TOWNSEND LETTER

The Examiner of Alternative Medicine

Monday, December 20, 2021

Hormone Therapies to Strengthen Our Immune Resistance to Viral Infections, Including COVID-19

By Thierry Hertoghe, MD

International Hormone Society

The best way to control the COVID-19 pandemic is to prevent people from becoming infected. Aside from putting on a mask, keeping social distance, and being vaccinated against the SARS-Cov-2 coronavirus, almost no measures of prevention are advocated by governments and in the media. Fortunately, most physicians working in the integrative or holistic field of medicine have a better overview of the problem. They are aware that the best prevention starts with stimulating a patient's immune system so that masks, social distancing, and vaccines might then become unnecessary. These measures could be reserved for the most fragile individuals of our society, patients of all ages with serious diseases as well as very old adults.

How can physicians help patients increase their resistance against infections? In

my experience, making changes in three domains significantly increases the immune system: diet, nutritional supplements, and hormone treatments. In this article, we will mainly examine what is possibly the most essential intervention to boost the immune system efficiently, the hormone therapies.

The first step is to obtain that patients **improve** their **diet**. Scientific studies tell us that a diet rich in fresh vegetables and fruits, sufficient protein-rich foods cooked at low temperature (and, thus, not burned) improves the immune system and decreases the number of infections. Avoiding sugar, sweets, and bread, which is made of hard to digest non-sprouted grains, has been shown to reduce the incidence of infections. Equally, the incidence of infection drops when people stop consuming dairy. Cow milk and its derivatives are not designed for human consumption but are mainly adapted to the digestive system of calves.

The second step is to take **immune-enhancing nutritional supplements.** Among the nutrients that show immune-stimulating potency against viral infections are zinc, iron, iodine, and vitamins A, C, and D.

The third and, in my experience, most important intervention to stimulate the immune system is to **correct deficiencies in immune-stimulating hormones** in patients.The most significant immune-stimulating hormones are likely as follows. Thyroid hormones are potent hormones to improve our resistance against viral infections. Thymosin alpha-1, the number one hormone of the thymus, might, in my experience, be the most potent of all the hormones that stimulate the immune system. Cortisol, at physiological doses, also enhances the immune system, particularly against viral infections. DHEA, melatonin, estrogens, and testosterone may be considered additional immune-stimulating hormones that help fight off viral infections.

First, let's discuss **thyroid hormones.** Patients with hypothyroidism are easily infected. In one study, about half of the participants complained of nasal obstruction (48%), one-sixth complained of rhinorrhea (16%), and one-fifth complained of headaches (20%), typical symptoms of the common cold. Thyroid therapy can efficiently make these complaints disappear.[1] The same might be valid for the flu. Patients infected with influenza (A) reportedly have T3 and T4 serum levels below the lower reference limit. [2] In my experience, thyroid therapy with recurrent flu can considerably decrease the incidence and recurrence of the flu in hypothyroid patients.

Some data suggest that thyroid hormones might help against coronavirus infections. In an observational study of 50 hospitalized patients with severe COVID-19 in Wuhan, China, the place of origin of Sars-CoV-2, most patients had serum levels of total T3 and TSH below the lower reference limit. Both of these levels normalized in people who survived the infection.[3] This suggests that the coronavirus affects the pituitary gland or the hypothalamus, resulting in a reduced secretion of TSH, itself causing a reduction of the secretion of thyroid hormones, including of T3. However, coronaviruses may also profoundly affect the thyroid gland.

During the SARS-CoV-1 pandemic in 2002-2004, also in China, two studies showed that the coronavirus profoundly damaged the thyroid gland of the patients who died from the infection. The follicular cells, which produce thyroid hormones, and the parafollicular cells, which produce calcitonin, in the thyroid gland are severely injured and tend to

disappear.[4-5] Reports in the media related the cases of two men who were dying from COVID-19 infection but who dramatically improved and survived with T3 supplementation.[6] A randomized controlled study is ongoing to determine whether providing T3 as a nasal spray during the first 7-10 days of COVID-19 might improve the survival rate of severely ill patients.

Thyroid therapy may also display beneficial effects against herpes infections. Rats rendered hypothyroid by taking the antithyroid drug methimazole accumulated 10 times more of the herpes simplex virus in their spleens than euthyroid rats did. In contrast, rats rendered hyperthyroid accumulated almost no herpes simplex virus: approximately 1,000 times less herpes simplex virus in their spleens than were found in euthyroid rats (and 10,000 times less than hypothyroid rats).[7] In hypothyroid patients, thyroid supplementation can reduce by 40% the risk of herpes zoster infection (shingles).[8] Interestingly, children with autoimmune thyroiditis have a 40 to 60% increase in prevalence of IgG antibodies against Epstein-Barr (also called herpes 4) virus in their serum. Because patients with autoimmune thyroiditis usually have lower thyroid hormone levels and a higher TSH serum level than healthy individuals, the high frequency of Epstein-Barr IgG antibodies may signify that lower thyroid activity may have contributed to infection by Epstein-Barr virus in these children.[9]

Hypothyroidism may also allow easier development of viral hepatitis. Patients with viral hepatitis have been reported to have lower serum T3 and T4 levels, as well as higher serum TSH and reverse T3 levels, [10] indicating a lower thyroid function. The lowest T3 levels and highest levels of reverse T3, which blocks T3 action, are found in patients affected by fulminant viral hepatitis, the life-threatening form.[11] The opposite is true when thyroid therapy is given to hypothyroid patients with hepatitis: clinical improvement, stimulation of liver and immune functions, and amelioration of their hormone status.[12]

Further evidence of protective effects of thyroid hormones against hepatitis viruses may be found in the laboratory tests of patients with chronic hepatitis B: a mean of 58% increase in serum TSH in the most ill patients whose livers have become fatty (steatohepatitis).[13] Thus, a lower thyroid function may facilitate the progression of the disease. The risk that hepatitis B progresses into the dangerous fulminant form increases at progressively greater drops of the serum T3 level and increasingly higher levels of the antagonistic reverse T3. The lower the serum T3 level is in patients with fulminant hepatitis, the less chance they have of surviving massive necrosis of the liver.[14] Patients infected by the hepatitis C virus also tend to have a certain degree of hypothyroidism, which may weaken their immune systems. One study reported that hepatitis C patients are at a three-fold higher risk of overt hypothyroidism and about two times higher risk of having antithyroid antibodies (as well as antithyroglobulin as antithyroid peroxidase antibodies) in their serum.[15] The lower the serum T3 total is, the more likely these patients present a severe form of cirrhosis and, thus, of dying. In general, the severity of viral hepatitis appears to depend on the level of free or total serum T3.[16]

HIV infections are also associated with an increased incidence of free serum T3 and T4 levels below the lower reference limit and a TSH above the upper reference limit. For each of these levels, approximately 20% of HIV patients are in the overtly pathological level versus 2.5% of the overall population.[17]

In my experience, the most efficient thyroid preparation to improve the immune system is desiccated thyroid at doses between 30 and 180 mg/day, depending on the patient's degree of hypothyroidism. The additional presence of T3, T2, T1, and T0 thyroid hormones next to T4 in the preparation makes this therapy more efficient at stimulating the immune system than T4 (thyroxine) alone, the usual medication for hypothyroidism. (Note that each number following the capital T indicates the number of iodine atoms incorporated into each different type of thyroid hormone.)

Thymosin alpha–1 is the most potent immune-stimulating hormone I know, particularly against the flu. Many of my patients who take subcutaneous injections of thymosin alpha-1 at a dose of 0.3 to 0.5 mg per day no longer seem to catch flu. If they do, tripling the dose in the early stage of the flu usually makes the infection disappear within hours. Treatments with a single but higher dose of 3.2 mg of thymosin alpha-1 together with the influenza vaccine have been shown to increase antibody production substantially in reaction to the influenza virus vaccination in patients who are vulnerable to infections, such as uremic patients (patients with kidney failure).[18] Such beneficial effects might, in my opinion, also occur with COVID-19 vaccination when thymosin alpha-1 is given simultaneously on the same day as the vaccine injection.

Thymosin alpha-1 is also a potent treatment for coronavirus infections. In 2002, thymosin alpha-1 was given to coronavirus patients who developed a severe acute respiratory syndrome during the first outbreak of a coronavirus pandemic in China. The hormone was found to control the development of the disease efficiently.[19] Thymosin-alpha-1's efficacy seems to be even more evident with the coronavirus that causes COVID-19. A controlled trial first published in May 2020 on 76 patients hospitalized for severe COVID-19 showed that the 36 patients who received 10 mg/day of subcutaneous injections of thymosin alpha-1 for seven days were three times less likely to die than the controls without the treatment (11% of treated patients died vs. 30% of controls). In addition, thymosin alpha-1 virtually eliminated the need for mechanical ventilation in these severely infected patients. Eighty-two percent fewer patients who received thymosin alpha-1 needed non-invasive mechanical ventilation than the controls did. Hospitalized patients with COVID-19 suffer from severe lymphopenia. The main effect of thymosin alpha-1 was to restore lymphocyte count, particularly the T lymphocytes CD4+ and CD8+ cells, which fight off viruses.[20]

Thymosin alpha-1 is, in my experience, surprisingly efficient in herpes infections. All my patients with recurrent and treatment-resistant herpes infections report important progress with thymosin alpha-1, having no or almost no infections, on condition they follow a healthy diet and avoid consuming sweets, chocolate, and alcohol. Studies in mice infected with herpes viruses confirm this finding. Subcutaneous injections of thymosin alpha-1 to mice infected with herpes simplex 1 and herpes simplex 2 viruses substantially decreased the morbidity and mortality of these infections.[21] In cell cultures, thymosin alpha-1 can decrease the replication of herpes simplex 1 and 2 viruses.[22] In kidney transplant patients with acute respiratory distress syndrome due to cytomegalovirus infection, thymosin alpha-1 treatment significantly increased survival and decreased morbidity. Doses were either 1.6 mg a day of

thymosin alpha-1 or 1.6 mg every two days. These doses increased the survival with an additional + 56% compared to patients who only received standard treatment. In survivors of the cytomegalovirus infection, thymosin alpha-1 increased the CD4+ lymphocytes and the immune ratio of CD4 to CD8 cells.[23]

Thymosin alpha-1 is also beneficial in patients with viral hepatitis. The hormone has been officially accepted by healthcare systems throughout the world for its potency to help patients survive and heal from viral hepatitis, particularly hepatitis B and C pathologies where levels of thymosin alpha-1 may be lower. In patients with chronic hepatitis B, serum titers of thymosin alpha-1 are approximately 30% lower.[24] For treatment of hepatitis B, thymosin alpha-1 has been reported to be more efficient than interferon-alpha. In one controlled trial, 50% of patients had complete remission with thymosin alpha-1 compared to 27% in the group taking interferon alpha at 12 months (6 months after the end of the treatment). [25] These superior effects of thymosin alpha-1 alone have been confirmed in other studies.[26-30] Thymosin alpha-1 has also been reported to improve the antibody production to hepatitis B vaccination.[31,32] For hepatitis C,thymosin alpha-1 alone is less efficient as a treatment. It should be considered an adjuvant treatment next to other therapies in contrast with its effects on hepatitis B where alone it may be very efficient. [33-37]

In HIV infections, the serum thymosin alpha-1 titer is paradoxically higher.[38,39] The higher level is a false positive result due to cross-antigenicity of thymosin alpha-1 with molecules produced by HIV patients. The last 18 amino acids of one end of thymosin alpha-1 have a 50% similarity with the last 18 amino acids of the HIV P 17/18 protein. [40] Thus, much of the higher level of thymosin-alpha-1 that is measured in the serum consists in fact of HIV P 17/18 proteins, not thymosin-alpha-1. Can thymosin-alpha-1 help HIV patients? Yes, in association with antiviral medication (azidothymidine) and interferon alpha, thymosin-alpha-1 increases the number of T cells and the CD4 to CD8 ratios in AIDS patients.[41,42] Moreover, in cultures of macrophages and peripheral blood mononuclear cells, thymosin alpha-1 treatment inhibits HIV infection.[43]

The third most important hormone for the immune system is **cortisol**. Since its discovery at the end of the 1940s, cortisol has been used efficiently to overcome viral and bacterial infections, particularly the flu. Before cortisone became available, influenza almost invariably killed patients with adrenal insufficiency.[44-45] During an outbreak of avian influenza in Malmo, Sweden, in 1957, autopsy studies of each of the five patients who died from influenza showed untreated adrenocortical insufficiency.[46] Dr. William Jeffries, an expert in cortisol treatment, reports that in the acute stages of the flu, there are remarkably low serum cortisol levels, while at the same time the cortisol secretion to ACTH injections is normal. This means that these patients with the flu have an ACTH deficiency. The virus blocks the production of ACTH by the pituitary gland. The lack of ACTH causes a drop in cortisol production by the adrenal glands and puts the patient in adrenal deficiency. In his famous book *Safe Uses of Cortisol*, Jefferies points to the great similarity between symptoms of acute flu and those of acute adrenal deficiency. He reports that taking cortisol supplements, even transiently, can impressively improve the outcomes of patients infected by the flu.[45]

The strategy to get rid of a flu infection is to make adrenal-deficient patients who are already taking cortisol increase the dose of hydrocortisone by 5 mg every 30 minutes (during a maximum of 2-3 hours) within the first minutes up to first six hours of the first symptoms of flu. When taken early, this treatment is very efficient. When cortisol is taken

later (e.g., 1 to 2 days after the start of the infection), it is a too late to achieve quick results by increasing the cortisol dose. In this latter case, I recommend cortisol-deficient patients increase their hydrocortisone dose by 50% over three to five days. People who are not under glucocorticoid treatment and who acquire the flu or other types of infection may transiently take a single dose of 20 to 30 mg in the first hours of the flu. This method may help them overcome the infection quickly in two-to-three hours. I also advise patients to take an additional and equivalent (to the cortisol) dose of DHEA. For example, if the additional dose of hydrocortisone is 20 mg/day, then the patient should take an additional 20 mg/day of DHEA. This helps to avoid excessive tissue breakdown. Several studies report that supraphysiological doses of glucocorticoids together with antibiotics accelerate and improve the recovery of acute pneumonia due to the flu.[47-50]

The intake of glucocorticoids has also been shown to decrease the duration of the common cold caused by rhinovirus. The treatment suppresses nasal inflammation and cold symptoms during the first two days of the infection.[51] In patients with suspected or confirmed severe COVID-19 infections, two studies have shown that the use of glucocorticoids decreases mortality by 20 to 30% and the need for mechanical ventilation by approximately 20 to 50%.Efficient doses of intravenous hydrocortisone were 200 mg per day. If dexamethasone is administered, then the dose is 6 mg per day. The duration of both types of treatment is 7 to 10 days.[52,53]

For shingles (herpes zoster infection), methylprednisolone, a synthetic glucocorticoid, at supraphysiological doses has been shown to reduce the persistence of pain when given within the first 5-10 days of the infection.[54.] For herpes zoster infection, Jefferies proposes to do it with hydrocortisone and provide 4 x 20 mg per day to patients during the two-to-seven days of acute pain until a substantial decrease in pain is obtained, which is when a progressive decrease in dose can be implemented.The dosage should be tempered off progressively over two-to-seven days with 4×5 mg less each time.[55] At that stage, I would also add an equivalent 4×20 mg/day of DHEA, then 4×10 mg/day, etc., to protect the body from excessive catabolism.

Cortisol also helps to fight off other types of virus infections. Patients with viral hepatitis B and cirrhosis have lower levels of cortisol than patients without cirrhosis. The lower the cortisol level is found in patients with hepatitis B, the more they suffer from a progressive increase in cirrhosis (liver fibrosis).[56] This suggests that cortisol might slow down the progression of hepatitis B. In cell cultures, cortisone has been shown to inhibit proliferation of polio, rabies, and yellow fever viruses.[57] Cortisol deficiency also plays a role in HIV infections.More than a quarter (27%) of patients with HIV infection have been reported to have adrenal deficiency and show symptoms of cortisol deficiency.[58] Physiological, but not supraphysiological, doses of cortisol to these patients help them better overcome the infection and have, in my experience, an immune-stimulating effect rather than an immune-depressing effect.

DHEA is a fourth important immune-stimulating hormone. DHEA blocks excessive immune-suppressing effects of cortisol. DHEA alone can stimulate the immune system and resistance against viral infections. For example, a DHEA analog has been shown to decrease the replication of influenza A virus in mice.[59] Subcutaneous DHEA injections have been shown to decrease the mortality from herpes simplex 2 virus infection substantially in mice, increasing their survival from 60 to 92%.[60] Subcutaneous injections of DHEA also substantially increased the survival of mice infected with Coxsackie virus from 0% survival to 80%.[61] Interestingly, androstenediol, a metabolite of DHEA, is

even more potent. The skin possesses the enzymatic equipment to make androstenediol from DHEA.[62] In the same experiment with Coxsackie virus, androstenediol treatment kept all mice alive. It is likely that most of DHEA's anti-infectious potency is obtained through its transformation into androstenediol because all the experiments with DHEA on infections in mice involved subcutaneous injections.

In one observational study, pregnant women with cytomegalovirus infection presented low serum DHEA sulfate levels. The authors of the study suspect that the cytomegalovirus decreases the synthesis of DHEA sulfate. They also observed that cytomegalovirus damaged the adrenal glands of the fetus.[63]

DHEA may counter a number of other viral diseases. For example, in vitro DHEA reduces the replication of the genital herpes virus. [64] In patients with hepatitis C virus, low serum DHEA sulfate levels are found, possibly contributing to the appearance or aggravation of the liver infection. [65] In patients with HIV who are showing a lot of symptoms in pain from the disease, serum DHEA sulfate levels drop to less than half of the DHEA sulfate levels in HIV patients without symptoms.[66-67] Moreover, a level of DHEA lower than 100 µg/dL or 2.7 µmol/L, which corresponds to the average at age 65, significantly predicts future aggravation into AIDS.[67-70] Other studies have shown that the lower DHEA sulfate levels are in HIV patients, the weaker their immune systems are with increasingly lower numbers of CD4 cells and differentiated and aggressive cytotoxic CD8 cells and with higher HIV viral load.[71] In HIV patients, each progression into a more advanced stage of HIV disease, is accompanied by a progressively greater decline in DHEA sulfate levels in the serum and a worse prognosis over the next year. Can DHEA treatment oppose HIV progression? A hint of an answer is given in several in vitro studies, which show that DHEA and a DHEA analog reduce the replication of the HIV virus at concentrations on the average five times higher than the average physiological level in adults.[72-74]

Melatonin is a fifth hormone that may help to increase our resistance against viral infections. Melatonin is found in every living being. In mice, melatonin has been shown to reduce substantially the severity and mortality of deadly encephalitis-inducing virus infections, such as with the West Nile virus, encephalomyocarditis virus, Semliki forest virus, and Venezuelan equine encephalitis virus, thereby improving survival by three to 13 times.[75-78] In the Aleutian mink inoculated with the Aleutian mink virus, subcutaneous implants of melatonin considerably reduced the animals' mortality rate.[79] In rabbits infected with the rabbit hemorrhagic disease virus, melatonin supplementation has been shown in three studies to decrease both morbidity and mortality of the rabbits considerably.[80-82]

The most important researcher in melatonin, Prof. Russell Reiter, published several studies presenting evidence that melatonin treatment may help prevent viral infections in general. He hypothesize that melatonin also increases patients' survival of Ebola virus and COVID-19 infections.[83-84] In patients with herpes infection, 2.5 mg per day of melatonin can produce complete regression of symptoms in 96% of patients, a result more efficient than 200 mg of the antiviral drug acyclovir (85% of patients have complete regression).[85] Melatonin can possibly also reduce the severity and duration of herpes infection because low melatonin levels have been found in patients with herpes zoster. In this study, the lower the melatonin levels were, the more severe the rashes and pain of herpes zoster were.[86] Can melatonin treatment increase our immune resistance to HIV infection? Observational data suggest yes. HIV-infected patients have lower salivary and serum melatonin levels. In AIDS, the advanced stage of HIV infection, the appearance of lipodystrophy is a sign of further aggravation and associated with significantly lower serum

melatonin levels.[87,88]

Estradiol is a sixth potent hormone to stimulate the immune resistance against viral infections. In mice made estrogen-deficient by removal of the ovaries, estradiol supplementation reduces the morbidity and increases the survival during an influenza A virus infection.[89-90] Estradiol treatment also significantly stimulates the production of antibodies against the influenza virus in estrogen-deficient mice. When estrogen-deficient mice receive the flu vaccine, estradiol treatment significantly stimulates the mice's production of antibodies against the influenza virus.[91] However, we are lacking data from human trials. A prospective cohort study did not show that estrogen therapy could significantly increase the production of anti-influenza virus antibodies in postmenopausal women after vaccination.[92]

Estradiol may also be helpful against hepatitis C. Patients with chronic hepatitis C have significantly lower 17-beta-estradiol levels than healthy controls.[93] In cell cultures, estradiol can reduce the replication of the hepatitis C virus.[94] Can estradiol also boost the immune resistance of women against HIV? The answer is likely a yes. In an interesting experiment, female monkeys (macaques) were made estrogen-deficient by removal of their ovaries. Without estradiol treatment, all monkeys became infected by inoculation of the simian immunodeficiency virus (SIV similar to HIV) into their vagina. However, estradiol treatment prior to the vaginal inoculation of the SIV, completely blocked transmission of the SIV. This protective effect was obtained by an effect of estrogen either within the vagina or, more likely, on the vaginal epithelium, because there is no inhibition of HIV transmission when the virus is inoculated with a syringe in the tissues situated beyond the vaginal epithelium inside the body.[95]

Testosterone is a seventh interesting hormone that may improve the resistance against viral infections, but perhaps less efficiently in the flu and more efficiently in coronavirus and hepatitis infections. In a trial on aged male mice with influenza, testosterone treatment modestly decreased the morbidity and mortality of influenza virus infection.[96] In men with hepatitis C, the effects of testosterone are more important. Fifty percent of men with active hepatitis C have low serum free testosterone levels. Progressively lower total testosterone is found when the hepatitis infection gradually worsens.[97] A small study of men with recurrent viral hepatitis C and who got a failing liver transplant for serious third or fourth stage of cirrhosis (liver fibrosis) is enlightening. Treatment of nine of the men with 1% testosterone gel for six months kept them alive with significant improvements in albumin, muscle strength, well-being, and disease scores. In the five other men without testosterone treatment, no improvement was noted and all patients died within less than three months after transplant.[98]

In HIV infection, testosterone may also have a protective role. In one study, 30 percent of men infected with HIV had severe testosterone deficiency with low total serum testosterone levels below 2800 pg/mL (200 ng/dL) or low serum free testosterone levels (levels below 65 pg/mL).[99] In another observational study, 37% of women with HIV had testosterone insufficiency. These female HIV patients with testosterone insufficiency suffered from significantly more fatigue and tended to report lower sexual desire, physical activity, and physical function as well as more stress feelings and more severe depression.[100]

In COVID-19, testosterone may protect men against severe acute respiratory syndrome (SARS). An Italian study showed that in men with severe COVID-19 and pneumonia who developed SARS, the testosterone level was on the

average three times lower than in men without SARS. A serum total testosterone level below 1450 pg/mL or 5 nmol/L, which is approximately 50% lower than the lower reference limit of young men, is particularly worrisome. Men with this low level had a 23 times higher risk of needing to be transferred to the intensive care unit, a sign of major aggravation of the infection. Their mortality was about 30 times higher than for men with testosterone levels above 5 nmol per liter (144.21 ng/dl) or 1450 g per mol.[101]

Conclusion

Correcting hormone deficiencies may prevent many patients from getting viral infections and may save the lives of people with viral infections, including COVID-19. Hormone therapy works through several mechanisms. First, many hormones strengthen our first immune barrier consisting of the skin and mucosa, making these areas more efficient in rejecting or eliminating pathogens. Second, hormones can stimulate not only the production but also the efficacy of white blood cells, including neutrophils, macrophages, and T- and B-lymphocytes, to attack and destroy intruders. Physicians can become considerably more efficient in protecting their patients against COVID-19 and other viral infections by diagnosing and treating hormone deficiencies in their patients in time.

Additional Information

You can learn more on hormone and nutritional therapies on **www.hertoghemedicalschool.eu**.

For scientific evidence, you can visit **www.intlhormonesociety.org**; there you will find scientific data and information on hormone research.

For more information you can contact isabel@hertoghe.eu.

CLICK HERE FOR REFERENCES