which have been done under normal living conditions.

**Denham Harman**

The procedure known as "caloric restriction" is the best known and best regarded method of slowing ageing and extending life-span at this time. The history of this is illustrative of this field in general and warrants a more detailed exposition.

**Clive McCay**

In 1934, **McCay** conducted an experiment in which he decreased the total caloric intake of rats to about 60% of what they eat normally, and he added essential nutrients to make sure there were not any deficiencies. The procedure was initiated early in life, and the restricted group grew more slowly, never developed fully, and did show a significant increase in life-span and a delayed onset of cancer and other diseases. This was the first demonstration of something which approximated real life-extension; and it was replicated, later, in various studies on rodents and other species, such that it became an accepted dogma that if you could slow growth, then you would slow ageing and extend survival. However, it was treated by the scientific community, including gerontologists, as mostly a curiosity until, some 50 years later in the 1980's, **Walford** adopted caloric restriction not only for human life-extension ("The 120-Year Diet, 1986" and "The Retardation of Aging and Disease by Dietary Restriction, 1988") but also as a model for studying the ageing process, itself. In other words, if you get life-extension via caloric restriction, and if you could discover how that works, one might understand a cause of ageing and invent pharmaceutical methods to mimic such mechanisms of life-extension; and such efforts are still in process even though caloric restriction has not really elucidated the ageing process and pharmaceutical caloric restriction has not yielded life-extension. Finally, a very expensive study began in the 1980's to test caloric restriction in the rhesus monkey (the "gold standard" for research). Designed by Ingram and conducted by Walford's associated, Weindruch, in 2012 (30 years after its initiation), the study failed to show any increase in life-span from caloric restriction in higher primates.

**Roy Walford**

**Donald Ingram**

**Rick Weindruch**

The preceding has been a cursory over-view of gerontology since the 1950's. Although necessarily superficial, it adequately serves our purposes here. Suffice it to say the following. Gerontology is the study of the ageing process or, more generally, how a system deteriorates over time. The embedded fallacy in that approach is the assumption that by studying the problem, then an understanding will emerge regarding the solution to the problem. It seems like a reasonable approach; but any understanding of a situation is perspective bound and people tend to look were there is prior existing light, even if in an irrelevant area, rather than attempt the more difficult task by investigating those areas that are relevant but undeveloped. We may ask, why has so much effort gone into studying caloric restriction for 70+ years when its effects on life-extension were always modest, at best, and besides that why would anyone recommend stunting the growth of children just to possibly gain a couple of years and lower the probably of cancer? Thus, in practical terms, restriction could never be deployed in normal living. Gerontology, during its tenure as a solution to ageing, has not yielded any real understanding of the ageing process nor resulted in any method to slow it and extend survival. There has been a plethora of theories (e.g., limited cell doubling, free-radicals, somatic mutation and auto-immune reactions, a "death hormone", late development genetic expression like Progeria, depletion of telomers or ends of chromosomes, etc.) but to no resolve. Gerontology is well funded and will continue to proceed along its own course. One needs to stay informed of events in that field; but we are better off looking elsewhere (i.e., developmental and regeneration biology) for solutions.

Consider these simple observations. The mouse has a life-span of not much more than a maximum of 3 years. This pertains to all strains of mice. In all of the thousands of experiments in mice, none have lived longer than that, even under sterile conditions and the best of husbandry. (As will be discussed later, the C57BL/6J in-bred mouse is the model of choice for doing ageing and life-span studies and a colony of such mice is a component of our program for screening therapies.)

**Mouse**

In contrast to the mouse, the humming-bird has been recorded to live, in the wild, for 12 years, traveling some 2,000 miles annually. How can this be? The mouse is obviously stronger and yet, even under optimal environmental conditions, lives only 25% as long as the humming-bird, while the humming-bird appears frail and works hard but lives 4 times longer. Obviously, it is the maintenance of the form, not the form itself.

**Humming-bird**

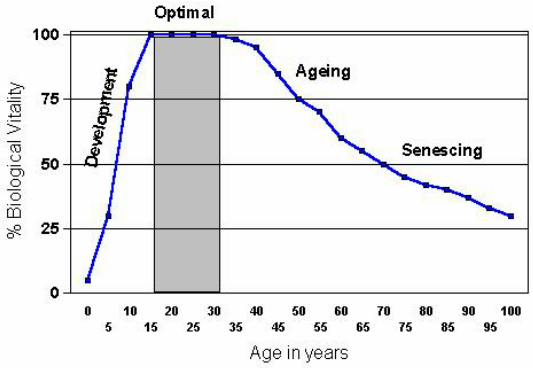
Even more curious, the naked mole rat can live to about 30 years while still baring young at that age and has a very low incidence of tumors and cardio-vascular disease. These animals live deep in the ground, feeding only on tree roots, in an extremely congested and septic environment - notably a toxic atmosphere of about 40% concentration of ammonium cause by their own urine. Again, how can this be? Obviously, it is the maintenance of the form, not the form itself.

**Naked Mole Rat**

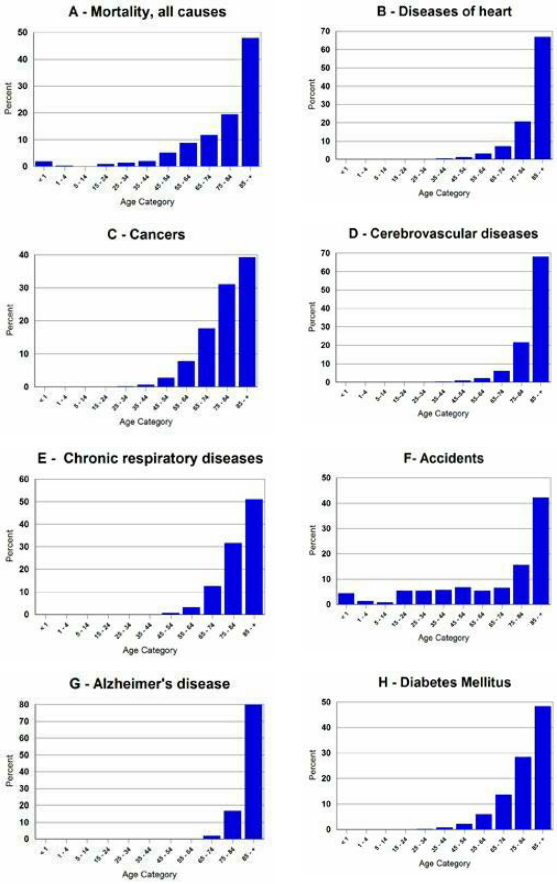
Ageing is a gradual failure in the maintenance of the form, and form/function is the reflection of cell number, rate, and quality. Beginning at about the age of 30, there is a progressive decline in biological vitality (cell number, rate, and quality), which leads to a decline in functionality and an increase in the probability of disease - inevitably ending in senility and death and a functional life-span of not much more that 80-90 years. Because this happens to all people and over a longer period of time, it is considered "natural", which, obviously, it is - given our present state of bio-medical technology.

**Ageing**

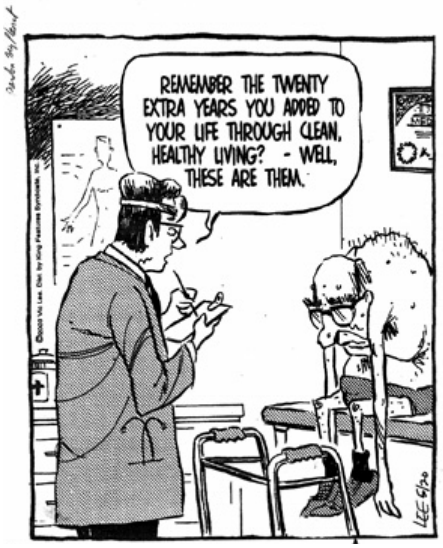
All humans develop along the same type of trajectory in terms of biological vitality. From birth to about age 15, the body increases in its vitality (cell number, rate, and quality). Vitality becomes optimal between the ages of 15 - 25. After about age 30, vitality declines progressively into senescence. The reversal of ageing would result in a stable biological vitality which a person had between the ages of 20 ± 5. That is the research objective.

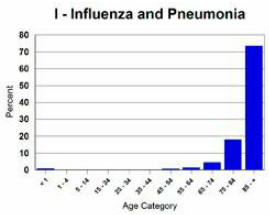


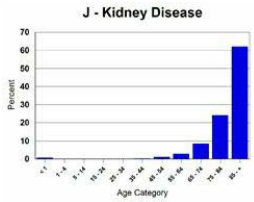

Concurrent with the above trajectory in biological vitality, the incidences of mortality and disease increase with age and the decline in biological vitality. Note the incidences in the diseases in the adjacent graphs - all increase with age. Also note, that there is virtually zero disease and mortality during the age range of 20 ± 5. Restoring that vitality is the aim of this science.




Thus, if ageing were cured, then disease would be minimal and, if it did occur, would be easier to cure and recovery would be rapid. Conventional medicine seeks to prevent death by curing diseases; but it is a little discussed fact that if we were to cure or prevent all of the major diseases which now afflict us, then we would increase the average life-expectancy by only about 12 years and force virtually everyone into advanced senility. That is why medicine, as now practiced, is failing and will fail in its mission.

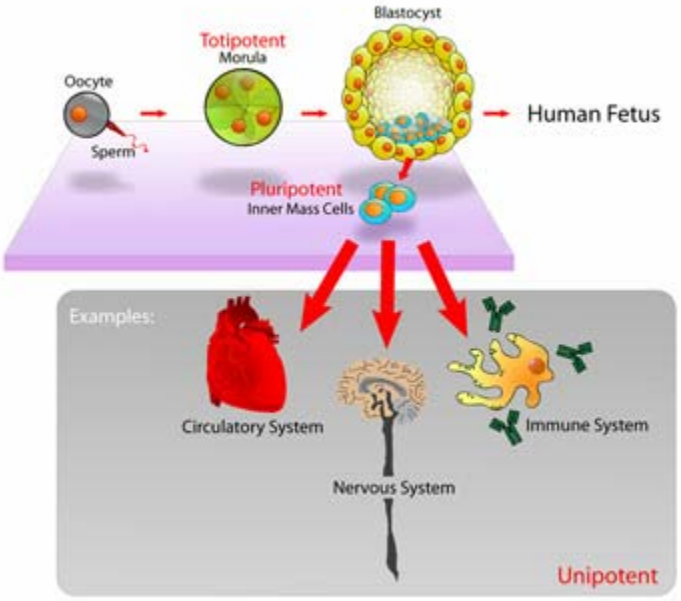



**The Era of Regeneration Biology.**

We are now entering a new era of research and medical applications - one based on the emergence of cellular and molecular biology, developmental biology and regeneration. We have already said that gerontology is unlikely to elucidate the ageing processes nor yield any significant life-extension modalities. Fortunately, since 2000, the field of regeneration biology has emerged with both strong science and strong funding. The basic idea is that rather than simply rely in reductionistic thinking and try to untangle the multiplicity of causes from the cacophony of effects, the more direct approach would be to assess whether or not a particular tissue has declined in biological vitality (again, cell number, rate, and quality) and then restore the cells in that tissue to their optimal condition. Granted, this description is overly simplistic but it serves the general purposes here. The key to this is in understanding how biological systems are created and maintained; and the diagram, below, is illustrative. The oocyte or ovum and sperm (A) unite to form an all potential (totipotent) cluster of cells (B), and that cluster of cells has the capacity to make many different (pluripotent) kinds of stem cells (C) which generate differentiated cells (D) that make the particular, working tissues which form the organs.




In all tissues, there are pluripotent, stem cells which replenish damaged differentiated cells or are quiescent until activated by unusual circumstances. Further, Yamanak (page 13) has demonstrated that differentiated cells can be induced to de-differentiate and re-construct themselves and then re-differentiate as new functional cells. This, then, is the key area of biology with the greatest likelihood of yielding regeneration therapies and which needs to be advanced.

The rate of progress depends on the amount of resources applied within a proper strategy and under ethical management, with "ethical" meaning people who are dedicated to advancing the science rather than their own self aggrandizement - economic or otherwise.

## In Summary

The foregoing has been a sweeping over-view of the history and the basic biology *vis a vis* Life-Extension Science.

1) We know where we want to go and our target is the development of a bio-medical technology which re-constructs and maintains cell number, rate, and quality (biology vitality) that one had at 20 ± 5 years of age. In this condition, function would be optimal, disease minimal and, if it did occur, easy to cure. Life-expectancy would be dramatically increased and death, relegated mostly to being voluntary rather than imposed by one's own nature. Such a technology is possible in the foreseeable future - indeed, it would seem inevitable at this point. This prospect represents a paradigm shift in the improvement of human nature, carries with it a new dimension in psychology, sociology, and ecological aspects, and entails both expanded opportunities and expanded responsibilities.

2) In this regard, we know where the science stands at present. It is fairly easy to stay in touch with critical developments as they occur; and the challenge is designing the strategy which will expeditiously and judiciously get us from where we are to where we want to be. We do not need a grandiose, centralized, Manhattan or Apollo type of project to bring about the solution - rather the approach must be measured, incremental, and actionable.

3) We know that the appropriate experimental, animal model is the C57BL/6J mouse for the screening of therapeutic ideas, and we know how to avoid the handful of artifacts which have routinely happened in past experiments and invalidated most of those studies. Further, we understand that the animal model is suggestive only and is for rapid screening and that we must focus on developing the Uniform Testing & Evaluation System so that experimental treatments can be done in participants in a manner that is ethical and scientifically valid. In other words, Life-Extension Science is validated in the biology of each single person, and we are our own experimental model.

4) We know that there are a variety of "Phase I" life-extension modalities which tend to maintain health and functionality and prevent or post-pone diseases and that these may increase life-expectancy by some 10 - 20% in most people. **Registrants** are directed to the **Life-Expectancy Calculation** to see how this might apply to you personally. Those can buy time; however, there are trade-offs in this regard, and unless one is philosophically right minded and also participating in the advancement of the final solution in terms of the cure of ageing, then these intermediate measure are perhaps ill-advised.

5) The three central components of the Life-Extension & Control of Ageing Program are: **i)** a specialized clinic for the application of Phase I and Phase II modalities; **ii)** the experimental animal colony for the screening of life-extension modalities; and **iii)** the strategy for advancing basic research in selected areas. These three components are necessary and are integral to each other.

6) In a recent survey on how long people wish to live, 60% chose a life-span of 80 years, which is the present average life-span. It is interesting that none chose less than 80 which is, itself, pretty well advanced. We can assume that these will not be interested much in Life-Extension Science for the time being; but they will be interested in health maintenance. 30% chose a life-span of 120 years; and about 10% chose 150. Less than 1% embraced the idea of avoiding death altogether. Those choosing 120 and beyond are our target audience for participants in this enterprise. That would translates to about 80 million people in the U.S.; and therefore, the world-wide group would be substantially more. With only a partial involvement of this number, progress could be made exponentially.

7) As originally said, the purpose here is to identify people who are positively interested in the subject of life-extension and control of ageing (either for oneself or future generations or both) in order to build a network of participants and bringing this science to its full realization, as quickly as possible. That is the goal of this communication; and once again, it begins by having interested parties **Register**. Pass it along.

Best wishes ....

*Chadd Everone*, Governing Trustee

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