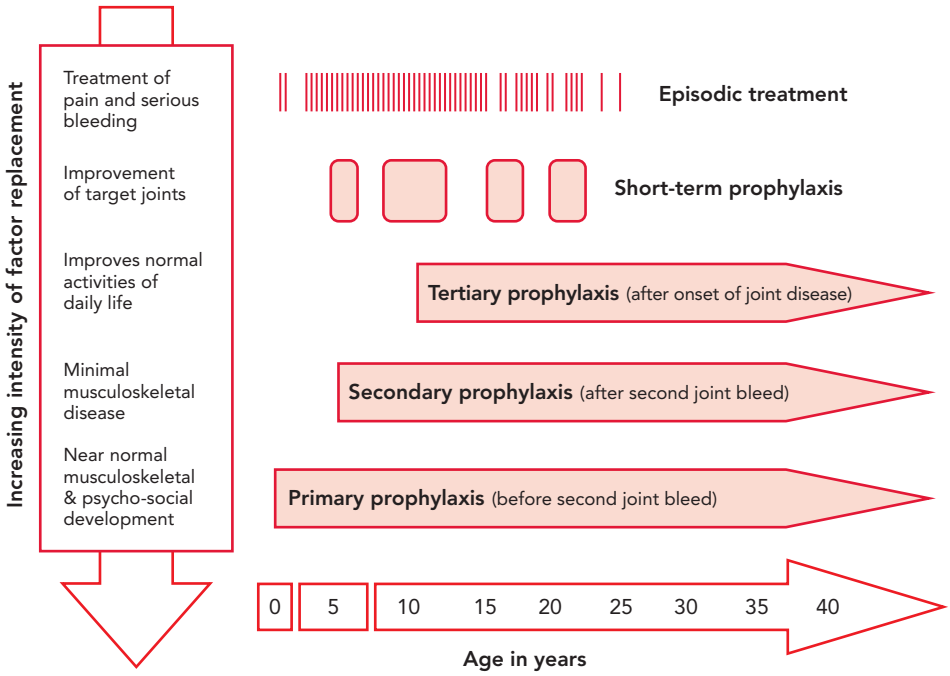
7 PLASMA FACTOR LEVEL AND DURATION OF ADMINISTRATION

7.1 Choice of factor replacement therapy protocols

1. The correlation shown in Figure 7-1 between possible factor replacement therapy protocols and overall outcome depicts the choices that one needs to make when selecting doses and regimen of clotting factor concentrates.
2. While enabling a completely normal life should remain the ultimate goal of factor replacement therapy, this cannot be achieved immediately in people with hemophilia in all situations.
3. The availability of treatment products varies significantly around the world and there will therefore always be a range of doses with which people with hemophilia are treated. Lower doses may increase as the global availability of treatment products improves incrementally over time.

FIGURE 7-1: STRATEGIES FOR CLOTTING FACTOR REPLACEMENT AT DIFFERENT AGES AND IMPACT ON OUTCOMES



Adapted from Blood Transfus 2008 Sep;6 Suppl 2:s4-11

4. Table 7-1 and Table 7-2 present commonly followed guidelines on plasma factor peak levels and duration of replacement that reflect the different practices in countries where there is no significant resource constraint (Table 7-1) and countries where treatment products are limited (Table 7-2).
5. With the lower doses for treating musculoskeletal bleeds listed in Table 7-2, it may only be possible to avoid major target joints and crippling deformities.
6. Higher doses listed in Table 7-1 have been shown to avoid joint damage, but the optimal dose needed to achieve this remains to be defined.
7. Observational studies documenting the musculoskeletal outcome of doses and protocols of factor replacement are extremely important in defining these issues.
8. Doses for prophylactic replacement of factor concentrates vary between different countries and also among centres in the same country.
9. **Commonly-used dosage for prophylactic factor replacement is 25-40 IU/kg 2-3 times weekly in countries with less resource constraints (see Section 1 for details). [1-3]**
10. **In situations where there are greater constraints on supply of factor concentrates, prophylaxis may be initiated with lower doses of 10-20 IU/kg 2-3 times per week. (Level 2) [4,5]**

TABLE 7-1: SUGGESTED PLASMA FACTOR PEAK LEVEL AND DURATION OF ADMINISTRATION (WHEN THERE IS NO SIGNIFICANT RESOURCE CONSTRAINT) [6]

	HEMOPHILIA A		HEMOPHILIA B	
TYPE OF HEMORRHAGE	DESIRED LEVEL (IU/DL)	DURATION (DAYS)	DESIRED LEVEL (IU/DL)	DURATION (DAYS)
Joint	40–60	1–2, may be longer if response is inadequate	40–60	1–2, may be longer if response is inadequate
Superficial muscle/no NV compromise (except iliopsoas)	40–60	2–3, sometimes longer if response is inadequate	40–60	2–3, sometimes longer if response is inadequate
Iliopsoas and deep muscle with NV injury, or substantial blood loss				
▪ initial	80–100	1–2	60–80	1–2
▪ maintenance	30–60	3–5, sometimes longer as secondary prophylaxis during physiotherapy	30–60	3–5, sometimes longer as secondary prophylaxis during physiotherapy
CNS/head				
▪ initial	80–100	1–7	60–80	1–7
▪ maintenance	50	8–21	30	8–21
Throat and neck				
▪ initial	80–100	1–7	60–80	1–7
▪ maintenance	50	8–14	30	8–14
Gastrointestinal				
▪ initial	80–100	7–14	60–80	7–14
▪ maintenance	50		30	
Renal	50	3–5	40	3–5
Deep laceration	50	5–7	40	5–7
Surgery (major)				
▪ Pre-op	80–100		60–80	
▪ Post-op	60–80 40–60 30–50	1–3 4–6 7–14	40–60 30–50 20–40	1–3 4–6 7–14
Surgery (minor)				
▪ Pre-op	50–80		50–80	
▪ Post-op	30–80	1-5, depending on type of procedure	30–80	1–5, depending on type of procedure

NV; neurovascular

TABLE 7-2: PLASMA FACTOR PEAK LEVEL AND DURATION OF ADMINISTRATION (WHEN THERE IS SIGNIFICANT RESOURCE CONSTRAINT)

	HEMOPHILIA A		HEMOPHILIA B	
TYPE OF HEMORRHAGE	DESIRED LEVEL (IU/DL)	DURATION (DAYS)	DESIRED LEVEL (IU/DL)	DURATION (DAYS)
Joint	10–20	1–2 may be longer if response is inadequate	10–20	1–2, may be longer if response is inadequate
Superficial muscle/no NV compromise (except iliopsoas)	10–20	2–3, sometimes longer if response is inadequate	10–20	2–3, sometimes longer if response is inadequate
Iliopsoas and deep muscle with NV injury, or substantial blood loss				
▪ initial	20–40		15–30	
▪ maintenance	10–20	3–5, sometimes longer as secondary prophylaxis during physiotherapy	10–20	3–5, sometimes longer as secondary prophylaxis during physiotherapy
CNS/head				
▪ initial	50–80	1–3	50–80	1–3
▪ maintenance	30–50 20–40	4–7 8–14	30–50 20–40	4–7 8–14
Throat and neck				
▪ initial	30–50	1–3	30–50	1–3
▪ maintenance	10–20	4–7	10–20	4–7
Gastrointestinal				
▪ initial	30–50	1–3	30–50	1–3
▪ maintenance	10–20	4–7	10–20	4–7
Renal	20–40	3–5	15–30	3–5
Deep laceration	20–40	5–7	15–30	5–7
Surgery (major)				
▪ Pre-op	60–80		50–70	
▪ Post-op	30–40 20–30 10–20	1–3 4–6 7–14	30–40 20–30 10–20	1–3 4–6 7–14
Surgery (minor)				
▪ Pre-op	40–80		40–80	
▪ Post-op	20–50	1–5, depending on type of procedure	20–50	1–5, depending on type of procedure

NV; neurovascular

References

1. Astermark J, Petrini P, Tengborn L, Schulman S, Ljung R, Berntorp E. Primary prophylaxis in severe haemophilia should be started at an early age but can be in dividualized. *Br J Haematol* 1999 Jun;105(4):1109-13.
2. Blanchette VS. Prophylaxis in the haemophilia population. *Haemophilia* 2010;16(Suppl 5):181-8.
3. Gringeri A, Lundin B, von Mackensen S, Mantovani L, Mannucci PM; ESPRIT Study Group. A randomized clinical trial of prophylaxis in children with hemophilia A (the ESPRIT Study). *J Thromb Haemost* 2011 Apr;9(4):700-10.
4. Fischer K, van der Bom JG, Mauser-Bunschoten EP, Roosendaal G, Prejs R, Grobbee DE, van den Berg HM. Changes in treatment strategies for severe haemophilia over the last 3 decades: effects on clotting factor consumption and arthropathy. *Haemophilia* 2001 Sep;7(5):446-52.
5. Wu R, Luke KH, Poon MC, Wu X, Zhang N, Zhao L, Su Y, Zhang J. Low dose secondary prophylaxis reduces joint bleeding in severe and moderate haemophilic children: a pilot study in China. *Haemophilia* 2011 Jan;17(1):70-4.
6. Rickard KA. Guidelines for therapy and optimal dosages of coagulation factors for treatment of bleeding and surgery in haemophilia. *Haemophilia* 1995;1(S1):8–13.