Approach to the bleeding newborn

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Bleeding in the newborn can lead to serious cardiovascular and neurological effects. Routine administration of vitamin K has reduced the incidence of hemorrhagic disease of the newborn, but abnormal bleeding can occur in babies from many causes. A practical approach to the diagnosis and treatment of bleeding in the newborn is described in this article.

Key Words: *Bleeding, Hemorrhage, Newborn, Vitamin K*

Une méthode de prise en charge du nouveau-né qui saigne

Une hémorragie chez le nouveau-né peut entraîner des effets cardiovasculaires et neurologiques graves. L'administration systématique de vitamine K a réduit l'incidence de syndrome hémorragique du nourrisson, mais des saignements anormaux peuvent survenir pour de nombreuses raisons. Cet article présente une méthode pratique de diagnostic et de traitement de cette hémorragie chez le nouveau-né.

Bleeding in the newborn is often a serious problem because of cardiovascular effects associated with a loss of blood and/or the damaging effects of bleeding on neonatal tissues, especially the brain. Forty years ago, hemorrhagic disease of the newborn occurred in 1% to 2% of newborn babies (1). With vitamin K administration routinely administered following birth, this problem is now rare in the normal newborn (2). Babies in the neonatal intensive care unit (NICU) more commonly have abnormal bleeding or conditions that increase the risk of bleeding (eg, thrombocytopenia with platelet count less than 100×10^9/L occurs in 12% of babies in the NICU [3]). A report of the Canadian Paediatric Surveillance Program suggested that practitioners may benefit from a simple approach to bleeding in the newborn (4).

The development of the hemostatic and thrombolytic systems has recently been reviewed (5,6). Many plasma coagulation and fibrinolytic factors are decreased in a newborn versus an adult; this is especially true for vitamin K-dependent and contact factors (6). The 'cascade' of coagulation and fibrinolysis has also been reviewed (7). A practical approach to the diagnosis and treatment of bleeding in the newborn is outlined in this article.

CLINICAL ASSESSMENT

Bleeding in the newborn may be manifested by signs of shock, anemia, signs related to pressure from 'hidden' bleeding (eg, intraventricular hemorrhage), or bleeding from the gastrointestinal tract, respiratory system or skin. With bleeding from the gastrointestinal tract, it is important to distinguish bleeding in the baby from swallowed maternal blood (an Apt test will distinguish fetal from adult hemoglobin). Bleeding in the baby may occur before or during birth (Table 1), presenting as cardiovascular or respiratory instability at birth and/or anemia.

Once abnormal bleeding in the newborn is identified, the first management approach is to ensure cardiorespiratory stability. A diagnosis to aid in more specific management may then be made.

An approach to the bleeding newborn is outlined in Table 2. A family history of a bleeding disorder, maternal illness with infection that may affect the fetus and maternal thrombocytopenia are uncommon occurrences but are important to identify. Maternal idiopathic thrombocytopenic purpura, even several years before a baby's birth, may be associated with neonatal thrombocytopenia. Thiazides in pregnancy have been associated with neonatal thrombocytopenia, and maternal acetylsalicylic acid use may inhibit platelet function of the baby. Anticonvulsants, rifampin and isoniazid may be associated with severe vitamin K deficiency, with bleeding in the newborn happening within the first two days of life (2).

Physical examination of the newborn helps to determine the support that the baby requires and the diagnosis (Table 3) (7). Bleeding in the well newborn suggests an inherited coagulation disorder, vitamin K deficiency or immune-mediated thrombocytopenia. Disseminated intra-

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TABLE 1: Possible causes of bleeding before or during birth

Origin of bleeding	Examples
Transfusion	• Fetal to maternal • Twin to twin
Placenta	• Placenta previa, abruption • Vasa previa • Cord accident
Baby	• Intracranial hemorrhage • Cephalhematoma, subgaleal hemorrhage • Abdominal organs (liver, spleen)

TABLE 2: A clinical approach to the bleeding newborn

History	• Family bleeding disorder • Maternal illness (eg, infection, HELLP syndrome) • Maternal drugs (eg, acetylsalicylic acid, coumadin, anticonvulsants)
Physical examination	• Well or sick baby • Hepatosplenomegaly • Bleeding sites • Physical abnormalities

HELLP Hypertension, elevated liver enzymes, low platelets

vascular coagulation (DIC) is more common in the sick newborn. Petechiae or purpura in the skin are more characteristic of thrombocytopenia, while bleeding from injury sites (eg, circumcision, heel lance) or the gastrointestinal system suggests other coagulation defects. However, more than 90% of babies with inherited coagulation disorders (eg, hemophilia) present after the neonatal period. Laboratory investigations are important aids in the diagnosis of bleeding disorders in newborn babies (Table 3).

LABORATORY ASSESSMENT

Bleeding abnormalities may be associated with respiratory distress syndrome, and intrapulmonary or intraventricular hemorrhage (8). Measures to potentially prevent or manage these abnormalities are beyond the scope of this article. Laboratory investigation should include an activated partial thromboplastin time (APTT), prothrombin time (PT) (or more commonly international normalized ratio [INR] to standardize for different reagents) and complete blood count with platelet count. Additionally, all sick newborns should have fibrinogen and fibrin degradation products (FDP) measured. (Fibrinogen concentrations may be normally less in premature babies, and FDP may be increased with liver disease or after blood transfusion as well as with DIC.) Blood should preferably be taken from a venous site. Capillary samples are more prone to errors, with clotting in samples including platelet clumping. Although blood from an arterial line may be used if measures are taken to minimize heparin contamination and protamine is used to neutralize any heparin that may be present (8), this should be reserved for situations when other blood samples cannot be obtained.

Coagulation tests should be ordered whenever the cause of bleeding is not clear. Reference values for coagulation tests at varying ages are available (5,6). In general, the following are considered abnormal:

- PT 17 s or more;
- INR 1.5 or greater;
- APTT 60 s or greater (preterm 80 s or greater in first day of life);
- fibrinogen less than 1.5 g/L;
- FDP present; or
- platelet count less than $100{,}000 \times 10^9$/L

While an INR 1.4 or less (or normal PT) rules out vitamin K deficiency, abnormalities in APTT without other evidence of DIC may require more detailed investigation. Measuring factor VIII may help distinguish DIC (low) from liver dysfunction (normal or high), although factor VIII may also be congenitally deficient. In many of these situations, consultation with a hematologist with paediatric experience is advisable to guide investigation and management.

Diagnosis and management of maternal thrombocytopenia may include intravenous immunoglobulin (IVIG), steroids and rarely fetal transfusion in an endeavour to minimize potential adverse effects on the fetus, especially

TABLE 3: Suggested clinical and laboratory approach to the differential diagnosis of bleeding in newborn babies

	Laboratory investigations			
Health status	**Platelets**	**INR (PT)**	**APTT**	**Possible diagnosis**
Sick	↓	↑	↑	Disseminated intravascular coagulation (usually low factor VIII)
	↓	N	N	Platelet consumption (infection, necrotizing enterocolitis, renal vein thrombosis)
	N	↑	↑	Liver disease, heparinization (usually normal factor VIII)
	N	N	N	Altered vascular integrity (eg, extreme prematurity, severe hypoxia and acidosis
Healthy	↓	N	N	Immune thrombocytopenia, occult infection or thrombosis, abnormal bone marrow function
	N	↑	↑	Hemorrhagic disease of the newborn (vitamin K deficiency)
	N	N	↑	Hemophilia
	N	N	N	Bleeding due to trauma or anatomic abnormalities, qualitative platelet abnormalities

↑ Increased; ↓ Decrease; APTT Activated partial thromboplastin time; DIC Disseminated, intravascular coagulation; INR International normalized ratio; N Normal

intracranial hemorrhage (9). While thrombocytopenia in the newborn is relatively common, it is not always associated with bleeding. Thrombocytopenia has varied etiology (Table 4) (3,9). Diagnosis may be helped by the microscopic examination of platelet size. Large platelets are more indicative of platelet consumption with new large platelets entering the circulation, while only small platelets may indicate disordered bone marrow function (9). Flow cytometry may be used to look for reticulocytes and immunoglobulins on the surface of platelets. If thrombocytopenia in the baby is otherwise unexplained, a maternal platelet count is useful (9). Alloimmune thrombocytopenia may be suspected on the basis of a low platelet count in the absence of other etiologies or the absence of response to a platelet transfusion. More specific platelet typing and investigation for antiplatelet antibodies may be required (10). Investigation for uncommon qualitative defects in platelet function requires specialized tests usually in consultation with a hematologist.

TABLE 4: Common causes of neonatal thrombocytopenia

Increased destruction	• Disseminated intravascular coagulation • Localized (thrombosis, hemangiomas, necrotizing endocarditis)
Decreased production	• Trisomy 13, 18 or 21 • Fanconi anemia • Syndromes (eg, Wiskott-Aldrich, thrombocytopenia, absent radius [TAR])
Other or mixed	• Rh disease • Exchange transfusion • Extracorporeal membrane oxygenation

MANAGEMENT

Management should initially be directed at promotion of cardiorespiratory stability, which may require replacement of intravascular volume and occasionally other cardiorespiratory support. Additional treatment should correct the underlying etiology (eg, infection). Although intramuscular injections are not recommended with a known bleeding disorder, it is rare to see problems with intramuscular injections of vitamin K or later immunizations using small needles even in babies with hemophilia. For the baby with bleeding, in addition to ensuring adequate vitamin K, many coagulation factor abnormalities may be corrected with intravenous administration of 10 to 15 mL/kg fresh frozen plasma (1). Use of cryoprecipitate may be indicated with factor VIII deficiency (congenital or acquired with DIC) and/or hypofibrinogenomia. The potential hazards of transfusion of blood products should be kept in mind. The risks may be lessened by the use of heat-inactivated products and with appropriate blood banking procedures. The complications of continued bleeding are potentially more severe.

Although no well controlled studies are available, suggestions have been given regarding indications for platelet transfusion (1,7). The following guidelines may be considered:

- for premature infants, platelet count of less than 50×10^9/L in a stable infant as clinically assessed and platelet counts of less than 100×10^9/L in a bleeding infant or if surgery is anticipated; and
- for term infants, platelet count less than 30×10^9/L in a stable infant and platelet count less than 50×10^9/L if there is bleeding or need for an invasive procedure.

More liberal criteria (eg, platelets less than 100×10^9/L) may be used for platelet transfusions when bleeding is severe (eg, DIC). Other therapy such as the use of IVIG for neonate alloimmune thrombocytopenia may also be helpful (7).

SUMMARY

Because bleeding in the newborn is often a serious event, the paediatric practitioner should approach the problem in a systematic manner. If bleeding is without apparent cause, all babies should have at least a basic laboratory evaluation. This may assist immediate management and help to determine whether there are future implications for the baby. Management should include potential prevention, measures to ensure cardiorespiratory stability, treatment of underlying problems and replacement of coagulation factors. In more complex cases, investigation and management may be guided by a consultation with a hematologist who may also assist in follow-up if ongoing problems are anticipated.

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