

STEROID HORMONES, VITAMIN B COMPLEX FACTORS, AND
LIPOTROPIC FACTORS IN THE TREATMENT OF
GERIATRIC CASES

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Max Jacobson, M.D.*
Frederick E. Greenbaum, D.Sc.*

Preliminary Report

INTRODUCTORY REMARKS

In the treatment of Rheumatoid Arthritis within recent years the limelight was focused on Cortisone and A.C.T.H. Factors. Both of these substances belong to the group of steroid hormones.

They are, therefore, chemically related to all other steroid hormones, like testosterone, estrogenic substances, progesterone, desoxycorticosterone, acetate, pregnelone, acetoxypregnelone, Reichstein's substance. These hormones all have a very close chemical structure and differ only in some of their side groups or chains. One would, therefore, expect that if one steroid hormone is effective, all other hormones ought to be effective also.

A number of investigators have demonstrated that it is the liver which is the responsible organ in the inactivation of estrogenic substance or other steroid hormone in the human body. If a defective liver then fails to inactivate estrogen or any of the other steroid hormones, trouble may result. High steroid hormone level is necessary for the treatment of any disease. Consequently, it was reasoned that, if adequate therapy for the damaged liver could be found, one should expect the liver to regain its power of inactivating steroid hormones.

*155 E. 72nd Street, New York, N. Y

Director of Research HANLEY LABORATORIES, INC., Philadelphia, Pa.

The Biskinds and their group of investigators (1) have demonstrated a partial solution of this problem. They have shown that a significant inter-relationship exists between Vitamin B complex deficiency and the inactivation of steroid hormone. This has become now an accepted scientific fact, so that a deficiency of vitamin B complex factors might well lead to a failure of the liver to inactivate excessive levels of steroid hormones. Among the vitamin B complex factors, Thiamine, which is not stored in the body, is particularly liable to temporary or chronic depletion, so that a daily intake of Thiamine becomes necessary. Such Thiamine as is needed is immediately used, the remainder being excreted or destroyed.

On the other hand, a number of investigators, (2), (3), and (4) have demonstrated the fact, that certain specific amino acids have catalytic as well as synergistic action upon the effectiveness of the vitamin B complex factors. Furthermore, it has been shown that certain substances such as Pyridoxine Hydrochloride, d. l. Methionine, Choline and Inositol act upon fat metabolism and are very helpful to a sluggish liver, causing a relief or repair of such a liver. These factors have come to be known as lipotropic factors. These lipotropic factors given by intravenous or intramuscular injection establish a relationship between high blood cholesterol and atherosclerotic plaques.

Lipotropic factors, such as Choline, d. l. Methionine, Inositol, and Pyridoxine Hydrochloride will reduce blood cholesterol levels, and a slight increase in Phospholipids after 6-10 weeks administration of lipotropic factors will occur. These lipotropic factors act also as catalytic and as synergistic substances for the utilization of the vitamin B complex factors.

From the above mentioned facts, we conceived the idea, that steroid hormones, irrespective of what kind of hormones are used, might be more effective if vitamin B complex factors as well as lipotropic factors were given simi-

taneously, due to the catalytic as well as synergistic action of these factors. In addition to the action of the vitamin B complex factors and the lipotropic factors upon the liver, there is an additional insurance for the complete inactivation of an excess of a steroid hormone, thus preventing any danger that an excess of such a hormone might produce.

The administration of these factors could be accomplished by the physicians giving to the patients three different injections, in close sequence, one consisting of the aqueous solution of vitamin B complex, another the injection of an aqueous solution of lipotropic factors, and the third injection an oil solution of the steroid hormones. However, instead of this rather cumbersome procedure, it occurred to us to combine in the same aqueous solution the vitamin B complex factors, the lipotropic factors and the steroid hormone in aqueous suspension.

In this way preparations containing 1 mg of natural estrogenic substance per cc. or 12.5 mg testosterone per cc., or 30 mg of cortisone acetate per cc. suspended in the aqueous solution of vitamin B complex factors and lipotropic factors can be used.

The clinical evaluation of these products showed that our theoretical considerations were correct, and that steroid hormones given in only small amounts are as effective as if massive doses of the hormones are given alone. Thus the clinical experience clearly demonstrated that the lipotropic factors and vitamin B complex factors have a catalytic and synergistic action and that every bit of the steroid hormone is utilized, so that doses of only 1/10~~X~~ to 1/30~~X~~ of the amounts of the hormones otherwise required are as effective, as though the hormones were given alone.

CLINICAL CONSIDERATIONS

In the field of modern therapy the treatment of the patient of advancing age becomes a problem of increasing importance to the general practitioner. In

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addition to the economic aspects which form a problem for the country as a whole, the basic problems the therapy involves are prophylactic and therapeutic. With the ever increasing knowledge of metabolic processes that constitute the changed condition as well as diseases which are more prevalent in the ages of fifty and over, it has become possible not only to ^{maintain} ~~maintain~~ the normal functions of aged patients, but also to prevent conditions or cure diseases that result from metabolic and glandular changes.

As early as 1925 ~~and 1926~~ one of us (H.J.) pointed to the importance of choline in connection with atherosclerosis, ^{and later} ~~and later~~, in 1947 ~~(5)~~ combination of choline with amino acids showed marked influence on conditions of fatigue, anemia, nervous exhaustion, etc. In a later article, ~~in 1945~~, ~~(5)~~ the influence of these combinations on ~~about~~ 1000 patients was reported, with an average of ~~eight to ten~~ ^{8 to 10} injections necessary for successful treatments, with marked improvement already shown after the first few injections in many cases.

The interrelationship between hormones and the B Complex group

Recent investigations have shown that no antibody or antibody formation is possible without the presence of the B complex factor. The interrelationship of sex hormones and B complex has led us to use suspension of ^{either} ~~either~~ male or female hormones in conjunction with the ^u ~~u~~ afore-mentioned factors in all cases pertaining to special afflictions in the field of gerontology and geriatrics. The main conditions treated with this hormone B Complex mixture were fatigue, circulatory disorders, resulting from middle ~~age~~ or old age deficiencies and their glandular unbalances, anemia, arthritis of glandular origin, nervous disorders, also cases of hearing disorders ~~(6)~~ or inherited deafness in otosclerosis ~~(7)~~. The preparations have been used either separately or mixed and it has especially been found that disorders in ^{MENOPAUSAL} ~~menopausal~~ women respond better to male hormone with B complex or to mixtures which contained more male than female hormones.

The steroid hormones with the vitamin B complex factors and diastrophic

factors act co-enzymatically in bringing about a more pronounced and prolonged effect in the special fields in which correction of glandular imbalance or treatment caused by it are required. These conditions comprise vitamin deficiencies, general debility, arthritis, etc.

The most obvious and gratifying results have been obtained in menopausal syndrome, circulatory disturbances, such as flushes, numbness, nervous tension, ~~and~~ joint changes. The recent ~~trials~~ and experiences prefer male hormone suspension, especially in circulatory disturbances, in combination with vitamin B complex factors and lipotropic factors to which we have given the name, Testramone (androgen compound). The combination of estrogens, vitamin B complex factors, and lipotropic factor we have given the name, Vitramone (estrogen compound). *

It is now a ~~generally accepted fact~~ that the Papanicolaou test is ~~essential~~ ^{essential} ~~order~~ to determine the need of glandular therapy. It can ~~however~~, ² be said that as a result of ~~three~~ ³ years ¹ treatment of ~~about~~ 150 cases of menopausal disturbances by one clinician, the following course of treatment is recommended:

^{1.0} ~~one~~ cc. of estrogen compound plus 0.3 cc. androgen compound given three times a week, ~~intramuscularly~~, for a total of 12 injections; then, in accordance with therapeutic responses, repeating twice to three times a month for maintenance therapy will give results far superior and ~~immediate~~, as compared with ~~injections containing glandular extract~~ of estrogenic substance or male hormones alone. There have been no side reactions in thousands of cases treated with this preparation in this special group. The results were excellent in 50 ~~per~~ ¹⁰⁰ percent of ~~the cases~~, fair in 40 ~~percent~~, and the remaining 10 ~~percent~~ ¹⁰ unchanged.

¹ ~~The~~ ² ~~remnant~~ ^{of} ~~arthritis~~ ^{of} responded especially to high concentration of male hormone. As we have in our preparation of androgen compound only 12.5 ^{mgm.} milligrams of testosterone, ~~two cc. every other day~~ ² for the first 10 days have been injected to obtain ~~clinical~~ results. ~~The treatment of rheumatoid arthritis that has been the center of interest in connection with steroid therapy, has~~

* These compounds were supplied by Harary Laboratories, Philadelphia 44 Pa

been retreating gradually from the exclusive position that had been heretofore occupied by this most powerful but equally dangerous remedy, reserving it almost exclusively for those cases in which there are complicating factors.

It should, however, be kept in mind that even in cortisone therapy, the addition of androgen type compounds have been considered as essential, in order to insure the anabolic protein metabolism. The therapy in which an-

H ~~one doctor has been~~ ² ~~androgen compound has been used~~ ² ~~in a course of two~~ ² ~~cc. of the androgen type compound every other day for the first 10 days; two~~ ³ ~~cc. androgen type compound~~ ^{was} ~~three times a week for an additional two weeks.~~ ³ ~~The number of cases treated were~~ ^{was} ~~23. There were no definite cures, but great~~ ³ ~~improvement in about 35 percent, lesser improvement in about 30 percent,~~ ³ ~~and the remainder unchanged.~~ ³

no 9 The combination of salicylates or novaldine and, most recently, small amounts of butazolidine, has improved the ~~effect and~~ therapeutic responses, ~~which will be mentioned in a later report.~~

no 9 In many cases of osteoarthritis, ~~which is still a field in which even the~~ ~~ketosteroid or cortisone (ACTH) therapy has admittedly given poor results,~~ androgen compound alone or in combination with aminopyrine and aminopyrine derivatives and salicylates, has ~~definitely~~ proven superior in effect and ~~certainly incomparably~~ less dangerous.

no 9 ~~There is no doubt that~~ the latest development in this field ~~represents one~~ ~~of the most gratifying therapeutic indications that, in accordance with the~~ ~~components of the preparation, is not only a powerful~~ ⁱⁿ ~~preventative~~ ^{at} ~~an~~ ^{onset} ~~equally powerful~~ maintenance of function, ~~beginning in middle age,~~ and an ~~equally~~ active therapeutic agent in geriatric conditions.

~~Very recently, the medical profession has been aware that hormone therapy~~ ~~can be worthless or sometimes even dangerous if improperly applied.~~ ~~and~~ ⁱⁿ ~~the~~ ^{the} improvement that the added B complex and lipotropic factors represent,

~~and aside from the fact that they enhance, deepen, and prolong the therapeutic intensity and range, these combinations can be considered as safety devices that will make this type of therapy, not only more effective but certainly less dangerous.~~

It is not within the framework of this report to enumerate the wide, ever-increasing, clinical field that now is being represented in gerotherapy, but the effect of estrogen type and androgen type compounds is most convincing for anyone who has tried it in this particular field. ~~In the younger group~~ ^{To men} (between 40 and 60) it is ~~more~~ ^{ed} recommendable to give this therapy twice or three times a year in courses of 10 to 12 injections (for each series, frequency ranging from ~~two~~ ³ or three times a week ~~to once a week~~. Careful examination of the ~~prostate gland will give the androgen type compound the preference.~~ From there on, for the groups over 60, a maintenance therapy ~~three~~ ³ to ~~four~~ ⁴ times monthly, with occasional interruption, will result in better function and improvement of ~~conditions like~~ fatigue, depressions, insomnia, ~~impotence,~~ etc.; but it is here preferable to add 0.3cc. of ~~the~~ estrogen type compound to ~~one~~ ¹ cc. ~~of~~ androgen type compound, ~~as a safety factor.~~ In ~~almost~~ ⁷⁰ ~~percent~~ [%] of this group the results were excellent; ~~an additional~~ 15 per cent were ~~considered~~ improved; ~~whereas only~~ 15 per cent showed no ~~appreciable~~ changes.

Although ~~the general trend of~~ male-female hormone therapy was generally based on one ~~milligram~~ ^{10 mg} estradiol to 20 ~~milligrams~~ ^{mg} testosterone propionate, a combination of ~~one cc. of~~ ^{1 cc.} estrogen type compound ~~corresponding to~~ (10,000 units) ~~of estrogenic substance,~~ in combinations of ~~one-half~~ ^{0.5} cc. androgen type compound ~~equivalent to six milligrams~~ ^(6 mg) testosterone, has been found to be more effective. ~~This only moves the increased therapeutic value created through the aforementioned factors, in spite of the small amounts of the steroid hormones.~~

Recommended in these ~~same~~ cases are two series of 12 injections, each in a ~~single~~ ¹⁰ injection three times a week, and only in very deficient cases a

third course being added. ~~this is preferable to a continuous therapy, and has shown better and longer lasting results.~~

no

Recently, cortisone acetate combined with lipotropic factors and vitamin B complex ^{was} were tried, and it was found that ~~the combination of cortisone with these factors makes it possible to use cortisone in much smaller doses and~~

had

~~had a more pronounced and prolonged action. Just as soon as cortisone is more abundantly available, another product containing cortisone acetate in combination with lipotropic and vitamin B complex factors will be given to the clinicians for geriatric cases.~~

In the extensive clinical practice of one of us (M.J.) many cases of geriatric conditions have been treated ~~but only a few illustrations of outstanding cases will be mentioned who have greatly benefited.~~

seen

~~let case~~ *up to 72 yrs of age with most gratifying results*

A 56 years old business man complaining of fatigue, fitful sleep, slight precordial sensation, with red blood count ^{million} 4,160,000, blood pressure 110:80, blood cholesterol 280, MPN 36, was treated with ~~testramone~~ ^{testosterone}, 1 cc. 3 times a week for a period of 4 weeks. He was advised to keep a well balanced diet and to abstain from alcoholic beverages during the period of treatment. After 4 weeks, the blood count was 8,450,000, ~~cholesterol~~ ^{cholesterol} 210, MPN 28. He had a feeling of being less nervous, was able to sleep and the precordial pain was already gone after two weeks of treatment. He was advised to come for a check-up in intervals of 2 months.

2nd Case

Age 92 male; patient complained of slight shortness of breath - in spite of the fact that he was ⁱⁿ remarkable condition for his age - he was able to walk 1 1/2 miles and was in full possession of his intellectual powers. He had begun to complain of palpitations of the heart, and of increased nycturia. His electro-cardiogram showed only slight signs of myocardiac weakness, other-

*Red cells 3.9 million
Hemoglobin 15%
white cells 6000*

wise normal. There was tendency toward slight secondary anemia probably due to frequent hemorrhages from a rectal condition he had suffered from for the past 40 years. The blood pressure was 130 over 90; pulse 85; urine examination showed traces of white blood cells; prostata slightly enlarged; three protruding hemorrhoids, of pea size, showed sign of recent bleeding; blood chemistry essentially normal. Patient was started on a series of combined $\frac{1}{2}$ cc. Testramone ^{→ t} - ~~Testramone~~ ^{→ v} Vitramone, 3 times a week for a period of 6 weeks. Circular disturbances disappeared; urination frequency, at night, reduced; blood count, 4,500,000 red cells and 6,000 white cells. ^{HEMOGLOBIN 85%} Patient could walk without any longer complaining of shortness ^{ness} of breath and felt generally well.

3rd Case

Housewife, 60 years of age, menopause for past 8 years, complaining of arthropathy in hands and knees, flushes, nervous tension, fatigue, blood: ^{Red count} 4,000,000:78%, hemoglobin, 6,000 white cells, blood pressure 150 over 100; Patient, being five feet 6 inches tall, was overweight (158 lbs.). She was advised to reduce carbohydrate and fat intake and abstain from alcoholic beverages during treatment. She received Testramone twice a week for 2 weeks, later combined with ^v Vitramone for another 3 weeks. After the first week, circulatory disturbances ^{UR} disappeared, patient lost 12 pounds, and after 3rd week the arthropathy and nervous exhaustion were considerably improved.

4th Case

^{female} Patient, age 87, suffering from osteoarthritis, lower back and shoulders; lack of appetite; depression; underweight; and general debility, although of full mental capacity; low blood pressure - 100 over 70; general stiffness of hands and shoulders; red blood count 3,8 million; 70% hemoglobin. Patient was started on a series of Testramone ~~was~~ ^{combined with VITRAMONE} 1 cc. 3 times a week ^{to} experienced remarkable recovery during first three weeks of treatment which has been maintained since. The final blood count, red, was 4.2 million and 80% hemoglobin.

not

In general, it can be said that the interaction of lipotropic factors and B complex and hormone in their effect on fatigue, nutritional and circulatory disorders and disorders of the skeleton is mostly based, ~~essentially assumed~~ *changes in* on ~~the influence upon the~~ *incidence to the* metabolism ~~of~~ *later years of life.* ~~Of course, all~~ ~~metabolic processes being influenced by B complex factors and protein, and by steroid components, there has been achieved, especially in aforementioned combinations, a greater effect than could be expected from any single factor of either B complex or steroids alone.~~ ~~It may be pointed out that the lipotropic factors are only present in comparatively small quantities, but a~~ ~~markedly~~

~~shown in cases of hearing disorders (6)(7).~~ *as the* these small amounts of amino acids and lipotropic factors act catalytic *ically* and synergistic *ally, and so the*

not

total activity is greatly enhanced
In addition, the B complex factors with steroids effect an improvement in metabolism. This can easily be explained through increased appetite, ~~the~~ *the* lack of ~~which~~ *which* often is a problem in the ~~elderly~~ *elderly*. Improved appetite makes the blood count rise and makes fatigue disappear. ~~These few illustrations very briefly described here, are representative of several hundreds of patients, of these groups.~~

men and women in

We have chosen these case illustrations to show rehabilitation of middle ~~aged and advanced aged men and women and the therapeutic influence in real old~~ *very old.* ~~groups, and there are~~ *Many* other patients who belong to groups in between these

who respond ~~quite~~ *well*, and even better, to the treatment with the hormone - B complex combination. ~~As there have been numerous reports emphasizing the necessity of B complex therapy and hormone replacement, with stress on the presence of lipotropic factors, this preparation was chosen for the purpose for which it has been used in this short report.~~ The authors present this ~~short~~ preliminary report to encourage other researchers to evaluate this kind of response in such conditions.

Of ~~specific~~ ^{special} interest are cases of malnutrition of concentration camp inmates. Through the fact that they survived the horrors despite their old age, these cases ~~are~~ particularly suited for this kind of investigation.

5th Case

female
Patient, formerly an inmate of concentration camp Theresienstadt, dismissed at the age of 76 with signs of malnutrition; abdominal distention; edema in both legs; blood pressure 140/90; red blood count 3.8 million and 70% hemoglobin; 8,000 white cells; urine, countless crystals and white cells; suffering from bad appetite, nervous exhaustion. She was started on Testramone-Vitramone mixture; 1 cc a week for one week; then for 3 additional weeks, 1 cc every other day; and for one month 1 cc each week. After first week, edema, apparently caused by beriberi, disappeared; patient regained appetite; lost depression; was alert; and could sleep again. Blood count became 4.5 million - 85% hemoglobin, 7,000 white cells. Patient suffered from cystitis which reduced capacity of the bladder. She was relieved through disinfecting therapy resulting in increasing capacity of the bladder.

6th Case

Patient, doctor's widow, 66 years old at time of discharge from concentration camp/suffered from serious circulatory disorders, respiratory allergy, inappetance, anxiety, nervousness and ^{Atrophic} vaginal ^{changes} disorder; no changes in blood count or blood chemistry. Started on Vitramone 3 times a week for three weeks, with an additional series of Testramone-Vitramone for another 3 weeks, she regained appetite, lost nervousness and vaginal discomfort after 2 weeks. Three weeks later, she was rehabilitated so much so that fatigue disappeared, she became active in her work as a teacher at a cooking school and today, at the age of 75, is fully employed; able to provide for herself.

Sex
1st
~~In addition to aforementioned two camp cases, there are hundreds of the advanced age group of camp inmates. It is essential to keep in mind that one can always classify adult camp inmates into the advanced age group as they age~~

prematurely and are particularly qualified to benefit from rehabilitation treatment to help them regain prematurely lost functions. ~~It is gratifying to see that these patients from the above mentioned treatment~~ benefit

CONCLUSIONS:

- #1. Steroid hormones, if suspended in aqueous solutions of Vitamin B Complex factors and lipotropic factors are much more effective if given by injection due to the catalytic and synergistic action of these factors.
- # 2. ~~As successful illustrations of these steroid hormones, suspended in aqueous Vitamin B Complex factors and lipotropic factors are natural estrogenic substance, testosterone, and cortisone acetate which have been thoroughly investigated clinically, and which have given most promising results where the injections of steroid hormone are indicated.~~
- # 3. Two new products, ~~Testramone and Vitramone are described. These ~~new~~ products are the outcome of extensive researches of the Research Department of Harvey Laboratories. The usefulness of these products in conditions like vitamin deficiencies, metabolic disturbances, general debility, arthritis and other geriatric conditions is outlined. They are of great value in the treatment of diseases of middle age and advanced age, known as the geriatric patient.~~
- # 4. ~~Of the many hundreds of geriatric cases treated by one of us (M. J) six outstanding case illustrations are briefly described and in all six cases great improvement and amelioration followed after a few weeks' use of these products.~~
- # 5. ~~The presence of~~ lipotropic factors and Vitamin B Complex factors with steroid hormones, in one ~~and the same~~ injection, makes it ~~possible~~ possible for the steroid hormones to be effective in doses much smaller than if steroid hormones are used alone. This is of great

Conclusions continued:

importance to the ^cphysicians, as it reduces greatly the cost, ~~of the preparation.~~

#5. As soon as cortisone acetate will be more freely available a third product will be ^{offered} given to the medical profession, ^{namely} a combination of cortisone acetate with lipotropic factors and Vitamin B₁ Complex factors, thus making cortisone effective in smaller doses over a longer period of time or even permanently.

~~Acknowledgments.~~

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