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AGING IS A PROCESS…….. NOT A DISEASE

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Aging starts at conception & Continues until death[1]

Growing old is a natural process our body has to pass through. It's a natural course of action human must suffer[2]. Aging is a slow complicated process affecting the physiology of our body. It's a silent process passed unnoticeable.

The advance of age is an extremely complicated procedure utilizing every cell and part of our mechanism of physiology that we have. As we grow older things begin to go wrong with us[2]. Our vascular system, digestive tract and respiratory system begin to show their age. But why does aging occur?

This article is dealing with the aging process of the skin only. Since skin show the changes that draws the attention of the person and others.

The skin is an organ with its surface area measuring about 1.5- 2 square meters (16 to 22 square feet); it is not merely a protective barrier. It serves to regulate excretion of metabolic waste products, regulates temperature, and has receptors for pain, tactile sensation, and pressure. The health and appearance of the skin, reflects the lifestyle, dietary habits and the age of the individual[3].

Aging process is associated with a loss of fibrous tissue, slower rate of cellular renewal, and a reduced vascular and glandular network. The barrier that maintains cellular hydration also becomes impaired. The subcutaneous tissue (hypodermis) flattens, particularly in the face, hands and feet.

Aging of the skin is influenced by many factors as ultraviolet radiation, excess alcohol consumption, tobacco abuse, and environmental pollution[4]. Increase in body weight and rise in blood sugar levels, disrupt the biochemical reactions and the very structural framework of the skin. All these factors lead to cumulative deterioration in skin appearance and function.

Age time line

What happens to the skin as person gets older[1]?

Age 25: Visible aging lines of the skin start to appear, and the skin replaces old cells more slowly.

Age 30: More fine lines develop as collagen and elastin start to breakdown and their production decrease. The delicate skin under the eye begins to thin.

Age 40: deeper lines begin to engrave around the mouth and the eyes. Furrows appear on the forehead and circles under the eyes.

Age 45 +: the skin becomes thinner, partly because of hormonal changes, and more sensitive to irritating environmental

factors and allergens. The skin loses much of its strength and elasticity.
Age 50 +: age spots start to appear; a common occurrence on more than 90% of fair skinned people.

Skin Changes with Aging[5]

1- The epidermal layer thins, but the number of cell layers remains unchanged.
2- The number melanocytes cells decreases, but increase in size. The skin appears thinner, paler, and clear (translucent), with large pigmented spots (age spots, liver spots, or lentigos) appear in sun-exposed areas.
3- The skin's strength and elasticity reduced due to the changes in the connective tissue, known as "Elastosis" in sun-exposed areas. The skin is leathery with weather-beaten appearance common to those who spend a long time exposing to sun as farmers and sailors.
4- The blood vessels of the dermis become more fragile easily bruised with sub-cutaneous bleeding called senile purpura.
5-The subcutaneous fat layer thins, reducing its normal insulation and padding. This increases the risk of skin injury and reduces the ability to maintain body temperature with danger of hypothermia in cold weather.
6- Sebaceous glands produce less oil as skin age. Men experience a minimal decrease, usually after the age of 80. Women gradually produce less oil beginning after menopause. This can make it harder to keep the skin moist, resulting in dryness and itchiness.
7- The sweat glands produce less sweat. This makes it harder to keep cool, and you are at increased risk for becoming overheated or developing heat stroke.
8- Some medications are absorbed by the fat layer, and loss of this layer changes the way that these medications work.
9- Growths such as skin tags, warts, and other blemishes are more common in older people.
10- With advance age the skin is thinner, more fragile with reduced subcutaneous fat layer which makes the skin at higher risk for injury. The ability to sense touch, pressure, vibration, heat and cold may be reduced.
11- Friction and rubbing on the skin can cause skin tears. Blood vessels are fragile and easily damaged. Bruises, and hematomas may form after even a minor injury, can occur anywhere on the body, as the outside surface of the forearms,
12- The older the skin the slower it can repair itself. Healing of the skin wounds may be up to 4 times slower to repair. This is the cause of pressure ulcers and infections.

Visible signs of aging[1]

Dark spots	Wrinkles/Sagging	Comedones	Rough, red or scaly

Aging Factors

A. Intrinsic (chronologic) [1]: Skin is at risk for degenerative effects seen in other organs, yet due to its visibility, the skin on the surface reveals many aspects of our inner health.
1) Genetic predisposition: cell aging is the process by which the cell becomes old and can't replicate, a process called "replicative senescence". This phenomenon could be due to:
(a) Random occurrence DNA mistakes: Skin cells are some of the most rapidly dividing cells in the body. Persistent accumulation of DNA damage induced by reactive oxygen species (ROS) is proposed to be a major contributor toward the aging process. The rapid replication of skin cells causes them to be intrinsically

vulnerable to replicative senescence, especially if efforts to protect skin cells from damage are not taken[6, 7].

(b) Telomeres: it's the protective DNA cap at the end of the chromosome that ensures chromosomal stability. It serves to protect our genetic data, make it possible for cells to divide, and hold some secrets to how we age and get cancer. Each time a cell divides, the telomeres get shorter. When they get too short, the cell no longer can divide and becomes inactive or dies. This process is associated with aging and cancer formation. So telomeres have been compared with a bomb fuse[8, 9].

2) Hormones: With aging, there is a decline in the level of sex hormones (estrogen, testosterone, dehydro-epiandrosterone sulfate), and growth hormone[10, 11]. These particular hormones have great influence on the skin. While escalating sex hormones during puberty increase the incidence of skin acne, declining hormonal levels with aging accelerate skin deterioration[12]. In women, changes of hormonal levels e.g. estrogen during menopause are associated with significant changes within the skin. Estrogens influence skin thickness, wrinkling, and moisture[13, 14].

3) High blood sugar levels: Glucose is a vital cellular fuel. Chronic glucose exposure has long been known to affect how the body ages by a process called glycation based on the accelerated rate of aging seen in diabetics[15]. Hyperglycemia accelerated skin aging, results in gradual development of diabetic complications. When sugars enter the circulation, they attach themselves to the amino groups of tissue proteins such as collagen to slowly rearrange their structure into damaged structure called "advanced glycation end products" which is destructive because they can undergo extensive cross-linking with other proteins to form strong chemical bridges. Once healthy collagen fibers lose their elasticity, becoming rigid, more brittle, and prone to breakage[16]. The skin will show widespread complications, such as thinning, discoloration, loss of elasticity, and tendency to rashes and infections.

4) Metabolic "Oxidative stress": The skin is the outermost barrier separating internal tissue from the environment. The regularly exposure to UV radiation and air pollution stimulate the production of "free radicals", which cause chaos in the skin cells. Prolonged exposure to free radicals leads to the appearance of pigmentation, wrinkles and sagging skin[17]. Oxidative stress breaks down protein (collagen), alters cellular renewal cycles, damages DNA, and promotes the release of pro-inflammatory mediators (cytokines), which trigger the generation of inflammatory skin diseases[18]. It also decreases the population of immune Langerhans cells, and the ability to migrate in response to tumor necrosis is significantly impaired in elderly subjects, which affect skin's ability to defend itself against stressors or infection that may impact its health[19].

B. External (photoaging) [3]: The intrinsic factors of skin are exacerbated by environmental (extrinsic) factors. One of the most important extrinsic factors in accelerated skin ageing is solar ultraviolet radiation (UVR), which induced chronic low grade inflammation through increase of cytokines, cyclooxygenase (COX-2) and metalloproteinases. Epidemiological and clinical studies have identified excessive sun exposure as the primary cause in various skin diseases including, premature aging, inflammatory conditions, and melanoma and non-melanoma skin cancers[20, 21].

1) Effect of UV exposure, chronic sun exposure[1].

(a) Damaged to dermal connective tissue.

(b) Alters normal skin metabolism.

(c) Depress immunity

(d) Stimulate oxidative stress & inflammation.

(e) Increase destruction of collagen by increase enzymes which result in loss of skin structure occurring with age.
(f) Depletion of anti oxidants (vitamin E & vitamin C) in the surface epidermal layer.
2) Environmental Toxins
a) Tobacco smoking: associate with increased plasma homocyteine. It contributes to many chronic diseases and reduced life expectancy[22,23]. The tobacco smoke produces oxidative stress, impairs circulation, and triggers DNA damaging reactions, making the skin more vulnerable to disease and aging[24,25]. "Smokers skin" is characterized by increased lines and wrinkles, uneven tone, dehydration, dull and frail skin[24]. Quitting smoking improves skin conditions and skin aging effect[24]. Smoking is a strong predictor of facial wrinkle formation and other aspect of premature skin aging[25].
b) Air Pollution: Effects of air pollution on the skin alone include dryness, premature aging, skin rashes, eczema and acne in both human and animal studies[26,27], in particularly hyper-pigmentation, wrinkles, and sluggish skin renewal[28]. An increase in soot and particles from traffic was associated with 20% more pigment spots on forehead and cheeks[28].
3) Emotional stress effect on the skin: "Stressful emotions age your skin[29]"
When stress signal send out by the brain, the responds is as follows:
1. Activating immune cells in the skin and inflammation results which may affect the skin aging.
2. Production of adrenaline: blood directed away from the skin towards the muscles which tends to get stiff results in more decrease of normal blood flow to the skin. Nourishment and Oxygen will be less and removal of waste and toxins will be inhibited. Eventually the skin will appears dull, pale, sallow and lifeless.
3. Stressful emotions as anger, frustration, anxiety and excitement stimulate the release of hormones and enzymes which increase oil glands production and results in clog pores, pimples and unhealthy pale appearance.
4. Increase production of cortisone hormone which weakens the body natural defenses and natural process of skin renewal and leaves the vulnerable to environmental pollution.
5. Stress increase the population of free radicals which speed the aging process by harming the DNA and results in premature aging.
6. Stress inhibits digestion; the body can't absorb nutrients from the food and undigested impurities will accumulate faster than the body can get rid of them.
4) Dramatic changes in weight: Obesity requires special attention to skin, as the forces gravity grow, they place greater stress on healthy skin. The thin, elastic layer of skin becomes more delicate and easily broken with venous stasis and dermatitis. Because the immune response is less efficient in obese people, the likelihood of infection is greater. As the body weight increases and the blood sugar level rise, the biochemical reactions disrupt the structural framework of the skin[30]. Combination of these factors leads to cumulative deterioration in skin appearance and function.

Radiation Energy[1]

Radiation Energy emitted by the sun composed of;

Ultraviolet	8.5%
UVC	0.5%
UVB	1.5% (5% of total UVR)
UVA	6.3% (90- 95 % of total UVR)
Visible Light	39%
Infrared (IR)	52%

What Are the Free Radicals[1]?

A Free Radical is any atom or molecule that has one or more unpaired electrons and is capable of independent existence.

The damaged caused by the Free Radicals are directed to:
1. Cell Wall Integrity
2. DNA, RNA (Cell Nucleus)
3. Intracellular Organelles
4. Collagen (Dermal)
5. Elastin (Dermal)
6. Keratin (Cell Walls & Intercellular Spaces)

UVA Characteristics[1]

1. Passes through window glass

2. Constant flux all year long
3. Passes through clouds (doesn't filter by ozone)
4. Present from sunrise until dusk
5. Present in tanning beds and electric welding

UVA wave length[1]

UVA "long wave" its length = 160-250 nm,
It penetrates deep into the epidermis & dermis.

Structure and Functional Damage[1, 3]:

1. Fibroblasts, Collagen, Deranged Elastin,
2. Langerhans Cells (immunity suppression)
3. Hair Follicles, Dermal Papillae, Vascular network,
4. Post UV inflammation & hyperpigmentation with Tanning (melanin production)

5. Photo Allergy and Photo Sensitivity
6. Primary cause of wrinkling
7. Minimal erythema reaction (burn)
8. Induce oxidative stress

UVB Characteristics[1]

1. Can't penetrate window glass
2. Varied flux (11am-3pm danger zone)
3. Can't penetrate clouds (filter by ozone layer)
4. Causes acute sunburn. Normal collagen damaged
5. Major cause of epidermal cancers.

UVB Penetration[1]:UVB" Mid wave" its length = 17-50 nm, it has a shallow penetration

Structure and functional damage[1,3]:

1. Highly damaging to Keratinocytes and DNA.
2. Acute Sunburn reaction
3. Absorbed within the Epidermis:
- Retention Keratoses (thick & rough)
-Actinic Keratoses
- Skin Cancers (non melanoma)

- Abnormal Pigment (melasma/age spots)
- Fine Lines (wrinkles)

Current existing UV Protection Means[1]

(1) Chemical absorbers: Sunscreen for UVB, sunscreen is generally aromatic compounds conjugated with a carbonyl group. These chemicals absorb high-intensity UV rays.

(2) Physical blockers = Sunblock for UVA, Physical blockers reflect or scatter UV rays; it acts as a small reflecting mirror. ? Absorption

The Photon "Nano particle" Trapping[1]

Totally new concept now perfected by James Beckman (USA) and Anatoli Ischenko (Russia).

It's a Silicon composite nano-particle which can give broad-spectrum protection against

UVA, UVB, and UVC spectrum action (99% effective). Its characteristics are:

1. Transparent to visible light (clear not white)
2. Chemically inert-no toxicity
3. Potential actual SPF of 1000

The nanocrystal bulk is a crystal lattice with average size of several tens of nanometers.

It works as follows:

UV energy in its smallest form is a "dot" of energy particle traveling as a wave. Its energy has enough force to pass between the Silicon Oxide nanoparticle (NC, Sio) through the electron field into the interspaces of the crystalline structure. But the energy spent in getting into the nanoparticle leaves less energy available to escape out of the intermolecular spaces of the silicon oxide nanocrystal, i.e. there is little energy available to allow the UV energy to exit from the other side of the nanoparticle.

The trapped UV energy simply converts to vibration and then to heat energy and is dissipated as heat. This is a very low heat and would not cause body surface to heat up more than one degree, so there is no discomfort nor heat damage.

Silicon Oxide nanoparticle

References

1. Beckman, J. "UV-Protective Silicon Nanocomposite Emulsions", presentation at Revitalizing Research in Kurdistan, Erbil, Iraq. December 14-16, 2010
1. 2. The Human Aging process and What We Can Do To Slow It Down. Aug 13,2010 www.immortalhumans.com/the-human-aging-process-
2. Skin Aging. LifeExtension. http://www.lef.org/protocols/skin_nails_hair/skin_aging_01.htm
3. Pontius, AT., Smith PW. "An antiaging and regenerative medicine approach to optimal skin health." Facial Plast Surg (2011): 29-34.
4. Aging changes in skin. Medline Plus, Aug 15, 2010. http://www.nlm.nih.gov/medlineplus/ency/article/004014.htm.
5. Chang AL., et al. "Association of facial skin aging and vitamin D levels in middle-aged white women." Cancer Causes Control (2010):2315-6.
6. Gilchrest BA, Eller MS, Yaar M. Telomere-mediated effects on melanogenesis and skin aging. J Investig Dermatol Symp Proc. 2009 Aug; 14(1):25-31.
7. Attia, EA., Seada LS, El-Sayed MH, El-Shiemy SM. "Study of telomerase reverse transcriptase (hTERT) expression in normal, aged, andphoto-aged skin." Int J Dermatol (2010):886-93.
8. Gao, YY., Luo D, Zhou BR, Li W, Min W, Lin BJ. "Mechanism of telomere shortening in photoaging model induced by 8-methoxypsoralen and ultraviolet A." Zhonghua Yi Xue Za Zhi (2010): 1698-702.
9. Chahal, HS., Drake WM. "The endocrine system and ageing." J Pathol (2007):173-80.
10. Makrantonaki, E., et al. "Molecular etiology of skin aging. How important is the genetic make-up?" Hautarzt. (2011): 582-7.
11. Makrantonaki, E., Zouboulis CC.. "Androgens and ageing of the skin." Curr Opin Endocrinol Diabetes Obes (2009): 240-5.
12. Verdier-Sévrain S."Effect of estrogens on skin aging and the potential role of selective estrogen receptor modulators." Climacteric. (2007): 289-97.

13. Kanda, N., et al. "Regulatory roles in sex hormones in cutaneous biology and immunology." J Dermatol Sci (2005): 107.
14. Van Boekel MA. The role of glycation in aging and diabetes mellitus. Mol Biol Rep. 1991 May;15(2):57-64
15. Pageon H., Técher MP, Asselineau D. Reconstructed skin modified by glycation of the dermal equivalent as a model for skin aging and its potential use to evaluate anti-glycation molecules. Exp Gerontol. 2008 Jun;43(6):584-8. Epub 2008 Apr 7.
16. Fisher GJ, Quan T, Purohit T, Shao Y, Cho MK, He T, Varani J, Kang S, Voorhees JJ. "Collagen fragmentation promotes oxidative stress and elevates matrix metalloproteinase-1 in fibroblasts in aged human skin." Amer J Pathol (2009) 101-114.
17. Masaki, H. Role of antioxidants in the skin: anti-aging effects. J Dermatol Sci (2010): 85-90.
18. Ogden, S., Dearman RJ, Kimber I, Griffiths CE. "The effect of ageing on phenotype and function of monocyte-derived Langerhans cells." Br J Dermatol (2011): 184-8.
19. Chang KC, Wang Y, Oh IG, Jenkins S, Freedman LP, Thompson CC, Chung JH, Nagpal S. “Estrogen receptor beta is a novel therapeutic target for photoaging". Mol Pharmacol. 2010 May;77(5):744-50. Epub 2010 Jan 28
20. Bauer A, Diepgen TL, Schmitt J. “Is occupational solar ultraviolet irradiation a relevant risk factor for basal cell carcinoma? A systematic review and meta-analysis of the epidemiological literature”. Br J Dermatol. 2011 Sep;165(3):612-25. doi: 10.1111/j.1365-2133.2011.10425.x. Epub 2011 Aug 18.
21. Kim ,EJ., et al. "Skin aging and photoaging alter fatty acids composition, including11,14,17-eicosatrienoic acid, in the epidermis of human skin." J Korean Med Sci (2010): 980-3.
22. Nicita-Mauro, V., et al. "Non smoking for successful aging: therapeutic perspectives." Curr Pharm Des (2010): 775-82.
23. Serri, R., et al. "Quitting smoking rejuvenates the skin": results of a pilot project on smoking cessation conducted in Milan, Italy." Skinmed (2010): 23-9.
24. Morita, A., et al. "Molecular basis of tobacco smoke-induced premature skin aging." J Investig Dermatol Symp Proc (2009): 53-5.
25. Pedata P, et al. "Interaction between combustion-generated organic nanoparticles and biological systems: In vitro study of cell toxicity and apoptosis in human keratinocytes." Nanotoxic (2011) May.
26. Vierkötter, A., et al. "Airborne particle exposure and extrinsic skin aging." J Invest Dermatol (2010): 2696.
27. Keefer A. “Air pollution Effects on the Skin”. Livestrong.com; Jun 11, 2010
28. How Emotions Can Cause Premature Aging. Rich Earth. Jan 31, 2012. http://richearthorganicspa.com/skincareblog/?p=1282
29. Clarke N. “Obesity & Skin Care”. livestrong.com, Aug 13, 2011. http://www.livestrong.com/article/79422-obesity-skin-care/#ixzz2EOARAfKm