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KEY ISSUES IN HEMOPHILIA TREATMENT

PART 2: ORGANIZING A NATIONAL PROGRAMME FOR COMPREHENSIVE HEMOPHILIA CARE

WORLD FEDERATION OF HEMOPHILIA
FÉDÉRATION MONDIALE DE L'HÉMOPHILIE
FEDERACIÓN MUNDIAL DE HEMOFILIA

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Key Issues in Hemophilia Treatment
Part 2: Organizing a National Programme for Comprehensive Hemophilia Care

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Further information on several of the issues addressed in this document is available from the secretariat. We intend to update this document periodically to include any new information. Should you wish to help us improve this document, please send your comments or suggestions to the WFH secretariat at, The World Federation of Hemophilia, 1310 Greene avenue, Suite 500, Montréal, QC H3Z 2B2, Canada.

Thank you.
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Introduction

A national programme denotes the project of organizing comprehensive care for persons with hemophilia in a given country. The structure of such a system is determined principally by the nature of the condition itself and its demands. The resources of a given country will also influence the way services are administered there. Whether services are administered by a hospital's general services—that also contend with the rest of the population—or by centres specializing in the treatment of hemophilia (usually within a hospital setting), depends on the human and medical establishment resources as well as the educational opportunities available in a country. How diagnosis is carried out in a given country affects who receives services and when. The important support of national and regional hemophilia societies, of registries and education programmes on hemophilia is essential to the smooth delivery of services to people with hemophilia. Blood products themselves must be carefully collected, produced, packaged, transported, and stored. Records of each stage of production and transport must be kept scrupulously, from the screening of each donation to the follow-up of each individual using the final product.

It is the responsibility of the national healthcare system, pharmaceutical companies, national hemophilia organizations, and the medical and paramedical establishment to cooperate in establishing, maintaining and reviewing the national programme for hemophilia services in a given country.

1 A Structured Approach

A national programme will

- reduce medical complications for people with hemophilia
- reduce hospitalization for people with hemophilia
- allow people with hemophilia and family members to remain consistent in the work-force
- improve life-expectancy and quality of life for persons with hemophilia
- reduce demand on healthcare resources

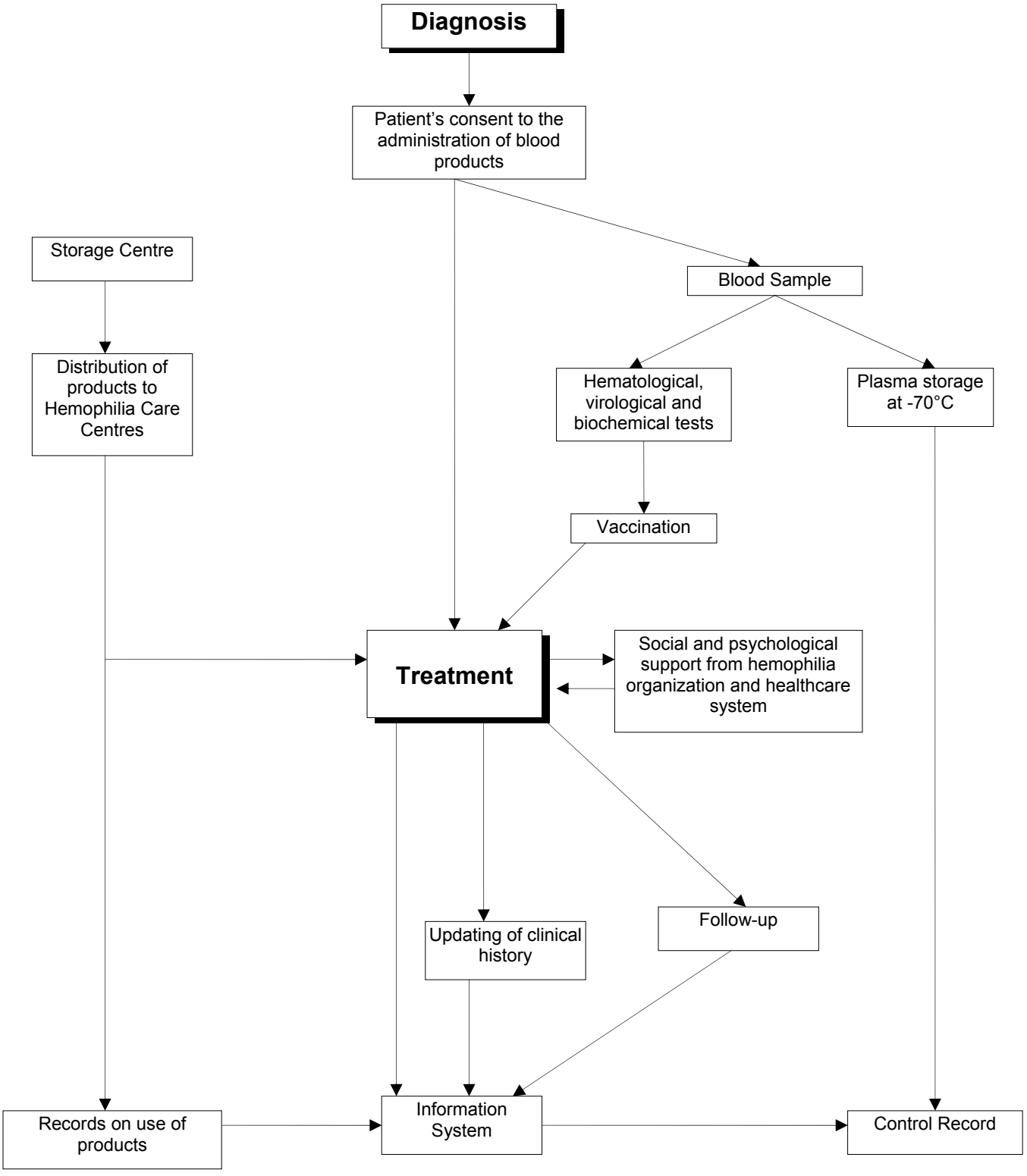
The national programme will also make it possible to

- coordinate resources for the most efficient delivery of services
- evaluate outcome on a national basis to achieve the most cost-effective delivery of extended services
- be used as a model for other chronic diseases

Hemophilia services touch many elements of health care: blood banking, transfusion, hematology, pediatrics, orthopedics, dentistry, physiotherapy, laboratory testing, and infectious diseases. The process of organizing a national programme will bring about improvement of these other aspects of the health system.

Responsibility for the programme should be assigned to a specific centre. This entity should support the hemophilia programme in coordination and collaboration with the national Red Cross/Crescent society , the national hemophilia organization, the Society of Hematology, and with blood banking and other interested parties.

Figure 1 Treatment cycle for an individual with hemophilia



2 Diagnosis

The first step in hemophilia care is its recognition and diagnosis. Every effort must be made to identify carriers, especially where the condition is severe. Even in cases of sporadic hemophilia, the mutation may have occurred a few generations previously, and every effort must be made to identify carriers if that is in accordance with the family's wishes. Identification depends on family history, gene tracking, on measurement of the relevant clotting parameters and, increasingly, on DNA analysis. Laboratory analysis is needed to establish a true diagnosis. It is essential that hemophilia A and hemophilia B be distinguished immediately so that appropriate treatment can be given.

3 Treatment Centres

Medical care for hemophilia is specialized. A person with hemophilia must receive services from healthcare workers who have expert knowledge of the bleeding disorder. The wide-ranging needs of people with hemophilia and their families are best met **through Hemophilia Treatment Centres (HTCs)*** rather than by individual doctors. These centres can provide treatment, or referrals for appropriate treatment. Services available at HTCs will vary according to the expertise and interest of healthcare workers in position at a given time, but in general the staff can expedite the proper diagnosing of hemophilia and give first aid and appropriate clotting factor therapy on demand.

The most sophisticated level of treatment, available through **Hemophilia Comprehensive Care Centres (HCCCs)**,† provides a full range of facilities for the coordinated comprehensive care of individuals with hemophilia. Depending on the expertise available at more local centres, an individual may not need to travel to an HCCC, but an understanding of comprehensive treatment is a must.

4 National Hemophilia Organizations

The effectiveness of the services received is greatly amplified by access to voluntary support groups, the most important of which is the local or national hemophilia organization. These national organizations may or may not be affiliated with the World Federation of Hemophilia (WFH). Eighty-eight such national organizations are currently affiliated with the WFH. The main role of national or local organizations is to educate individuals with hemophilia and their families and to encourage their collaboration in treatment. Hemophilia organizations also play an essential advocacy role by lobbying governments to provide better treatment for the hemophilic population.

Hemophilia organizations can also provide up-to-date factual information to their members, as well as practical help and friendship.

* Hemophilia Treatment Centre (HTC) Medical centre providing basic diagnosis and treatment for inherited bleeding disorders. Hemophilia Treatment Centres are usually linked to Hemophilia Comprehensive Care Centres.

† Hemophilia Comprehensive Care Centre (HCCC) Medical centre providing a full range of facilities for the diagnosis and management of inherited bleeding disorders.

Table 1 Facilities available at centres of expertise

	General Hospitals	Hemophilia Treament Centres	Hemophilia Comprehensive Care Centres
Patients	Local, public access	Patients referred by General Hospital	Responsible for at least 40 people with severe hemophilia
Treatment	Simple bleeding, first aid, emergencies	Minor surgery, dental procedures, psychological and social support	Treatment of musculoskeletal complications; other medical complications; major surgery
Diagnostic tests	Basic coagulation tests	Coagulation tests and factor assays	Factor and inhibitor assays along with coagulation tests
Staff	One doctor with expertise and interest in hemophilia	Hematologist, nurse, dentist, physiotherapist, social worker	Hematologist, orthopedic surgeon, dentist, nurse, genetics councilor, psychologist, physiotherapist, occupational therapist, social worker
Laboratory	Routine hematology including coagulation	Coagulation laboratory	All tests necessary for the definitive diagnosis of hemophilia and other inherited bleeding disorders
Prevention	Identification of obligatory carriers and referral of possible carriers for investigation		Carrier detection and prenatal diagnosis
Education programme	With the local chapter of the national hemophilia organization	With the local chapter of the national hemophilia organization	With the national hemophilia organization

5 Planning Your Own System

Within each country the exact requirements expected of both HCCCs and the smaller HTCs is defined by health authorities.

People with hemophilia may have developed relationships with a chosen centre for various reasons, and this centre may not be within their administrative or geographical health area. Individuals with hemophilia often refer themselves directly to a particular hemophilia treatment centre, bypassing customary consultation with their family doctor, because of the specialized knowledge required for treatment, and because of their own understanding of their condition.

In planning the provision of services for people with hemophilia, health authorities must take into account the following of particular considerations if access to comprehensive care is to be achieved.

- classification of severity of cases and accommodation of the variability of the condition
- the *complexity* of hemophilia and its various medical complications translate into a need for a diversity of services

- The *amount* of treatment a given individual needs varies during their growth and lifetime. What they will need is unpredictable
- expertise in treatment of hemophilia patients will not be available uniformly across the country
- ease of access to blood products to support home treatment programmes
- the prevalence of side-effects of therapy is a significant problem; the need for treatment and counseling must be figured in
- Fortunately fewer and fewer cases of HIV and hepatitis infections occur, but in cases where they do, on-going care of people with hemophilia who do become infected must be considered.
- mildly affected individuals may need little more than review and access to treatment in the event of a bleed. More sophisticated treatment may be required for these individuals at times.

6 Laboratory Diagnosis and Monitoring

Coagulation laboratories, set up as part of general hematology services in local hospitals, act as referral points for patients diagnosed as having a bleeding disorder.

Many of the tests required to diagnose and manage *hereditary* bleeding disorders are in general use for the treatment of any patient presenting with abnormal bleeding or clotting symptoms. A few more sophisticated tests do require the specialists that are available only in larger centres. An essential component of all coagulation testing is the use of regulated standards and quality control.

It is recommended that there be at least one national laboratory capable of carrying out these tests, including those requiring carrier detection. This laboratory should be a part of a hemophilia comprehensive care centre and should have easy access to such a laboratory.

The following information can be collected and used to monitor the effectiveness of comprehensive care:

- bleeding incidents since the last consultation
- treatment since the last consultation: type of product used, amounts in units, lot numbers, efficiency of treatments
- musculoskeletal assessment of joint flexibility and muscle strength
- records of progress in physiotherapy and exercise programmes
- inhibitor screening
- radiology or scanner images of joints subject to recurrent bleeding or pain
- screening immunity to blood-borne viruses and appropriate vaccination when available
- immunological assessment if HIV positive
- psychosocial assessment

Table 2 Basic tests required for persons with hemophilia

Test required	Frequency
Hepatitis C (HCV)	Once a year
Hepatitis B (HBV), including HBsAg, HBsAb, HBcAb (IgG)	Once a year
HIV 1, HIV 2	Once a year
Inhibitor screen and, if needed, inhibitor assays	Once a year
Billirubin and ALT	Once a year
Factor VIII and IX Assays	First and second year
Tests for infectious diseases appearing regionally	According to need

Every severely affected child should be seen at six-month intervals by a doctor with hemophilia treatment experience. Every severely affected adult should be seen at least once a year. Individuals with moderate or mild hemophilia or a related disorder may be seen less frequently, unless they have received blood products. Those people known to have medical, social, or psychological problems in addition to their

bleeding disorder may need more frequent consultations. Follow-up is facilitated when easy-to-understand visual aids are used to explain treatment and changes in treatment to families. Recording treatment details on a calendar-type chart is recommended. This enables patients to track their own progress and gives them a direct way of comparing their own case with those of others with equally severe hemophilia. Such charts are especially valuable when monitoring target joints for prophylaxis.

7 Training a Comprehensive Care Team

The need for training is felt at two levels:

- team training for healthcare workers to explain the comprehensive hemophilia programme and the services delivery structure
- training for individual healthcare workers, either at the local or national level or as part of an international training programme

These individual programmes should include

- for doctors: use of concentrates, clinical issues and therapeutic protocols, management of comprehensive hemophilia care centres, specialized training for hematologists, training in orthopedic surgery, clinical genetics
- for nurses: diagnosis, treatment of bleeds, infusion, homecare training skills
- for physiotherapists: musculoskeletal treatment
- for laboratory staff: diagnosis, tests, and monitoring
- for blood bank staff: preparation and storage of blood products; record-keeping and tracking
- for dentists: dental hygiene and treatment
- for social workers: psychosocial problems of persons with hemophilia

Centre staff should practice good record-keeping. No centre of this nature can exist without very good secretarial support. Periodic training should be modified according to local health customs. It may be necessary to use international training sessions as an incentive to develop the interest of regional health professionals.

8 Education Programmes

The medical consequences and the cost of treating hemophilia can be significantly reduced with a good prevention programme and the development of homecare therapy. However, experience has shown that transmission of information in a traditional way does not produce satisfactory results.

There is a consensus that bleeding disorder education programmes must be reviewed with a view to obtaining the real and active participation of the patient, his or her immediate family and that of medical staff. One must take into consideration the psychological condition of the person with the disorder. The phenomena of dependence and overprotection between parents and children with hemophilia is an example of something which must be watched for. Education programmes help the person with a bleeding disorder to assume responsibility for his or her care. As well, thorough information on safety issues must be included in the education programme. In order to achieve these objectives, a national education plan should be prepared with the help of professional educators and the national hemophilia society.

Cost related to treatment of hemophilia will be reduced relative to the success of education programmes. When education programmes have a significant impact on the behavior and attitude of people with hemophilia and their families, savings can be significant.

9 Social and Psychological Support

Special mention must be made of social and psychological support as it is so often overlooked and this can have serious

repercussions. A diagnosis of hemophilia affects every aspect of an individual's life and the lives of his family members. Psychosocial support is therefore necessary and can be provided through

- ready access to experienced social workers and psychologists
- ongoing education of both families and healthcare workers
- facilitating a programme of services whereby the individual with the disorder can participate fully in all aspects of his or her care

In collaboration with medical and nursing services, professional and volunteer psychosocial services should provide

- general information on hemophilia and its treatment, growing up with hemophilia, hemophilia and sports, activities, travel and vacations, details on education and employment, the availability of state or local benefits
- specific information on marriage and parenthood, access to genetic counseling and prenatal diagnosis
- practical help for people with chronic disorders; referrals to specialized agencies for specific problems.

While both the social and psychological aspects of comprehensive treatment are usually hospital-based, there is much to be gained by visits to families in their homes, by meeting teachers, guidance counselors, or prospective employers in the workplace, and by encouraging contact with other affected families outside the hospital setting.

The hemophilia carrier needs careful counseling and support, especially if the bleeding disorder in her family is severe. Motivation for testing, and even for acting on the test results, varies from family to family and from country to country. Regardless of the circumstances, carrier detection should never be attempted without sensitive and confidential counseling, and a mechanism to ensure follow-up on individuals identified as carriers.

DNA analysis for the purpose of carrier detection should be carried out in compliance with local customs and values.

10 Safety and the Patient's Right to Decide

Someone with severe hemophilia may require fifty or more treatments each year and may be exposed to products made from the plasma of literally hundreds of thousands of donors. Until recently few doctors talked with their patients about the risks involved in blood transfusion. Nor have hospitals considered asking patients to sign a consent form before receiving blood or blood products.

There is a growing realization that patients should be advised of the risks and benefits involved, and of the alternatives open to them. As part of the process of encouraging the patient and his or her family to assume responsibility for their treatment, there is also a growing sense that the treating doctor should obtain the patient's consent prior to any administration of blood or blood products.

The question of who is responsible for securing a patient's informed consent should be addressed, and when consent is obtained it is recommended that a note be added to the medical record.

11 Administrative and Financial Issues Pertaining to National Programmes

11.1 Safety Control of Imported Blood Products.

Although blood products now have a high level of safety, like other medicines, they should never be considered completely free of risks.

It is important to maintain active surveillance of both donors and recipients for blood transmitted diseases. Both the U.S. Food and Drug Administration and the European Commission of Pharmacology of

the Council of Europe attempt to maintain the highest standard for products and to ensure safety by placing strict requirements on manufacturers.

It is very important for a country wishing to implement a national hemophilia programme to train personnel in the safety control for imported blood products and establish solid working relations with the U.S. Food and Drug Administration and/or the European Commission of Pharmacology of the Council of Europe.

11.2 Transportation

All licensed antihemophilic factors (except porcine factor VIII which must be stored frozen) require storage at 2°–8°C to permit use through the expiration period printed on each container. While some non-refrigerated storage is acceptable, long periods of non-refrigeration necessitate shortening of the expiry period. Every package of antihemophilic factor includes a vial of sterile water which serves as the diluent for the freeze-dried factor. Freezing must be avoided to avoid bursting the vial and loss of diluent. Non-refrigerated storage temperatures should never exceed 25°–30°C in order to avoid the loss of coagulant activity.

Since factor can be shipped anywhere in the world within a few days, transportation storage temperatures become a concern only when the recipient lacks the facilities to maintain temperature requirements until transfer is made to the final storage and distribution facility. Extremes of temperature below freezing or greater than 30°C must be avoided at all times.

It is expected that shipment temperatures can be adequately maintained using corrugated shipping containers. Lining is with polystyrene and varying amounts of frozen refrigerant can be employed until it is ascertained that receiving facilities are adequate and product can be immediately transferred.

After prolonged transport or storage it is advisable that the specific coagulant factor activity be checked against the manufacturing estimate as printed in the bottle.

In the case of home therapy, it is imperative that consumers who will eventually be storing the factor receive a clear and unequivocal message that temperatures must be controlled if they are to gain maximum advantage from infusions.

11.3 National Storage Facilities

Facilities for the storage and distribution of factor must include comprehensive inventory management and physical security.

As every dispensing vial of factor is received by each intermediate and final storage facility, its arrival and duration of stay, along with its storage conditions, must be recorded in a comprehensive written inventory. When each vial is distributed from that facility, the disposition must be recorded. Once entered into an inventory, the record must not be deleted. A chain of possession is established by recording its next destination. In this manner each vial can be traced through each step to its final destination and back. From the time plasma is collected, tested, manufactured, distributed, and stored in intermediate facilities, several years can pass. It is imperative, in the event of product recall, that all facilities handling the factor be able to account for every vial of factor received and distributed. Access to records and inventory must be restricted to authorized personnel.

A single vial of factor concentrate containing 1000 iu may have a retail value in excess of US $900 but, along with diluent and infusion, the set can fit easily in a small pocket.

11.4 An Information System

A hemophilia registration centre would preferably be equipped with adequate computer equipment and software that can

be used for clinical and public health evaluation. Three types of data are required:

- Hemophilia patient: patient, doctor, source of services, demography, clinical, joint disease data, hospitalizations, laboratory and outcome data to evaluate the system
- Inventory control and tracking of factor use (see paragraph 6.11..3, above)
- Inventory control for plasma samples (see Figure 6, p. 18)

When information is collected according to international standards, results can be made available for study and comparisons with other countries. This allows for evaluation and improvement of services over time.

11.5 Administration of a National Programme

Successful programmes set annual objectives with priorities. The effectiveness of the programme is evaluated annually in order to make necessary adjustments to meet national goals.

The most effective programmes have organization charts designed, and appoint programme directors. Taking into account the numerous tasks involved in achieving these objectives, we believe that this programme director's position should be full-time, at least for the first year. After one year, experience will show if other responsibilities can be attached to this function.

11.6 Financial Considerations

The following check list contains the budget items that should be taken into consideration in developing a national comprehensive care system for hemophilia. Many of these are shared with other healthcare programmes. Health officials responsible for safety should be conscious of the need for funds for recurring expenses such as the maintenance of laboratory equipment and testing material. For example, the cost of such things as the plastic bag and other disposable components necessary to obtain a liter of plasma by plasmapheresis (at lease five or six are used) is fairly high. The cost for this kind of thing must carefully be accounted for.

Table 3 Budget items for a national programme

Supplies
Concentrate and diluent
Transport
Insurance
Packaging
Handling
Import duties
Delivery from airport to storage
Storage costs
Distribution costs
Training
Local training: Transportation and accommodation costs
Training outside the country: Air transportation and accommodation costs
Equipment
Computers
Refrigerators and freezers for HTCs and HCCCs
Coolers/scooters
Recurrent costs
Salaries: national programme coordinator, messengers, social benefits for employees
Vaccination programmes
Laboratory staff
Laboratory tests
Laboratory disposables: syringes, needles, bags, etc.
Liaison newsletter
Prenatal diagnostics
Data base
Computer training for personnel
Unforeseen expenses 15%

12 Clinical Audit of a National Programme

The ultimate purpose of an audit is to improve patient services. Effective audit assesses both patient expectations and measures the standard of their health

services in terms of available resources. These include medical and paramedical personnel, facilities for treatment, therapeutic products, and costs.

Within a country, extensive confidential and comparative auditing can be carried out among various centres, including patient demographics and the use of therapeutic materials. It can be performed by an annual collection of data by mail. However, an audit performed by personal visits provides the opportunity for a friendly, objective and entirely confidential appraisal of a centre. It also affords time to collect patients' views on their care.

Medical audit of a centre should be carried out by a hemophilia specialist from a geographical area not served by that centre. Someone knowledgeable in hemophilia care is essential because of the specialized nature of comprehensive hemophilia care. Keys features of an audit are available on request.