

SCIENTIFIC STUDIES ON GEROVITAL H3

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Gerovital-H3 - Its regenerative effects

In 1956, Aslan brought forth her work "A new method for the prophylaxis and treatment of old age with Novacaine-Substance H3" at the institute of chemical physiology, Berne, Switzerland (1) and at the "Deutsche Therapiewoche" congress in Karlsruhe, Germany (2).

Since then, over the past 42 years, valuable literature on Gerovital-H3 has accumulated consisting of the confirmation of Aslan's geriatric-method, and Gerovital-H3's regenerating and prophylactic actions.

Studies conducted by the National Institute in Bucharest and those carried on by other authors have pointed out the general action exerted by Gerovital-H3 on the aging process, and its action on chronic diseases, the frequency of which increases with advancing age (3,4).

Clinically, Gerovital treated patients show more desire to live, diminished depression and anxiety, increased physical and intellectual capacities, diminished extrapyramidal rigidity, better skin, hair and nail trophicity, less senile spots and keratosis, growth and regimentation of the hair color, increased muscular strength and joint mobility and faster knitting of accidental fractures.

Gerovital and regeneration

Aslan checked these clinical facts experimentally (5), the research showed Gerovital-H3 to have regenerative effects on the liver tissue, bone marrow and it shortened the time required by bone knitting after experimental fractures in rats (5).

An experimental study was conducted by Aslan on 1840 rats, it made evident an 18% to 21% life span extension in the treated rats as compared to control rats injected with saline solution.

The treated old animals also displayed better general trophicity, thick and glossy fur, higher resistance to acute diseases, increased resistance to exercise and better answers to memory and behaviour tests as against the control group. At the age of 24 months, the treated animals with Gerovital-H3 scored better in learning and memorizing the maze (6), (see figure 1 below).

The histological examination of the hearts removed from animals treated with

Aslan's Gerovital-H3 revealed connective invasion more reduced than in the controls; the degenerative modifications of the renal tubes were fewer and less severe in the treated animals as were the involutive changes found in other organs.

The laboratory studies conducted on *Drosophila melanogaster* revealed a 22.7% life span extension in individuals cultivated in a medium containing 0.005mg Gerovital-H3/ml, in comparison with control group (p 0.01). Similar results were obtained with secondary cultures of monkey renal cells.

Gerovital-H3 in a concentration of 0.4ml% induced the extension of the post-mitotic life span renal cells by 16%, meanwhile the normal signs of aging were noted in the untreated cells (7,8).

Gerovital-H3 effects on aging embryo fibroblasts of the rat and their life span in cultures were studied by Officer (9). He noticed that Gerovital-H3 added to the cultures in the 7th to 9th passages reduced the time required by cell replication, which thus continued for 2 to 5 generations more than in control cultures. When added to cultures in which the replication had ceased, Gerovital-H3 extended cell life span, it also prevented the spontaneous change into a continuos cell line.

Regarding the regeneration of cells, I recall Schedel's experiment with procaine injections around a wound (10). This enabled him to cure an ulceration caused by Rontgen therapy. The histologic examination of the wound revealed the appearance of the granulation tissue after a 3-week treatment along with the accumulation of the so-called "regeneration cells" around many vessels (see figure 2 over).

The age-related accumulation of lipofuscin within the nervous cells is now well known, so the action of Gerovital-H3 was studied on rats under 6 to 18 months old. Histologically and histochemically, the number of entirely lipofuscin-loaded pyramidal and Purkinje cells from the brain cortex and cerebellum was much lower (19.4 in treated vs. control animals- 72.8) (11,12).

In an experiment study on the nootropic effects of Gerovital-H3 upon the central nervous system in rats, it was noted that Gerovital-H3 had protective consequences against anoxia by curarization or closed circuit (13).

Gerovital- protection against infection

The higher resistance to infections of the patients under Gerovital-H3 treatment was also remarked on by Aslan (14), her observations showed that;

- 69.1% of the patients under long-term treatment with Gerovital-H3 did not catch

any disease.

- Overall the death rate in the Gerovital-H3 group was 3.3% compared to a much higher rate of 12.9% in the control group.
- The patients under long-term Gerovital-H3 treatment were less prone to infectious diseases, both in the cases of seasonal influenza epidemics and whenever the environmental conditions favoured the onset of acute respiratory pathology (15).
- The prophylactic studies which consisted in administering Gerovital-H3 to people over 40 years old indicated the decrease in morbidity rates leading to the reduction in the number of sick days off work by 39%, when compared to the pre-treatment period (16).

(Ed.- In fact the Romanian government was so impressed by this potential productivity/ economic improving potential, that it subsidised the cost of the Gerovital-H3 to its people!)

Further experimental researches conducted by Raskova (17) showed that procaine injected into mice increased their resistance to *Shigella shigae*; (and when maintained by periodical procaine injections) this resistance was passively transmitted to their offspring!

With subsequent investigations, I will try to pinpoint the mechanism by which Gerovital-H3 enhances the organism's defence ability, but for now, •Gerovital-H3 prevents or alleviates chronic diseases which are caused by mechanisms closely dependent upon the general involution of the organism and implicity of the immune structures and functions.

•Some researchers found out that low auto-antibody levels in aged people treated with Gerovital H-3 over long periods (18), this data points to Aslan's treatment ability to hamper the impairment of those structures susceptible to become antigen sources for the production of auto-antibodies. This treatment appears as effective in preventing auto-aggression phenomena in the aged. As the lymphocyte binding ability decreases with advancing age, Gerovital-H3 preserves lymphocyte reactivity on which the cell-mediated immune response is based.

The increased resistance of the organism against the manifold environmental aggression (infections, toxins, stress) is also prevented by the decline in cortisol levels (19).

Dr. Aslan published her findings on the functional study of the cortex and basic

nuclei in aged and young people by way of conditioned vascular reflexes (20,21). Since then Tzobkallo C.T. has confirmed these results by means of experimental salivary conditioned reflexes.

These authors claim that small doses of 1-2mg procaine/ Kg body weight injected subcutaneously stimulate the higher nervous activity. Large doses of 10-20mg procaine/ Kg body weight have an anti-depressing effect (22) (see figure 3).

Gerovital- experiments in the USA!

Experiments using procaine according to Aslan's method were conducted in the united states, where they concentrated upon mental disorders.

In a double-blind trial on 30 elderly patients, Zung using Gerovital-H3, placebo and imipramine emulated Aslan's Gerovital-H3 efficiency in depressed people (23). Data published by the American authors drew attention on the change induced by aging and depressive states in the enzymatic activity of the nervous cell, as well as the antidepressive effect of Gerovital-H3 (24,25).

These studies have provided a view of potential importance regarding the Gerovital-H3 antioxidant action (26). The author found out that Gerovital-H3 exerted an inhibition on the generation of the superoxide radical in a nonenzymatic system. It was shown that Gerovital-H3 determined a decrease in the erythrocyte susceptibility to auto-oxidation, and it was suggested that this geriatric product might play an important role in the erythrocyte antioxidant protective mechanisms.

In a study on the prophylactic effects of the treatment with Gerovital-H3, it has been discovered that there are significant increases in the serum HDL-C concentrations (good cholesterol) of the HDL-C percentages of the serum total cholesterol, decreases in the triglyceride levels and a tendency to return towards the normal lipid profile (table available upon request) (26).

Gerovital-H3, the original procaine-based product, exerts its effects on the atherogenesis process by several interdependent mechanisms, consisting either in diminishing the level of plasmatic lipoproteins and lipids, or in the effect exerted on the erythrocyte membrane (an increase in membrane fluidity and a protection against osmotic hemolysis), or by the antioxidant mechanisms reducing the oxidative stress exerted on the membrane structure and on the HDL (see figure 4).

On the occasion of the International Scientific Manifestation "Medizinischewoche" in Baden-Baden Germany (November/ 1985), while concluding the Gerontology and Geriatrics Section, Prof. Dr. Paul Luth (Germany) remarked "Gerovital-H3

treatment and Aslan's method represent the most efficient therapeutic procedure in Pregeriatrics (40-65 years old) and Geriatrics (more than 65 years old) in the prevention of aging disorders and chronic diseases."Gerovital-H3 is still made in Romania to Dr. Ana Aslan's original formula. It is available in 100mg tablets or 5ml injectable ampoules. English instructions are made available with every purchase.

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The anti-depressant effects of Gerovital-H3 treatment

As people grow old, the brain undergoes macroscopic, microscopic, biochemical and electrophisiological changes. The number of neurons (nervous cells) decrease, dendridic changes occur (the link among cells), as well as neurofibrillas and plates (described by Marinescu and Block) appear in the nervous cells.

Recent data shows that neuron losses do not occur in all the brain's area (for instance, the parietal area). There are markers which confirm the aging process: ischemia, plates of lipofuscin, neurofibrillas (a net of intraneuronal fibres very frequent in Alzheimer's disease). The prefrontalis and frontalis are the areas most altered by aging. Changes also occur within the cerebral vascular system: haemorrhages, atheromatous plates and obstruction of some small vessels.

The cognitive changes are quite normal in the elderly (the topic is still under discussion). Nevertheless, old age brings about changes of the intellectual ability). The impairment of the cognitive functions begins about age of 35-40, although being insignificant till the age of 60-65. The primary memory (sense memory) and the long-term memory do not change. On the contrary, the short-term memory (from 1 hour to 1 week) is altered. The elderly can hardly remember the names and the events that happened and the things they read over this period. The use of calendar and written notes help them most. It is very easy for the elderly to remember knowledge stored in the past to which their lifetime experience is added.

Effects of Old Age

The decrease of the psychomotor activity is another important feature of old age, which is obvious in everyday life (the subtle movements lose their accuracy, the reaction speed lowers). With normal aging these changes do not infringe upon the elderly's independence and ability to meet their own needs.

The above mentioned changes are normal in the elderly. Biochemical changes of the neurotransmitting systems (GABA, dopaminic, cholinergic and serotonergic) and the influence of some exogenous factors bring forth the metabolic changes which cause depression's onset. In the presence of an old patient with cognitive impairments and changes of behaviour, the geriatrician and the psychologist should distinguish the trilogy:

- is it a normal change?
- are they the indices of a depression?
- is it an incipient Alzheimer's disease?

In general, the patients suffering from depression exaggerate their sufferings, while those with Alzheimer's disease or with other incipient dementias deny or minimise them.

Depression

Depression is one of the elderly's major diseases. It is also frequent in adults. Depression is a syndrome (a series of symptoms) including physiological, emotional and cognitive symptoms. The criteria worked out by The American Psychiatric Association in The Diagnostic and Statistical Manual of Mental Disorders (3rd revised edition) include:

Change of appetite and weight;

- Sleep disorders;
- Inner strain or belated motory reactions;
- Lack of energy, fatigue;
- Nervousness;
- Concentration and memory disorders;
- Lack of pleasure and interest in almost any kind of activity;
- Tendencies of guilt;
- Thought or attempt of suicide.

The presence of 5 of these symptoms shows a major depression fit. These symptoms are often assigned to normal age, both the physician and the patient being mostly concerned with physical diseases and ignoring depression.

In the elderly, depression occurs within a complex clinical and social context. The older patient may suffer from 2-3 or even more diseases, some of them leading

to infirmities, and the social relationships may be non-existent. The diagnosis of depression should be preceded by a thorough analysis of the patient's present state and case history. The clinical history, physical examination and biological check-up, as well as a study of the social background are current possibilities of assessing the diagnosis of depression.

Some authors consider that many elderly have a depressive state. According to the National Health Institute of Bethesda, 30% of the elderly (over 65) suffer from depression. Other researchers mention a higher rate - 50% and even more in the elderly of the 8th, 9th and 10th age decades. This suffering often remains hidden, unknown, being masked by physical diseases, and neither the patient nor the care staff, homes for the aged, nursing homes for the elderly people recognise it.

Despite the great progress of diagnosis, treatment and care of these patients, many aspects of depression are still unsettled. For the readers of this article interested in the promotion of an active life, it is important to know:

- The conditions and factors responsible for the depressive states;
- The peculiarities of depression in the elderly, and
- The treatment.

For women who lead a life of deprivation i.e., widows stressed and lacking a moral and economic support - often suffer from depression. After the age of 65, chronic diseases such as cancer, stroke, diabetes, mellitus, deforming and painful arthritis, by their nature multiply the implications and induce a depressive state. Half of the patients suffering from depression have several episodes during their lifespan. Suicide and suicidal tendencies are frequent after the age of 80.

Polymorbidity

Depression in the elderly is not quite different from the adult's depression. After the age of 65, polymorbidity (association of several diseases in the same patient) is very frequent. The somatic disorders - cardiovascular, digestive, respiratory, loss of weight - raise several questions as concerns the positive and differential diagnosis. 20-30% of the patients have a depression which is mostly masked by an organic symptomatology. The visceral symptomatology is expressed subjectively only under the form of cenestopathic symptoms of a hypochondriac type. These symptoms mostly occur in adult women. Certain disorders which point out "de facto" a visceral suffering may be wrongly assigned to a depressive state. The phenomenologic analysis of depression's symptomatology will reveal the circadian variation, much more obviously in the morning when the incidence of suicide is at its greatest.

Therapy

Any depressive symptom may impair life's quality, so a therapy is absolutely necessary. The treatment may be medical and psycho-social. To be effective, the treatment should be administered over a period of time and in optimum doses.

Since 1945, Prof. Aslan had been injecting procaine into patients with painful arthritis in order to relieve their joint pains. Many of her patients noted an improving memory, less depression, more energy and a generalised feeling of well-being. These results encouraged her to carry out additional studies to test the effects of procaine on thousands of patients. She found that by adding an antioxidant, the procaine molecule was stabilized and the effects were more than with procaine alone. She called her improved form, Gerovital-H3.

Aslan said that "due to the effects of its main active elements, the procaine and procaine's metabolites - paraaminobenzoic acid (PABA) and diethylaminoethanol (DEAE) -, Gerovital-H3 belongs to Pregeriatric and Geriatric drugs having an eutrophic effect on the organism". Starting from 1949, she noticed an obvious improvement of the physical state in old people. Gerovital-H3 acts upon the human body participating in the regulation of the intermediary metabolism, acetylcholine synthesis and inhibits the monoamineoxidase (MAO). MAO is an enzyme that catalyses the breakdown of monoamines (dopamine, epinephrine and norepinephrine) which play a transmitter role between nervous cells. A MAO inhibitor blocks a breakdown of certain monoamine neurotransmitters and that can be used to treat depression. Robinson and his colleague, in the 'Lancet' magazine, Feb., 1972 (1), showed that starting around the age of 40, the level of MAO increase is directly related to the aging process and depression phenomena.

Gerovital-H3 has a certified antidepressive effect, especially in light and moderate depressive syndrome, thanks to its MAO-inhibitory effect. The antidepressive effect of Gerovital-H3 as well as the lack of any side effects can be accounted on the fact that it is a reversible and competitive-MAO inhibitor.

Paul Luth (2) mentioned that "procaine influence on the patient's psychic condition was signalled for the first time in the medical literature by Aslan". Subsequent to Aslan's investigations on the psychic effect of procaine (3), Pfeiffer (4) carried out pharmacological studies on demethylaminoethanol (DMAE) action and noticed a mental stimulation. This study placed emphasis on the relations existing between DMAE and acetylcholine. DMAE breaks through the blood-brain barrier taking part in the metabolic process of the nervous cells fixing their proteic and lipid fractions and changes into choline and acetylcholine.

Hrachovec, from Los Angeles University, published in 1972 the results of a

comparative study showing that Gerovital-H3 has an inhibitory effect upon the MAO-brain, liver and the heart of the rabbit (5).

Gerovital-H3 Mechanisms

Yau made a pharmacological study upon Gerovital-H3 and summarised as such its basic mechanisms (6):

- it competitively and reversibly inhibits the MAO;
- it acts as an antidepressive through the modification of the monoamine level in the brain and it is very selective in the oxidative desamination inhibition;
- the oxidative desamination of monoamines is done in such a way as to eliminate the hyper-blood-pressure peaks so typical after administering other MAO inhibitors.

McFarlane proved the increasingly inhibitory action of Gerovital-H3 upon MAO from 17.8% to 87.7% depending on the dose administered (7). McFarlane appreciated Robinson's important contribution to the understanding of a biochemical modification connected with the ageing process. He noticed that Gerovital-H3 induces a stronger MAO inhibition than the normal procaine hydrochlorate and its action is reversible and competitive (8).

Depression Treatment

William Zung from Duke University, North Carolina, applied Gerovital-H3 treatment for 28 days, using the double-blind method, on three groups of patients who suffered from depression (9). One group of patients aged 60 were submitted - before, during and after the treatment - to a battery of psychological tests (Zung is the author of a well-known scale of psychological tests) which proved the Gerovital-H3 efficiency in the treatment of depression.

In a double-blind study (10) conducted on depressive patients, the antidepressive effect of Gerovital-H3 was evaluated by means of psychiatric and psychological investigations. The tests on depression showed a higher percentage of improvement for Gerovital-H3 treated patients. The following items were alleviated: depressed mood, sociability and fatigue-70%, agitation-60%, anxiousness and hypochondriasis-45%.

Durk Pearson and Sandy Shaw noted in their book, "Life Extension" (a national best-seller): "here is how you might be able to better handle depression... MAO increases in activity with age, thus resulting in lowered levels of these signal-transmitting brain chemicals. Procaine - or the procaine compound Gerovital-H3

(GH3) developed by Dr. Ana Aslan of Romania, is a mild reversible MAO inhibitor. When using most MAO inhibitors, it is necessary to avoid excessive dietary intake of monoamine precursors such as the amino acids tyrosine and phenylalanine to avoid too high levels of the monoamines, which can lead to higher blood pressure. Procaine - or GH3 - does not interfere".

Recently, I did a double-blind study (unpublished) on 50 patients with low, moderate and severe depression. After two series of treatments, the difference was statistically significant between the patients with Gerovital-H3 and placebo. The Hamilton score was constantly positive and the medium reduction was significant ($p=0.0001$) much more so for Gerovital-H3 than for the placebo. All the statistics were proved with the technique of Covariance analysis.

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Gerovital-H3 treatment in Osteoarthritis

In 1946, Aslan published her first research on Novocaine (1). In 1951, she studied the effect of procaine on experimental arthritis (2).

"After the first results with Novocaine injections, I tried this treatment on patients with arthritis and those with a tendency to ankylosis. Because these diseases are chronic, I administered novocaine for each patient with more injections. With great joy, I noticed an improvement in the local symptoms, and even more importantly a great improvement in their overall general condition. Before the treatment, the patients avoided any movement due to pain and now they were willing and wanting to walk, sitting up to read and talking. The biggest reward was noticing an increase in their interest in life and for their family".

Aslan remembered, too: "On April 15, 1949- an American GI, with arthritis arrived in my clinic. He had terrible pains and his articulations were blocked. I explained to him my ideas about novocaine and after receiving his permission, I gave him an intra-arterial injection with 1%- novocaine. After 10 to 15 minutes, his knee was mobile and he could flex his leg outright. What happiness! I administered his treatment for a further two weeks and he was completely recovered" (3).

Clinical (5,6,7,8,9) and experimental studies (2,10) previously conducted by Aslan et al. have pointed out the effects of Gerovital-H3 therapy in arthritis. Concerning the chronic degenerating disease under the effect of the eutrophic Gerovital-H3 treatment, an obvious amelioration of the clinical signs was particularly noticed in osteoarticular diseases (11,12,13). In a study performed in 1982 (4) on 2643 patients, Aslan noticed that it became evident that pains ceased in 62.2% of the patients, and articular mobility and periarticular muscular tonus were ameliorated in 51.8% of the cases. Repeated radiological examinations indicated a gradual amelioration of osteoporosis and other dystrophic osteoarticular modifications.

I conducted a study on 100 elderly patients admitted to the National Institute of Gerontology and Geriatrics (NIGG) in Bucharest. They were aged 60 to 89 and suffering from moderate to severe arthritis involving one or more joints. Two groups of 50 patients were made up being very similar in age, sex and rheumatic diseases.

In both groups, arthritis involved more often the spine than the peripheral joints, in which hip-arthritis was slightly less prevalent than knee-arthritis, the latter being more frequent in women than men did. Patients with severe organ or system pathology were not included. No patient with abarticulare rheumatism was included in the groups under study, nor patients with clinical, paraclinical or radiological signs suggesting another type of rheumatism, nor those having a positive test for the rheumatoid arthritis. I noted a significant number of patients suffered from Heberdenosis, which was much more frequent in women than in men.

Two reasons for admission of the patients included pains in the affected joints, limitation of movements, myalgia, joint swelling and declining muscular strength. The patients under study were divided into the following clinical forms who display joint pains persisting at rest; moderate limitation of movements (with 10% to 30% of the normal joint movement capacity; accompanying phenomena which point to 'warm up' arthritis processes-rubor, swelling, heat; reduction of joint space and the presence of osteophytes (diagnosed radiologically). Severe forms with marked pains; who display over 30% deficits of joint function; marked joint swelling; a certain degree of invalidity that forced the patient to use an aid such as a stick or frame- for walking.

Radiologically, the patients displayed reduction of joint space and osteophytosis.

The distribution of these two clinical forms was sensibly equal.

As far as associated morbidity of the patients is concerned, the obvious prevalence of cardio-vascular diseases was first followed in order by neuro-psychiatric, respiratory and digestive complaints.

Gerovital-H3 treatment was administered to the patients in the first group as follows: one i. m. injection daily in the morning for 18 days, followed by 12 days of Gerovital-H3 pills, twice daily: 9:00 A.M. and 4:00 P.M. Similarly, the patients in the second group received Placebo injections and pills. No other drug was given, nor any local therapy applied.

Treatment efficacy was assessed by comparing prior and post-treatment values of the following parameters recorded in all patients of the two groups:

- pain as a subjective parameter and its characteristics;
- joint mobility assessed by goniometry and movements based on tests specific to each joint;
- muscular tone by muscular check-up;

- accompanying phenomena: joint swelling, instability, crepitations;
- overall functional capacity of joints affected by arthritis.

Some parameters reflecting the patients' general condition such as arterial blood pressure, circadian rhythms and psychic state were also checked in parallel. In the two groups (Gerovital-H3 and Placebo) the clinical signs of progress was recorded as the following:

In the Gerovital-H3 group the following was recorded:

- (1). Pain: A remarkable alleviation in 34% of cases, satisfactory alleviation in 54% of cases and no effect in just 12% of the cases;
- (2). Joint Mobility: Improved in 56% of cases and remaining unchanged in the rest;
- (3). Muscular Tone: Improved in 41% of cases and no change in the rest.

I didn't notice any side effects during the treatment with Gerovital-H3.

For the Placebo group:

- (1). Pain: A satisfactory alleviation in only 11% of cases and no influence upon the remaining ones;
- (2). Joint Mobility: Improved in only 4% of cases and there was no change for the rest;
- (3). Muscular Tone: Unchanged in 100% of the patients.

Conclusions

Clinical symptoms dominated by pain and limitation of movements was positively influenced in the case of the first group of patients, (i.e. those under Gerovital-H3 treatment). Their psychic condition was obviously improved. The small amount of positive outcomes recorded in the patients from the second group, (i.e. the Placebo group) by the slight alleviation of joint pains can be explained in terms of the patients resting while hospitalized, which is likely to have diminished the degree of pain felt.

Previous studies carried out at the National Institute of Gerontology and Geriatrics in Bucharest have proved that Gerovital-H3 exerts a beneficial effect

on the vascular, nervous and metabolic components involved in the genesis of degenerative rheumatism (4,6,7,8,10,11,12). The positive properties of Gerovital-H3 treatment can be explained as:

- (A). The antalgic action either controlling or reducing the pain caused by irritation of the nervous network from the spongiotic or by osteophitic presence;
- (B). The anti-inflammatory effect exerted through the AMPc, stimulated by the moderate rise in circulating catecholamine levels;
- (C). Improvement of capillary permeability and the favourable intervention in the bioenzymatic disorders at the level of the joint cartilage considered primum movens in the process of joint degeneration.

Gerovital-H3 can be the drug of choice in the management of arthritis in Geriatrics, because of its beneficial effects on the distressing, sometimes invalidating clinical phenomena and because of its paucity of side effects.

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Old age humoral dysmetabolism

The functions of an aging individual show in the totality of the changes of the metabolic and neurohormonal modulation.

The dominant feature in elderly people is a great liability under stressful conditions', as a consequence there is a decrease in the total water content of the body and hydroelectrolytic turnover, as well as cellular and humoral dysmetabolisms. Advancing age brings about a general anabolic deficit, a reduction of tolerance of carbohydrates, an increasing in biochemical values of lipids and hemocoagulation components, and a diminution of the cellular energetic potential. Each of the functions having its own development and aging time-table.

Gerovital-H3 has a positive effect on the cell metabolism and on the cell membrane. There are studies where the emphasis was placed on Gerovital-H3 intervention in the intermediate metabolism favoring ATP synthesis (1). This hypothesis was based on the discrepancy between the favorable trophic effect and the reduced O₂ consumption. This finding seems to point out procaine similarity with antioxidative abilities. Since 1962, Ficher and Klotz (2) insisted on procaine's antioxidative effect. Other studies carried out on yeast (3) pointed out procaine action on the enzymes involved in oxireduction. Research on liver homogenate revealed procaine intervention on oxidative phosphorylation of glucidic metabolism (4).

Energetic Metabolism

Energetic Metabolism undergoes modifications during the life cycle at the level of energy production, storage, transformation and liberation.

The cell oxygen consumption decreases progressively with age:

At the age of 20: a man's basal metabolism is of 42.5 1.6 cal./sq.m./h; A female's metabolism is of 36.7 2.7 cal./sq. m./h.

At the age of 40: a man's metabolism is of 38 2.9 cal./sq.m./h and 35.9 2 cal./sq.m./h. in females.

However, this diminution of the cellular oxygen consumption is neither regular nor uniform; as a compensation, while tissular activity of oxidative phosphorylation decreases, the glycolytic activity increases and some anaerobic energy-generating processes are intensified.

The reduction of the energetic potential is brought about by the diminution in the number and volume of the mitochondria, of the oxidation substrate and of respiratory enzymes. Unlike other structures, the heart tissue shows an accentuation of oxidative and phosphorylating couplings. The low capacity of an aging organism in pathological conditions reflects the low energetic potential of the cells.

The controversial results of the studies on basal metabolism in the elderly depend on the normal and pathological factors that may influence it. The elderly's physical state, the muscle activity one develops, as well as one's bone pathology, neuromuscular coordination, psychological state and integument's aging degree may influence on production or loss of heat.

With the advance in age, in parallel to the decrease of oxygen consumption, we also may see modifications of the thermoregulation. In conditions of average temperature, the body maintains constant temperature even in advanced ages. However, it presents difficulties for its adaptation to extreme temperatures. As the years pass by, as a consequence of a poorer blood flow in the skin, temperature records has a tendency to decrease, so that the response to the low environmental temperatures will be slower. On the other hand, by the integument aging through atrophy, dryness, reduced elasticity and modifications of the capillaries structure, this diminishes the capacity of water elimination through the skin, explaining the elderly's difficulty of adaptation to caloric stress.

Lipid Metabolism

The normal indicators of the lipids metabolism inscribe themselves on a curve with maximum values in the 6th and 7th decades of life. In long-lived people, biochemical constants are significantly equal to those of young adults. Directly related to the quantity of cholesterol, total blood lipids increase at the age of 70 as compared to the values recorded at 30 years. The increase is especially on account of the esterified cholesterol (low density) and of the cholesterol bound to beta-lipoproteins (with a tropism to the vascular wall). The relation of lecithin to cholesterol decreases. Kurth's studies (5) on procaine action on the lipids metabolism recorded favorable results in atherosclerotic subjects in whom the function of the cell membrane was corrected. Also, the arteriosclerotic dysproteinemias became normal as a result of procaine administration. The author noticed the clearing of serum as well as the decrease of cholesterol levels.

In order to point out the antiatherogenous action of Gerovital-H3, Aslan carried out a study on 25 subjects aged 72-90 to procaine treatment for 4-11 years (1); an equal number of patients were used as controls. The author studied lipoprotein lipase activity in vitro as well as different lipids-fractions after both heparin injections and the activation of the endogenous lipoprotein lipase. Lipoprotein lipase activity reached the average values 13.01 2.01 in the treated subjects, as against 8.75 1.77 in the controls (the normal value is 15 1.6). An obvious dislocation of the lipoproteins fractions was noticed after the heparin injection, with the modification of the beta/alpha-lipoprotein gradient (80% in the treated subjects, as against 15% in the controls). The modifications of the coefficient beta/alpha specific to the post-heparin lipoproteins tallied with the lipoprotein lipase enzymatic activity in vitro.

The inference maybe thus drawn is that one of the important links in the atherosclerotic dyslipidosis chain is also subjected to the eutrophic treatment with Gerovital-H3. This data may be correlated with the reduced number of trombotic accidents in aged subjects treated with Gerovital-H3.

Comparative studies on Gerovital-H3 and procaine action carried out by Greppy and Sgardiigli (6) showed the higher efficiency of Gerovital-H3. Gordon and colleagues (7,8) conducted comparative studies on American procaine and Gerovital-H3. The experiments revealed too the higher efficiency of Gerovital-H3.

Protein Metabolism

Enzymatic structures and protein biochemistry undergo modifications in elderly people. Quantitative modifications are noted in the activity of monoaminoxydase (MAO), aldolase, myosin, adenosine-triphosphatase and phosphofructokinase. Studies published (9,10) draw attention to the modification induced by aging in

the enzymatic activity of the nerve cell as well as to the intervention of procaine at this level. The increased MAO activity could play an important role in the biochemical modifications induced by aging and depressive states. Depressive states have been correlated with the reduction of central amines (11) which is due to the increase of MAO. The anti depressive effect of Procaine (Gerovital-H3) has been pointed out by Bucci and Saunders (12), Siggelkow (13), Cambel (14), MacFarlane (9,10), Zung (15) and other researchers.

The total contents of seric proteins remain unchanged. A modification in the ratio of albumin to globulin will be observed: from 1.38 0.03 at the age of 25 it becomes 1.02 0.02 at the age of 75.

Quantitative modifications are observed in the protein contents of muscles, brain and liver. The net muscle mass decreases. Cytoplasm proteins tend to form inactive complexes, so that the fibrils protein structures increase. A diminution of active protoplasmic mass, and along with it, a reduction of the total potassium content of the body will be observed.

Carbohydrate Metabolism

Carbohydrate Metabolism presents two important phenomena in the aged:

1. The accentuation of the anaerobic phase of glycolysis, and in consequence the diminution of oxidative phosphorylation processes;
2. The reduction of the tolerance to glucose.

The aspects related to the statement of a tolerance reduction to glucose with the advance in age, and to the physiological or physiopathological mechanisms which lead to this situation are not yet completely elucidated. It was considered that there is a "real" decrease of the tolerance to glucose with the advance in age, in both sexes, this being shown by glycemia (fasting blood sugar) and by dynamic tests. Some researchers consider that for each decade of age after 50, the fasting blood sugar increases by 1 to 2 mg./dl., and postprandial blood sugar increases by 5 to 6 mg./dl.

There are four age-related factors that are incriminated in bringing about modifications in Carbohydrate Metabolism.

- An inadequate Insulin Input;
- Decrease of the body net muscle mass;
- Increase of the adipose mass tissue, and
- Reduction of the cell sensitivity to Insulin independently of any effect of **adiposity**.

It is considered that previous estimation as to the influence of age upon the decrease of the tolerance to glucose have been exaggerated, as it is not taking into account among other parameters, the correlation of diabetes mellitus, overweight and other existing chronic diseases.

However, the correlation between fasting blood sugar and advance in age was statistically proved, considering the modifications due to overweight.

As years pass by, a slight unbalance will be observed in the glucose homeostasis. However, this is not an absolute rule and it is more or less accentuated by the frequent association of chronic diseases and obesity.

The inadequate Insulin Input

A reduced insulin secretion has been initially considered as an important factor in reducing the tolerance to glucose in the elderly.

This opinion is being revised today considering the following:

·Most of the studies show that the advance in age does not lead to reducing the insulin liberation by a stimulation with glucose;

It has even been demonstrated that plasmatic insulin concentration increase in the old, whence it may be deducted that their intolerance to glucose could be determined by a diminished capacity of plasmatic insulin to stimulate the utilization of plasmatic glucose. It is also supposed that there may be a deficient insulin metabolism- a supposition based on data showing a diminution with age of the plasmatic insulin clearance.

Reduction of the body net muscle mass

With the advance in age, a correlation has been stated between a reduction of the muscle mass and the reduced tolerance to glucose.

Increase of the adipose tissue

It is known that the process of hypertrophy and hyperplasia at the adipocyte level is accompanied by a reduced insulin-receptivity, but the inner mechanism by which obesity is determining it is not explained. On the other hand, during the aging process an increased frequency of obesity is observed. However, replacement of the muscle-mass by adipose tissue takes place even if the body weight remains unchanged. Specific transformation in the adipose tissue, associated to above mentioned, may cooperate in modifying the glucidic

homeostasis.

Decrease of the cell sensitivity to insulin

It was emitted the hypothesis that, with age there might exist a decrease of the cell sensitivity to insulin in the target organs, independently of the degree of obesity.

However, there is not sufficient proof to support this hypothesis which is contradicted by the fact that it is a normal sensitivity to insulin associated to a normal tolerance to orally administered glucose.

Conclusions

On the basis of the above considerations it may be said that:

- Glucidic homeostasis is not necessarily modified by the aging process.
- When glucidic homeostasis appears to be modified by the aging process, a modification manifested by a reduced tolerance to glucose and apparition of the age-related hyperglycemic syndrome, there may exist a loss of the insulin normal action "in vivo".

A parallel drawn between diabetes mellitus and the aging process suggests that diabetes mellitus could represent a model for the latter and some common elements being observed:

- The rigidity of the arterial wall;
- An increased incidence of coronary atherosclerosis;
- The thickening of the basal membrane of the capillaries;
- Anomalies of lipids metabolism.

Gerovital-H3, as an intact molecule, and through diethylaminoethanol (DEAE) and paraaminobenzoic acid (PABA) intervenes in the metabolic regulation.

According to Laborit (16), substances having this type of action, play an important role in the cellular reactivating, and thus we may deduce an enhancement of activity at the cellular level leads to improved energy levels.

Gerovital-H3 treatment in Rheumatology

Comparative studies present certain peculiarities of the human osteoarticular with aging: osteopeny, degenerative modifications of the intervertebral discs, the

reduction of the osseous capital. The decline of the muscle force, (more evident in men,) represents a primordial sign of aging and begins to manifest after the age of 30. The capacity of muscular and osteoarticular effort requires a longer adaptation period and falls may happen during the effort.

The normal aging of the osteo-articular system may be appreciated with the aid of quantitative and qualitative indicators. The bone involution after the growing period shows that the bone volume diminishes progressively with the advance in age, with some peculiarities in women. The psychological osteopenia and the involutive modifications of the other elements of the osteo-articular system may be accentuated in old people by protein, calcium and vitamin D deficiency, in various digestive and endocrine diseases, or due to iatrogenic causes. Age related changes in the joint can be found in almost all people over 65. Joints become increasingly misshapen. Aging of cartilage is associated with biochemical modifications. The content of water decreases, but proteoglycan content remains unchanged, thus undergoing changes. Metabolical changes in cartilage or changes in joint biomechanics make easier the development of the osteoarthritis process. By its frequency and medico-social implications, arthritis and rheumatoid arthritis have an important place in rheumatology.

Osteoarthritis

Osteoarthritis is the most common form of arthritis in the elderly. Millions of people suffer from pain, limitation of motion and disability because of osteoarthritis. There is an exponential increase in arthritis with advancing age. In the last decades more adult people are suffering degenerative alterations of joints because of obesity and lack of physical movement. Is there a relationship between aging and osteoarthritis?

As I mentioned, aging is facilitating the development of arthritis, but the normal changes of the bone and joint are not those of osteoarthritis.

The earliest events in osteoarthritis occur in the cartilage: decreased total proteoglycan content and shortening of the glucosaminoglycan branches. The continuity of the surface of cartilage is disrupted. The most important change in arthritis is the fibrillation of the cartilage with the focal erosions. In the meantime changes in subchondral are occurring, leading to an decrease in the density of bone with a consequent reduction in the mobility of the joint. We do not know the exact nature of the events that initiate arthritis. Trauma, aging, occupations, metabolic diseases, life-style and genetic factors cause alterations into the structure of cartilage that facilitate osteoarthritis. The most common joints that are affected are the hip, knee, carpometacarpal, and the spine.

The clinical use of Gerovital-H3

Many studies prove the positive effect of Gerovital-H3 in arthritis (1,2,3,4,5,6,7,8).

I studied 100 subjects suffering from moderate to severe arthritis admitted to the prophylactic treatment center at the Nat. Inst. of Gerontology & Geriatrics-Bucharest, 1985 (7). From the beginning in 1946, Prof. Ana Aslan tried to discover explanations to the complex biological phenomena with special attention to arthritis. In 1947, Aslan started administering procaine in cases of trophic troubles of the extremities, sometimes with spectacular results. This is what she declared:

“After one injection in the femoral artery, given to a patient with embolism at the level of the inferior extremity, I noticed the almost instantaneous disappearance of pain. Then, for the first time, I had the idea to apply the same method in certain diseases with pain, like rheumatism-specially at the level of knee articulations-which produces immobilization and thus long-lasting incapacity”.

Later on, Prof. Aslan used that method of treatment with procaine arterially administered to patient with arthritis, and she presented the results obtained with the first 50 cases at a scientific session of the Romanian Academy back in 1950. Starting in 1949, Aslan started applying procaine treatment in an old people's home (based on the fact that such patients present frequent cases of arthritis). Besides an improvement of the local movement, she noticed an obvious improvement of the physical and psychological state of the elderly.

She then initiated experimental arthritis research which evinced particularly favorable effects on animals treated with procaine. Gerovital-H3 has a positive effect on cell metabolism and on the cell membrane. There are studies where the emphasis was placed on Gerovital-H3 intervention on the collagen metabolism in arthritis. Aslan demonstrated the positive effect of her treatment on experimental arthritis studies (3). In my career, I've treated thousands people with arthritis all over the world. I studied one group of elderly people under treatment with Gerovital-H3 suffering from moderate to severe arthritis involving spine, peripheral joints, hips and knees (7).

Gerovital-H3 was administered one injection daily for 18 days followed by 12 days of Gerovital-H3 pills daily. I assessed the efficacy of the treatment comparing pain, joint mobility, functional capacity of the joints and muscular tone before and after the observation. In parallel, I noted the psychic mood and the circadian rhythm of blood pressure. Clinical symptoms like pain and joint mobility have had a remarkable alleviation in 34%, respectively in 56% and the muscular tone of the patients was improved in 41%.

I want to emphasize that during the Gerovital-H3 treatment no side effects were noted. The beneficial effect of Gerovital-H3 treatment is due to its antalgic action, an improvement of capillary permeability and the favorable intervention in the bioenzymatic disorders at the level of the joint cartilage. Gerovital-H3 can be the

drug of choice in the management of mild clinical arthritis forms and can be administered with non-steroidal anti-inflammatory drugs (NSAIDs) in severe arthritis.

Preventative treatment

From the age of 40, we can start an arthritis' Preventive Treatment with Gerovital-H3: one course of 25 pills over 12 days (one pill twice daily between the meals) and then a 2 week break. The cycle is then resumed. It is possible to do a milder prophylactic treatment only with pills in a series of 25 pills during 12 days with an interval of 45 days in between.

Curative treatment

At the beginning of arthritis or in a clinically advanced form, I recommended Curative Treatment: a course of 1 injection daily for 12-days followed by a 2 week break and then one course of 25 pills over 2 weeks – in total 6 courses of 12 injections and 5 courses of 25 pills-yearly. Gerovital-H3 treatment can be individualized; we can shorten or extend the breaks depending on the results, arthritis gravity and the accompanying diseases. Taking into consideration cost-results and side effects, with incipient and mild clinical form of arthritis, Gerovital-H3 treatment is superior compared to NSAIDs.

Rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic inflammatory arthritis. The clinical features vary widely ranging from a mild disease to a progressive one. The pattern is influenced by sex, age, endocrine and genetic factors. RA may begin in the aged, or may be encountered in an already "old" form, whose symptoms begin in the adult age. The clinical picture is more faded, often oligosymptomatical.

In many old people, RA is no longer active and a sick patient presents symptoms and a better prognosis for seronegative elderly onset. Symptoms such as morning stiffness, fatigue, weight and appetite loss precede the onset of RA. Usually, the onset of RA afflict metacarpophalangeal joints and later on may involve hips, knees and shoulders. Extra-articular symptoms are rare in old people. At this age we have to differentiate RA from polymyalgia rheumatica, amyloid arthropathy and arthritis.

Gerovital-H3 treatment is indicated in the incipient stage of RA. Its anti-inflammatory effect is exerted through the AMPc stimulated by the moderate rise in circulating catecholamine levels in synovia (5,6). Because RA is a very distressing and an invalidating disease, Gerovital-H3 with its affects of less fatigue, less stiffness and its antidepressive effect is beneficial.

Low back pain

Low back pain afflicts one out of every four adults and old people. Many of them can not get out of the bed because of Low Back Pain and they are using anti-inflammatory and pain killing drugs with many side effects. After surgery within one year 50% to 60% of the patients will have the same low back and leg pain. The best care of back pain is the multidisciplinary approach. The loss of disc height is called disc degeneration and sometimes arthritis. Conservative treatment should be used before surgery and can be helpful to relieve pains following back surgery.

Gerovital-H3 has a strong indication in low back pain because of its anti-degenerative effect and to relieve muscle spasm. Gerovital-H3 is administered locally and I.M. After a couple of days, the patient is more relaxed and is sleeping better. To help relieve the pain it is possible to apply Gerovital-H3 into certain points. For maximum results, the patient has to be treated daily for the first two weeks. Depending on their condition (arthritis, degenerative disc, spondylolisthesis, sacroiliac treatment etc.) physical therapy should also be applied to help take away the swelling that accompanies the ailments.

Gerovital-H3 - classic antiaging medicine

Ed.- In numerous issues of the IAS Anti-Aging Bulletin over the last 3-years, Dr. Dumitru has extolled the virtues of Gerovital-H3, the original anti-aging drug developed by Professor Ana Aslan. As Dr. Dumitru was the right-hand man of Ana Aslan, the Director of the Bucharest Institute of Gerontology and Geriatrics after her death and her personal physician in her final years, there can be no one better placed in the world to discuss her work.

In this summary, Dr. Dumitru outlines the benefits, side-effects, contraindications, and administration of what is still one of the world's most commonly used anti-aging supplements.

The history of Gerovital-H3 began in 1946 when Ana Aslan, Professor of Internal Medicine at the University of Timisoara thought about all the suffering in old age. As a result she discovered a new type of medicine and proved for the first time, a scientific efficacy against the aging process.

Her life was not easy, on the contrary, she had to fight against all the misconceptions regarding cronos-age, and most of all, against the opinions of many colleagues.

After her first scientific results, Aslan introduced in 1956 for the first time at the International Congress of Gerontology and Geriatrics (G. & G), in Merano-Italy,

the concept of Gerontoprophylaxis. Let me tell you about what Aslan named "Decalogue" which after some time I referred as "Alan's Ten Commandments."

- Food- a secret to an extended life.
- Physical movement.
- Training for aging.
- Sex at any age.
- The drug of intelligence-Gerovital-H3.
- Stress and aging.
- Cosmetics and age.
- The elderly' s leisure.
- Loneliness, depression and music.
- The art to prevent chronic diseases.

This synthesized the importance of general recommendations to delay the aging process and maintain a healthy and active life.

In 1964 working at The National Institute of Geriatrics & Gerontology in Bucharest, I was directly involved in the scientific programme of Gerovital-H3 studying one topic: "The effects of Gerovital- H3 in outpatients." Over more than 10 years I elaborated on five scientific papers regarding its effects on healthy elderly people, chronic degenerative diseases and the possibility to partially reverse the aging process. From 1978 until 1990, as a Director of The Nat. Inst. Of G. & G and as a chairman of scientific topics, I have introduced new topics and methodologies to study this drug.

Many scientists from the US, Germany, UK, Japan, Austria, Italy and Romania etc. have studied Aslan's Product and more than 400 articles have been published in scientific journals. Many symposiums, conferences and scientific sessions at International Congresses have been dedicated to present and to discuss the effects of her treatment.

After 54 years and after hundreds of thousands of healthy and sick people from all over the world have received Alan's treatment, what can I say, (as a close collaborator of Aslan) about her and her famous product-Gerovital-H3?

- * Alan's Method of Geriatric Treatment and her product Gerovital-H3 is most efficient in the Pre-geriatric-stage of life (40 to 65 years) and Geriatrics (after 65).
- * More than 15 books were written about Aslan's work and her life.
- * Even today, in all the world's continents you will find Aslan's Geriatrics Clinics.
- * Ana Aslan is one of the most important personality's in the history of G. & G. because she especially fought the aging process and was against the sufferings of old age.

Here we are now, at the start of the second millennium and after more than 40 years of Gerovital research. I want to share two of my thoughts to doctors and to patients, because not all of the physicians recommending Gerovital-H3 had a training in Romania, and many people are taking this medicine over the counter . What is it necessary for the doctors who are using Gerovital treatment to know?

When I asked Aslan how do you fight the aging, she answered:

"Old age is full of suffering and pain and I regard this as a parasite of life which develops slowly. I declared war on aging. As a gerontologist and a geriatrician you have to explain to healthy and sick people, what it means to grow old, and what they have to do in order to improve the quality of their life. My treatment is a solution and Gerovital-H3 is not only a treatment, it is a philosophy and a hope".

In 1946, Aslan published her first research on Novocain and stated:

"After the first results with Novocain injection, I tried this treatment on patients with arthritis. Because these diseases are chronic, I administered each with more injections. With great joy, I noticed an improvement in the local symptoms and in their overall general condition. The biggest reward was to notice an increase in their interest in life. This lead me to the hypothesis on Novocain's general effect on the neuro-psychical system. After doing pharmacological research, this conviction crystallized in my mind."

Her adventure began in Timisoara, the city of Romanian revolution that took place in December 1989, and continued onto Bucharest. As soon as Aslan began publishing and sharing her treatment, more and more people started to visit her and the Institute in Bucharest. The Institute was situated in an anonymous place but gradually became the Mecca of the ill. Scientists came to learn from her and to undergo personally her treatment. Their spoken and written words are proof of the effectiveness of her method and product, Gerovital-H3, which has bought so much relief and hope to the suffering.

The Characteristics of Gerovital- H3

The solution of Gerovital-H3 contains the following active principles:

- Procaine hydrochloride 0.100009
- Benzoic acid 0.006009
- Potassium metabisulphite 0.005009
- Disodium phosphate x 12H2O 0.000509

And the excipient, distilled water up to 5 ml.

The Gerovital H3 sugar coated tablets contain:

- Procaine hydrochloride 0.100009
- Benzoic acid 0.006009
- Potassium metabisulphite 0.005009
- Disodium phosphate x 12H2O 0.000509

And the excipients: maize starch, mannitol, gelatine, talc, magnesium stearate, sugar, PVP K30, CMC-Na(400-600 MF 7), Aerosil, Tween Tween 80, Titanium dioxide, Schellack, Yellow wax and Carnauba wax.

Pharmacokinetics Absorption

The radio-pharmacokinetic studies have shown that Gerovital-H3 is quickly absorbed after administration. During the first 240 minutes the two metabolites, diethylaminoethanol (DEAE) & para-amino-benzoic acid (PABA) are produced and absorbed. This result is due to procaine and esterase's action of splitting Gerovital-H3. The absorption of DEAE & PABA takes place in a competitive manner, which means that the two metabolites compete for the active sites of the mechanism that governs the absorption. The age of the subject is what differentiates the absorption of DEAE, the older tissue having a greater affinity for it.

Distribution

Radio-cromatographic experiments have showed that Gerovital-H3 splits into DEAE and PABA, which bind the plasma proteins no matter the route of the administration. PABA binds specially to the light molecular weight plasmatic proteins. The distribution of Gerovital-H3 and its metabolites is fast, both for i.m. or oral administration. At the tissue level procaine crosses the biological membranes acting upon their fluidity, and facilitating the process that imply trans-

membranary transport.

Metabolism

Once absorbed by the animal organism, procaine undergoes the first stage of hydrolysis into the blood and liver resulting in DEAE and PABA (Figure 1). Radio pharmacological experiments proved that in a second stage hydrolysis, DEAE splits into ethanol amine, glycine and urea. By certain methylation processes together with "base exchange" reactions, the ethanol amine enters the synthesis cycle of choline and then acetylcholine as a next step. After injecting ^{99m}Tc -DEAE to rats, radioactive marker was found in the ethanol amine and acetylcholine extracted from brain and blood homogenates. There exists a saturation limit for metabolism of DEAE after which the substance is eliminated.

Characteristics and mechanisms of action

* The addition of benzoic acid to procaine increases absorption from 15% to 32% (as compared to isolated procaine), the fraction that enters the organic phase of butanol, induces a greater access of procaine into the hydrophobic cellular compartments.

* Eutrophic properties.

* Procaine as a molecule and DEAE are cell membrane modulators.

* Monoamineoxidase (MAO) reversible inhibitor. The procaine hydrochloride normalizes the body's production of certain neurotransmitters by monitoring the degrading action of MAO

Excessive levels of MAO is a common cause of mental depression. Gerovital-H3 is a reversible antidepressive monitoring the action of MAO rather than destroy the MAO as do traditional antidepressant drugs.

* A deficiency in PABA can causes stress, digestive disorders, fatigue, headaches, irritability and graying hair. By stimulating the intestinal flora, PABA aids in the production of vitamin K, folic acid and thiamine.

* DEAE aids in the production of choline which is a precursor of acetylcholine. DEAE is effective in relieving migraine and tension headaches.

* Antioxidant and lipid-lowering effects. Gerovital-H3 exerts an inhibition on the generation super oxide radical in a non enzymatic system.

* Gerovital-H3 has a lipid lowering effect consisting of either diminishing the level of plasmatic lipoproteins and lipids, or increasing the membrane fluidity. This protection against osmotic hemolysis, or its antioxidant mechanism reduces the oxidative stress exerted on the membrane structure and on the low density lipoprotein (LDL).

Indications

- * Gerovital-H3 is indicated for people older than 40 years to retard the aging process and as a preventive and curative treatment for chronic degenerative diseases.
- * Moderate and light depressive syndromes.
- * In troubles concerning attention, concentrating, cognitive process and in balancing the neuro-vegetative distonies.
- * Chronic fatigue syndrome.
- * Sleep disorders.
- * Tegument dystrophies, trophic ulcers, atonic wounds.

- * Osteoarthritis, degenerating rheumatism, osteoporosis and during fracture consolidation periods.
- * Sexual management- improving sex drive.
- * Parkinson disease and Parkinson syndromes.
- * Due to the inhibition of the generation of the super oxide radical, Gerovital-H3 is a powerful antioxidant, a free radical quencher.

Outcome of Gerovital-H3 treatment

- * Desire to be active and more ability to cope with the environment.
- * Improves affective tone, psychic and vegetative balance.
- * Diminished extra pyramidal rigidity, improved gait and exercise capacity .
- * Balanced endocrine functions with oestrogens reappearance and reactivation of androgens and sex drive.
- * The alleviation of chronic disease symptoms, arthritis, varicose ulcers.
- * Improves the Quality of Life retarding the rhythm of aging and having a role in preventing chronic diseases.

Posology and mode of administration

Before starting the treatment you must perform two tests: first inject 1ml i.d., and after 24 hours, 2ml i.m., this is in order to establish the possibility of an allergic reaction to Gerovital-H3. If after the test no allergic reactions appear (such as rash, itching, eruption, general reaction of the organism with headache, vertigo, cephalic heating sensation or a metallic taste), the treatment may be continued. These effects disappeared with the treatment by respecting the post-injection rest period. It is seldom necessary to reduce the dose. Usually these side effects occur only in patients of more than 80 years of age.

In the experience of many hundreds of thousands of patients that have completed this treatment, an intolerance has only occurred in 1 in 7000 cases.

Preventive treatment of chronic diseases and to reverse partially the aging process, consists of 4 courses of 12 injections and 4 courses of 24 pills. Starting from the age of 40, the prophylactic treatment with pills only is recommended in a series of 25 tablets during 12 days, with an interval of 2 months. First day, 1/day, 2 hours after breakfast increasing to the 12th day when 2 pills per day are taken (2 hours after meals, for example one at 10:00 AM and another at 4:00 PM). There should a series of 5 treatment courses in the year , which should be increased to 6 per year for people over the age of 65.

Curative treatment in chronic diseases requires 6 courses of 12 injections, and 5 courses of 24 pills, yearly. One course of 12 injections over 4 weeks (three injections per week); 2 week break followed by one course of 24 pills over 12 days, and after a further 2 week break, the cycle is then resumed. After the i.m. injection the patient should take a 10 to 15 minutes rest.

Limits of use- Contraindications

Gerovital-H3 should not be used together with eserine or prostigmine, and at the same time with sulphanides, because of the competition on the bacterial metabolism.

Precautions

Take care when administering Gerovital-H3 in epilepsy cases or high blood pressure. The treatment does not interfere with the vigil state or the reaction aptitude if the recommended pause after injection is adhered to. There have never been any observed cases of drug dependence. There is no evidence regarding human fetus' risk.

Over dosage

The intoxication with Gerovital-H3 occurs only over 400mg in i.v. rapid injection and manifests as convulsions, hypotension, coma. The treatment to apply is non-specific, the same as for any acute intoxication. Chronic intoxication has never been observed.

Special remarks

It is possible to dilute Gerovital-H3 in glucose or NaCl 9%, and also to be mixed with cortisone drugs.

Information for the patient

Gerovital-H3 belongs to the class of drugs whose general action is upon the organism, especially in depression and overworking due to stress and over activity, also in arthritis and in other degenerative diseases.

Gerovital-H3 is recommended to people older than 40 who present symptoms of

tiring, to those suffering from chronic disease, to prevent chronic disease or to partially reverse the aging process.

The treatment has both prophylactic and curative purposes and it is used alone or in association with other drugs in case of depression, rheumatic diseases, Parkinson or systematic arteriosclerosis.

The treatment method

It must be administered two hours after the meals, either by oral or by i.m. injection mainly at the beginning of the treatment: I recommend a 10 to 15 minutes rest.

Where Gerovital-H3 is not recommended

It is not recommended in the following circumstances: severe liver disease, renal failure and severe arterial high blood-pressure. Also, it is not recommended in feverish states and in association with sulphonamides, eserine and prostigmine.
Precautions regarding the treatment with Gerovital-H3

You must inform your physician about the following circumstances:

- * you suffer from another disease.
- * you are allergic.
- * you are taking some other drugs-self medication.
- * before starting the treatment you must undergo an intradermic test (1 ml) and also an i.m. test (2 ml) to reveal a possible allergy to procaine.

The treatment with Gerovital-H3 should be under medical supervision, mainly in the first series of injections in order to establish the optimal dose, and eventually to reduce the doses of previously used drugs or even cancel them.

Method of administering Gerovital-H3

The usual injectable dose is 1.5-2.0 mg/kg of body weight and day. This means 1 ampoule in an i.m. injection.

The usual oral dose is of 2 sugar coated tablets a day.

The patient has to follow Alan's method presented to specialists. Other schedules of treatment will be established by the physician adapting them to the patient's characteristics: age, associated diseases. If the patient forgets to take one or more doses, the treatment should be respectively lengthened. Do not change the prescribed doses by your own will. Go to your physician whenever you think that the drug's efficiency is either too little or too strong.

What are the possible side-effects of Gerovital-H3?

Rarely, at the beginning of the treatment the patient may observe slight vertigo, metallic taste, cephalic heating sensation. These effects disappear during the treatment. Even if the first tests do not point out an allergic reaction to procaine, the subsequent occurrence of coetaneous reactions determine that you should go to your physician.

What else should be taken into account?

- * You must take the drug after meals.
- * Maintain a 10 to 15 minutes rest after the Gerovital-H3 injections.
- * The product must be stored in a dry place, at room temperature, respecting the validity date mentioned on the packing.
- Keep out of children's reach.

Who was Ana Aslan ?

Ana Aslan is renowned for her essential contribution to gerontological research as well as for having patterned the best geriatric treatment influencing the aging process. Ana Aslan was the first person to rule out the fatalistic approach to aging, providing a new method in gerontology by opening the way to the prevention and treatment of old age.

I worked with Professor Ana Aslan for 25 years, from 1963, first as a researcher, then as chief physician and afterwards as the Director of the National Institute of Gerontology and Geriatrics in Bucharest, Romania, between 1978 and 1990.

In the last 3 years of her life, Aslan chose me as her personal physician and three months before her death she asked me to do some personal things, including to write a book about her life and her work. So I took notes at her bedside as a moral testament.

In addition to her life, she talked of her views of politics, religion, euthanasia, dying, death and love. As such I had the opportunity to know her private thoughts and personal thinking.

On her 90th solemn birthday celebration at the Romanian Academy in Bucharest on May 22nd, 1987, on behalf of the Romanian National Institute of Gerontology and Geriatrics, I said; "I want to express my emotion and say how difficult it is to talk about Ana Aslan, being such a complex personality, the story of Gerontology might as well be the story of Aslan."

"Ana Aslan's life can be seen in her work. She has battled courageous fights, all for the service of good, to make man's dream to live with dignity for as long as possible. Now we celebrate the inventor, the scientist, the physician, and the

professor. For 35 years since 1952, she has led us as the first Institute of Gerontology in the world. Ana Aslan is the Ambassador of Gerontology and a brilliant woman. As a scientist she is an inventor, not an imitator. She has played such an important role in Gerontology at the world level. She has given the world decades of research that revealed that Gerovital-H3 is the most effective treatment in geriatrics. Ana Aslan is the original contributor in the basic research concerning cellular and molecular aging, and researching her product reaction in the body. She has a special empathy for the elderly and has always fought to improve their condition all over the world. She worked with others to initiate the General Assembly of the United Nations Organization on aging, held in Vienna, 1983. Aslan has a remarkable understanding and appreciation for beauty and culture. At one time she visited Hippocrates grave and on which she stated, "I now realize how small I am."

As a disciple and collaborator, and being inspired by the University Hymn, I declare "Viva Academia! Viva Professores! Viva Ana Aslan!"

Aslan's distinctions

1. Commander of the order "Meritor Della Republica," Italy, 1969
2. Commemorative Gold Medal, Nicaragua, 1971.
3. Cross of Merit, first class Order of Merit, Germany, 1971.
4. Hero of Socialist Labor, Romania, 1971.
5. "Augusto Pinaud," Medal, Venezuela, 1972.
6. Cavalier de la Nouvelle Europe, Prize Oscar, Italy, 1973.
7. Knight of the Order "Les Palmes Academiques," France, 1974.
8. International Prize, "Eva," Italy, 1974.
9. Commander of the Order "De Orange Nassau," Holland, 1975.
10. "L'Ordre du Merite," Grande Officier, Senegal, 1976.
11. "Dag Hamarskjöld," International Prize, Italy, 1977.
12. "Dama di Collare Del Santo Graal," Nice, 1978 (granted by Italy)
13. Honorary Foreign Citizen and Honorary Professor of Sciences, Manila, Philippines, 1978.
14. President and Honorary Guest of the Symposium, "Ageing Comes of Age," Philippines Academy, Philippines Association of Geriatrics and Gerontology, 1978.
15. Officer of the Order "Merito Della Republica Italiana," 1979.
16. La Medaille et le Prix "Leon Bernard" La 35eme Assemblee Mondiale de la Sante, 1982.

Aslan is quoted in the following

- 1.

Who's Who in America (1972)
2.

Who's Who in the World (1971)
3.

Who's Who of Women (1971)
4.

British Encyclopaedia (1974)
5.

Who's Who of Intellectuals (1976)
6.

The International Men of Achievement (1976)
7.

International Biographical Association of England (1978)

Dr. Dumitru comments

We are witnessing a spectacular alteration of the age pyramid. Furthermore the process of the demographic aging of the population will continue to increase in the coming decades.

I feel obliged to sound an alarm at the apparition of this phenomenon unique in human history, at least in relation to how the appropriate tactics and strategies should be adopted.

Human society has the duty to benefit in an organised way from the knowledge, experience, wisdom and the free time of the elderly.

Activity, as a way of life for aging and aged people, creates for them a mental and physical well being, changing old age into a useful period, not only at the individual and family level, but at the social level too.

The traditional image of the elderly incapable of working, needing help, care and with a tendency for solitude is being re-evaluated. Elderly people do not appear as a homogenous category of population, but as a very heterogeneous one, from the demographic, medical and social standpoint.

The concept of the "elderly" from the social standpoint is becoming outworn and out-of-fashion, and is frequently considered in a merely functional sense related

to the elderly's capacity of assuming a role in the community.

Interdisciplinary researches are apt to offer solutions for promoting an Active Old Age. As a supporter of an optimistic conception of the third age, in the data that I am submitting, I will propose measures to forming a new attitude towards this last stage of life.

"The everlasting ageless youth" has always been one of the great desires and concerns of mankind. Especially in the latter decades, if the thoughts of the last thousand years were put into a microscopic lens then the complex equation of human aging would begin to reveal some of its unknown values, however man cannot accept the idea of aging and death.

I have discussed the topics of aging and old age with my patients during the last 40 years of my pregeriatric and geriatric practice; these years having been dedicated to scientific research relating to the aging diseases; their prevention and treatment.

I worked for 25 years at the National Institute of Gerontology and Geriatrics in Bucharest, of which I was the Director and the closest co-worker of the famous Romanian physician- Ana Aslan for 11 years. I have had the opportunity to examine patients of different ages from all over the world, to know their thoughts, their concerns and their varied questions. For example, I've talked with many young people, for whom aging, death and disease were states, which they hadn't accepted yet as a possibility during their life. Other young people I have dealt with had diseases and pain and wished an end as quickly as possible. Some considered that they ought to try everything as soon as possible and had no respect for their health. Some women believed the menopause was the starting of their old age and other healthy old (often-centenarian) people who were in full activity pleaded for the beauty of this age and regarded life from the height of their wisdom. Of course there were also their children abandoned those elderly who had severe chronic diseases and were living alone having. All this has been a fantastic lesson for my pregeriatric and geriatric practice.

But only fate made me the personal physician of Professor Ana Aslan during the last three years of her life. During this time we became closer in spirit and in our long conversations she shared many of her private thoughts of her life experience fighting against old age and its sufferings.

Asking her many questions that I was concerned about gave me the opportunity to learn the convictions of one of the most famous personalities in the world, her ideas were pioneering in the fascinating field of Gerontology and Geriatrics.

In the afternoons and in the evenings on the terrace of her apartment at the

Otopeni Clinic, (where she was convalescing), she told me her thoughts, and interrupted only by nightingale trills, she talked of the 84 countries she had visited. The people, their cultures, the famous personalities she'd met, and normally, about the history of her only son- Gerovital-H3- the product that could improve the quality of life.

After 40 years of age (which is a critical period from a biological point of view), many people begin to ask; "What is old age? What about the aging process? How can we fight against it? Can old age be delayed or prevented? What are the factors accelerating the aging process? Should we learn to die? Has a person the right to dispose of his or her own life and decide when the end is to be? What about sexual activity in old age? Can it be improved? How will relations between the generations be affected? What is the older persons role in society and family?" and so on.

My understanding of the concerns of gerontology schools in the United States, Great Britain, Germany, France and Romania regarding the "Life Extension Research" and from my geriatric practice, in time, I appreciated that "those good habits" give strength and active life in aging.

Today we have discovered what was originally thought to be a compulsory condition of old age, namely the presence of heart disease, arthritis, diabetes, depression. Presently and especially in the near future these are (and will) no longer are the facts of aging.

Everything depends on the way you live from birth to death and what kind of supplements you are taking.

The behaviour is based on the way of thinking to remain young, on the strategy to fight against gaining weight, to prevent paralysis, to fight against the stress and to maintain a young at heart spirit.

In the following pages, I will try to answer some of these questions and to draw the way to live, remain active and to retain dignity in older age.

"To grow old in a beautiful and dignified way is at the same time a science and an art." Ana Aslan.Ana Aslan.

The aging process and old age

Ana Aslan remembered with pleasure a question asked by many reporters and research workers; "What made you in the 1940's- when very few people thought about geriatrics- dedicate yourself to the study of aging and to the care of old people?"

Ana Aslan's answer was always full of nostalgia; "At the age of 50 I changed my career and I started another life dedicated to Geriatrics. I was a specialist in Internal Medicine and Cardiology and in 1945 on January 1st, I received a congratulation card, which I keep with my precious possessions. This card was signed by many of my patients who wrote- On the occasion of your birthday a group of old patients, some of life's broken toys, wish you good health and many happy years! - I read and re-read- these words many times and they continued to stir me and even to obsess me. I told myself, that in fact, these broken toys could be mended, and I wondered what help I could give old people? Those words and that card, together with the impulse given by one of my professor's, were the seed which sprang in my mind and made me dedicate the rest of my life to the study and treatment of old people. It was the elderly showed me that TIME is the killer of organic substance and it puts its definite imprint on the human organism."

In our contemporary society, we are witnessing two essential tendencies, the aging population and the technical progress.

The understanding of demographic tendencies, therapy and recovery from the diseases of old age are priority problems with economical, political and social implications.

Each of us is a witness to a spectacular increase of the average life span, which increased from 40-50 years in the last century, and now, to more than 78 years old. Grandfathers take care of their grandchildren, and their great grandchildren, and they share with them their life experience, a feat not possible before in the history of mankind.

In the year 2000 those over 60 years old will represent 15-20% of the total population of the earth. The rate of those over 65 increased from 200 millions in 1950's to 400 millions in 1985, and to an estimated 600 millions in 2000, and to more than 1 billion in 2025!

What are the implications of the presence of such a segment of elderly within the population? Should they stay outside of the normal social life? The answer to these questions has an impact not only on Gerontology, but in philosophy, religion, politics and economy too.

Geriatrics deals with the medicine for the elderly, and Gerontology studies the modifications of the human organism in time, as such Gerontology can define the aging process and can distinguish between aging and disease. Alone they cannot answer and solve the fundamental aging questions, but together they become a powerful science.

- Aging is a plurality of normal changes of mankind due to the lapse of time, the change in the frame of mind and in the physical condition of each of us.
- Disease is an accident, a pathological process, abnormal, which can occur occasionally in childhood, adulthood and is not compulsory in old people.

Disease can be prevented, treated, or if it becomes chronic it can be alleviated. Disease can also often hide aging and for this reason we should pay attention to the change due to time "per se."

The aging process is suggestively illustrated in Figure 4. It shows the increasing presence of aging from the period of embryo, childhood, adulthood and into old age.

In this conception, old age is the last period of the life, when the aging signs become evident; signs such as the gerontoxon (or arcus senilis), a degenerative change in the cornea occurring in persons over the age of 50 and the ceasing of the menstrual cycle etc.

For the reader it is very important to know that aging is subjected to the influence of genetic and environmental factors. Under the influence of these factors, the aging rhythm can be normal, accelerated, or delayed.

Each person has his or her own biological clock, which can function normally, or it may have an accelerated or delayed function.

The nutrition, physical, environmental factors, way of life, presence or absence of diseases, stress and the eutrophic treatment with Gerovital-H3 influences the aging rhythm.

After the age of 40, the proportion between muscular and fat tissue changes. Around the age of 60- 30% of the muscular mass is replaced by fat tissue. The articular flexibility, muscular strength, pulmonar ventilation, vascular elasticity and cardiac efficiency decrease with advancing age.

Visual acuity and ovarian function are among the first changes, which announce the period of senescence. In bone structure, important changes take place, which should be prevented with the necessary steps.

At the age of 65 we can no longer do what we did at the age of 30 and this fact we all understand.

Old age is often a "state of mind" and the human spirit is the strongest treatment, which should be fed with understanding, useful constructive work, love,

tolerance, kindness and friendship.

Old age can be a period of pain, loneliness and disease, with high medical cost and social complexity; Grieg described it as "diminishing also has its beauty," Juvenal however, said, "old age is worse than death."

In everyday life, in literature, in fairy tales, old age aureole is not missing. In popular wisdom, the old man appears as a positive character, kind and clever. The elderly are capable of useful activities for themselves and for others, they can solve difficult situations, to value their creativity. They are a treasure of wisdom and preserve a "living history," they are the keepers of history, and by vocation, character and inspired choice, become as much important as inventors.

When I asked Aslan, "what is aging and old age and how do we fight it?" she answered,

"Old age is full of suffering and pain and I regard this as a parasite of life which develops slowly and whether you know it or not, it takes hold of us. From the age of 50 onward, I declared war on aging and old age. Gerontology and Geriatrics have enough possibilities to slow down the aging process and to delay old age onset. We are obliged to guard against and to explain to healthy or sick patients, what it means to grow old, and what they have to do in order to extend their life in conditions of quality. My treatment and my method is a solution, Gerovital-H3 is not only a treatment, it is hope, and when there is no hope, there is nothing."

Ana Aslan's incredible adventure

(IN HER OWN WORDS) "I accepted that I had to leave Bucharest in order to be by myself. This was not easy for me, but in those years, the air that I was breathing was not enough. Brilliant lights are attractive to creative spirits, but they can also deprive you of sight. The magnificent oaks have too much shade, and under their magnificent crown you can find the smallest trees. Their seeds should be taken by the wind to fertile places."

Ana Aslan had many personal ideas, one of which was to start a medical school in Timisoara, the western Romanian town situated on the banks of the Bega channel.

It was here that she met Dr. Pius Branzeu, a student under the famous Professor Loriche. She discussed his methods of Novocain treatments on post-operative incisions and later learned about Dos Ghali's method of intravenous administration of Novocain in patients with bronchial asthma.

Ana Aslan passionately studied Professor C.I. Parhon's work as well. After 30

years of clinical and experimental observations, Parhon reached the conclusion that aging is a disease and that it can be treated. In 1908 he published his observations of two cases of senile osteomalacia and in 1925, he introduced the term Ilikibiology, meaning morphological, chemical and physiological variations related to age.

"I taught at the medical clinic in Timisoara and learned the basic notions of gerontology. I read all the works of Marinescu, Parhon, Metchnikoff, Charcot and Burger (the principle disciples of gerontology) and I also maintained a relationship with Dr. Parhon. Since 1946, he was the Director of the Institute of Endocrinology in Bucharest and the chair of the Endocrinology Department of the University there. I returned to Bucharest once a month just to talk to him."

"Parhon was a pioneer in gerontology. He treated aging patients with extracts of epiphysis, gonads, insulin and vitamin E, in 1909 he published the first book in the world of endocrinology and in 1955 published the book Biology of Ages, which was translated all over the world."

"Parhon had a universal mind and was a wonderful man. Our privileged relationship was in the field of gerontology; this was where his heart was. He believed in rejuvenating and ardently maintained that life cannot be only a one-way direction. He knew everything, botany, zoology, endocrinology, psychiatry and anthropology. His mind was like an encyclopaedia! Above all, Parhon was a man of great generosity and dedication. He sacrificed many things for medicine, even including some family relationships, he was quite different from Danielopolu but without the two, I would not be what I am now!"

In 1946, Aslan published her first research on Novocain, The Novocain Action on the Respiratory Rate when injected in the Human. "After the first results with Novocain injections in the vascular embolias, I tried this treatment on patients with arthrosis and those with a tendency to ankylosis. Because these diseases are chronic, I administered each with more injections. With great joy, I noticed an improvement in the local symptoms, and even more importantly, a great improvement in their overall general condition. Before the treatments, the patients avoided any movement due to pain, and then they were willing and wanting to walk, sit up and read, and talk. The biggest reward was to notice an increase in their interest in life and for their families."

"These improvements also came along with much more restful sleep for the patients. This led me to the hypothesis on Novocain's general effect on the neurophysical system. Maybe it had effects here as well as locally. I noted these observations for two years until I could test my hypothesis."

"On April 15, 1949, a GI Medical student with arthrosis arrived in our clinic. For 3

weeks he'd had terrible pains and blocked articulation. I explained my idea about Novocain to him and after receiving his permission, gave him an intra-arterial injection with 1% Novocain. His knee was mobile immediately and he could flex his leg outright. What happiness! I administered this treatment for another two weeks, after which he completely recovered."

"There was a nice park close to the clinic in Timisoara, and one April afternoon while I was there I noticed an old man. He was leaning on his crutches and when sitting down, he laid his head in his hands. I later saw him in one of Van Gogh's paintings! He embodied despair. My attention then turned to an old couple who was walking with small steps, patiently leaning on one another. They did not talk, but their dry wrinkled faces told enough about their many years. Their gait was a symbol of their fraternity and support they have given, and will continue to give, to each other for the rest of their lives."

"I then said to myself, why can't I help these people? Why do they have to suffer such pain and suffering? If this young man had started to walk after the injections I had given him, maybe these people could be helped? They could smile again and regain their own sure steps."

"I did not go to Bucharest at the end of the week as I had been doing on the weekends. Instead I returned to this park. All I could focus on was old people. I was overwhelmed with age; I began to feel an unusual sympathy. Something had touched me deep down, and I began my quest. At night I thought about the Novocain shots Loriche had administered around wounds. If such rapid healing occurred, couldn't it benefit these people as well? I became obsessed."

"After doing pharmacodynamic research in 1946 with Dr. Danielopolu, this conviction crystallised in my mind between 1947-1949. I was using Novocain to treat bronchial asthma according to Dos Gahali's method and to treat arthritis and emboias according to Loriche's method."

"I practically ran to Bucharest with my results! Dr. Danielopolu advised me to share this with Parhon immediately. His words to me were, "Novocain has an effect on aging. You should carefully carry out this research. Come back to Bucharest and lead our Experimental Department here. I'll make all the arrangements, just say you'll come." I agreed and in a few months I was back in Bucharest."

This adventure that began in Timisoara continued in Bucharest. But it was here that the struggle really began. In order to clear up the Novocain mechanism of action in arthritis, Aslan followed its effects on experimental arthritis induced by formaldehyde (according to Seyle-Brownlee's method).

"In the fall of 1949, I wanted to present my first observations to the Academy of Medicine. It was then that I realised the envy-taking place among my colleagues, and how it was increasing. In a chorus, Milcu, Lupu, Nicolau and Benetato were adamantly against it. "You need at least 25 cases" they argued. Finally, they refused to include my research in the agenda being set for the Academy's meetings. It doesn't matter, I told myself, Alzheimer presented his observations on a single case, and Hodgkin on only six!"

"After Parhon left the Institute of Endocrinology, those that followed caused me much frustration. (They did, however, do one good thing, for which I want to thank them, they agreed with my resignation and return to Bucharest)."

"With the passing of time I learned that the opposition made me more and more ambitious. I knew that I was right and I had to prove it. Life would be too dull without controversy, and in my case, unfortunately, the controversies overstepped the bounds of academic dispute. All of this doesn't matter now, I forgave them many years ago."

"It was the co-operation with Parhon that does matter. He was very good to me and was convinced by the results I was obtaining. He was my moral support, and it is because of him that I continued with my research."

As soon as Aslan began publishing and sharing her method, more and more people, most of them ill, started to visit the Institute. The Institute, situated in an anonymous place, gradually became the Mecca of the ill.

Scientists came to learn from her as well as to undergo treatment. Some remained perplexed, listening to the testimonies of the old people who had regained the joy of life, returned to their favourite activities, found peace in their battles with insomnia. More importantly, they found their place in society, a society who before had alienated and repulsed by them. Their spoken and written words are proof of the effectiveness of her treatment, method and product, Gerovital-H3, which had bought so much relief and hope to the suffering.

Many physicians came to the Institute for training in gerontology and geriatrics, and to learn Aslan's method. In return, Aslan visited them in their countries to acknowledge and celebrate their results. With special appreciation, she remembered Dr. Marion Bucker Bode of Germany. Besides leading a center of geriatrics, she also had serious concerns for research. She talked also of Dr. Pop Michel of Cyprus, these and many others, were considered her disciples in the fight against aging.

Some of the many testimonials

After visiting the Institute in September of 1958, Academician R. Bacov, Director of the Pavlov Institute in Moscow, wrote, "I found the activity carried out at the Institute of Professor Aslan to be very interesting. The problem they focus on fascinates the world. I think Professor Aslan has found a real way to maintain the activity of the nervous system and to prolong the normal functioning of the entire organism. I myself am convinced that Aslan's method is a success. Thank you for the wonderful demonstration of your results."

Robert A. Homes, M.D., chief physician in a hospital in Washington D.C., confessed that he learned much from Aslan's revolutionary treatment. Hollings E., Senator S.C., Washington D.C., expressed his admiration for a real mother nature, as well as Senator Howard W. of Nevada, who remarked on the wonderful work in such an important field.

Professor Aslan thoroughly studied and diversified the research, a fact that was noted in the pharmacology department of Harvard University as well.

These were world-wide acknowledgements, the Minister of Health in Belgium, Nameche Louis, stated that he was "impressed by the social action developed by Aslan and convinced of the prophylactic results."

Ever since 1966, Lord Amulree of London appreciated "the work Aslan developed in order to cover all of Romania with a network of care centers for the elderly. These could very well be imitated by other countries and I hope this wonderful work by Professor Aslan will be very wide spread."

Dr. Iderwal de Carvalbo, Professor of psycho-pathology at the Sao-Paulo University in Brazil was "full of admiration for all he saw and felt at the Institute when he personally noted the stateliness of Aslan's work and the magnificent results in treating aging with Gerovital-H3 and Aslavital."

From the Institute of Geriatrics and Gerontology of the University of Florence, Italy, Professor Francesco Antonini, "admired the work carried out with such intelligence."

A letter of gratitude from Professor Mario Giacorezzo from the Medical Clinic of Rome University, thanked Aslan "for this masterly lesson."

Journalists, writers and poets whose fantasy took them beyond the limits of reality soon visited the Institute seeing the results in old patients. For example, Galina Seredrinkova wrote, "Faust's dream, the alchemists fight for life has been solved by the well known woman of our century, Ana Aslan. The gratitude and enthusiasm towards her talent and her deep scientific thinking includes anybody between the walls of her institute."

A news journalist by the name of A. Umar, considered Aslan's results not only prestigious for Romania, but for the entire world.

During her life, Aslan received thousands of letters. They came from the most remote parts of the world. Sometimes the letters were directed with no address, but a simple "Ana Aslan" on the envelope. The country and address was not necessary, the entire world knew of her!

In most letters, patients expressed their thanks, for regaining strength, hope and confidence. They expressed their gratitude for her competence and devotion.

She had four secretaries who helped her answer each and every one. They had a difficult job, working in the rhythm and time that Aslan demanded. She did not consider this impressive correspondence as simple politeness and responsiveness, but rather as a constitutive part of her own medical activity as a doctor. The exchange with research institutes, such as the "Institute of Aging" in the United States and in Kiev, meant contact.

From her travels and fame, Aslan made friendships everywhere. Many of them became patients and followed her treatment for years and years. One of these was Mr. Hans Matguart of Germany; he was a man of remarkable culture, honour and honesty. After he learned of Aslan's death (a month after she had actually died), he took a plane to Bucharest. He went to her grave and quietly remained there for some time, as homage and out of respect. He went on to address me; "It is a pleasure for me to speak about Professor Ana Aslan, as she was, in my opinion, a world authority and a remarkable person. My first encounter with her took place in 1982. Ana was herself an old woman, but yet maintained all of her mental capacity. Her long medical experience proved very useful. Ana was also being treated with Gerovital-H3. Her intellectual capacity, maintained to the end of her life, is proof of the drug's success."

"I had begun my treatment (Aslan's therapy) on August 12, 1980 and continued without an interruption. She herself personally cared for me. She examined me and decided on which type of therapy. For ten years, at regular intervals, I have been treated with Gerovital-H3 by injections and by pills. I am now 76 years old; therefore I started therapy when I was 65. Since then, I have continued leading negotiations in my field and making all the necessary decisions about my activities. Would I still if I wasn't using Gerovital-H3? I definitely say no!"

"In the last 10 years I have accomplished my daily tasks with great joy. When we think that the normal man retires at 65 or earlier, then these 10 years are even more astonishing. I have held honorary positions and been appointed several times as president of different organisations. This activity is proof of my capacity.

It should also be mentioned that in the last 10 years I have also had no serious disease, more proof of healthy conditions due to Aslan's therapy."

"Throughout these 10 years I have often talked with others in this long term treatment, and not once have I heard a negative word. Of course this therapy cannot make miracles alone. Positive results only appear when regular treatments are given and the physician one is dealing with is seen regularly."

"Above all, I hope her knowledge will be spread to all the people in this country and to all of human-kind."

During this visit, Mr. Matquart was intrigued and puzzled about why her death had not been immediately announced. "Ana belonged to mankind, not only to Romania. Surely, Belu cemetery would have been full with people from all over the world?" But under communism, the people of Romania had no possibility to taste and to know of Ana Aslan's international success.

Biological basis of Gerovital-H3 treatment

Ana Aslan at the Institute of Gerontology and Geriatrics in Bucharest, Romania experimented with Gerovital-H3 between 1951 and 1958. Since 1951, Aslan stopped the use of hydrochloric-procaine; the research results materialised a different product with a new formula- Gerovital-H3. In the new formula, adding benzoic acid to procaine and inducing a greater access of procaine into the hydrophobic cellular compartments modified the pharmacological action of hydrochloric-procaine.

Between Gerovital-H3 and hydrochloric-procaine there is a difference of pharmacological action. Hazard showed that the procaine-based product has a stability of 6-months, whereas the Aslan product has a much increased stability of 2 years and 6-months.

Once introduced into the human body, the procaine molecule is hydrolysed by procainesterase into two metabolical fractions; Paraaminobenzoic acid (PABA) and Diethylaminoethanol (DEAE). The absorption of the two metabolites is better when they result from the in-vivo hydrolysis of Gerovital-H3 than administered as such. The absorption takes place in a competitive manner, which means that the two metabolites compete for the active sites or mechanism that govern the absorption. The DEAE's absorption is particular to the brain as compared to other organs.

The procaine from Gerovital-H3 has a greater capacity of wadding the medium (pH), due to benzoic acid, reducing the degradation speed of the product. DEAE splits into Ethanolamine, Glycine and Urea. Ethanolamine enters the synthesis

cycle of Choline and then acetylcholine.

In the case of Gerovital-H3, the chromatographic techniques showed that there are intact procaine molecules in the blood and heart of experimental animals 6 hours after the product was administered. There are two possible explanations for the important difference in the procaine metabolism.

It is considered that hydrochloric-procaine is differently metabolised depending on the pH of the solution. At a pH of 7, the procaine is permeated "en masse" into the blood, but at a pH of 3.3 the procaine is gradually set free from the blood.

An acid solution will decrease the sudden release of the substance, a quality that Gerovital-H3 possesses. Cohen (1) shows that benzoic acid will arrange itself in space in such a manner that it protects the procaine molecule at its weak point from the action of procainestherasis. Important are also the K ions, which amplify the procaine action at the level of the nervous, and the muscular system (2). Gordon (3) has compared Gerovital-H3 and Procaine and found that there are significant statistical differences in favour of Gerovital-H3. The experiments carried out by Aslan (4) showed significant differences between Gerovital-H3 and Procaine inducing the vascular conditioned and unconditioned reflexes in old patients.

Gerovital-H3 acts upon the human body both under the form of an intact molecule and through the hydrolysis products PABA and DEAE, which participate in the regulation of the intermediary metabolism.

Gerovital-H3 favours the acetylcholine synthesis and it is a source of folic acid. In fact, a series of researches suggest the hypothesis that procaine, by means of the PABA, can stimulate the intestinal flora and the production of folic acid, vitamin K and tyramine.

The cellular effect of the Aslan product bears different characteristics and dimensions regarding the organ in question and its role within the body. The improvement of the superior nervous activity presents a particular importance. Yau (4) made a pharmacological study upon Gerovital-H3 and summarised its basic mechanism as,

- Gerovital-H3 competitively and reversibly inhibits monoamineoxidase (MAO).
- Gerovital-H3 acts as an antidepressive through the modification of the monoamine level in the brain.
- Gerovital-H3 is very selective in the oxidase desamination inhibition.

- Gerovital-H3's oxidative desamination of monoamine is done in such a way as to eliminate the hyper-blood-pressure peak, so typically present after administering of other MAO inhibitors.
- Gerovital-H3 is considered to play a role in maintaining the physiological status of the nervous cell membrane, restoring the equilibrium between the processes of excitation and inhibition at the level of the cortical and subcortical systems.
- Gerovital-H3 exerts an important regulatory action upon the nervous vegetative centers.

Further experiments reveal procaine's anabolic action. Studies on Infusoria (Colpidium colpoda and Vorticella) show the proliferation of cells as a result of a weak procaine solution (6).

The investigations on rats drew the attention of procaine's anabolic affects improving the quality of the hair. Berger obtained similar results with 6mg procaine/ Kg bodyweight in a study on 3-month old rats (7). On the other hand, Verzar used 25mg procaine/ Kg bodyweight (the amount which inhibits oxidoreduction) and did not notice any modification (8). In order to solve these contradictory results, Aslan initiated a study on 1800 white rats treated with Gerovital-H3 (9). The results pointed out an improved general tropicity, an increased resistance to pulmonary disease and less myocardial modifications. Fewer spontaneous tumours occurred in the treated group as compared against the controls.

Gerovital-H3 action upon the lipid mechanism is reflected by the hypotrope, heparinoid and lypoconverting characteristic (10). Aslan's procaine-based product exerts its effects on the atherogenesis process by several mechanisms;

- Gerovital-H3 diminishes the level of plasmatic lipoproteins and lipids.
- Gerovital-H3 exerts an effect on the erythrocyte membrane (an increase in membrane fluidity and a protection against osmotic hemolysis).
- Gerovital-H3 has an anti-oxidant mechanism that reduces the oxidative stress exerted on the membrane structure. Russu et al. Found that Gerovital-H3 exerts an inhibition on the generation of the superoxide radical in a non-enzymatic system (11).

It has been shown that Gerovital-H3 action on the lipid metabolism results in modifications in the serum total cholesterol, changes of the lipoprotein fractions ratio and changes to the unsaturated fatty acids content (11).

The international confirmations

Mention must be made of the fact that the research concerning Gerovital-H3 therapy has been simulated in over 500 medical and scientific publications.

The experiments utilising the original Aslan product and method confirm the efficiency and efficacy of Gerovital-H3.

The data presented at the 10th Congress of the International Association of Gerontology in Jerusalem in 1975, and at the European Congress of Clinical Gerontology in 1977, made available new evidence of the efficiency of Gerovital-H3.

The work of the special session at the Jerusaeum Congress regarding old age pharmacology were dominated by the research focussed upon the mechanism of Gerovital-H3 action.

A special interest was generated by the mechanism of Gerovital-H3's action, particularly from several American scientists who presented papers of double-blind placebo controlled trials.

Among them was Professor William Zung from Duke University, North Carolina who in his study applied the treatment for 28 days on his patients who were suffering from depression (12).

One group of patients aged 60 were submitted before, during and after the treatment to a battery of psychological tests. Professor Zung, a well known and respected author of psychological tests, proved the Gerovital-H3 efficiency in the treatment of depression.

Within the same session, the American authors, M. Kurland and M. Hayman from Palm Springs, California, presented the double-blind results performed with Gerovital-H3 on 63 patients suffering from depression and aged 45 to 80 (33 using Gerovital-H3 and 30 using placebo). Under observation there were several types of depression; manic-depression, reactive depression, organic cerebral depression, chronic reactive depression and alcoholic depression.

The results proved that Gerovital-H3 efficiency in all the tests applied, the differences between the two groups showed a great statistical significance ($p>0.001$).

Particularly valuable results were communicated by McFarlane M.D. who proved that Gerovital-H3 inhibits MAO (13). It is a known fact that the MAO levels increase with advancing age (14). McFarlane certifies the lack of any adverse

reactions with Gerovital-H3 and he also confirmed that Gerovital-H3 is a reversible and competitive MAO inhibitor.

The success enjoyed by Gerovital-H3 at the Jerusaem International Congress in June 1975, was remarked upon by Professor Nathan Shock (USA) in the closing speech of the Congress. That recognition came shortly after another world-wide known gerontologist, Alex Comfort (England), in an article published in the magazine "Mechanism of Ageing and Development", where he made positive remarks upon Gerovital-H3 and Aslan's method.

On the occasion of the International meeting "Medizinischewoche" in Baden Baden, Germany in November 1983, whilst concluding the Gerontology and Geriatrics section, Professor Paul Luth said "The Aslan method and treatment represent the most efficient therapeutic procedure in Geriatrics." (15)

Aslan's method of prophylactic and curative treatment with Gerovital-H3

As a medical professor from 1947 to 1949, Ana Aslan was inspired by the works of Lorich. Aslan started administering procaine in cases of arthritis and in trophic troubles of the extremities with sometimes spectacular results (1).

This is what Ana Aslan declared from the very beginning; "After one injection in the femoral artery given to a patient with embolism at the level of the inferior extremity, I noticed the almost instantaneous disappearance of pain. Then, for the first time, I had the idea of applying the same method in certain diseases with acute pain, which produce immobilization and thus long-lasting work incapacity."

Like other great discoveries, the clinical observation facts did not fail Aslan, as they represented the beginning of a period of original and fundamental studies which contributed to the prophylaxis and treatment of aging and chronic disease. Thus, in that period, another clinical observation was pointed out by the patients who stated that after the injections (given into the artery of the extremities), pain was relieved in all the body. "I believe, a general effect was obtained," concluded Aslan.

Starting in 1949, Aslan began applying her treatment in a nursing home. Besides an improvement of the local phenomena, she noticed that the physical and psychical state of the old men was becoming better. That was the time when Aslan initiated experimental research which had particularly favourable effects on all the treated animals.

I want to emphasize that, besides introducing the procaine treatment against the aging process and degenerative illnesses Aslan had other original contributions lying at the base of the treatment and method bearing her name.

- Aslan introduced long-term procaine therapy.
- Aslan used procaine in intramuscular injections according to her own schedule, which represented a true therapeutic novelty, since previously procaine had only been used for local anaesthesia, or in short-term cures injected either subcutaneously, intravenously or, more rarely, intra-arterially.

The special moment arrived when procaine was prepared to the new formula now known as Gerovital-H3. This is more active and has practically no side effects if administered in therapeutic doses.

Gerovital-H3 was experimented with at the Institute of Gerontology and Geriatrics in Bucharest, between 1951 and 1958. In 1957, Aslan started comparative investigations to establish the effectiveness of the oral treatment. To achieve the same results like in the parenteral treatment, the oral dose has to be doubled.

I must also state that at the Bucharest Institute, to evaluate the effects of Gerovital-H3 treatment, since 1952, a clinical study has been initiated. This study, due to the thousands of patients observed over a 25 year time scale makes this clinical study unique in the world.

Gerovital-H3 is a complex drug acting like the procaine molecule with its two hidrolisis products; PABA and DEAE. The addition of benzoic acid, potassium and disodium phosphate increase the effects of Gerovital-H3 biotrophic treatment.

Indications for Gerovital-H3

Gerovital-H3 is indicated for people older than 40 years in order to retard the aging process and as a preventative and curative treatment for chronic degenerative diseases. Gerovital-H3 has been shown to be efficacious in all the following :

- moderate and light depressive states.
- in troubles concerning attention, concentrating, cognitive processes and in balancing the neuronegative distinies.
- chronic fatigue syndrome.
- sleep disorders.
- tegument distrophias, trophic ulcers, atonic wounds.

- osteoarthritis, degenerating rheumatism, osteoporosis and during fracture consolidation periods.
- sexual management and improving sex drive
- Gerovital-H3 is an active anti-atherogenous factor and recommended in cerebral and peripheral atherosclerosis and in the treatment of post-infarct and hemiplegia consequences.
- Parkinson and Parkinson syndromes.
- Gerovital-H3 ameliorates the hair resistance and quality, repigmentation, reduces the alopecia (hair loss), head skin seborrhea and helps eliminate the pruritus.
- due to the inhibition on the generation of the superoxide radical, Gerovital-H3 is a powerful antioxidant, a free radical quencher.

Outcome of Gerovital-H3 treatment

Aslan's treatment produces a general transformation of the organism manifested as follows;

- desire to be active and to live, better memory, enhanced concentration ability and attention, improved optimism.
- improved affective tone and psychic and vegetative balance.
- increased self-caring abilities and exercise capacity.
- more ability to cope with the environment and increased resistance to infections.
- balanced endocrine functions with oestrogens reappearance and androgen reactivation.
- improved visual, auditory and olfactory acuity.
- diminished extrapyramidal rigidity, improved gait and increased mobility.
- better skin, nails and mucous trophicity.
- hair growth stimulation with a tendency to repigmentate the hair and a more trophic aspect.

- better blood vessel reactivity.
- the alleviation should also be mentioned of the clinical symptoms of the chronic diseases; chronic rheumatism, atherosclerosis, bronchial asthma, psoriasis, vitiligo, varicose ulcers.
- improves the quality of life retarding the rhythm of aging and preventing the chronic diseases.
- improves the sex drive.

Administering method for Gerovital-H3

The long term treatment with Gerovital-H3 has been extensively established with Aslan et col. For over 40 years at the National Institute of Gerontogoy and Geriatrics in Romania, in compliance with Aslan's methods.

At the beginning, Gerovital-H3 was administered only as injections. The tolerance has always been tested before starting the treatment; one subcutaneous injection of 1ml on the first day, followed by an intramuscular injection of 2ml the next day.

If no local or general reactions occur, proper treatment can be started. In the experience of more than 300,000 patients that completed this treatment in Romania, an intolerance only occurred in 1 in 7000 cases.

In 1957, Aslan started clinical and experimental comparative investigations in order to establish the effectiveness of the oral administration.

The dose of active substances had to be doubled to achieve the same results as in the parenteral treatment. Considering this fact and the difficulty raised by the accurate management in certain patients, Aslan established a combined schedule made up of both oral and parenteral approaches as follows;

- PREVENTATIVE– Treatment of chronic diseases and aging consists of 4 courses of 12 injections and 4 courses of 24 pills, ie, one course of 12 injections over 4 weeks (ie, 3 injections per week), a 4-week break then one course of 24 pills over 12 days (one pill twice daily between meals), a 2-week break and then the cycle is resumed.
- Starting from the age of 40 years, the prophylactic treatment with pills only is recommended in a series of 25 tablets during the first 12 days, with an interval of 2 months;

1st day, 1 tablet/ day, 2-hours after breakfast, increasing to the 12th day when 2 tablets per day are taken, (again 2-hours after meals, for example one at 10AM and another at 4PM).

There should a series of 5 treatment courses in the year, which should be increased to 6 per year for persons over the age of 65.

CURATIVE– Treatment in chronic diseases requires 6 course of 12 injections, and 5 courses of 24 pills, yearly, ie, one course of 12 injections over 4 weeks, a 2-week break, one course of 24 pills over 12 days (one pill twice daily between the meals); 2 week break. The cycle is then resumed.

Depending upon the outcomes the physician and patients can either shorten or extend the breaks. The first and second course of injections can be administered daily in order to study the individual reactivity.

Gerovital-H3 treatment can be individualised according to the disease/ diseases accompanying the aging and the patients biological age.

In arteritis, actively influenced by Gerovital-H3, the route of administration is intra-arterial. Aslan recommended the intra-arterial route in arthrosis and arthritis, especially when the knee joint is involved, and the intravenous route for cerebral spasms.

Contraindications

Gerovital-H3 should be avoided by anyone suffering or utilising the following;

- allergy or sensitivity to Gerovital-H3 (or Novocain).
- Gerovital-H3 cannot be used together with eserine or prostigmine.
- Gerovital-H3 can not be used at the same time as sulphanides.
- Gerovital-H3 should not be used with an antibacterial treatment.

Side effects

Gerovital-H3 side effects are relatively uncommon and may occur principally only after injections, but the frequency is very reduced (according to the statistics there is 1 case for every 7000 patients).

The minor side effects consist of a heating sensation and metallic taste, these effects disappear during the treatment.

The major side effects are related to the skin; macular eruption, rash and itching which determine the interruption of the treatment and the remake of the tolerance test (1ml injected id.) after the eruption has disappeared. The treatment of the side effects consist of the administration of the usual antiallergic drugs if the eruption persists after the arrest of Gervotal-H3.

In spite of its monoamineoxidase (MAO) inhibitor character, Gerovital-H3 does not interfere, as the conventional MAO inhibitors do, with the Tyramine from food (ed.- commonly called the cheese affect), which means there is no known incompatibility with Gerovital-H3 and food.

The interaction with sulphanides is because of the competition on the bacterial metabolism.

Overdosage may occur only after 400mg in iv rapid injection and the treatment is the same as for any acute intoxication.

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