Alpha

WINTER 1982 VOL. 4, NO. 2

HEMOPHILIA

A QUARTERLY NEWSLETTER DEVOTED TO HEMOPHILIA LETTER

Alpha Moves to Protect Hemophiliacs Against Risk of AIDS

Addressing the current concern over Acquired Immune Deficiency Syndrome (AIDS), the National Hemophilia Foundation has recommended that existing treatment methods for hemophilic patients continue, since it is not yet clear what is causing AIDS. Currently engaged in a nationwide surveillance study with the Centers for Disease Control (CDC) to help clarify whether the spread of AIDS is related to blood product use, the Foundation also recommended that elective surgery be delayed and that, as before, cryoprecipitate be used for newly diagnosed patients, patients with mild hemophilia, newborns and children under 4. With fewer than one percent of AIDS cases having occurred in hemophiliacs, experts in the treatment of hemophilia agree that the risk of contracting hepatitis remains the greater threat to these patients.

Alpha Therapeutic Corporation has moved quickly to protect hemophilic patients by excluding plasma donors who may be potential carriers of AIDS. "So long as there is any question about the involvement of blood products, Alpha is taking all possible steps to reduce the potential risk for the hemophiliac receiving our factor VIII and factor IX concentrates," said Dr. Clyde McAuley, Alpha's medical director.

Alpha's new donor screening and education program seeks to eliminate plasma from any individual considered at high risk for transmitting AIDS, specifically male homosexuals, IV drug users and Haitians. Alpha has always checked potential donors for fever, weight loss and other physical signs which may be associated with AIDS. The Alpha screening program provides the prospective donor with background information on AIDS, the severity of the disease and a description of the high-risk groups. Then the donor is asked if he belongs to any of the high-risk groups. If the donor answers yes, he will be excluded from donating plasma for use in the manufacture of factor VIII and factor IX concentrates. Alpha is requiring all its suppliers of plasma to apply the same donor screening procedure. Further, Alpha does not operate donor centers in prisons, which have a large high-risk population, nor does Alpha purchase plasma from prisons.

"Thus," said Dr. McAuley, "since there is no known laboratory test that will identify a potentially infectious individual, we have made every effort to eliminate donors who might have AIDS, through a program of education and asking potential donors if they fall into any of the high risk groups."

At the end of 1982, more than 800 cases of AIDS had been reported, with the vast majority appearing in male homosexuals. The disease seems to disrupt the body's immune system, decreasing a patient's ability to fight off disease; thus, some infection-causing organisms which are not a particular threat to persons with intact immune systems can become life-threatening in persons with AIDS. In the later stages of the disease, some patients develop Kaposi's sarcoma, a rapidly advancing cancer.

A Message from your Editor...

Winter is here, the excitement of the holiday season is over, and it's time to plug along until spring comes. From the reports we have had from various summer camps, it sounds like a lot of hemophilic patients had a lot of fun over the summer. We heard about one very interesting camp in New Zealand, not just for the boys but also for the parents. Once they all get to camp, however, they are separated; while the boys are off with the counselors enjoying life at camp, the parents get counseling by staff. The point is to break the parents of the overprotection syndrome many of them fall into. Counselors stress it is better for the boys to do what all boys want to do, and in so doing learn to set their own limitations, than to have restraints imposed on them that they may later rebel against. Physical hurt to a child may be less of a problem than psychologic damage to an adult who has not been allowed to establish his own guidelines, limitations and value system. We can only imagine that boys and parents both return home from camp having learned a great deal about life.

We at Alpha have something new for hemophilic patients – our Profilate® Antihemophilic Factor (Human) is now a purer product. We think this product is ideal to meet the needs of today's hemophilic patient – a patient who is active and self-reliant, eager to participate in life, meeting challenges and caring for himself. He needs a high-purity, low-fibrinogen factor VIII concentrate, with no extraneous protein. He doesn't have time for troublesome allergic reactions or bleeding episodes that resolve slowly.

Thanks to a new manufacturing process, fibrinogen and total protein have been significantly reduced. This makes Profilate a cleaner, clearer product. Low fibrinogen and low total protein mean more than purity – they also mean higher factor VIII activity, with increased specific activity per ml and per unit. That helps resolve bleeding episodes more quickly, with lower volume infusions. (Please see prescribing information on page 4.)

Profilate is also the only product supplied with a 40-micron filter – a filter that's small enough to filter out microaggregates, which increases the safety factor. And big enough to permit free flow without clogging. The filter simplifies concentrate administration and there is no loss of factor VIII activity following filtration.

Don't forget the XVth World Federation of Hemophilia Congress, to be held in Stockholm, Sweden, June 27 to July 1, 1983. For more information, write to

XVth World Federation of Hemophilia Congress
Stockholm Convention Bureau
JAKOBS Torg 3
S-11152, Stockholm, Sweden

We hope to have some reports from the Congress for you in a future issue. In the meantime, if you have any questions or comments about the newsletter or Alpha Therapeutic Corporation, please call at 800-421-0008 or (213) 225-2221 collect and ask for A.J. Winkelman.

Sincerely,
ALPHA THERAPEUTIC CORPORATION

GRO-C

A.J. Winkelman
Director of Marketing, Protein Therapeutics and Lipids

HEMOPHILIA LETTER is published periodically for physicians and other health-care professionals involved in the management of hemophilic patients, as a service of Alpha Therapeutic Corporation. All inquiries should be addressed to Editor, BGM Publications, 145 North Robertson Blvd., Beverly Hills, CA 90211 USA.

NSAIDs Successfully Relieve Pain of Hemarthroses

P Thomas, B Hepburn, HC Kim and P Saidi: Nonsteroidal Anti-Inflammatory Drugs in the Treatment of Hemophilic Arthropathy Am J Hematol *12:131-137, 1982.*

Because there are few suitable anti-inflammatory analgesics for hemophilic patients, it has long been difficult to relieve the pain of arthropathy. In general, such patients should avoid nonsteroidal anti-inflammatory drugs (NSAIDs) which can adversely affect platelet function and hemostasis.

Researchers at Rutgers sought to determine whether ibuprofen and choline magnesium trisalicylate (CMT) could safely be used for the pain of chronic hemophilic arthropathy. Eight hemophilic men participated in the study, seven of whom were on home-care infusion programs. Six suffered severe factor VIII deficiency, one had moderate factor VIII deficiency and one had moderate factor IX deficiency. All had x-ray and clinical evidence of severe hemophilic arthropathy and all took analgesics for pain.

CMT or matched placebo was randomly assigned at the beginning of the study; CMT placebo crossover occurred at six weeks. The men took two tablets twice daily. At 12 weeks, administration of ibuprofen or matched placebo was instituted. Crossover occurred six weeks later. Subjects took one tablet four times a day. They kept a record of bleeding episodes and infusions during each six-week interval.

Investigators obtained complete joint evaluations, bleeding times, platelet counts, platelet aggregation studies and salicylate levels. Patients answered a questionnaire about side effects at weeks one, three and six. They gave a subjective assessment of pain relief by answering questions regarding joint pain during and between bleeding episodes, and regarding joint stiffness.

Well Tolerated and Helpful

Over the two six-week periods, subjects took NSAIDs at regular therapeutic doses with no increase in clinically significant bleeding or increase in factor infusion. Seven patients completed the CMT trial and six completed the ibuprofen trial. Patients' subjective impressions of pain relief suggest the drugs did relieve pain and stiffness between bleeding episodes.

Investigators found no increase in frequency or severity in intra-articular bleeding during NSAID therapy. They found results of joint examinations changed little over the study period and changes in range of motion and degree of synovitis seemed related only to episodes of recent bleeding. They noted too that changes in joint swelling were invariably related to recent hemorrhage.

Patients tolerated both CMT and ibuprofen well with no significant gastrointestinal bleeding or distress. No patient showed a consistently abnormal bleeding time. No statistically significant difference between bleeding times occurred during the drug and placebo intervals, nor did platelet aggregation during drug trials significantly differ from aggregation in placebo trials. There was no correlation between results of platelet aggregation studies and bleeding times. The drugs provided little relief from the pain of acute hemarthroses. Investigators did not notice any anti-inflammatory effect of the drugs objectively.

> "...ability to better distinguish causes of different types of pain with NSAID therapy might enable patients to avoid inappropriate factor infusions when they mistake pain of chronic arthritis for a bleeding episode."

Although the number of subjects was too small to compare the efficacy of CMT and ibuprofen, five patients chose to remain on one of the two drugs. Some of the patients noted that with the drug they were better able to differentiate the pain of chronic arthritis from that of hemarthrosis. It is thought that ability to better distinguish causes of different types of pain with NSAID therapy might enable patients to avoid inappropriate factor infusions when they mistake pain of chronic arthritis for a bleeding episode.

Results of this pilot study suggest that CMT and ibuprofen can be safely administered to patients with hemophilia under close supervision for periods up to six weeks. Investigators urge, however, that platelet aggregation studies and bleeding times be performed on all subjects to identify individuals sensitive to the drugs.

CT Scan Assists Pseudotumor Diagnosis

CS Kitchens: Computed Tomography in Two Cases of Hemophilic Pseudotumors. Am J Hematol *12:277-280, 1982.*

Pseudotumor is a rare and serious complication of hemophilia in which blood accumulates along the long bones, within the pelvis or along the bones of the hands. On x-ray, these hematomas can resemble primary bone tumors. Because corrective surgery may be especially risky if pseudotumors have not been correctly diagnosed, routine radiographic examination and arteriography may not be sufficient for exact evaluation of patients with pseudotumor.

This article presents two patients with pseudotumor of the femur for whom computed tomography (CT scans) significantly influenced diagnostic decisions and treatment outcome. On preliminary evaluation, the first patient showed only a pathologic fracture of the upper left femur. A CT scan, however, revealed a large cystic mass extending from the midfemoral area to the symphysis pubis. Bone destruction made reconstruction of the leg impossible; amputation was successful.

> "...routine radiographic examination and arteriography may not be sufficient for exact evaluation of...pseudotumor."

The second patient suffered massive swelling of the left leg with femoral nerve damage. A CT scan showed a large cystic mass extending from the lower third of the left femur proximally to the symphysis pubis. The leg was successfully disarticulated.

Physicians and patients enjoy dinner festivities at the 20th anniversary celebration of Orthopaedic Hospital's Hemophilia Center, held November 5 and 6, 1982. Steven Emerson, left, chats with Lois Boylen, M.D., Director of Adult Care at the Hemophilia Center.

Two Reviews of Plasma Exchange for the Treatment of Patients with Inhibitors

Reduces Antibody Levels, Enhances Factor VIII Activity

JG Erskine: Plasma Exchange in Patients with Inhibitors to Factor VIIIC. Plasma Ther Transfus Technol *3:123-130, 1982.*

Treatment options for bleeding episodes available to hemophilic patients with inhibitors to factor VIII are limited. Bleeding episodes are not affected by the presence of inhibitors, but inhibitors make treatment difficult. Seventy-five percent of affected patients are classified as strong responders; they tend to develop high levels of antibody that persist for a long time. Further challenge with factor VIII raises already high inhibitor titer levels. Weak responders maintain low titers that do not rise on challenge; they may even disappear spontaneously.

Treatment of patients with inhibitors is complicated by the fact that inhibitors may redevelop quickly after infusion with any blood product containing factor VIII. Thus treatment of patients with mild hemophilia should be conservative – withholding factor VIII-containing blood products and correcting hypovolemia with albuminoid solutions. Physiotherapy, use of splints and rest may be useful.

When life-threatening hemorrhage requires use of factor VIII products, it takes large quantities to neutralize circulating antibody and produce free factor VIII coagulant activity. This treatment is usually effective for only a few days. Continuous infusions of factor VIII have also been tried. Some work has been done infusing animal factor VIII concentrates, but inhibitor titers still rise after one week and allergic reactions can occur.

A wide variety of immunosuppressive agents have been used to eradicate antibody-producing cells. Results have been disappointing. Initial studies suggested that prothrombin complex concentrates (PCCs) might contain a substance that could bypass factor VIII inhibitor activity. Mechanisms of action remain unclear, however, and the role of PCCs remains to be defined.

> "Rapid removal of immunoglobulins results in reduction in antibody levels that is sufficient to allow infusions of factor VIII concentrates to produce circulating coagulant activity."

The basic procedure of plasma exchange is much like standard plasmapheresis and must be performed in a specialized center. It is important that plasma-exchange patients be tested for presence of hepatitis B antigen; patients who are HBsAg-positive pose problems for cell separators. Good venous access is important in these patients; peripheral vein cut or femoral cannulation to achieve flow can be dangerous. Heparinization should be kept to a minimum and should be reversed at the end of the process.

Volume of exchange and frequency and duration of treatment are important considerations. The patient shows a rapid rise in antibody levels immediately after plasmapheresis. Treatment should be continued until hemorrhage has subsided or until the patient's inhibitor level has fallen sufficiently to permit factor VIII infusions to create effective circulating levels of factor VIII coagulant activity. (Daily exchanges of at least three liters appear necessary in most patients.) Choice of replacement fluid is important – ideally, a mixture of an albuminoid solution and an equal volume of fresh plasma should be given. Small volumes of normal saline can also be given.

An intensive plasma exchange schedule has several potential benefits for the treatment of patients with inhibitors. Rapid removal of immunoglobulins results in reduction in antibody levels that is sufficient to allow infusions of factor VIII concentrates to produce circulating coagulant activity. By adding immunosuppressive drugs, further antibody production may be limited. Risk of hepatitis could be eliminated if albuminoid solutions were used. Further study of this treatment is required, but it seems it could improve prognosis for hemophilic patients with inhibitors to factor VIII.

Plasmapheresis Benefits Patient Dramatically

S Salmassi, S Ilangovan and DO Kasprisin: Treatment of Hemophilia A with Factor VIII Inhibitor by Plasma Exchange Transfusion. Plasma Ther Tranfus Technol *3:131-136, 1982.*

Plasmapheresis, or exchange transfusion, was first used successfully to reduce inhibitor concentration in 1973. Exchange transfusion seems to decrease the amount of inhibitor sufficiently to allow infused factor VIII to work to stop bleeding.

This paper describes a 27-year-old man brought to the emergency room after a fight. He was bleeding severely from the jaw and mouth. Interstitial hemorrhage extended to his face, scalp, and jaw, and interfered with his speech and breathing. He did not respond to massive doses of factor VIII and fresh frozen plasma (FFP). Factor VIII inhibitor had previously been 35 units. After treatment with factor IX, inhibitor titer was 11 units.

Emergency plasmapheresis was performed; 4260 mL plasma were removed over three days and FFP and cryoprecipitate were used as replacement. After the first plasmapheresis, inhibitor titer decreased to four units, and factor VIII activity increased to seven percent after administration of 2800 units of factor VIII. After the second plasmapheresis and treatment with factor VIII, the inhibitor titer was decreased to 0.5 unit, and bleeding was markedly decreased. After the third plasmapheresis and treatment with factor VIII, the patient's bleeding stopped and the hematoma and edema resolved.

Specialist's Update

Dental Care Should Not Be Neglected

Carol K. Kasper, M.D., Department of Medicine, University of Southern California School of Medicine; the Coagulation Laboratory of the Hemophilia Center at Orthopaedic Hospital, Los Angeles; Member of the Editorial Board of the Journal of the American Medical Association.
From Hereditary Plasma Clotting Factor Disorders and Their Management, Description of Disorders, *February 1982.*

Regular professional dental care should be encouraged in patients with hemophilia. To this end, patients may need referral to a dentist who is knowledgeable about hemophilia and willing to provide the special care the hemophilic patient needs. Cleaning of the teeth is usually accomplished with minimal trauma and rarely is there a need for plasma products. In fact, minor bleeding from the gums after vigorous brushing or professional cleaning is easy to control. Orthodontia may be carried out as in non-hemophilic patients. When cavities can be filled without anesthesia, or with a light anesthetic gas or an intravenous anesthetic, there is little chance that the patient will experience serious bleeding.

> "...patients may need referral to a dentist who is knowledgeable about hemophilia..."

If regional block anesthesia is attempted, the patient's clotting factor level should be raised to 50 percent within an hour before the procedure. Patients given regional block anesthetics without plasma product preparation sometimes develop massive hematomas at the side of the face which may dissect into the neck. Patients also need plasma products before excision of periodontal tissue. For tooth extractions, patients receive enough of the appropriate plasma product to raise the plasma clotting factor level to 50 percent (or as high as possible if only fresh-frozen plasma can be used) within the hour before surgery.

Patients with von Willebrand's disease receive cryoprecipitate or plasma even if their levels of factor VIII coagulant activity are normal. EACA (epsilon amino caproic acid, an anti-fibrinolytic agent) is given on the day of extraction and for about ten days thereafter in a dose of 40 mg/kg four times a day. Because EACA and prothrombin complex concentrate cannot be given together, patients with hemophilia B must be treated either with concentrate alone, or with plasma plus EACA. A strict diet of cold fluids for several days after extraction helps to preserve clots. With the use of one preoperative dose of plasma products, plus several days of EACA and dietary restrictions, most extractions are accomplished as outpatient procedures without rebleeding.

Profilate®
Antihemophilic Factor (Human) Lyophilized

Brief Summary

INDICATIONS
Antihemophilic Factor (Human) Profilate is indicated solely for the prevention and control of bleeding in patients with moderate or severe Factor VIII deficiency due to hemophilia A, or acquired Factor VIII deficiency. Antihemophilic Factor (Human) is not indicated in the management of bleeding in patients with von Willebrand's disease.

CONTRAINDICATIONS
There are no known contraindications to the use of Antihemophilic Factor (Human).

WARNINGS
Viral hepatitis may be transmitted by this product. Patients with mild deficiencies, who consequently have not received multiple transfusions of blood or blood products, are at greatest risk. In this situation, the benefits of Antihemophilic Factor (Human) administration must be carefully weighed against the risk of viral hepatitis; single donor products should be preferentially utilized whenever feasible.

PRECAUTIONS
Antihemophilic Factor (Human) should not be administered at a rate exceeding 10 ml/minute. Rapid administration may result in vasomotor reactions.

Approximately five to eight percent of hemophilia A patients develop inhibitors to Factor VIII. Rarely, other patients acquire similar inhibitors. The management of patients with inhibitors requires careful monitoring, especially if surgical procedures are indicated. In patients with inhibitors, the response to Antihemophilic Factor (Human) may be much less than would otherwise be expected and larger doses are often required. Patients with high inhibitor levels may not respond to Antihemophilic Factor (Human) at all.

Nursing personnel and others who administer this material should exercise appropriate caution in handling because of the risk of exposure to viral hepatitis.

ADVERSE REACTIONS
Adverse reactions can include urticaria, fever, chills, nausea, vomiting, headache, somnolence or lethargy. Some patients develop reactions of a mild nature following the administration of Antihemophilic Factor (Human). Adverse reactions may be on an allergic basis. If a reaction is noted and the patient requires additional Antihemophilic Factor (Human), product from a different lot should be administered.

Massive doses have rarely resulted in acute hemolytic anemia, increased bleeding tendency or hyperfibrinogenemia.

Profilate does contain blood group isoagglutinins and when large and/or frequent doses are required in patients of blood group A, B, or AB, the patient should be monitored for signs of intravascular hemolysis and falling hematocrit. Should this condition occur, thus leading to progressive hemolytic anemia, the administration of serologically compatible type O red blood cells should be considered.

CAUTION
Federal (USA) Law prohibits dispensing without a prescription. Single dose container for intravenous administration only. Discard any unused contents. Discard administration equipment after single use.

Profilnine™
Factor IX Complex (Human) Lyophilized

Brief Summary

INDICATIONS AND USAGE
Factor IX Complex (Human) Profilnine is indicated solely for the prevention and control of bleeding in patients with Factor IX deficiency due to hemophilia B, where bleeding cannot be controlled by the use of plasma.

CONTRAINDICATIONS
None known.

WARNINGS
This product is prepared from units of human plasma which have been tested and found nonreactive for hepatitis B surface antigen (HBsAg) by an FDA-required test. However, presently available methods are not sensitive enough to detect all units of potentially infectious plasma, and risk of transmitting hepatitis is still present.

Patients with mild Factor IX deficiencies, who consequently have not received multiple transfusions of blood or blood products, are at greatest risk. In this situation, the benefits of Factor IX Complex (Human) administration must be carefully weighed against the risk of viral hepatitis; single-donor products should be preferentially utilized whenever feasible.

PRECAUTIONS
Factor IX Complex (Human) should not be administered at a rate exceeding 10 ml/minute. Rapid administration may result in vasomotor reactions.

Nursing personnel and others who administer this material should exercise appropriate caution in handling because of the risk of exposure to viral hepatitis.

ADVERSE REACTIONS
Adverse reactions may include urticaria, fever, chills, nausea, vomiting, headache, somnolence, lethargy, flushing or tingling. For most reactive individuals, slowing the infusion rate relieves the symptoms. For those highly reactive individuals, a different lot may be satisfactory.

Adverse reactions characterized by either thrombosis or disseminated intravascular coagulation have been reported following administration of similar Factor IX Complex (Human) concentrates. In particular, patients who receive Profilnine concentrate postoperatively or with known liver disease should be kept under close observation for signs and symptoms of intravascular coagulation. Continued administration should be left to the discretion of the physician.

CAUTION
Federal (USA) Law prohibits dispensing without a prescription. Single-dose container for intravenous administration only. Discard any unused contents. Discard administration equipment after single use.

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5555 Valley Blvd., Los Angeles, CA 90032

It Takes a Team.

The ultimate in hemophilia management is the maintenance of the patient with hemophilia as an independent, self-supporting individual in his own community.[1]

And it's not something one person can achieve on his own.

Clotting factor concentrates provide the means for effective control of bleeding in the hemophilic patient and the prevention of crippling for most patients.[2] And working together, the hemophilia specialty team can help boys and men with hemophilia to be more active and productive members of society.[3]

The Alpha Team Is Complete

Profilnine Factor IX Complex (Human) for the management of hemophilia B completes the Alpha team of clotting factor concentrates. New Profilnine Factor IX Complex (Human) for the patient with hemophilia B, and Profilate Antihemophilic Factor (Human) for use in the management of moderate to severe hemophilia A.

Order with Confidence

- *High Potency*—ideal for self-administration by syringe, with Factor VIII and Factor IX potencies up to 50 units/ml
- *Stable*—Profilate is stable at room temperatures up to six months and Profilnine for one month, to facilitate travel and a more normal lifestyle
- *Fast, Easy Reconstitution*—usually reconstitutes in less than 10 minutes, so delay and patient discomfort are minimized
- *Hepatitis-Tested Twice*—both individual units of plasma and the end product are tested and found non-reactive for HBsAg
- *Heparin-Free*—no heparin to complicate lab profiles

Profilate
Antihemophilic Factor (Human)

Profilnine™
Factor IX Complex (Human)

Put the Alpha Team on Your Side

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5555 Valley Blvd., Los Angeles, CA 90032

References:
1. E Sergis, MW Hilgartner: "Hemophilia" *Amer J Nurs* 72:2011-2020, 1972.
2. MW Hilgartner: "Comprehensive Care of Hemophilia" DHEW Publ No (HSA) 79-5129, 1979.
3. LM Aledort: "The Management of Hemophilia: A Perspective" *Drug Ther* 1:55-59, March 1971.

Please see reverse side for brief summaries of prescribing information.

Hepatitis B Linked to Treatment Frequency

RT Card, M Dusevic and BE Lukie: Coagulation Factor Therapy for Hemophilia: Relation to Hepatitis B and to Liver Function. CMA Journal *26:34-36, 1982.*

The cause of liver disease that complicates hemophilia in many patients is unknown. Investigators have postulated it may be a basic feature of hemophilia, it may result from viral infection or it may be related to use of pooled rather than single-donor concentrates to control bleeding episodes. Researchers at the University of Saskatchewan, Saskatoon, examined 36 hemophilic patients for the effects of frequency of infusion and type of coagulation factor therapy on the incidence of hepatitis B and on liver function.

Ages of these patients, all of whom attended the bleeding clinic at University Hospital during 1977 and 1978, ranged from two to 63 years. Treatment was analyzed through a review of the clinic's records and patients' answers to a questionnaire verifying findings.

Patients were divided into two groups—26 patients requiring factor infusions more than once a year (23 of whom required infusion more than once a month), and ten patients treated less frequently. Patients who had received factor VIII or IX concentrates were placed in one group and those who had received only cryoprecipitate or whole blood were placed in another group. (Until recently, factor concentrates have not been widely available in Saskatchewan, and so there were a large number of patients who had been treated exclusively with single-donor products.)

Researchers found three-quarters of the patients (including 45 percent of patients treated exclusively with single-donor products) had antibody to hepatitis B surface antigen, as determined by high SGOT levels. Researchers could not demonstrate a significant relationship between SGOT level and treatment type—these observations failed to support the contention that therapy with multiple-donor products poses a greater threat of liver disease than

(Continued at the bottom of next column)

therapy with single-donor products. Because elevated SGOT was significantly more common in patients treated more than once a year, their results suggested that patients who require treatment more than once a year are at increased risk for hepatitis B.

New Findings on Two Bleeding Disorders

Definition of von Willebrand's Disease Widens

JL Miller and A Castella: Platelet-Type von Willebrand's Disease: Characterization of a New Bleeding Disorder. Blood *60:790-793, 1982.*

This article describes a newly observed bleeding disorder that shares some but not all of the features previously described as von Willebrand's disease. Physicians at SUNY Upstate Medical Center, New York, suggest that this disorder features an intrinsic abnormality at the surface of the platelet that affects platelet-VIII/von Willebrand's interactions. They propose that this disorder be termed "platelet-type von Willebrand's disease."

Investigators studied five members of three generations of one family. All had histories of bleeding following minor trauma or surgery. All showed decreased factor VIII-ristocetin cofactor activity, selective decrease of the higher molecular weight VIII/von Willebrand's multimers, and increased platelet agglutination at low concentrations of ristocetin added to platelet-rich plasma. These patients showed no enhanced binding of VIII/von Willebrand's by normal platelets. Their platelets did show a significant increase in ability to bind factor VIII/von Willebrand's factor from normal plasma.

> "...this disorder features an intrinsic abnormality at the surface of the platelet that affects platelet-VIII/von Willebrand's interactions."

Further study of platelets is needed to elucidate platelet receptors for factor VIII/von Willebrand's factor as well as the cellular pathways of plasma factor VIII/von Willebrand's factor metabolism. Study should thus lead to better treatment for patients with this type of disease.

Families Suffer Combined Factor V and Factor VIII Deficiency

U Seligsoh, A Zivelin and E Zwang: Combined Factor V and Factor VIII Deficiency among Non-Ashkenazi Jews. NEJM *307:1191-1195, 1982.*

Although separate genes control normal function of factors V and VIII, hereditary combined factor V and factor VIII deficiency has been documented in 26 unrelated families of Jews deriving mainly from the Mediterranean basin. A rough estimate of frequency of this disorder is one in 100,000 non-Ashkenazi Jews. Investigators studied factor V and factor VIII clotting activities (VIII:C) and factor VIII antigenicity (VIII:RAG) in 115 members of seven unrelated families. The most commonly noted symptom in affected family members was excessive bleeding after surgery, abortion or childbirth. Hemarthrosis was never noted.

This study confirmed that the level of factor VIII:RAG is normal in affected persons with the combined factor V and factor VIII deficiency, as it is in hemophilia A. It was also confirmed that the mode of inheritance of the disorder is autosomal recessive. Only 33 percent of obligate carriers could be identified by a significantly diminished level of factor V:C or VIII:C, or both. The ratio of factor VIII:C to factor VIII:RAG did not help define the carrier state. Researchers concluded that the decrease in factor VIII:C in the combined deficiency could stem from a deficiency of protein-C inhibitor.

HEMOPHILIA LETTER
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(address correction requested)

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625X82 Printed in U.S.A. January 1983