Deferral of Blood and Plasma donors -- Medications (7/28/93)

DATE: July 28, 1993

FROM: Acting Director, Office of Blood Research and Review, Center for Biologics Evaluation and Research

SUBJECT: Deferral of Blood and Plasma Donors based on Medications

TO: All Registered Blood Establishments

The recommendations in this memorandum apply to collection and distribution of blood and blood products intended both for transfusion and for further manufacturing.

I. INTRODUCTION

Blood products manufactured from donors receiving certain medications may contain significant levels of these medications. Transfusion of these products could result in adverse effects to certain recipients or to the developing fetus of a pregnant recipient.

Many factors should be considered when determining the potential harm of a drug present in a blood product. These include the drug's half-life, its mean and peak plasma concentration, the time that the drug was taken relative to the time of donation, the drug's long-term storage in the body, the dose that produced teratogenic effects in animals and humans, and the time during gestation at which the drug is most teratogenic relative to the time of transfusion. In addition, the blood product (and thus the level of drug) may be diluted if pooled or when transfused into the recipient's plasma volume. The level of drug may also be diluted or concentrated by the fractionation process.

II. RECOMMENDATIONS FOR DONOR DEFERRAL

a. Proscar (finasteride)

Proscar (finasteride) is a drug recently approved for the treatment of symptomatic benign prostatic hypertrophy (BPH). It is an inhibitor of the enzyme, 5 alpha-reductase, which converts testosterone into 5 alpha-dihydrotestosterone (DHT). As such, its use by men with BPH may result in shrinkage of the enlarged prostate gland and improvement in maximum urinary flow rate. Levels of DHT return to normal approximately 2 weeks after discontinuing Proscar.

Proscar is not indicated for use in women or children and is contraindicated during pregnancy (pregnancy category X)(21 CFR 201.57(f)(6)(i)). Studies in pregnant rats given oral doses of finasteride (3/100 the recommended human dose) showed abnormalities in the reproductive organs of their male offspring.

Women who are or may become pregnant are cautioned to avoid exposure to the drug either by direct contact with a crushed tablet or through contact with the semen of a male taking this medication.

It is thus potentially possible that if a donor who is receiving Proscar donates blood which is then transfused to a woman who is or will soon become pregnant, the male fetus exposed to this drug in the blood product may suffer deformity of his reproductive organs. It is particularly noteworthy that the teratogenic dose in the rat studies was a small fraction (3/150) of the recommended human dose.

With these concerns in mind, the FDA recommends that any donor taking Proscar (finasteride) be deferred from donating blood or plasma for at least one month after receipt of the last dose.

b. Accutane (isotretinoin)

Accutane (isotretinoin) is a retinoid which inhibits sebaceous gland function. It is indicated for the treatment of severe, recalcitrant cystic acne. This drug is contraindicated in pregnancy (pregnancy category X). Major fetal abnormalities, including neurologic and cardiovascular deformities, related to Accutane administration have been documented. Effective contraception must be used for at least one month before, during and one month after therapy.

If a donor who is receiving Accutane gives blood or plasma which is then given to a recipient who either is or soon becomes pregnant, there may be a risk to the developing fetus due to Accutane in the transfused blood product.

Taking into consideration the potency of the drug as a teratogen and the possibility that it may be present in the blood for long periods, the FDA recommends that any donor taking Accutane (isotretinoin) be deferred from donating blood or plasma for at least one month after receipt of the last dose (FDA memorandum, February 28, 1984).

c. Tegison (etretinate)

Tegison (etretinate) is a retinoid. It is indicated for the treatment of severe, recalcitrant psoriasis. This drug is contraindicated in pregnancy (pregnancy category X). Major fetal abnormalities related to Tegison, including neurologic and skeletal deformities, have been reported. Effective contraception must be used for at least one month before, during and for an indefinite period of time following therapy. Blood levels of 0.5 to 12 ng/mL have been reported up to 2.9 years after treatment was concluded. The length of time necessary to wait after discontinuation of treatment to assure that no drug will be detectable in the blood has not been determined. The significance

of undetectable blood levels relative to the risk of teratogenicity is unknown.

If a donor who is receiving Tegison gives blood or plasma, and the blood product is transfused to a patient who either is or soon becomes pregnant, there may be a risk to the developing fetus due to Tegison in the transfused blood product.

Taking into consideration the potency of the drug as a teratogen and the possibility that it may be present in the blood for long periods, the FDA recommends that any donor who has taken or is taking Tegison should be permanently deferred. (This supersedes the previous 3-year deferral period mentioned in the Blood Bank Inspection Checklist Instructions and the Plasmapheresis Inspection Checklist Instructions.)

d. Human Pituitary-Derived Growth Hormone

Human growth hormone is indicated for the long-term treatment of children who have growth failure due to an inadequate secretion of normal endogenous growth hormone. Prior to 1985, human pituitary-derived growth hormone (pit-hGH) was available in the U. S. Several cases of an extremely rare neurological disease called Creutzfeldt-Jakob disease (CJD) were reported in recipients of pit-hGH. The likelihood of young adults developing CJD was so remote that it was concluded that pit-hGH must have been inadvertently contaminated with the transmissable agent of CJD.

Animal studies suggest that it may be possible to transmit CJD by transfusion of blood products from a person who has been infected with CJD-but who is asymptomatic. Thus, there is a remote but finite chance that CJD may be transmitted through the blood or plasma of pit-hGH recipients who are asymptomatic yet harboring the agent of CJD. There are currently no means of testing to detect such infected persons.

The FDA recommends that any donor who has received injections of pit-hGH be permanently deferred. Such deferral is not necessary for donors who have received only recombinant growth hormone (FDA memorandum, November 25, 1987).

III. OTHER MEDICATIONS NOT LISTED ABOVE

It is the responsibility of the medical director of the blood establishment to determine policies for deferral of donors taking medications other than the ones mentioned above. Donor deferral policies should consider the medical indication for the drug and the possible effect of the drug on the recipient of the blood product, or on the fetus, if the recipient is pregnant.

Blood establishments should have written procedures describing the circumstances and procedures for medical director review of blood donor suitability with regard to medication usage, and

should keep records of such donor suitability evaluations that occur.

Questions regarding this policy may be directed to the Division of Blood Collection and Processing, (301) 227-6487, FAX (301) 227-6431.

Gerald V. Quinnan Jr., M.D.