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AIDS AND PREVENTIVE TREATMENT IN HEMOPHILIA

THE lives of hemophiliacs have been transformed by advances in treatment during the past decade. The demonstration in 1937 by Patek and Taylor[1] that a fraction isolated from plasma could correct the coagulation defect in this disease provided the impetus for subsequent efforts to isolate and concentrate the deficient factor, later designated factor VIII. It was not until 30 years later, however, that cryoprecipitate, shown by Pool et al.[2] to contain factor VIII, came into widespread use. The availability of this material meant that patients could be treated with concentrations of factor VIII that could not be obtained from fresh whole plasma. Techniques of concentrating and storing the factor were also developed to the point at which stable, lyophilized concentrates became available commercially and provided a means for ambulatory care of hemophiliacs, most of whom learned to administer the material themselves.

Remarkable changes have occurred during the past decade with this program of self-administration of a factor VIII preparation. It has provided a means of early and preventive treatment and has minimized hospital admissions among hemophiliacs.[3,4] The program has given patients a new degree of freedom and independence in managing their disease. Besides decreasing the need for hospital admissions, it has diminished the number and severity of complications. The availability of concentrates of factor VIII has also allowed safe surgical treatment of acute problems and repair of severe joint deformities. Thus, life style and life itself have changed for many hemophiliacs.

The risk associated with exposure to plasma from multiple donors, however, has long been a concern in the care of these patients,[5] primarily because of evidence of virus-induced liver disease. Hepatitis is a common event in the histories of many of these patients. Objective evidence of hepatitis B, obtained by liver biopsy and by serologic tests, has been described in several reports.[6-8] Transmitted diseases other than the various types of hepatitis have not been a problem, however, and until recently there has been no clinical evidence of an unusual susceptibility of this population to opportunistic infections.

Now we are becoming aware that treating hemophiliacs with factor VIII preparations may exact a high cost. Reports from the Centers for Disease Control include three hemophiliacs among cases of acquired immunodeficiency syndrome (AIDS).[9] Only recently recognized, this syndrome is associated with abnormalities of immunoregulation and a profound susceptibility to opportunistic infections; it is eventually fatal in many patients. AIDS has been described in homosexuals, heroin addicts, and Haitians, as well as in hemophiliacs. Whether it is secondary to multiple antigenic exposures, to a specific transmitted agent, or to some other mechanism is not yet known.[10] The three hemophiliacs described by workers from the Centers for Disease Control had serologic abnormali-

ties of immunoregulation and diseases that one usually sees only in immunosuppressed patients.

This issue of the *Journal* contains two reports on asymptomatic hemophiliacs in Cleveland and in Milwaukee, some of whom had an immunoregulatory disorder characterized by an abnormal ratio of OKT4 to OKT8 cells.[11,12] Functional studies in some of the patients confirmed the presence of this abnormality, which consists of an increase in the number of suppressor (OKT8) cells. Patients receiving lyophilized commercial concentrates of factor VIII appeared more likely than those receiving cryoprecipitate to have abnormalities of T-cell subpopulations. In view of this finding, current modes of treatment must be scrutinized. Concentrates are prepared from pooled plasma from 2000 to 5000 donors, lyophilized, and packaged in vials containing 200 to 1200 IU (1 IU is equivalent to the activity found in 1 ml of normal plasma[4]). Cryoprecipitate, on the other hand, is prepared in the blood bank from the plasma of individual donors; each bag finally contains about 100 units of factor VIII in a relatively small volume. The commercial preparation is more concentrated than the cryoprecipitate, and its unitage is more reliable, but the advantage of the cryoprecipitate is that the recipient is exposed to only one donor per bag. In the hemophiliacs studied,[11,12] the difference between those receiving concentrate and those receiving cryoprecipitate does not seem to be explained by the fact that there was less treatment in the latter group, but one may wonder whether exposure to fewer donors is crucial.

Ease in obtaining the commercially prepared lyophilized concentrates of factor VIII has made the ambulatory program possible. The average patient requires about 40,000 units yearly,[4] and provision of this amount of cryoprecipitate to each of the nation's 12,000 hemophiliacs would certainly stress the capacity of blood banks. It would also be difficult to design a home-infusion program with cryoprecipitate therapy, since the material must be stored in the frozen state. The present program has been extremely successful and would be given up by physicians and patients only with great reluctance. Yet it is time to consider doing so, even though we may not have enough evidence to demand such a radical change.

The fact that hemophiliacs are at risk for AIDS is becoming clear.[9,13-15] If the use of cryoprecipitate will minimize this risk, the current home-infusion program needs to be revised. The studies reported in this issue demonstrate in vitro abnormalities of immunoregulation, but the numbers are too small for definitive comparison of the risks of different modes of treatment. Unfortunately, the data are consistent with a greater potential for AIDS in the population treated with concentrate. Physicians involved in the care of hemophiliacs must now be alert to this risk. Preventing the complications of the present treatment may have to take precedence over preventing the complications of hemophilia itself.

JANE F. DESFORGES, M.D.

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The Evolution of Health Planning

PUBLIC Law 93-641, the National Health Planning and Resources Development Act of 1974, provided direct federal financial support for both state and local health-planning agencies. It mandated the development of health-system plans by health-planning councils, a majority of whose members would be consumers, at the state and local levels. Furthermore, P.L. 93-641 also required each state to conduct a certificate-of-need program to regulate the introduction of new institutional health facilities and services.

The Reagan administration is opposed to health planning on the grounds that it interferes with competition in the health-care sector. However, Congressmen Henry Waxman (D-Calif.), Edward Madigan (R-Ill.), and Richard Shelby (D-Ala.) recently arrived at an agreement that would continue the basic rudiments of the health-planning process in this country.[1] This compromise proposal, the "Health Planning Block Grant Act of 1982," would require states to revise but continue their certificate-of-need programs and would provide limited funding for local health-planning agencies.

Under P.L. 93-641, health planning often seemed unconnected with the real world of health-care financing and delivery. Health planning can be justified in