

6 The Role of Prophylaxis

This chapter provides answers to these questions:

- What is prophylaxis?
- What are the different types of prophylaxis?
- Why give prophylaxis in hemophilia?
- When should prophylaxis be started?
- What is the family's role in prophylaxis?
- How should the benefits of prophylaxis be assessed?
- What are the barriers to long-term factor prophylaxis?
- When should prophylaxis be stopped?
- How is prophylaxis different for hemophilia A and hemophilia B?
- What research is currently being done on prophylaxis in hemophilia?
- What is the future of factor prophylaxis?

Victor Blanchette, M.D., FRCPC

*Director, Comprehensive Care Hemophilia Program,
The Hospital for Sick Children, Toronto, Ontario*

Vicky R. Breakey, M.D., FRCPC

*Clinical Fellow, Division of Hematology / Oncology,
The Hospital for Sick Children, Toronto, Ontario*

Manuel Carcao, M.D., FRCPC, M.Sc.

*Associate Director, Comprehensive Care Hemophilia Program,
The Hospital for Sick Children, Toronto, Ontario*

Man-Chiu Poon, M.D., FRCPC

*Director, Southern Alberta Rare Blood and Bleeding Disorders
Comprehensive Care Program, Calgary, Alberta*

Georges-Étienne Rivard, M.D., FRCPC

Director, Centre d'hémostase, CHU Sainte-Justine, Montreal, Quebec



Test Your Knowledge

.....

What country was the first to use long-term factor prophylaxis for boys with severe hemophilia in the 1960s?

(For some help in finding the answer, see page 3 in this chapter.)

(The correct answer is on page 17-18.)

■ What is prophylaxis?

Prophylaxis refers to factor concentrate treatment that is given in anticipation of bleeding, to help prevent bleeds from occurring. There are two very important points about this preventative approach to treatment. First, factor concentrates are infused *before* bleeding has occurred. Second, the aim of treatment is to help prevent bleeding.

■ What are the different types of prophylaxis?

There are several types of prophylaxis:

- short-term prophylaxis
- long-term prophylaxis
- primary prophylaxis
- secondary prophylaxis

Short-Term Prophylaxis

Short-term prophylaxis is treatment given for several days or a few weeks. For example, short-term prophylaxis can involve factor infusions given to control bleeding during and after surgery. Or, it can involve factor infusions for a joint that has had frequent bleeding within a short period of time that shows signs of inflammation (for example, swelling) and/or loss of range of motion.

6 The Role of Prophylaxis

Long-Term Prophylaxis

Long-term prophylaxis refers to the regular infusion of factor concentrates over a long time, generally at least one year and often much longer. For example, long-term prophylaxis can involve factor infusions starting at an early age and given throughout childhood to prevent bleeding into joints. Or, it can involve factor infusions following a bleed into the brain (intracranial hemorrhage) to prevent it from happening again.

Primary Prophylaxis

Primary prophylaxis refers to factor infusions given before any joint damage has occurred because of repeated bleeding.

Secondary Prophylaxis

Secondary prophylaxis refers to factor infusions given after joint damage has already occurred because of repeated bleeding. Bleeding that occurs while on prophylaxis is sometimes called *breakthrough bleeding*.



MYTH:

THE BLOOD OF A CHILD ON PROPHYLAXIS CLOTS NORMALLY.

REALITY:

Typically, prophylaxis raises a child's factor VIII or IX levels to only 20 or 30 percent of normal levels immediately following the infusion. Levels fall to close to 1 percent of normal just before the next infusion. Prophylaxis is not a guarantee against bleeds and joint damage.

■ Why give prophylaxis in hemophilia?

Factor prophylaxis is useful to help prevent bleeding and joint damage in children with hemophilia. Frequent bleeding into joints (in particular ankles, knees and elbows) is common in boys with severe hemophilia, but occurs much less often in boys with mild and moderate hemophilia. The goal of prophylaxis is to raise the factor levels of boys with severe hemophilia to within the range of mild/moderate hemophilia by giving regular infusions of factor VIII or IX.

The success of prophylaxis was first shown by a group of doctors in Sweden, who began a program of long-term factor prophylaxis in boys with severe hemophilia in the 1960s. Their results, reported in the early 1990s after 25 years of follow-up, were so impressive that prophylaxis for boys with severe hemophilia is now considered as the standard of care in countries that have access to safe factor concentrates in sufficient supply.

The ultimate goal is to protect joints so that they can work normally. Prophylaxis helps children with hemophilia be active, attend school regularly and participate in life as fully as possible.

6

The Role of Prophylaxis

■ When should prophylaxis be started?

This is a key question. Some physicians feel that primary prophylaxis should be started after the first joint bleed and certainly by the age of two years. Others note that the pattern of joint bleeding varies from one boy to another, and recommend waiting until he has experienced two bleeds into the same joint within a short period of time before starting prophylaxis.

All hemophilia treaters agree that it is important to start long-term prophylaxis before repeated bleeding has occurred — this helps avoid the development of any joint damage.

■ What is the family's role in prophylaxis?

The family plays a key role in the success of prophylaxis beginning with the decision of when to start. Your hemophilia care team will explain various approaches that are used to introduce prophylaxis and you can decide together what would be best for your child.

Throughout the time that your child is on prophylaxis and until he is old enough to make decisions for himself, your key role is to make sure that the prophylaxis plan is followed. You will need to...

- Keep an accurate diary of his bleeding episodes and treatments.
- Take your child to the clinic for regular check-ups. His hemophilia doctor and nurse will review the prophylaxis plan with you, including the amount and type of factor concentrate to infuse and the frequency and timing of infusions (ideally given in the morning).



6 The Role of Prophylaxis

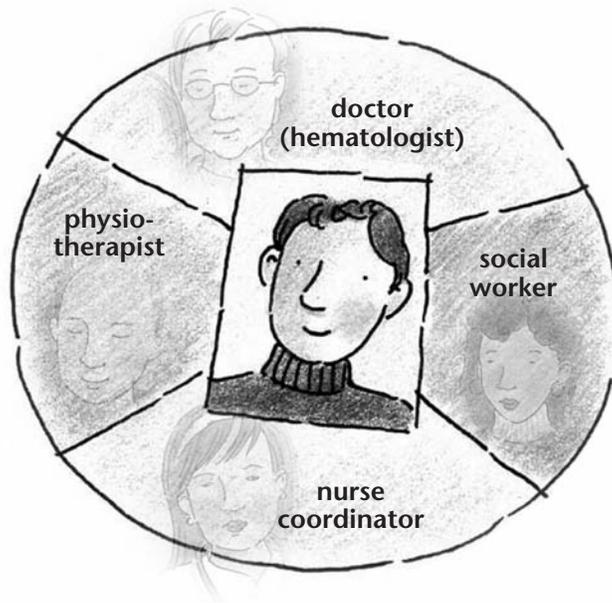
- Learn how to give factor infusions. Your child's hemophilia nurse will teach you all the steps.
- Take over prophylaxis care when you become comfortable giving factor infusions and treatment at home.

Many families find home therapy improves their quality of life and decreases the number of visits to the hospital.

One final and very important point — this is a team effort. The team includes your child and you, and the core members of his comprehensive care team. Everyone on the team has an important role in making sure that the prophylaxis plan is successful. Your child's hemophilia team has lots of experience with ways to start a family on a prophylaxis program. They will work with you to find the approach that is best for your child.

Please remember that you should always feel free to ask questions and be prepared to learn from members of your hemophilia treatment team and other families with children on prophylaxis.

“Prophylaxis has worked well for my son; he does most things that other children do. The at-home treatment has given us so much more control.”



6

The Role of Prophylaxis

■ How should the benefits of prophylaxis be assessed?

Since prophylaxis is demanding for the patient and very expensive for the health care system, it is important to evaluate the prophylaxis treatment plan on a regular basis. This evaluation should include:

- Regular review of the patient's treatment diary to assess the frequency and type of bleeding.
- Studies and tests to assess joint health, for example... X-rays and ultrasound to detect soft tissue changes such as swelling of the synovial lining, magnetic resonance imaging (MRI) to detect changes in the joint cartilage, bone and tissues.
- Regular detailed check-ups with the hemophilia treatment centre physiotherapist using a standard musculoskeletal evaluation. This includes assessment of joint function, loss of motion, and whether there is early or advanced joint disease.
- Regular assessment of the patient's ability to perform the activities of daily living (self-care, personal hygiene, dressing, eating, mobility and movement) on his own.
- Assessment using quality-of-life measures to determine what impact hemophilia is having on the person's overall enjoyment of life.

Test Your Knowledge

.....

What are the four different types of prophylactic clotting factor therapy?

(For some help in finding the answer, see page 1 of this chapter.)

(The correct answer is on page 17-18.)

■ What are the barriers to long-term factor prophylaxis?

The major barriers to prophylaxis are cost and the difficulty in finding veins (venous access) in very young boys with severe hemophilia. Factor concentrates are expensive and life-long prophylaxis costs hundreds of thousands and in some cases even millions of dollars. Fortunately, in Canada, the cost of factor concentrates is covered by our health care system.



The challenge of venous access is a real problem when prophylaxis is started at a very early age, especially in very young boys who are often chubby, and in whom it may be very difficult to locate a vein to infuse a factor concentrate. In such boys it may be necessary to place a central venous access device (generally a port-a-cath) to make it easy to take blood and infuse factor concentrates. This requires a small operation.

Parents will be taught how to access the Port at home. The major complications with Ports are infection of the blood and clot formation in the veins (thrombosis) and around the tip of the catheter. Ports are usually used only when the doctors and parents find it very hard to find a vein to insert the needle. Your hemophilia physician and nurse can speak to you about whether this could be useful for your child.  For more information, see **Chapter 7, Home Infusion.**



6

The Role of Prophylaxis

■ When should prophylaxis be stopped?

We do not know. In Sweden, prophylaxis is generally continued throughout life. In most other countries, adolescents and young adults decide whether to continue prophylaxis or not. If prophylaxis is stopped, it is very important to treat all joint bleeds early with factor concentrates in order to preserve the benefits of early prophylaxis given during childhood years.

■ How is prophylaxis different for hemophilia A and hemophilia B?

The dose of factor needed per infusion and the frequency of infusions varies. For example, the frequency of infusions needed for effective prophylaxis in boys with severe hemophilia B may be less than for boys with severe hemophilia A — this is because factor IX lasts longer than factor VIII in the bloodstream after it is infused. The *half-life* of factor VIII (the time it takes for half of the factor to disappear from the person's bloodstream) is approximately 10-12 hours, while the half-life of factor IX is approximately 20-24 hours.



■ What research is currently being done on prophylaxis in hemophilia?

The Canadian Dose Escalation Primary Prophylaxis Study, started in 1997, has provided us with very important information about prophylaxis in very young boys with severe hemophilia A.

- Boys with severe hemophilia A were started on once-weekly infusions of factor VIII.
- If unacceptable bleeding occurred into muscles or joints, the frequency of infusions was increased to twice weekly.
- If unacceptable bleeding into muscles and joints continued to occur on this more intense prophylaxis protocol, the frequency of factor VIII infusions was increased to alternate days.

This step-by-step approach, adapted to the bleeding patterns of each individual child with severe hemophilia A, is seen as an ideal way to introduce prophylaxis. In addition, it may reduce the need for central venous access devices that carry some risk of infections and thrombosis.

6 The Role of Prophylaxis

■ What is the future of prophylaxis?

Prophylaxis is likely to remain the standard of care for young children with severe hemophilia A and B for several decades. Cure of hemophilia by gene therapy is the ultimate goal but this treatment is not yet advanced enough to be used with patients.

An exciting new development in the treatment of hemophilia A is the creation of new factor VIII preparations that last longer when infused than the factor VIII concentrates that are available now. The first clinical trial of an extended half-life factor VIII product is in progress. If successful, factor infusions to prevent bleeds could be given less frequently. Work to develop long-acting recombinant factor IX preparations is in progress.

 For more information, see **Chapter 16, The Future of Hemophilia Care.**

