

Intensive Care Nursery House Staff Manual

Neonatal Coagulation Disorders

BACKGROUND AND PATHOPHYSIOLOGY: Neonatal bleeding results from disorders of platelets, coagulation proteins, and disorders of vascular integrity. While healthy newborns have low levels of some coagulation proteins, this is normally balanced by the paralleled decrease in fibrinolytic activity.

CAUSES OF NEONATAL BLEEDING:

1. Platelet Disorders

A. Thrombocytopenia (platelet count $<150 \times 10^9/L$) occurs in 1-4% of term newborns, 40-72% of sick preterms and 25% of ICN admissions; of these, 75% present before age 72h. Causes include:

- **Decreased platelet production** occurs in congenital infections (*e.g.*, CMV, Rubella, HIV), certain syndromes (*e.g.*, Thrombocytopenia Absent Radius, Fanconi), sepsis and Hemolytic Disease of Newborn.
- **Increased platelet consumption**, occurs in:
 - Maternal auto-immune disease (*e.g.*, ITP, SLE) -Asphyxia/Shock
 - Neonatal Alloimmune Thrombocytopenia -Maternal thiazide intake
 - IUGR with toxemia of pregnancy -Necrotizing enterocolitis
 - Thrombosis (due to catheters, hemangiomas) -Sepsis
 - Hemolytic disease of the newborn -Exchange transfusion
 - Heparin-induced thrombocytopenia -Polycythemia/Hyperviscosity

B. Impaired platelet function is rare in the newborn except for:

- Decreased platelet adhesiveness associated with **indomethacin** therapy
- Von Willebrand's Disease

2. Coagulation Protein Disorders

A. Congenital factor deficiencies:

- X-linked recessive: Hemophilia A (Factor VIII) and Hemophilia B (Factor IX)
- Autosomal recessive (rare): Factors V, VII, X, XI, XII, XIII, afibrinogenemia

B. Acquired deficiencies: Most common is Vitamin K deficiency.

3. Combined Platelet and Coagulation Factor Disorders:

A. Disseminated Intravascular Coagulation (DIC) occurs secondary to inappropriate systemic activation of normal clotting mechanisms after endothelial injury. Infants have low platelet counts and fibrinogen levels, prolonged PT and PTT, and elevated Fibrin Degradation Products.

B. Hepatic Dysfunction due to several causes (*e.g.*, shock, infection, inherited conditions); most have prolonged PT and decreased factor and fibrinogen levels.

4. Disorders of Vascular Integrity such as hemangiomas or vascular malformations, that may rupture and directly bleed, or sequester platelets and secondarily cause bleeding.

SIGNS AND SYMPTOMS vary with the cause of bleeding, magnitude of blood loss and the underlying disease. Signs of abnormal bleeding tendency include petechiae, excessive bruising, prolonged bleeding from puncture sites, umbilical oozing, gastrointestinal bleeding, hematuria, pulmonary hemorrhage, subgaleal hemorrhage and

intracranial hemorrhage. When blood loss is large, the infant may present with signs of hypovolemia (pallor, weak pulses, tachycardia, hypotension, metabolic acidosis).

DIAGNOSTIC EVALUATION OF ABNORMAL BLEEDING:

1. History:

- Family history of bleeding disorders or neonatal deaths (but may be negative even with inherited disorders)
- Maternal history of bleeding disorders, medication intake, previous neonatal deaths, auto-immune disease
- Perinatal: Toxemia of pregnancy, IUGR, infections, antepartum bleeding
- Neonatal: History of asphyxia, birth trauma, administration of Vitamin K, gender (X-linked disorders)

2. Neonatal physical examination:

- Signs of bleeding
- Signs of hypovolemia
- Other malformations
- Signs of infection (hepatosplenomegaly)
- Hemangiomas, vascular malformations
- Other illness (*e.g.*, NEC, hemolytic disease)

3. Laboratory investigation:

A. Initial screen

- CBC, differential, smear
- Prothrombin time (PT)
- Fibrinogen
- Platelet count
- Partial Thromboplastin Time (PTT)

Draw blood from non-heparinized source (or ask Laboratory to add Heptasorb).

B. If Neonatal Allo-Immune Thrombocytopenia (NAIT) is suspected, send mother's and infant's blood for platelet count and typing. With NAIT, maternal platelet count is normal and, in most cases, the mother will be HPA-1 negative (Only 2% of population is HPA-1 negative.). Infants with NAIT are at risk for serious intracranial hemorrhage. **For severe thrombocytopenia, platelet transfusion is indicated. Washed maternal platelets (to remove antibody) are the treatment of choice. If not practical, HPA-1 negative platelets are the second choice, but are difficult to obtain. Random-donor platelets should be used if other choices are not available. IVIG therapy will often increase the platelet count.**

C. Subsequent evaluation: If abnormal bleeding is not secondary to an underlying illness and **appears to be a primary coagulopathy, obtain Hematology consult immediately.** They will direct subsequent evaluation and treatment.

MANAGEMENT: For secondary bleeding disorders, treat underlying disease.

Replacement of clotting factors is often necessary:

1. Severe, life threatening bleeding:

- Maintain adequate circulating blood volume. (See: Neonatal Shock, P. 101)
- Send blood for clotting studies (See 3A above).
- If clotting defect is not known, consider giving all of the following:
 - Vitamin K 1 mg IV **slowly over 1 min** (Rapid infusion of Vitamin K can cause cardiac dysrhythmias).
 - Fresh Frozen Plasma 10 mL/kg over 5-10 min.
 - Platelets 1 unit
 - Cryoprecipitate 1 unit

- Send repeat clotting studies in 4-6h
 - Obtain Hematology Consult if bleeding is not controlled quickly.
2. **Bleeding with known abnormal clotting screening tests** (See 3A above).
 - A. Prolonged prothrombin time (PT), normal PTT, platelets and fibrinogen:**
Give Vitamin K 1 mg IV **slowly over 1 min** (Rapid infusion of Vitamin K can cause cardiac dysrhythmias). Repeat PT in 4h. If not improved, consider Hematology Consult to R/O specific factor deficiency.
 - B. Prolonged PT and PTT:** Give Fresh Frozen Plasma 10 mL/kg and Vitamin K 1 mg. Send repeat clotting studies in 2h.
 - C. Low fibrinogen:** Give cryoprecipitate 1 unit.
 - D. Thrombocytopenia:** Serious bleeding usually does not occur unless there is severe thrombocytopenia (*i.e.*, $<20 \times 10^9/L$). With “sick” infants (*i.e.*, other severe disease; receiving assisted ventilation), bleeding may occur at higher levels. Therefore, for these infants, use platelet transfusions to maintain platelets $>50 \times 10^9/L$. Platelets should be type and Rh specific, irradiated, and CMV negative (If infant is possibly immunocompromised). (For treatment of NAIT, see 3B above.)
 3. **For any bleeding problem that is not controlled adequately and quickly, obtain Hematology Consult.**
 4. For significant bleeding from any cause, consider **cranial ultrasound**, especially in preterm infants.

Table. Products for Treatment of Coagulopathies.

<u>Product</u>	<u>Factor Content</u>	<u>Usual Dose</u>	<u>Indications</u>
Fresh frozen plasma	All factors	10-20 mL/kg	Disseminated intravascular coagulation (DIC); liver disease; protein C deficiency
Exchange transfusion*	All factors, platelets	Double volume	Severe DIC; liver disease
Factor VIII concentrate	Factor VIII	25-50 U/kg	Factor VIII deficiency (Hemophilia A)
Factor IX concentrate	Factor IX	50-100 U/kg	Factor IX deficiency
Vitamin K		1-2 mg	Vitamin K deficiency
Platelet concentrate	Platelets	1-2 units/5 kg [‡]	Severe thrombocytopenia
Intravenous gamma globulin	IgG	1-2 g/kg	Severe sepsis; thrombocytopenia due to transplacental antibodies

*If fresh whole blood is used.

[‡]Response to platelets can vary markedly, depending on underlying condition.