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**Death, Aging, Rejuvenation (Part 4)**

**By Aleksandr Kavokin, MD,PhD**

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Biological clock

Obviously you need biological clock to time and alarm the point when you need to die and when you need to age. Aging is the same death as in those one-day butterflies, but a little bit prolonged one. Not immediate kill but gradual shut down of protection mechanisms – immunological, genetical repair, and just other necessary functions of proliferation. As soon as those functions turned off – an organism starts to deteriorate and wear off.

Interesting that our organism is not a static thing. We probably replace all molecules in our body within relatively short period of time. Obviously water is replaced completely every couple months. Water is 60% of our body. Other molecules are replaced as well. Thus, human being is just some unstable chemical organisation around genetical information. Molecules swirl and disappear like crazy. DNA in cells maybe is not changed so fast, but the cells themselves change quickly in most of cases. There is no need to age just because of wearing.

Biological clocks are necessary and there is no doubt they exist.

The theories of aging that consider death as a sequence of events caused by external causes – like oxidations and accumulation of genetical errors should anyway include the idea of Internal Biological Clock as well. Simple example is menopause in women. Somewhere at 40–55 all women undergo menopause. Unavoidable. Though there were reports of childbirth at 60 yo but considering one chance in billions, it is just a joke. Males have their equivalents too. All people after certain age change their immunological, hormonal, metabolic levels and so on. Majority of organs decrease their function . Thymus involute. Fat cells overgrow others, muscle cells degenerate etc. The same happens to all other multicellular animals and plants.

Now the real question: Is it possible to break the biological clock or at least slow down and rejuvenate?

Possible methods of rejuvenation.

### 1. Telomeres lengthening and other genes regulation.

Several genes that might play role in aging described recently. Telomerase encoding genes are the most discussed. In theory, if we lengthen the telomeres (these are the ends of chromosomes that are shortened with each division by very interesting mechanism), we could overcome cell tendency to lose ability for proliferation. Hence, we have "immortal cells". Hence, immortality or at least longevity is reached – cells divide indefinitely and repair organism. Basically, to restore telomeres length we need to activate production of or to introduce into the cell an enzyme named telomerase. To reach each cell in the body we would use viral vectors or smallRNA. Working with virus production and then cell transduction I would say it is difficult, very difficult. There are too many obstacles to use them

efficiently. SmallRNAs would be more promising. In any case, when you go from theory to practice problems rise exponentially. Biggest question: will it work? Immortal cell (cell which is able to divide indefinitely) does not mean immortal body. One of the outcomes would be uncontrollable cell growth and, hence, cancer. Actually scientists discuss telomeres mostly in connection with cancer. They are very cautious saying about the rejuvenation. Mass media extrapolates the findings to possibility of longevity and further rejuvenation.

My guess would be that telomeres are some of the "final cogwheels" in the Internal biological clock. It is useful to divide the clock on intracellular and whole body levels just for understanding. But in reality the levels are not separable, they continue one into another. It is easy to understand that intracellular production of any protein, any enzyme depends on transmembrane regulation. Hormones activate receptors that activate DNA transcription and protein production. Other genes that play role in cellular aging are described recently as well. I do not know how to use this method at present time

### 2. Hormone replacement.

When I studied in med school, several time I met mentions about hormonal side effects that cause a person to look much younger. Well known for example are: If a woman in menopause suddenly resumes menstrual cycles and looks younger than her age, we might suspect an ovarian Tumour producing excess of estrogen. If a person has thyrotoxicosis – excess of hormone thyroxine – he/she loses weight and looks much younger Persons with manic phases of bipolar disorder look younger, more energetic. Certain hormones – corticosteroids for example – might be increased or decreased in elderly. Couples that look younger were shown to have increased level of sexual relationships. Again, that supposedly should significantly change the hormonal levels.

If we give a person some of those synthetic hormones – estrogen, thyroxine – we can sometime reproduce the younger looks.

It is not the same as plastic surgery or skin creams and massages. It invigorates whole body. Skin as well. There is heavy price – recent debates are waxing and waning – if estrogen replacement increases or decreases risks of cancers (uterine, breast, ovarian etc.) Thyroxine excess takes heavy toll on cardiovascular system. Psychiatric disorders (mania for example) was linked to certain changes in

neurotransmitter levels. Certain psychotropic drugs change the ratios. Supposedly they can be employed for rejuvenation. Unfortunately, you would rather receive a psychosis than younger look.

On internet you can find massive information about hormones that rejuvenate you. I saw some websites that list practically any major hormone: estrogen androgens corticosteroids growth hormone thyroxine DHEA melatonin and some others as a drug that leads to rejuvenation.

The websites often have references to scientific literature. Most of the websites just sell you those hormones or offer courses of hormone therapy.

My personal opinion would be that blind replacement can cause more harm than lead to any desired rejuvenation.

Useful information that I would extract from the item is that A) Practically every hormone in the body is involved. B) Certain means of rejuvenation are actually documented. That gives hope.

I do not use hormones personally. If I would employ them, I would use them in very small quantities to

mimic physiology and in special controlled conditions that I will describe below. The doses that are used in regular therapy are actually way to high compare to the natural levels of a healthy organism.

### 3. Antioxidant therapy.

As we discussed, in the best case antioxidants are the method for longevity, not rejuvenation. I use mega-doses of antioxidants available over the counter. I use only those that I consider safe. I have a lot of doubts they give measurable effect. Anyway I use them. Would not throw away.

### 4. Caloric restriction.

I use it as well. 60% of regular meal – is way to much – you would barely move your feet. I regulate it. My opinion: if you increase your activity, you can eat more. Just balance your food and motions. Though I might be wrong.

### 5. Hypothalamic regulation.

This is scary level. Hypothalamus is the area of your brain that sits on the base of your skull. Why do we discuss hormones above? Well, hypothalamus contains hundred of centres that regulate your metabolism and first of all, hormonal status. Studies of hypothalamus are complicated – mostly there are postmortem studies of brain sections. To perform functional study you need to use micro-neurosurgical techniques (still very rude) and try to register changes in a hundred or so cells out of several billions. Changes would include minuscule production (nano and Pico grams) of poorly defined neurotransmitters. The infinitely small quantities of those neurotransmitters are produced by only few out of hundreds cell connections and exist only several nanoseconds. In general to study this area is more difficult than to look for a needle in a haystack. If you consider that there are only few centres have appropriate expertise, you would understand why the progress is relatively slow. Even

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fewer labs study rejuvenation. Though there were reports that transplantation of hypothalamic tissue from younger animals to older could result in rejuvenation-like effect.

I mention this level because A) hypothalamus regulates production of bunch of intermediate messengers that in turn activate hypophysis, that activate adrenal glands, ovaries, thyroid gland etc (maybe many other areas in the body) that in turn produce the hormones discussed above. (Full description you could find in a textbook of Endocrinology) B) because of complexity of hypothalamus it is a good candidate were a "supreme cogwheel" of biological clock may reside. One hint would be proximity of epiphysis – small pea-like gland that produce melatonin and regulates circadian rhythms. It would not be surprise that all that is interconnected in the hypothalamus. One of objection – what is about worms? They do not have hypothalamus as it is. But they age and die as well as humans. Explanation would be that worms also have nervous system and some other part of it may play the central role in the biological clocks. Another explanation would be that there is no such centre at all, everything happens on the lower levels.

I was interested in methods of rejuvenation since childhood. Maybe I read too many science fiction. When I was in medschool I saw some mentions of unusual phenomenon in magnetic radiation. To make story short, eventually I found a book – 400 pages of fine script. I found the book in Central Medical Library in Moscow. Even our relatively large library in Russian State Med U did not have this book. In addition I read the dissertation thesis, that were related to that book. Several Russian scientists developed relatively complicated theory, done many hundreds of experiments. Theory is a little bit complex, involves discussion of stress and adaptation syndrome. Obviously hypothalamic area

also discussed. I am not big fan of that theory. But result the authors described were striking: they were able to restore menopause in rats, prolong rats life span almost twice and more important repeat it again and again. By the description from the book "rejuvenated rats" looked the same as young, but were just bigger in size. Well, you saw a lab rat, you know that older rats have rare hair, bleak eyes, are in menopause etc. Young rat, in opposite, would have bright red eyes, very sleek hair, menstruations, etc. This is no surprise – all growth of hair, production of oil by skin, production of moisture in lacrimal glands and so on are regulated by the hormones. The same is true for rats as well as for humans. Authors described the methods that they found mostly empirically. Moreover they tested some methods on humans and described treatment of variety of diseases – asthma, gastritis, peptic ulcers, low grade skin cancers (non-melanoma) just to name few. As I understand they did not describe rejuvenation in humans. Though later there were some mentions in literature. Authors describe zones of activation, training and stress. In general the methods are difficult to apply – they require permanent control of organism condition for many months, maybe years. Control of hormonal level and control of blood work. In addition parameter would vary from individual to individual. In modern medicine it is much faster and more reliable to cut out skin cancer with knife or give powerful proton pump inhibitors for a gastric ulcer.

I realized that I used some of the methods described, even before I read that book. Since then I added some more methods for my own use. Mostly I use the methods that I feel safe and efficient. For example transplanting of hypothalamus would be out of question. It is a wacking unsafe procedure. Recently there were reports that DHEA, melatonin or other hormones could make miracles: older people feel as young. I would wait confirmation of the effects. Some authors suggest rejuvenation may

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be reached by individually designed cocktails of hormones. I would think that any hormone given makes more mess than regulation. Practically every hormone described have loops and pathways that prevent overproduction. If you just replace the hormones by giving the substitute, you wack the production of your own hormones those that injected as well as many others. All hormones are complexly interrelated. Individual cocktails would be better, but the doses described in literature are wacking. Again I might be wrong. Maybe everything is so simple – just get cocktail and you will jump as a newborn bunny.

Considering different information from different sources, I would propose following theory:

To rejuvenate yourself you need to recreate the hormonal and metabolic level of young organism.

This is actually very difficult to reach: your organism have all the means to produce all the necessary hormones. Levels of hormones in elderly are not so far from the levels in youth actually. The difference is several percentages, not several folds. But biological clock switch to underproduction. The idea is to cheat the biological clock and to restore the youth levels. The most difficult part is to get into the window of optimal production. You can not go too low – just wouldn't have any effect on rejuvenation. You can not go above the optimal level – it will cause stress and even more deterioration. So approach is very individual. There is no quick effect – you can not rejuvenate from looking 50 to looking 30 overnight. You really need a lot of commitment and time. The methods which you choose are not of so great importance. Practically any action toward your body would cause changes in your metabolic and hormonal status. Physical exercise, herbs, yoga, hormones (low doses) etc – we could list thousands.

Personally I used available antioxidants, slight caloric restrictions, herbs (some of substances in herbs like ginseng, Echinacea, etc mimics hormones in their chemical structure), self-hypnosis, neurolinguistic programming (NLP), auto-training, different exercises, lactic bacteria, etc. Important is the ability to adjust the level of treatment – reduce the dose of herbs or increase dose of exercise etc.

Methods of control are of much great importance. The described methods include measurement of hormonal level and of certain fractions of cells in the blood work(that is also regulated by hormonal and metabolic reactions)

If I would have a clinic of rejuvenation therapy I would probably use many of those methods – they are objective and reproducible. But they require blood work.

For individual use there some subjective methods exist. They are described in literature as: If you are in the condition of rejuvenation you feel great energy, hunger, restlessness. Your sleep would be normalised, you are fighting regular infections much more efficiently – inflammatory reaction might be exaggerated, but they last shorter time. Your eyes would glisten as in youth. You will feel constant euphoria and need in doing something. There are some other subjective criteria. Personally, I would add: you will notice that your nails and hair grow like crazy in those conditions.

The biggest problem is how to hold in this condition of rejuvenation for a prolonged period of time. You really can not go overboard – super activation would just wack all your system. You can not go under activation – just no any useful effect. You need to get it is just right. Solution is tight, continuous control.

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Boy, it's really tough in the modern stressful environment (would not describe all the junk that I had in recent years), but it is possible. Dedication is your solution. Some formulas to calculate doses of stimuli are described in the literature, but I feel it is easier to go with individual subjective feelings. Below there is an animation that contains some simple elements of NLP and might help to tune a brain a little.

Now, what did I get by using those methods? Well not much, but I hope for more. At present time I am 35 yo I do not really have good control group in my personal experiment. Sometime people asked me if I am younger than my brother (He is younger than me for several years). Maybe it is some sort of control group. When I come into a bar (can not say often, maybe once in a year with friends) waiter often asks my ID. It is funny also because I do not use alcohol. So, to drink a Coke I need to show ID, being 35 yo. Sometime people ask me are you 18 or 19 When I played water polo at Yale, undergrads told me they thought I was freshman (as I guess also 18 or 19). That time I was 33. Teenagers often start to talk to me in the way if I am another teenager. And so on.

So, in general it is really hard to measure rejuvenation. All measurements are mostly subjective. Even in well designed scientific trial you find either some description of biochemical changes (which doesn't say you anything about rejuvenation as it is) or some subjective descriptions – "patients felt much better, felt rejuvenated and invigorate". How much rejuvenated? How many years were reversed? It is very difficult to estimate. If I say to a person that I have MD and PhD, he says "aha". Mentally they immediately adjust and now they say that I am probably 30. OK. Sometime they just say: you look so young.

Again 35 is not the age where you really can brag that the methods worked. I would wait couple more decades to say that there was measurable effect. Unfortunately. You do not have the right for a mistake. If a method did not work , you can not go back and change it. You already are behind for several years.

But my personal, subjective feeling is that the methods do work. I believe that it is possible by tight control maintain the level of younger organism. It just requires a lot of work.

Below there is animation that might help to tune in the desired "optimal rejuvenation condition". Animation requires Flash file player I use that animation for myself. I doubt that it will necessarily help

you. Maybe 1 out of 10. If you are not sure, don't touch it. The animation contains some simple NLP information.

### Animation

Basically looking at the animation couple times a week for 5 min should start the tuning process (at least I feel so). You should target at the condition when you feel inexhaustible energy, euphoria, normalized sleep, and some feelings that is hard to describe – like a fine tingling in your fingertips, subjectively it feels like a pouring energy. It is difficult to explain, but when you feel you understand it. If you do not feel anything, it means it did not work, forget it.

So to finish I would say that Rejuvenation is difficult but probably possible to reach – at least in a certain

degree. A.K.2004

Aleksandr Kavokin, MD,PhD

### **Death, Aging, Rejuvenation (Part 3)**

**By Aleksandr Kavokin, MD,PhD**

Aging

How did aging appeared?

If mechanism of Death was chosen by evolution, how was aging chosen?

Why for example at certain age animals do not die instantly and just give the room for the next generation. Nurturing is one explanation at least for human society.

But lets say new generation of young adults already reached puberty . Why would not old generation die in an instant. Why do they age?

Actually there is nothing impossible. Some butterflies grow couple years, mate, produce new generation and die in one day. Some plants live 1 year, some live 2 years and then invariably die. Some live 1000 years. Lemmings, having overgrowth of population, just go and massively commit suicide in the sea. No questioned asked.

Why aging in other animals take several years?

It might be selected by cut-throat evolution during another catastrophe.

A relatively mild Cataclysm happened in the same time when all adults died programmed to do so. Older animals would survive the disaster. But they died instantly from internal timer. Younger generation did not tolerate the mishap.

All species that did it – just disappeared. Younger animals were not adapted to new conditions. Only animals with mechanism of aging were selected. Maybe the aged animals are not so good as younger ones. They already slightly deteriorated. But it is better than nothing.

Anyway. It makes sense why Death and Aging were selected during the Evolution.

– continued in Part 4

Aleksandr Kavokin, MD,PhD

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