

THE SCIENCE OF AGING AND LONGEVITY

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ABSTRACT

Aging is characterized by a progressive loss of physiological integrity, leading to impaired function and increased vulnerability to death. This deterioration is the primary risk factor for major human pathologies including cancer, diabetes, cardiovascular disorders, and neurodegenerative diseases. Aging research has experienced an unprecedented advance over recent years, particularly with the discovery that the rate of aging is controlled, at least to some extent, by genetic pathways and biochemical processes conserved in evolution. This review enumerates nine tentative hallmarks that represent common denominators of aging in different organisms, with special

emphasis on mammalian aging. These hallmarks are: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient-sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication. A major challenge is to dissect the interconnectedness between the candidate hallmarks and their relative contribution to aging, with the final goal of identifying pharmaceutical targets to improve human health during aging with minimal side-effects.

KEYWORDS: Aging, Genetic pathways, biochemical processes, hallmarks, genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient-sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, altered intercellular communication.

Aging as a disease^[4]

Longevity is the more academic ways we describe antiaging bunch of people that don't know

what they're talking about but aging is a disease and longevity are perfectly valid ways to talk about this subject. So let's talk about aging as a disease. If there's something that's wrong with you. and it's a rare thing, It has to be less than 50% of the population, that's definitely a disease, and then people work their whole lives to try and cure that condition. so, what's the definition of aging and it says, well, it's a deterioration in health and sickness and you can die from it, typically you do. Something that sounds pretty much like a disease, but the caveat is that if more than half the population gets this condition, aging, it's put in a different bucket. Which is first of all, that's outrageous, cause it's just a totally arbitrary cutoff. But we're ignoring the major cause of all these diseases. Aging is 80 to 90% the cause of heart disease, Alzheimer's. If we didn't get old and our bodies stayed youthful, we would not get those diseases. if you turn the clock back, in tissues, those diseases go away. So aging is the problem and instead through, most of the last 200 years, we've been sticking band-aids on diseases that have already occurred because of aging and then it's too late. so there are a couple of things. One is we want to slow aging down so we don't get those diseases and when they do occur, don't just take a band aid on, reverse the age of the body and then the diseases will go away.

General phenomenon in the body that underlies aging^[4]

That's contentious because scientists like to come up with new hypothesis. During the two thousands, scientists settled on eight or nine major causes of aging. They call them hallmarks because causes was a little bit too strong, but these eight or nine causes, at least for the first time allowed us to come around that they are actually genes called longevity genes. They rallied around this new map of aging with these causes of hallmarks. And they can get to that, but that's the information in the cell that they call the epigenome.

Epigenome^[4]

Aging is a loss of information in the same way that when you xerox something, a thousand times you'll lose that information or you try to copy a cassette tape. Or even if you send information across the internet, some of it will get lost. That's what I think is aging. And there were two types of information in the body. There is the genetic information, which is digital. ATCG the chemical letters of DNA, but there's this other part of the information in the body. that's just as important, it's essential, in fact, and that's the systems that control which genes are switched on and off in what cell at what time in response to what we eat, et cetera. And it

turns out that 80% of our future longevity and health is controlled by the second part, the epigenetic information, the control systems

Process of aging^[4]

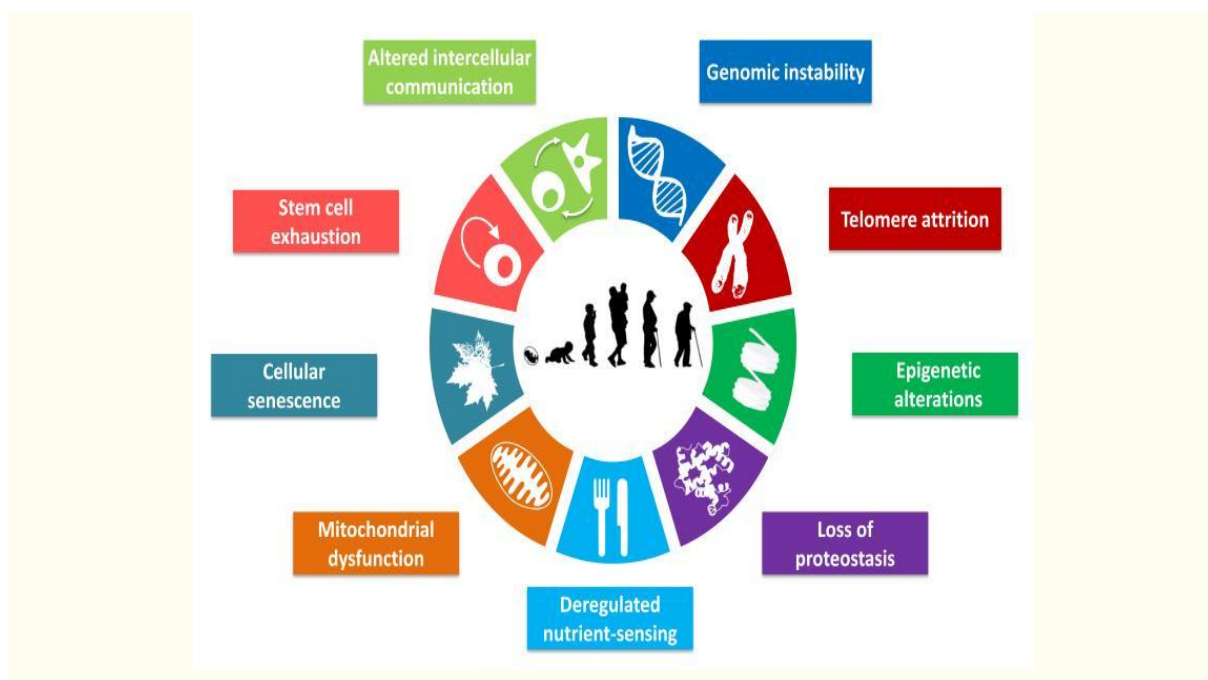
DNA is six foot long. So if you join your chromosomes together, you get a six foot post-sale. So there's enough to go to the moon and back eight times in your body. And it has to be wrapped up to exist inside us, but It's not just a bundle of string, it's wrapped up very carefully in ways that dictates which genes are switched on and off. And when we're developing in the embryo, the cell marks the DNA with chemicals that says, okay, this gene is for a nerve cell. Your cell will stay a nerve cell for the next a hundred years, if you're lucky. Don't turn into a skin cell that would be bad. And those chemicals, there are many different types of chemicals, but one's called methylation. These little methyl will mark which songs get played for the rest of your life. And there are other that change daily. But in total, what we're saying is that the body controls the genome through the ability to mark the DNA and then compact some parts of it, silence those genes, don't read those genes and open others, keep others open that should stay open. And that pattern of genes that are silent and open, silent, open, is what dictates the cells type the cells function. And then the scratches are the disruption of that. So genes that were once silent and you could say, it's a gene that is involved in skin. It's starting to come on in the brain, shouldn't be there, but we see this happen and vice versa, the gene might get shut off over time during aging. Cells over time, lose these structures, lose their identity, they forget what they're supposed to do and we get diseases. We call that aging and we can measure that. In fact, we can measure it in such a way that we can predict when somebody is going to die based on the changes in those chemicals. These are some sorts of changes that underlie the outward body surface manifestations of aging, that most of us are familiar with, graying of the hair, wrinkling of the skin, drooping of the face, C shaped spine. A hallmark, of aging, that most of us are familiar with.

The hallmarks of aging^[5]

The scheme enumerates nine hallmarks described in this review:

1. Genomic instability
2. Telomere attrition
3. Epigenetic alterations
4. Loss of proteostasis

5. Deregulated nutrient sensing
6. Mitochondrial dysfunctions
7. Cellular senescence
8. Stem cell exhaustions
9. Altered intercellular communications.



Direct relationship between body Size and Longevity or duration of life^[4]

There is, but that doesn't mean that you're a slave to your early epigenome nor have to your genome. The good news is that the epigenome can change. Those loops and structures can be modified by how you live your life. And so if you're born tall and I wasn't, and I wished at the time I did grow, but no matter what size you are, you can have a bigger impact on your life than anything your genes give you. 80% is epigenetic not genetic. So the first one relates to food, blood sugar, insulin. fasting is good for us, having elevated blood sugar, glucose and insulin ages us more quickly.

Ways to slow aging^[4]

1. Fasting

We live in a world now where there's at least three meals a day, and then we've got companies selling bars and snacks in between. So the feeling of hunger, some people never experienced hunger in their whole lives. It's really, really bad for them. It was based on the 20th century view that you don't want to stress out the pancreas and you try to keep insulin

levels steady and not have this fluctuation.

What we actually found, across this field of longevity is that when you look at first of all animals, whether it's a dog or a mouse or a monkey, the ones that live the longest by far 30% longer and stay healthy are the ones that don't eat all the time actually was first discovered back in the early 20th century, but people ignored it. And then it was rediscovered in the 1930s, Claude McKay did Clark restriction. He put cellulose in the food of rats, so they couldn't get as many calories even though they ate. And those rats lived 30% longer, but then it went away and then it came back in the 2000's in a big way, when a couple of things happened, that there were longevity genes in the body that come on and protect us from aging and disease. The group of genes are called sirtuins and there are seven of them. If you have low levels of insulin and another molecule called insulin like growth factor, those low levels turn on the longevity genes. One of them that's really important is called SIRT1. But by having high levels of insulin all day, being fed, means your longevity genes are not switched on. So you're falling apart, your epigenome, your information, that keeps your cells functioning over time, just degrades quick. Your clock is ticking faster by always being fed.

2. Effect of hunger

Though you get used to the feeling of not eating, but there are some studies that are being done at the National Institutes of Health that are able to simulate the effect of hunger, but still provide the calories. And it's looking like there's a small component that's due to hunger, but most of it, actually, is because you've got these periods of not being fed and then the body turns on these defensive genes.

There's a really interesting experiment that was published maybe a couple of years ago by Rafael de Cabo down at the NIH. What he did was he took over 10,000 mice and gave them different combinations of fat, carbohydrate, protein. And he was trying to figure out what was the best combination. And then he also cleverly had a group. Well, two groups, one that was fed all the time or ate as much as they wanted and the other group was only given food for an hour a day. And it turns out they ate roughly the same amount of calories, 'cause of course in an hour they're stuffing their faces. It turns out it didn't matter what diet he gave them, it was only the group that ate within that window that lived longer and dramatically longer.

So the conclusion is, and mice are very similar to us, metabolically, I think that tells us that it's not as important, what you eat, it's when you eat during the day.

Fruits for antiaging or longevity^[6]**1. Watercress**

The health benefits of watercress don't disappoint! This nutrient-dense hydrating leafy green is a great source of: calcium, potassium, manganese, phosphorous vitamins A, C, K, B-1, and B-2. The health benefits of watercress don't disappoint! This nutrient-dense hydrating leafy green is a great source of to all cells of the body, resulting in enhanced oxygenation of the skin. Packed with vitamins A and C, the antioxidants in watercress may neutralize harmful free radicals, helping to keep fine lines and wrinkles away.

2. Red bell pepper

Red bell peppers are loaded with antioxidants which reign supreme when it comes to anti-aging. In addition to their high content of vitamin C — which is good for collagen production — red bell peppers contain powerful antioxidants called carotenoids. Carotenoids are plant pigments responsible for the bright red, yellow, and orange colours you see in many fruits and vegetables. They have a variety of anti-inflammatory properties and may help protect skin from sun damage pollution, and environmental toxins.

3. Broccoli

Broccoli is an anti-inflammatory, anti-aging powerhouse packed with: Vitamins C and K, a variety of antioxidants, fiber, folate, lutein, calcium. Your body needs vitamin C for the production of collagen, the main protein in skin that gives it strength and elasticity.

Disease related to aging

Age-related diseases are illnesses and conditions that occur more frequently in people as they get older, meaning age is a significant risk factor. According to David Hogan, gerontologist, and professor of medicine at the University of Calgary, the following are the conditions of the more common age-related diseases.

1) Cardiovascular disease^[7]

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels.

They include

- Coronary heart disease – A disease of the blood vessels supplying the heart muscle.
- Cerebrovascular disease – A disease of the blood vessels supplying the brain.
- Peripheral arterial disease – A disease of blood vessels supplying the arms and legs.

Heart attacks and strokes are usually acute events and are mainly caused by a blockage that prevents blood from flowing to the heart or brain. The most common reason for this is a build-up of fatty deposits on the inner walls of the blood vessels that supply the heart or brain. Strokes can be caused by bleeding from a blood vessel in the brain or from blood clots.

Symptoms

- Chest pain.
- Pain, weakness or numb legs and/or arms.
- Breathlessness.
- Very fast or slow heartbeat, or palpitations.
- Feeling dizzy, lightheaded or faint.
- Fatigue.
- Swollen limbs.

2) Alzheimer's disease^[8]

Alzheimer's disease is a progressive neurologic disorder that causes the brain to shrink (atrophy) and brain cells to die. Alzheimer's disease is the most common cause of dementia — a continuous decline in thinking, behavioral and social skills that affects a person's ability to function independently.

Symptoms

Memory loss

Loss in ability to make decisions and judgements

Changes in personality and behaviour

Depression

Apathy

Social withdrawal

Mood swings

Molecules for longevity^[9]

1. Metformin

Metformin is a drug given to type two diabetics to bring down their blood sugar levels. But it's been found that looking at tens of thousands of veterans and all those, that those type two diabetics live longer than people that don't even get type two diabetes. So it's a longevity drug. The one wants to build muscle should stop taking Metformin because they're never

going to get muscle, or it's going to affect their ability to build up muscle. But that's not true, what Metformin does to you, it actually just reduces your ability to have stamina because it's inhibiting your body's ability to make energy. And so what happens is when you're on Metformin, you do fewer reps. Those muscles that you do build up on Metformin, have the same strength and have much lower inflammation and other markers of aging. You just won't have that extra 5% size of muscles. So if you want large muscles, don't take Metformin and you'll be fine during your exercise.

2. Berberin

Berberine is a substance that comes from Tree Barco. what's remarkable about berberine is that you can eat enormous quantities of food and not feel as if you've eaten enormous quantities of food. it works very similarly to Metformin where some of the AMPK pathway and the mTOR pathway, et cetera. it is effective at boosting energetics in the body, just like AMPK and Metformin does. There are some human studies that exist, clinical trials showing that it increases insulin sensitivity. but you need your cells to be insulin sensitive. You don't want a lot of blood sugar floating around that can't be sequestered into cells. so this is anti type two diabetes.

3. NR (Nicotinamide riboside)

Nicotinamide riboside is an alternative form of vitamin B3 with few side effects. It is commonly marketed as an anti-aging product. Your body converts it into NAD⁺, which fuels all of your cells. While NAD⁺ levels fall naturally with age, boosting NAD⁺ levels may reverse several signs of aging. studies have shown that taking NR increased serum NAD in subjects by 40–50% after 8 weeks. Oral supplementation with NR has been shown to increase NAD⁺ levels in multiple tissues, along with increased SIRT activity, improved mitochondrial function and regenerative potential of stem cells. In humans, NR supplements are considered safe to take in the short-term, and effectively and reliably boost NAD⁺ levels. NR may improve blood pressure and aortic stiffness, is available to skeletal muscle, and exerts anti-inflammatory properties. NR has not been effective in improving glucose or insulin sensitivity.

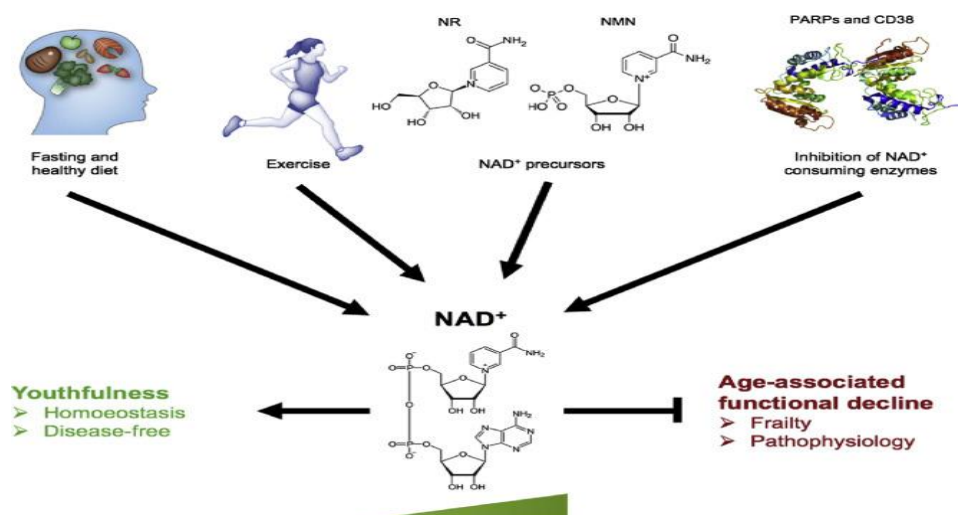
4. Vitamin B3 (Niacin)

The vitamin niacin has a life-prolonging effect, as demonstrated in roundworms. Vitamin B3, also known as niacin and its metabolite nicotinamide in the worms' diet caused them to live for about one tenth longer than usual. Both niacin and niacinamide are great at helping your

skin look and feel healthier, and protect you from the effects of aging by helping your cells repair and defend themselves. Niacin has the added bonus of helping to reduce bad cholesterol and increase good cholesterol, which niacinamide doesn't do. The price of other precursor supplements that may increase NAD⁺ in humans, such as NR and NMN, are very high compared to niacin, which is cheap and readily available. These results show that niacin can elevate human NAD⁺ in muscle and blood and potentially in other tissues as well. Niacin can cause mild-to-moderate serum aminotransferase elevations and high doses and certain formulations of niacin have been linked to clinically apparent, acute liver injury which can be severe as well as fatal.

5. Resveratrol

Resveratrol is the best-known chemical for extending the lifespan of various organisms. Extensive recent research has shown that resveratrol can extend the lifespan of single-celled organisms, but its effects on the extension of animal lifespans are marginal. Resveratrol supplementation has been shown to prolong lifespan in approximately 60% of the studies conducted in model organisms. ability to inhibit AAPH-induced senescence and apoptosis, restore the age-related cognitive impairment caused by D-gal administration. An exciting study conducted by researchers at the University of Exeter and the University of Brighton have found that exposing senescent (aged) cells to resveratrol made the cells not only look younger, but behave like younger cells. Resveratrol supplements are possibly safe when taken by mouth in doses up to 1500 mg daily for up to 3 months. Higher doses of up to 2000-3000 mg daily have been used safely for 2-6 months. But these higher doses are more likely to cause stomach upset. Resveratrol can have a two-fold effect, both neutralizing free radicals and boosting antioxidant levels.



Anti aging treatment^[9]

Ageing is a treatment to delay or stop the ageing process. There are many treatments that can help combat ageing, using both surgical and non-surgical procedures. Damage from too much sun exposure can take its toll and be responsible for most of the visible ageing of the skin. As well as photo-ageing, repeatedly spending time in the sun with lack of sunscreen can lead to skin cancer alongside damage. There is no treatment that deals with all skin issues and that will have the same result on every individual. A dermatologist can determine what would be the best procedure and whether a combination of treatment is needed.

1. Botulinum toxin therapy

More commonly known as Botox, Dysport Xeomin, botulinum toxin injections help reduce frown lines (glabellar lines) in between the Eyebrows and crows feet at the corners of the eyes. This treatments works by keeping the muscles in these areas from tightening. There is usually no recovery time for this cosmetics procedure, but it can take up to a week to see the effects. The result typically last about 3 to 4 month.

2. Dermabrasion

Used to treat wrinkles, age spots, and sun damage, dermabrasion uses a special rotating brush to remove the outer layer of the skin from small areas of the face. New, smoother skin grows in to replace it. The new skin will look red or pink for a few weeks, and you may have some scabbing or swelling for a few weeks after the treatment. It can take weeks or months to see the full results. You may need to take time off from work or other commitments. You may need only one treatment, but people with deep scars or significant signs of aging skin may need more than one derm abrasion.

3. Microdermabrasion

Like dermabrasion, this treatment removes the topmost layer of skin. But instead of a rotating brush, microdermabrasion uses a special machine to spray tiny particles on the skin. It is less abrasive dermabrasion and takes less time to heal. It can be used on all skin types, but you may need several sessions to achieve the desired results. Many people include microdermabrasion as part of their anti-aging skin care routine.

4. Chemical peels

During a chemical peel, your doctor uses an acid to peel away the outermost layer of skin. It removes age spots and wrinkles, and gives you a brighter skin tone. Your skin will need some time to heal after the peel and will appear red for a week or two. Depending on the type of

peel you receive, you may need to have more than one treatment to achieve the results you want. Woman Undergoing Laser Skin Treatment.

5. Fractional laser skin resurfacing

For this treatment, your doctor uses a special laser to treat narrow columns of skin. The laser damages deep layers of skin, which stimulates new skin cell growth. The damaged area peels away and reveals smoother, younger-looking skin. Fractional laser skin resurfacing can help treat wrinkles and fine lines. Although your skin will not likely need time to heal after fractional laser skin resurfacing, you may have some redness, pain, peeling or scabbing. You may need several treatments over a few weeks to get the results you want.

6. Dermal fillers

Fillers are substances that a doctor injects into your skin to fill out wrinkles and lines. Some popular fillers include collagen, hyaluronic acid gel, and fat. You can use fillers on your lips, face and hands. In most cases, you don't need any downtime after getting a filler, and you will see the results right away. Fillers last from 2 months to 3 years, depending on what type you get. Collagen is one of the shortest lasting fillers, while injections of your own fat last 1 to 3 years.

7. Nonablative skin rejuvenation

Non ablative skin rejuvenation uses lasers and other types of energy to treat wrinkles, age spots, and loss of skin tone. This type of treatment does not remove the outer layer of skin, and you don't usually need any recovery time. You may need several treatments to achieve the best results, and it can take up to a few months to see the full effects.

Ayurveda on longevity^[10]

"Healthy Aging" was the theme of World Health Day this year. This should be a decadal research mission for Ayurveda. Advancements in agriculture, science, technology, and biomedicine have increased human life expectancy, while the same have also contributed to the fall in the birth rates. As a result, for the first time in human history we will soon have more geriatric population as compared to the young. Elderly population of India is expected to share about 12.4% of the total population by 2026. India needs to be prepared to handle this demographic shift, especially the healthcare issues of the elderly, otherwise long life without health will certainly be a agony for them. Against this background, the World Health Day aphorism for this year – "Good health adds life to years" was pretty consequential and

evocative. It is especially challenging for the Ayurveda community because geriatrics is one of its core strengths.

The Indian population is growing fast; it has grown from about 450 million in 1961 to 1200 million in 2011. In the last 50 years, the global life expectancy has gone up from 52.65 to 69.41, an astounding 16.76 years. In all history, such a remarkable change in both life expectancy and falling birth rates was never seen. In India, the life expectancy has gone up by 25 years in the same period! The quantitative and qualitative change in the population makes demands on policy makers, governments, and administrators to change their outlook toward people at large and older people in particular.

It is well understood that the needs of the older people are different than those of youngsters, especially in respect of their healthcare needs. There is also a subtle shift in size and composition of the family leading to a large number of older people living all alone without support. Delivery of healthcare to the population takes a place of importance in a civilized society. The way the weakest members of the society are treated, speaks volumes about human development in the society. The policy on older people recognizes that “old persons have to cope with health and associated problems, some of which may be chronic, of a multiple nature, requiring constant attention and carrying the risk of disability and consequent loss of autonomy.” The national policy details a number of changes needed in the healthcare delivery mode, but it is not clear when these will actually be implemented. The policy speaks of healthy aging, but does not state precisely how this is to be achieved. Why is the Ayurveda knowledge system not being harnessed by policy makers to develop a uniquely Indian “integrative research program” for healthy ageing?

The concept of Vayasthapana in Ayurveda deals with preserving the youthfulness of a body irrespective of its age and restricting progression towards senescence, along with enhancement of longevity, intellect, physical and mental strengths, and prevention from diseases. Rasayana Tantra, one of the eight branches of Ayurveda is dedicated to rejuvenation, regeneration, immunomodulation, and healthy aging. The process of degeneration and wear out increases with age and maintenance of normal function obviously requires special efforts. The scope of Rasayana therapy is not necessarily restricted to herb or formulation, but includes a combination of meditation, yoga, daily and seasonal diet, lifestyle interventions, and personal and social behavioral conduct too. All these measures that assist in the maintenance of healthy body tissues consisting of Saptadhatu are grouped together as

Rasayana. If one invests adequately in the creative design and implementation of a long-term Indian research program for the elderly based on Ayurveda principles, a definite output will be that elderly population not only in our society but also globally can remain healthier and require lesser need of curative interventions.

“Achar Rasayana” is another Ayurvedic strategy for regulating the behavioral social conduct, which ensures a healthy life in a healthy society. In modern times when individuals are exposed to different types of societies in their life time, the ability to adapt to the behavioral modes of that society alone can ensure social health of the individual. In fact “Achar Rasayana” is of greater relevance in today's highly mobile society than it was when first proposed. Life should be like a Banyan tree giving shade and shelter to others, and send out its aerial roots earthwards to propagate the philosophy of providing shade and shelter. We cannot do away with ageing, but we can make it healthy and comfortable.

Ayurveda classic Sharngadhara Samhita quotes that we naturally deplete with each decade of life. Ayurveda observes natural dominance of vata dosha in old individuals and vata dominant diseases are expected more in this age group. Thus degenerative and debilitating diseases like osteoarthritis, Alzheimer's disease, dementia, stroke are commonly seen in older populations. Contemporary medicine has not yet been able to either prevent or retard the progress of these age-related disorders, and that is the reason why elderly people look toward Ayurveda with hope. Ayurvedic interventions are being tried for various health areas like skin, and brain aging, etc. however, more wholesome and systematic scientific programs to establish the safety and efficacy of Ayurvedic therapies are required. Unfortunately, most of the studies pertaining to Rasayana till date have truncated the concept and therefore are mainly restricted to selecting formulations. The non-pharmacological interventions related to lifestyle, diet, and panchakarma therapies that Ayurveda advocates have been overlooked. Whole system management will be the appropriate study design to demonstrate the benefits of Ayurveda's understanding of geriatric interventions including bold therapies like Kutipravesik Rasayanas. Biological effects of Ayurvedic interventions monitored during such studies may give new insights for modern biology and medicine. As WHO advocates, it is not important to add just years to your life but add life to your years. With help of wisdom of Ayurveda Shastra and advancements in Science, we can make life livable and more pleasant while it exists.

CONCLUSION

‘Aging is still not considered as a disease across the globe; but it is indeed a major cause of severe diseases and disorders. Antiaging products such as creams, pastes, et cetra are well known to most of the sophisticated communities but, these products are just to look young phenotypically or mostly are applied on face.

Instead of just looking young phenotypically by applying products, it is possible to be young from within or genotypically by just changing the lifestyle; not entirely, but just making small changes can create a larger difference in our mental, physical and social wellbeing and the lifespan of an individual can be increased along with minimizing the consequences of aging related disorders or maybe complete deletion of these disorders and hence can leave happier and healthier life.

And Yes, we believe that it is possible, not entirely naturally but, including synthetic molecules on which the research is being made and there are majority of chances that these molecules along with minute changes in sedentary lifestyle will be included in our daily lifestyle for longevity.

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