

Wceim Pharma

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INTEROFFICE CORRESPONDENCE

DATE: July 27, 1983
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SUBJECT: T4/T8 RATIOS IN HAEMOPHILIACS

Attached a report from a recent meeting in San Diego, U.S.A.

Comments

- I. The severity of the T4/T8 imbalance is related to the number of doses of factor VIII concentrate administered. The Dutch Red Cross has not studied this parameter (Breederveld, XVth World Federation of Hemophilia Congress, Stockholm 1983, Abstract No. 264).
- II. "We have not shown that factor VIII concentrate is related to AIDS - only that factor VIII therapy is related to low helper/suppressor ratios."
- III. "Hemophiliacs who develop AIDS have only two obvious risk factors in common with other AIDS groups: that of contracting hepatitis B and that of massive exposure to foreign antigens". How is the T4/T8 ratio in patients who have been treated with intermediate purity factor VIII concentrates as compared to Armour's high purity Factorate?

Regards

GRO-C

Dr. Hans Kjellman

Reference

Hager T JAMA 1983; 249: 3277

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But note that
it also states that
1981 before recipients
are highly correlated
revised studies.

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What is role of Factor VIII therapy in inducing helper suppressor ratio reversals in hemophiliacs?

As others have already shown, hemophiliacs receiving clotting factor VIII therapy may develop an imbalance in T lymphocytes similar to that found in patients with acquired immunodeficiency syndrome (AIDS). According to a new report delivered at the recent meeting of the American Society of Clinical Oncology in San Diego, the severity of this T-cell imbalance is related to the number of doses of factor VIII concentrate received.

The unexpected incidence of AIDS in hemophiliacs—14 cases so far confirmed by the Centers for Disease Control, Atlanta—led James J. Goedert, MD, of the Investigative Epidemiology Branch, National Cancer Institute (NCI), Bethesda, Md, to hypothesize that a transmissible agent in factor VIII concentrates may somehow be involved. To investigate this, he looked at one of the apparent markers for AIDS—an abnormal ratio of helper to suppressor T lymphocytes. In normal blood, the ratio of helper to suppressor cells is about 2:1. In most AIDS victims, however, this proportion is reversed; a decrease in helper and an increase in suppressor cells can lower the ratio to as little as 0.2.

Goedert and co-workers at NCI and the Naval Medical Research Institute, Bethesda, examined the treatment files of 44 patients with severe hemophilia—24 with hemophilia A and 10 with hemophilia B—who were registered at the Comprehensive Regional Hemophilia Center in Hershey, Pa. Thirty of the hemophilia A patients received regular therapy with clotting factor VIII, seven hemophilia B patients regularly received factor IX, and seven received no clotting factor. The computerized patient files allowed researchers to pinpoint the precise doses, brands, and batches of clotting factor involved and the dates of treatment received by specific patients.

One of the 44 patients was an admitted homosexual. Another three had lymphadenopathy, considered a possible prodrome of AIDS.

The investigators found that patients receiving factor VIII therapy had significantly lower helper/suppressor cell ratios than factor IX recipients or patients who had never been treated with either clotting factor. This effect seemed to be dose dependent: In general, patients receiving more than 556 vials of factor VIII during the course of the study had the lowest helper/suppressor ratios. Factor IX recipients did not have altered ratios.

It also appears that specific batches of factor VIII—especially those produced in 1981—are more highly correlated with lower helper/suppressor cell ratios. Additional studies to confirm this observation are in progress.

Goedert warns that this preliminary study should be interpreted with caution since the number of patients is small and clotting factor use alone does not account for all variations in helper/suppressor ratios. For example, to a lesser degree, patient age was also correlated—the older the patient, the higher the helper/suppressor ratio. Goedert also found that children who received factor VIII in the upper half of the dose range had an average helper/suppressor ratio of 0.97, while adults receiving factor VIII in the upper half of the dose range had an average ratio of 1.12. And, he emphasizes, "we have not shown that factor VIII concentrate is related to AIDS—only that factor VIII therapy is related to low helper/suppressor ratios."

Still, the study gives researchers more leads in their search for an agent of AIDS transmission. "Hemophiliacs who develop AIDS have only two obvious risk factors in common with other AIDS groups: that of contracting hepatitis B and that of massive exposure to foreign antigens," says Goedert. "Both of these risk factors are associated with clotting factor concentrates, making them plausible vehicles for an AIDS-type immunosuppressive factor," he concludes.—by TOM HAGER