*Help for aids*

# Updates on DHEA, Dextron Sulphate, DDC and Interferon-gamma

AIDS
U•P•D•A•T•E
• By Sean Hosein •

### SPECIAL REPORT ON EL-10 OR DHEA

DHEA is a hormone produced by humans and other mammals, EL-10 is an artificial version of this hormone. The function of DHEA in the body is not yet clear, but it is known that blood levels of DHEA vary with age. During puberty the amount of DHEA is high but it begins to decline by the age of 20. The Canadian government has announced that EL-10 is to be tested in humans as an anti-AIDS drug but this has yet to happen.

A recent article (*JAMA* 1989;261:1149) has reported that as HIV infection worsens, levels of DHEA fall, reaching their lowest level when AIDS develops. Research indicates that while DHEA does not appear to have a direct anti-viral effect, it can affect the immune system in a number of ways.

When DHEA was given to mice suffering from viral infections, it allowed over 90% of the infected mice to survive, while only 60% of the untreated mice lived. The hormone allowed the animals to produce more antibody making cells and it also raised the levels of a type of white blood cell known as the monocyte. Monocytes eventually turn into macrophages; the main target of HIV. Macrophages play an important role, roving throughout the body destroying invading viruses and other parasites.

Viral infections are thought to result in increased levels of immune suppressing hormones. DHEA may protect the body from the effects of such harmful substances and thus may be of use in treating viral infections.

People with HIV infection often develop various skin disorders ranging from psoriasis to cancer. The skin is known to have a group of resident immune cells that have the T4 receptor which makes them vulnerable to HIV. A recent study of DHEA (*Journal of Medical Virology* 1988;26:301-314) reports that when it was injected into the skin of test animals, its protective effects were greater than when it was given orally. It is possible that the hormone activates the skins's special immune cells. DHEA has been applied to the skin when used to treat psoriasis.

DHEA may also have anti-cancer properties. Women with breast cancer have been found to have low levels of this hormone while mice treated with DHEA were protected against tumour formation. *Cancer Research* 1979;39:1129-1132 and *Carcinogenesis* 1984;5:57-62.

Advantages of DHEA include its low toxicity, its ability to penetrate the blood brain barrier and it can be given by mouth. *Journal of Medical Virology* 1988;26:301-314.

### ANTI-HIV AGENTS
### DDC

In 1985 both DDC and AZT were found to have anti-HIV properties, yet so far only AZT has been licensed for treating HIV infection. In an earlier trial, DDC was found to cause some nerve damage when given in high doses. Now results of new trials with this drug in 61 people with ARC or AIDS have been published; DDC, even in reduced doses, seems to be able to lower the level of virus production without causing severe and lasting damage to nerves. While some patients experienced side effects, most improved after two months. The levels of T4 cells also increased in the majority of patients and there was a decrease in the incidence of opportunistic infections in those patients receiving a high dose of the drug. The researchers think that a regimen of alternating AZT with DDC; one week with AZT the other with DDC may be a way to avoid the worst of the side effects of both drug. *Annals of Internal Medicine* 1989;110:189-194.

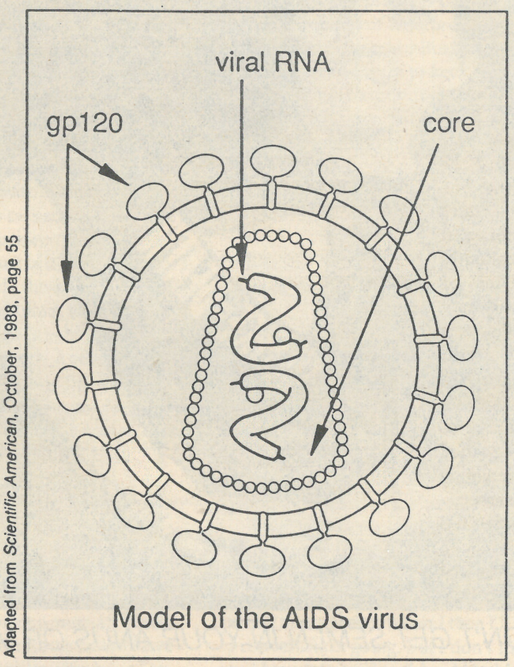
### Dextran Sulphate

Dextran sulphate, a substance with potent anti-HIV effects, was recently used in an 8 week trial in a group of 34 patients with HIV infection. The drug was given orally, 3 times per day at a dose of between 900 to 5400 mg per day. The molecular weight of the drug was between 7,000 to 8,000.

The scientists concluded that dextran sulphate did not cause any significant side effects. The drug may have caused half of the patients in the trial to decrease their level of T8 or suppressor cells. Apart from that it did not reduce the level of HIV replication, or levels of the molecule Beta-2-microglobulin; the concentration of which increases as HIV infection worsens. The researchers noted that the substance p24, which is associated with HIV production, could not be detected in the blood of one patient after 16 weeks of taking the drug at a dose of 1800 mg/day. Thus it may be possible that after prolonged treatment with dextran sulphate patients could obtain some benefit. The researchers have planned more trials to see the long term effects of this drug. *Annals of Internal Medicine* 1989;110:183-188.

### Carbovir

Carbovir is a substance similar to AZT. Like AZT, carbovir has shown powerful anti-HIV activity but it also appears to be less toxic. Extensive research is underway with this promising substance although it has not yet reached human trials. The latest results from mice indicate that the drug is not well absorbed when taken by mouth but better absorbtion may occur when it is given with food as happens with a similar antiviral, DDC. *Antimicrobial Agents & Chemotherapy* 1989;33:171-175.




Adapted from *Scientific American*, October, 1988, page 55

Model of the AIDS virus

### AZT

Since 1986 Canadian doctors have been studying the effects of AZT on a group of 72 HIV infected people. While they have yet to issue a final report on their research, a preliminary warning has been issued. They noted that when patients stopped taking AZT for 6 weeks (to allow time for the drug to be removed from their bodies) HIV production increased. The doctors suggested that AZT therapy should not be stopped whenever possible as this can lead to increased HIV replication. *Journal of the American Medical Association* 1989;261:865-866. Similar results have been seen in patients on anti-HIV drugs who stop taking their drugs even for a short time.

### INFECTION FIGHTERS
### Drugs for MAC

People living with AIDS (PLWAs) often become infected with mycobacteria (shortened to MAC), which can cause pneumonia and bone marrow infections. MAC infections are the commonest bacterial infections seen in PLWAs and along with the increase in MAC infections seen in AIDS, it appears that MAC infections are also increasing in non-AIDS cases as well. Standard anti-MAC therapy is often useless and there is a need for new antibiotics. Test tube studies of three drugs amikacin, ciprofloxacin and imipenem showed that of the three, only amikacin had any significant effect; it stopped the bacteria from growing. However, when the three drugs were combined the bacteria were destroyed. Further testing with the animal model continues but no human testing has been planned. *Antimicrobial Agents & Chemotherapy* 1989;33:176-180.

Meanwhile two PLWAs infected by MAC were given interferon-gamma (IFN-gamma) for four weeks as a treatment. The drug appeared to reduce the level of mycobacteria in their blood. These researchers plan to begin a pilot study of IFN-gamma with more patients who have MAC infections. IFN-gamma was obtained from the Biogen corporation, Cambridge, Mass. *Journal of Infectious Diseases* 1989;159:599-600.

### Help for Herpes

Herpes simplex virus (HSV) can cause serious infections in PLWAs. For many years the drug acyclovir (zovirax) has been used to treat such infections but increasingly, more and more cases are being reported where HSV has become resistant to acyclovir. Fortunately the drug foscarnet (made by Astra pharmaceuticals, Toronto), which has potent action against several viruses has proved useful in a case of acyclovir resistant herpes. *New England Journal of Medicine* 1989;320:287-300. A disadvantage of foscarnet is that it must be given intravenously.

### Success against CMV

Cytomegalovirus (CMV) is a virus which can cause a variety of infections in PLWAs some of which can lead to death. A drug which is beginning to see greater use against the virus is ganciclovir. However, ganciclovir does not destroy CMV, it only stops it from making new viruses (replicating). Now interferon-beta (IFN-beta) has potential as a new anti-CMV therapy as test tube studies show it to have potent effects against the virus. A Japanese study of IFN-beta in 8 immune suppressed transplant patients showed that they were able to completely recover from pneumonia caused by CMV. IFN-beta is licensed in Japan for treating skin cancer and hepatitis and is made by Toray industries Inc., Tokyo. *Journal of Medical Virology* 1988;26:363-373.

### Toxo

People with severe HIV infection are at risk for infection by the parasite toxo (toxoplasmosis gondii) which causes meningitis (an inflammation of the tissue covering the brain and spinal cord) and which may result in death. The treatment of choice is amphotericin B, a highly toxic therapy. Now scientists have found that a derivative of amphotericin B called N fru AmB which is less toxic than its parent drug, has immune boosting effects when used in mice. The new drug also retained the antibacterial and antifungal properties of amphotericin B. N fru AmB is made by X-TEC labs in France. *Immunology Letters* 1989;20:63-67.

Another compound with anti-toxo potential is non-toxic MPL (monophosphoryl lipid A) which is derived from a bacterial poison. When given to mice infected with toxo, MPL enhanced their survival. MPL has previously been tested in cancer patients and is made by Ribi ImmunoChem Research Inc, Montana, USA. *Journal of Biological Response Modifiers* 1988;7535-539.

### Thrush

Candida albicans is a yeast which can cause infections in HIV infected people, usually appearing as a white coating on the tongue. A drug with promising anti-candida properties is cilofungin. No clinical trials of this drug have been reported. *Antimicrobial Agents & Chemotherapy* 1988;32:1901-1903.

### CANCER

Interferon-beta (IFN-beta) is showing promise as a possible treatment for KS according to researchers in the USA. There, scientists have been giving patients with KS IFN-beta intravenously three times per week, starting with small doses and increasing the dose to the maximum tolerable amount, which is so far is about 318 million international units. The drug seems to hold the cancer in check and while it does have side effects, patients are able to tolerate them. IFN-beta also seems to prevent the immune system from becoming weaker. Interferon beta is made by Triton Biosciences, California. *Journal of Interferon Research* 1988;8 supplement 1 pg s87.