TreatmentUpdate 17

By Sean Hosein
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I. ANTI-HIV AGENTS

A. AZT: Treatment or prophylaxis?

Is it best to use AZT earlier, or later? As prophylaxis, or as treatment? As early intervention in the asymptomatic stage, or when symptoms of HIV disease appear? We hope that the information and discussion in this issue will help physicians and their patients to formulate their own risk/benefit analysis and to select the best point in the spectrum of HIV disease for the use of this drug.

B. AZT versus THA: results from France look promising for THA

As HIV is known to infect brain cells (**Science** 1990;249:549-553), it is not surprising that in advanced HIV disease, brain damage can occur. In the case of Alzheimer's disease, in which dementia also occurs, researchers suspect that a virus is at the root of the problem, and have used the drug THA (Tetrahydroaminoacridine or Tacrine) in experiments on subjects with Alzheimer's disease with some beneficial effects. Scientists think that THA may also be of use in treating the memory loss and other neurologic complications that occur in some patients with AIDS.

Results of THA trials in France were reported in **Treatment Update #10**, but at that time were based on only 2 months of the trial. The researchers now have released the findings of their 7-month study. The trial, at l'Hôpital Paul Brousse, Villejuif, and l'Hôpital de l'Université Internationale, Paris, involved 62 males and 8 females. Sixty-two subjects had ARC. Forty-five subjects took AZT (either by itself or in combination with THA, and in doses between 600 to 1200 mg/day); 25 subjects took THA (by itself or in combination with AZT, and in doses between 150 to 250 mg/day). Eighteen subjects took only THA, and 19 subjects took only AZT. Subjects took AZT for an average of 27 weeks and THA for an average of 24 weeks.

Seven subjects died in the AZT group, while none died in the THA group, a statistically significant result. Sustained decreases in HIV p24 antigen were seen in the THA group, along

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with sustained increases in the CD4+ (T4) cell count. The incidence of opportunistic infections was greater in those on AZT than in those on THA. **VI International Conference AIDS**, San Francisco, 1990 revised abstract SB 458.

Researchers in England have given THA to 7 subjects (1 AIDS, 6 ARC) whose CD4+ cell count ranged from 150 to 300 cells. THA was given at 25 mg 3 times per day for the first week, and then the dose was doubled to 150 mg/day for the next 12 weeks. No changes in p24 antigen, CD4+ levels, or weight were noted. **VI International Conference AIDS, San Francisco, 1990 abstract SB 457. It is not clear why the results from the UK differ from those from France, but the French trial is known to be** using ultra-pure THA (purified by the Synthese et Recherche company in Anthony, France) and this may account for the difference. In the USA, THA is made by Parke-Davis Pharmaceuticals (Morris Plains, New Jersey), which is said to be seeking "Treatment IND" status (investigational new drug) for the drug from the FDA. In Canada, THA is made by Pharmascience (Montréal) under the brand name Alzyme in 25 mg capsules.

C. *AZT: Cancer Risk?*

Scientists at the National Institutes of Health, Bethesda, Maryland, have been conducting a long-term follow-up of HIV-infected subjects who were among the first users of anti-HIV agents. Their research suggests that this group of subjects appears to have a higher-than-normal incidence of cancer, specifically non-Hodgkin lymphoma (NHL).

Researchers examined the medical records of 55 subjects who had been enrolled in three different anti-HIV drug protocols: (1) AZT alone, (2) AZT with acyclovir and (3) alternating AZT and ddC. At the time of entry into the 3 different trials, subjects had either AIDS or advanced ARC (oral yeast infections and more than 10% weight loss per month), and all subjects had **fewer than 300 CD4+ cells at the beginning of whichever trial they entered. Eight subjects developed NHL and 7 were given treatment with chemotherapy and/or radiation.**

After 3 years of anti-HIV therapy, the entire study group's risk of developing NHL was nearly 50% (46.4%) (and the rate will exceed 50% if more people in this group develop NHL). Most of the subjects who developed lymphoma had had fewer than 100 CD4+ cells for 17.8 months. All of the subjects received anti-HIV therapy for between 13 to 35.5 months. The development of lymphoma may have been a result of the long-term survival of these subjects, combined with their HIV-induced immune suppression.

Although NHL is known to occur in subjects with HIV infection, as an AIDS-defining condition it accounts for only 3% of such cases. The researchers at Bethesda say that the development of NHL may affect the survival of subjects who use anti-HIV agents, but they also suggest that attempts at keeping the CD4+ cell count above 100 cells should be made, perhaps by using AZT or other anti-HIV agents earlier in the course of HIV disease. (For an examination of the risks and perceived benefits of early intervention with AZT, see p. 3-4.)

Researchers at the National Cancer Institute (USA) have been conducting long-term observational studies of HIV-infected subjects. One group of 130 subjects from New York and Washington, followed over a 10-year period, has been found to have an 18% incidence of NHL. **Lancet** 1990;336:248-249. (Cancer trends in the northern industrialized countries suggest **that the incidence of NHL and of many other cancers is rising rapidly in the population as a whole. Lancet** 1990;336:474-481.) In people with HIV infection, the reason for the increase in NHL, as opposed to other forms of cancer, is not fully understood. Perhaps there is a specific virus that takes advantage of the suppressed immune system to trigger the development of cancer. But there is also the distinct possibility that AZT and related drugs promote its development.

Once NHL develops in people with HIV infection, it is usually very difficult to treat and affected people have short life expectancies, so researchers say that it is important to find the lowest effective dose of drugs such as AZT. In the USA, it is estimated that in 1990, 36,000 people will develop NHL, and 18,000 people will die as a result of complications associated **with it. Annals of Internal Medicine 1990;113:276-282.**

Including agents with anti-cancer potential, such as beta-carotene, in clinical trials might benefit people at risk of developing NHL. For a review of the properties of beta carotene and a pilot study in HIV-infected people, see **TreatmentUpdate #7** and **Federation of American Societies for Experimental Biology Journal** 1989;3:1927-1932. Beta carotene is sold in health food stores.

D. *AZT: viral resistance has serious implications for early intervention*

As larger numbers of HIV-infected people have begun to use AZT, limits to its usefulness have become more apparent. One of the major factors affecting its efficacy is the development of strains of HIV which are resistant to doses of AZT that can be tolerated by humans.

At the University of California (San Diego), research on AZT resistance has been taking place for the past 2 years; scientists have found that virus from 42 HIV-infected subjects who had no prior exposure to AZT was susceptible to inhibition by AZT. Virus taken from 31 subjects with AIDS or advanced ARC developed resistance more quickly than virus taken from people with earlier-stage HIV disease. This was a statistically significant difference. After 1 year of AZT administration, nearly 90% of people with late-stage HIV disease (AIDS/advanced ARC) had HIV which was resistant to AZT. This was contrasted with the group who had earlier-stage HIV disease, in which only 31% of the subjects were resistant to the virus. A lower CD4+ cell count was predictive of the chance of resistant

strains of HIV emerging with 1 year of AZT use. People with CD4+ counts of less than 100 cells had an 89% chance, with CD4+ cells in the range of 100-400 a 41% chance, and with more than 400 cells, a 27% chance of developing resistant strains of HIV within 1 year. The emergence of AZT-resistant HIV appeared sooner in subjects who were on very high-dose AZT (1200 to 1500 mg/day) than on lower doses (500 to 600 mg/day). **Journal of Acquired Immune Deficiency Syndromes** 1990;3(8):743- 746.

One of the problems with this study is that the laboratory techniques used to grow HIV-infected lymphocytes could have resulted in the underestimation of the number of resistant viruses. More sophisticated analytic procedures will be required before the phenomenon of resistance can be properly studied. **Perhaps such a system is now here—at the VI International Conference on AIDS, San Francisco, results of a new testing system (assay) for studying AZT resistance were announced by Dr. David Ho.**

A study using this HIV-resistance assay included 15 HIV-infected subjects (3 asymptomatics, 5 ARC and 7 AIDS), 10 of whom used AZT. Two of the untreated subjects had AZT-resistant strains of HIV. All 10 subjects using AZT had strains resistant to it (6 subjects had strains deemed "highly resistant"). Four of 6 subjects with rapid disease progression had highly AZT-resistant virus. In some subjects nearly all the virus in their blood was resistant to AZT. **VI International Conference AIDS**, San Francisco, 1990 abstract SB 81.

In a study of 9 subjects, conducted by the Centres for Disease Control and Burroughs-Wellcome, HIV-resistance developed after 9 months of AZT use. **VI International Conference AIDS**, San Francisco, 1990 abstract SB 86.

E. *AZT: Early Intervention in Canada & the USA results in no difference in disease progression*

Canadian physicians/investigators have conducted a long-term study of AZT intervention in subjects with early-stage HIV disease. All 74 subjects were asymptomatic and were matched to a group of similar controls who did not receive AZT. The 74 subjects were given a schedule of increasing **doses of AZT: 600 mg/day for 10 weeks, 900 mg/day for 9 weeks, and then 1200 mg/day for 9 weeks. This was followed by a "wash-out" period of 6 weeks, after which subjects were** given either 1200 mg/day or the next highest dose of AZT they were able to tolerate. The difference in rates of disease progression between the two groups was not statistically significant. **VI International Conference AIDS**, San Francisco 1990 oral presentation THB 18.

To determine the effect of AZT on the "functional status and well-being" of subjects with early ARC, researchers at the University of California conducted a study of 71 subjects in a placebo-controlled trial of AZT (1200 mg/day). Their results show that after 6 months, most scores on function and quality of health had improved for the placebo group while some scores had declined for the experimental arm (AZT group) compared to values at study entry. These differences were statistically significant. Over the following 6 months, subjects on AZT declined less than those on placebo. By the 12th month, values for both groups were similar to pre-trial scores. **VI International Conference AIDS**, San Francisco, 1990 oral presentation THB 19.

Another clinical trial of AZT in early ARC was conducted in Denver, with the collaboration of the Burroughs-Wellcome Co. This double-blind, placebo-controlled trial enrolled 218 subjects and used 800 mg/day AZT in the experimental arm. All subjects had symptoms of ARC and their CD4+ cell counts **were between 200 to 500. Initially, the group receiving AZT demonstrated increases in the CD4+ cell count, but after the sixth month of the study, the differences in CD4+ cell counts were not statistically significant. There was no difference in disease progression over an average of 9 months. VI International Conference AIDS**, San Francisco, 1990 poster SB 422.

F. *AZT: Early intervention is problematic*

The recommendations of the Food and Drug Administration (FDA) and the National Institutes of Allergy and Infectious Disease (NIAID) to use AZT in symptom-free HIV-infected people with CD4+ cell counts less than 500 are based on results obtained from the American trial ACTG 019 **American Journal of Medicine** 1990;89:335-344. This trial was a double-blind, placebo-controlled study of AZT with three arms: high-dose (1500 mg/day), low-dose (500 mg/day), and placebo. Statistical analyses were performed on 1338 subjects who, at study entry, had less than 500 CD4+ cells. The reasons why 500 CD4+ cells was chosen as a criteria for entering the trial are unclear. Moreover, subjects were enrolled in the trial on the basis of just one CD4+ cell count.

Subjects were followed for an average of 55 weeks. Eleven subjects in the low-dose group developed AIDS, in comparison to 14 in the high-dose group and 33 in the placebo group, statistically significant results. More subjects in the high-dose group developed anemia than in the low-dose group. There **were some problems with this trial. Nine percent of subjects in the placebo arm appeared to be using AZT. It can be argued that the trial was not double-blind as clinicians had access to the** MCV (mean corpuscular volume) values which are known to rise with AZT use. Despite these problems, it is likely that for every 100 symptom-free patients who take the drug, 4 will not experience disease progression for 55 weeks (the length of this study). For more information on this trial see **TreatmentUpdate #14.**

The assumptions which underpin the NIAID and FDA recommendations on AZT use were recently questioned in an editorial in the journal **Lancet.** 1990;1:821-822. They have been

further scrutinized in new research which raises questions about the use of AZT in asymptomatics. Below, we outline the major assumptions and summarize the critical responses which they have received.

• It is assumed that the benefit received by 4% of subjects on AZT—delayed progression to AIDS of 1 to 2 years—will be extended to the other 96%, should they continue to take the drug for several years. However, research on "time-to-disease progression" graphs suggests that this is unlikely. What is likely is that AZT delays progression for about 7 months, the limited time a result of the emergence of resistant strains.

• It is assumed that the course of the disease is irreversible, so intervention should be made as early as possible. However, AZT, if given after symptoms appear, can in fact reverse the course of disease and thereby render the person symptom-free (for a limited period of time).

• It is assumed that in low-dose early intervention, low toxicity of AZT will be maintained. However, the toxicity of AZT may be cumulative.

• It is assumed by patients who take AZT during the asymptomatic stage of their infection that although AZT will not be ultimately sufficient, some other anti-HIV agent will become available later, before their disease progresses. However, this may not necessarily be the case. There is little data on the clinical course of subjects who have experienced disease progression despite use of AZT.

• It is assumed that the only way to use AZT is by itself. So the question becomes at which stage of the disease AZT, by itself, is most effective. However, studies of cancer chemotherapy suggest that combination chemotherapy is often more effective than single-agent therapies in dealing with resistant tumours. Subjects who use AZT now may be denying themselves the opportunity of using other agents, or combinations of AZT and other anti-HIV drugs, later on in their disease. **Lancet** 1990;1:821-822.

Indeed, research presented at the VI International Conference AIDS, San Francisco, suggests that subjects who previously used AZT did not benefit as much from other therapies, as compared to subjects who had never taken AZT or used it only for a short time. Such therapies include hypericin, ddI and AzdU (Azidouridine). **VI Intl. Conf. AIDS**, San Francisco, 1990 publication 2061 (Hypericin), abstracts SB 471 (ddI) and THB 83 (Azidouridine).

• It is assumed, by among others, Burroughs-Wellcome, the manufacturer of AZT, that resistance to AZT develops slowly in asymptomatic subjects because the virus is thought to replicate at a slower rate than it does in subjects with AIDS/advanced ARC. However, Dr. David Ho has conducted studies which suggest that "resistance develops rapidly, even at lower doses" of AZT. This is something which should be taken into account before people are given AZT, according to Dr. Ho.

On one hand, the NIAID is recommending that AZT be used in early HIV disease because of the apparent short-term benefit seen in the American trials ACTG 016 and 019. On the other hand, the 3-year Canadian study of AZT in early HIV infection has found "no difference in clinical outcome." According to Dr. Ho, resistance to AZT might explain the different results of the Canadian study and the 1-year American trials. "If you start patients on AZT early, they have its benefit early and you see a slowing of disease progression. But once they progress, they no longer have the benefit of AZT because of resistance, and their course from that point on would be more rapid. Early versus late treatment may be very much the same. We won't know until we do large studies comparing them." Dr. Ho does tell his asymptomatic patients about this dilemma. He says that about half of them choose AZT.

At a recent symposium on the use of AZT in early HIV disease, the NIAID refused to hear a preliminary analysis from the large, ongoing Department of Veterans Affairs study on early intervention with AZT. This study, which has been under way for 2 years, has so far found no "statistically significant difference" in progression to AIDS among asymptomatic subjects (who had between 200 to 500 CD4+ cells) on placebo or AZT. The Anglo-French MRC/Concorde 1 study is attempting a similar trial. In October 1990 they will perform an interim statistical analysis to determine if there is any benefit from AZT in early HIV infection. **Journal of the American Medical Association** 1990;263:1605 and 1990;264:670. Indeed, according to Canadian researchers, ACTG 016 and 019 do not provide data indicating if the benefits of AZT are "additive in terms of overall survival and quality of life." **Annals of Internal Medicine** 1990;112(10):721-722.

G. *AZT: Ethical problems for ddI/AZT trials*

The results from clinical trials/research discussed above raise ethical questions about the comparative AZT/ddI trials taking place in Canada and the USA. The comparative trials have, as a control arm, subjects who receive AZT. Comparative trials are touted as an ethically advanced, non-placebo form of clinical trial; as subjects who do not receive the experimental drug at least get a drug which is seen as a standard of care. Having subjects receive a standard of care reduces their risk of participating in a trial. However, the status of AZT as a standard of care is being increasingly questioned. The limited duration of its beneficial effects during symptomatic disease, its apparent lack of efficacy in ultimately affecting disease progression, and its possible potential for enhancing the subsequent development of lymphoma raise serious questions about its status as a standard of care. If AZT is not a standard of care, and may in fact pose a risk to subjects, then it cannot ethically operate as a comparative control.

It would be very easy for subjects enrolled in the comparative AZT/ddI trial to infer the nature of their drug without resorting

to having it analyzed. For instance, MCV (mean corpuscular volume) blood values greater than 95 would suggest that AZT were being administered. Similarly, should a subject choose to have his or her uric acid levels measured, higher-than-normal levels might suggest that ddI was being metabolized.

II. IMMUNE BOOSTERS

A. *The Thymus gland and HIV*

The thymus gland, located in the chest, plays an important role in the development of certain white blood cells, helping them to mature into various types of T-cells. The gland also acts as a storage centre for T-cells, and releases hormones which affect the immune system. Because the immune deficiency seen in AIDS is similar to that seen in children with rare thymus disorders, early in the 1980s researchers began to investigate the functioning of the thymus gland in people with HIV infection. French researchers have found that subjects with advanced HIV infection have low levels of a thymic hormone called thymulin. Also, American and Danish researchers have found abnormalities in thymic hormone production in subjects who were HIV-infected but who did not have AIDS. Initially, they thought that they found elevated levels of the thymic hormone thymosin-alpha$_1$ in their subjects. Further investigation revealed that these subjects had high levels of an inner or core protein of HIV (called p17) in their blood. Parts of p17 resemble thymosin-alpha$_1$ and their detection systems treated the two substances as one. Actual levels of thymosin-alpha$_1$ are decreased in subjects with HIV infection.

At autopsy, the thymus glands from people with AIDS are often reduced in size and appear to be damaged. Some of this damage may be due to direct infection by HIV. However, there may be another mechanism whereby HIV infection results in thymus damage. As previously mentioned, part of HIV, p17, resembles part of the crucial thymic hormone thymosin-alpha$_1$. When antibodies are produced against this HIV product, it is likely that they attack not only HIV but also thymosin-alpha$_1$ and possibly the thymus gland as well. Indeed, at autopsy, the thymus glands from people with HIV infection have the appearance of glands which have come under severe attack by antibodies. **Science** 1986;232:1135- 1137. Further work on the p17/thymosin connection has resulted in the development of an anti-HIV vaccine called HGP-30. The implications of therapy for HIV disease using HGP-30 are discussed in the section on vaccines in this issue of **TreatmentUpdate**. For more information on possible thymic hormone replacement therapy in HIV infection, read the following articles on thymopentin and also amino acids.

B. *Thymopentin may delay progression to AIDS*

Various thymic hormones have been used to try to restore the depressed immune function seen in people with HIV infection. In many cases, they have been used for short periods of time only, with little or no success. The thymic hormone which appears to have the greatest potential for treating HIV disease is thymopentin, a synthetic version of the active portion of the thymic hormone thymulin. Several controlled clinical trials of thymopentin in HIV disease have been undertaken.

Researchers at the University of Bari, Italy, have conducted a placebo-controlled clinical trial of thymopentin in 41 subjects with HIV infection. All subjects had persistently swollen lymph glands as well as some symptoms of ARC such as night sweats, diarrhea, and weight loss. Subjects had approximately 300 CD4+ (T4) cells and 600 CD8+ (T8) cells at the beginning of the trial. Twenty-nine subjects were in the experimental arm of the trial and received 50 mg of thymopentin by injection under the skin three times per week for about 1 year.

Just over half of the subjects in the experimental arm of the trial had an increase in their absolute CD4+ cell count, which rose to just over 500 by the fourth month. This increase was sustained for the 12-month period of the trial and was statistically significant. The level of CD8+ cells decreased in the thymopentin group. Subjects in this group also appeared to have a more normal level of antibody production. Nine subjects who received thymopentin reported a disappearance of such symptoms as diarrhea, night sweats, and weight loss. Two subjects also had a reduction in the size of their lymph glands. Four subjects in the placebo group of the trial appeared to have worsening symptoms. No subject in either arm of the trial developed AIDS at the end of the study period. **Journal of Laboratory and Clinical Medicine** 1989;113:139-144.

More recently, trials of thymopentin took place in Cleveland and San Francisco, using HIV-infected subjects, with or without symptoms. In the San Francisco study, 47 subjects were assigned to the experimental arm and received thymopentin (50 mg injections under the skin, 3 times per week for six months), while 44 subjects were placed in the control arm and received a placebo. No subject who received thymopentin progressed from his/her stage of HIV disease. This is in contrast to the placebo group, in which 4 subjects worsened (2 AIDS, 2 ARC), a statistically significant result. Asymptomatic subjects who received thymopentin maintained their CD4+ cell counts, % CD4+ cells, and CD4/CD8 ratios, while all these values in the placebo group declined. The level of HIV p24 antigen remained stable in the experimental arm but rose by 36% in the placebo group. In approximately 25% of the subjects who received thymopentin, the level of Beta$_2$-microglobulin returned to normal. In contrast, only 3% of subjects in the placebo group had a normalization of Beta$_2$-microglobulin levels. No side effects as a result of thymopentin administration were noted. **VI International Conference AIDS**, San Francisco, 1990 abstract SB 485.

In a smaller trial, conducted to assess the long-term effects of thymopentin, favourable changes were seen in markers of HIV infection (CD4+, Beta$_2$-microglobulin, and p24 antigen), which

were sustained over a one-year period of thymopentin administration (dosage as above). In the placebo group, 1 subject developed AIDS and 2 developed ARC, compared with 1 subject who developed AIDS while on thymopentin. As the trial had only a small number of subjects, these differences were not statistically significant. **VI International Conference AIDS**, San Francisco, 1990 abstract SB 484. The thymopentin used in these two studies was provided by the Immunobiology Research Institute, Annadale, New Jersey. Another recent trial of thymopentin in subjects with kidney **failure showed that the hormone was able to increase the %CD4 cells. (Although these subjects did not have HIV** infection, such people often have impaired immune systems as a result of kidney failure.) **Current Therapeutic Research** 1990;47(5):911-915.

C. Increasing thymic hormone release through amino acids

Until thymopentin becomes more widely available, doctors may wish to find more accessible ways of raising the level of their patients' output of thymic hormones. Italian researchers have published the results of their successful attempts at raising **thymic hormone levels in subjects with cancer. People with cancer, like those with AIDS, have altered and abnormal immune functioning. While this may be a result, in part, of the** immune-suppressing effect of chemotherapy given to such people, subjects with cancer who have not been given chemotherapy have also been found to have suppressed immune systems. Research suggests that this immune suppression is a result of substances released by tumours. People with cancer have also been found to have reduced levels of the thymic hormone thymulin, regardless of their age or the type of tumour. Reduced levels of thymulin have also been found in people with HIV infection.

Italian researchers have been able to raise the level of thymulin in subjects with cancer by giving them a combination of the **amino acids arginine and lysine. Arginine is known to cause the brain to release growth hormone (GH). While it does not** cause additional growth in adults, GH is thought to act on the thymus gland, causing it to release thymic hormones. In the Italian trial, 10 subjects with cancer, who did not receive chemotherapy, were given 1 gram arginine with 1 gram lysine orally, 4 times per day for 30 days. Statistically significant increases occurred in the total T-cell count as well as in the CD4+ (T4) cell count. Statistically significant increases were also seen in the levels of GH produced by these subjects. **International Journal of Immunopharmacology** 1990;12(4):365-371. **The amino acid preparation used in this study (Lysargin) is made by Baldacci SpA (Italy). Capsules containing the amino acids arginine/lysine can be purchased from health food stores in the USA. Some body-builders are known to use GH-releasing amino acids as part of their training programme. Such** athletes often take supplements of arginine on an empty stomach in order to maximize the eventual penetration of the arginine into the brain. (Amino acids compete for entry into the brain. After a meal, there is an abundance of many amino acids. Taking arginine on an empty stomach several hours before a meal ensures that high concentrations of it accumulate in the blood, and increases the chances of its entering the brain.) Anecdotal reports suggest that, by themselves, high concentrations of arginine can lead to an increase in herpes virus replication. Lysine is thought to inhibit the replication of such viruses and that may be the reason for its inclusion in the formula used in Italy. **In Canada, health food stores are prohibited from selling capsules containing single amino acid concentrates. The safety of using GH-releasing amino acids over the** long term in HIV-infected subjects is unknown.

Growth hormone may also have other benefits as well. Subjects on long-term use of high-dose (cortico) steroids, such as prednisone, often suffer from protein loss and impaired wound healing, and so are at increased risk of infections. Researchers at the Mayo Clinic (Rochester, Minnesota) have found that injections of GH (0.1 mg/kg/day) have been able to reverse the protein loss in subjects receiving steroids. **Journal of Clinical Investigation** 1990;86:256- 272. The use of GH in elderly subjects has also been shown to cause increases in weight. **Thus, there is the possibility that one day GH may be used in clinical trials to arrest the weight loss seen in the HIV wasting syndrome.**

As yet, the long-term effects of giving humans supplemental GH are unknown and its effects on subjects with HIV infection have yet to be studied. In the USA, synthetic human GH is made by Eli Lilly & Company, Wayne, New Jersey and also by Genentech Inc., San Francisco, California.

III. VACCINES

A. HGP-30: Vaccines as therapy

One of the reasons HIV may be able to subvert the body's immune system is that different components of HIV resemble various components of the body; parts of the virus are thought to be similar to certain hormones, antibodies, and growth factors. As antibodies are produced against HIV, they may also "cross-react," or attack the components of the body which resembles HIV. Some scientists think that if an anti-HIV vaccine is given to people, the anti-HIV antibodies produced as a result of the vaccination might also attack the body. **Medical Hypotheses** 1990;31:155-156.

However, in 2-year trials of the Salk HIV vaccine, most of the **subjects do not appear to be suffering any ill effects as a result of having been vaccinated. In most subjects, the vaccine appears to have halted the further decline of their immune** systems. In the next issue of **TreatmentUpdate** we will report on progress in vaccine development and testing, including the Salk HIV vaccine, as well as on research taking place in

England, France, and Zaire.

Researchers at the National Cancer Institute and George Washington University have developed a synthetic molecule—called HGP-30— which mimics p17 and p24, the core proteins of HIV. Antibodies produced against HGP-30 attack p17 and p24 as well. In experiments with rabbits immunized with HGP-30, high levels of antibodies against HGP-30 do not appear to cause any ill effects. In laboratory experiments, these antibodies effectively neutralize HIV. Tests with 19 non-HIV-infected human volunteers show that immunization with HGP-30 causes the production of antibodies to p17 and/or p24. The vaccine was not associated with any toxicity. Another advantage of this vaccine is that it appears to activate CD8+ (T8+) cells. These cells play an important role in controlling HIV infection, and Norwegian researchers have found that CD8+ cells produce a novel anti-viral substance. It is thought that this vaccine may boost the levels of antibodies to the core proteins in HIV-infected people and may thus serve as a form of therapy, delaying progression to AIDS. Plans are under way in California to implement phase I trials of HGP-30 in HIV-infected subjects later this year. VI International Conference AIDS, San Francisco, 1990 oral presentation SA 76.

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P.O. Box 190712
Dallas, TX
US, 75219

Being Alive
4222 Santa Monica Blvd
Los Angeles, CA
US, 90029

BETA (Bulletin of Experimental Treatments for AIDS)
San Francisco AIDS Foundation
P.O. Box 6182
San Francisco, CA
US, 94101

CDC AIDS Weekly/DAITS
P. O. Box 5528
Atlanta, GA
US, 30307

Critical Path AIDS Project
2062 Lombard Street
Philadelphia, PA
US, 19146

Info-Traitements
Comité des personnes atteintes du VIH du Québec
3600, avenue de l'Hôtel-de-Ville
Montréal, Québec H2X 3B6

National AIDS Manual
1 Saltoun Road
London, England
SW2 1EN

Notes from the Underground
PWA Health Group
31 West 26th Street, 4th Floor
New York, New York
US, 10010

Positive Immunity
13579 Summit Avenue
Blue Ridge Summit, PA
US, 17214

Project Inform
347 Dolores Street, Suite 301
San Francisco, CA
US, 94110

PWA Coalition Newsline
PWA Coalition, Inc.
31 West 26th Street
New York, NY
US, 10010

Sida 90
ARCAT-SIDA--CIVIS
57, rue Saint-Louis-en-l'Isle
75004 Paris, France

Test Positive Aware
1340 West Irving Park Rd., Box 259
Chicago, IL
US, 60613

The Body Positive
Body Positive of New York
208 West 13th Street
New York, NY
US, 10011,

Treatment Issues
Gay Men's Health Crisis
129 West 20th Street
New York, New York
US, 10011

TreatmentUpdate / TraitementSida
~~Sean Hosein, Editor~~
AIDS ACTION NOW! TIE Project
324-517 College St.
Toronto, Ontario
Canada M6G 1A8

Up Front Drug Information
Body Positive Resource Centre
5701 Biscayne Blvd., Suite 602
Miami, FL
US, 33137

Vancouver PWA Society Newsletter
1447 Hornby Street
Vancouver, BC
Canada V6Z 1A8

Washington HIV News
Whitman-Walker Clinic
1407 "S" Street NW
Washington, DC
US, 20009