Approach to a bleeding neonate

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Introduction:

- Neonatal bleeding is associated with such catastrophes because of the relatively small total blood volume of newborn infants as well as the tendency to be concealed in some cases.
- Bleeding disorders had been reported to be a contributor to newborn morbidity and mortality in various centres in different parts of the developing world.

Physiological peculiarities of neonatal hemostasis:

- Although, the platelets count is the same for adults as well as preterm and term babies (150 400 × 10 /l), preterm babies are more prone to bleeding due to easy bruising arising mainly from ***increased fragility of their blood vessels***.
- The plasma levels of fibrinogen and clotting factors V and VIII in newborns are also near adult levels while those of factors ***II, VII, IX, X, XI, XII and XIII are very depressed*** in newborn infants. These deficiencies are worse in preterm infants because hepatic synthesis of clotting factors ordinarily increase with gestation.
- Anti-coagulation factors like ***antithrombin III, plasminogen and Proteins C and S are also remarkably low at birth.*** These deficiencies in the anti-coagulation factors protect neonates against abnormal bleeding despite the physiologic deficiencies in the clotting factors.
- Therefore, laboratory values of these parameters in the neonatal period should be interpreted with consideration for the maturity and age of the patient.

Evaluation of a bleeding neonate:

- The first essential step in the evaluation of a bleeding neonate is to establish whether the bleeding infant is ***well or sick***. An ill baby may have fever, hypothermia, lethargy or irritability, feed refusal, feed intolerance, poor colour or abnormal cry.

Features of abnormal bleeding:

- This may include spontaneous umbilical oozing, oozing from injection and venepuncture sites, cephalohaematoma and subgaleal haematoma, petechiae, purpura, easy bruising and ecchymosis.
- Other manifestations include post-circumcision bleeding, bleeding into muscles and joints, mucosal bleeding like malaena, haematochezia, heamatemesis and haematuria. It may also be concealed in the cranium (usually within the ventricles, cerebral tissues or in the subarachnoid spaces) and manifest with features of raised intracranial pressure like seizures and altered sensorium.

A detailed history and complete physical examination is, therefore, essential in establishing the aetiology and severity of bleeding.

History:

- *Bleeding occurring soon after birth* may be due to neonatal thrombocytopaenia (autoimmune or alloimmune), disseminated intravascular coagulopathy (DIC) or haemophilia.
- *Classic vitamin K deficiency bleeding (VKDB)* occurs typically between the 2 and 5 days of life, while the late form occurs between the 4 and 12 weeks of life. Babies who are exclusively breastfed or babies on nil per oral and prolonged antibiotic therapy are particularly prone to *late onset VKDB* especially if they are not given prophylactic vitamin K soon after birth.
- *Maternal febrile illnesses* associated with exanthema or jaundice during pregnancy may suggest intrauterine TORCHES (toxoplasmosis, rubella, cytomegalovirus, herpes, Epstein Barr virus and syphilis) infection. Such intrauterine infections cause nepnatalhrombocytopaenia.
- *Previous bleeding episodes in the mother* may suggest autoimmune thrombocytopaenia following Immune Thrombocytopaenia (ITP) and systemic lupus erythematosus (SLE).
- *History of perinatal events* like abruptio placentae and asphyxia are also usual in neonatal bleeding due to DIC. DIC occurs commonly in neonatal intensive care units as a complication of neonatal sepsis.
- *Maternal ingestion of drugs* like phenytoin, isoniazid and non-steroidal anti-inflammatory agents may increase the hepatic metabolism of vitamin K and

predispose to VKDB. Quinine and sulphonamides therapy may also cause immune-mediated maternal and neonatal thrombocytopaenia.

- *History of previous neonatal bleeding and recurrent neonatal deaths* may suggest neonatal alloimmune thrombocytopaenia (NAIT) although this may occur in the first pregnancy in about 40 to 50% of cases.
- *Family history of bleeding may suggest inherited disorders* particularly haemophilias, von Willebrand disease and clotting factor deficiencies. Parental consanguinity may also predispose to disorders of platelet functions like Bernard-Soulier syndrome.

Physical findings:

- *Examine for the tell-tale signs of bleeding* - uncontrolled oozing, purpura, petechiae, ecchymosis, pallor and features of circulatory collapse,
- *Examine for etiology - specific signs –*
    - Microcepahly, chorioretinitis, cataract and hepatosplenomegaly occur in TORCHES infection.
    - Prolonged jaundice and hepatomegaly may occur in hepatic diseases.
    - Seizures and apnea as well as severe respiratory distress may occur in severe cases of intracranial and pulmonary bleeding respectively.
    - Congenital hydrocephalus may occur from intra-uterine intracranial haemorrhage occurring in NAIT.
    - Rapidly-enlarging haemangioma may result in Kasabach-Merritt syndrome.
    - Limb deformity especially absent radii occur in TAR (thrombocytopaenia, absent radii) which is a cause of inadequate platelet production.

Laboratory investigations:

Laboratory investigation	Interpretation
Complete blood count (CBC)	• **The haematocrit (Hct)** • May be abnormally low (<0.45) following severe blood loss and in the presence of TORCHES infection. • **Leucocyte count:** • Usually normal except in some cases of NAIT when neutropaenia may occur. • Increase or decrease in sepsis • **Platelets counts**: • Thrombocytopaenia is associated with DIC, septicaemia, TORCHES infection, NAIT, maternal immune thrombocytopaenia, Kasabach-Merritt syndrome and congenital disorders like TAR, Trisomy 18, Fanconi anaemia and Wiskott Aldrich syndrome. • **Congenital thrombocytopaenia**– • Monitor maternal platelet counts. • This issignificantly reduced in autoimmune cases while it is within normal limits in alloimmune cases. • In NAIT, the mother is usually negative for the platelet antigen PAI-1a while the baby is positive for PAI-1a. Instructively, the PAI-1a platelet antigen is the commonest. • **Qualitative platelet defect**: • VKDB, liver disease, haemophilia, vonWillebrand disease and disorders of platelet function like Glanzmann thrombastenia are associated with normal platelets count

Peripheral blood smear	• Fragmented erythrocytes and burr cells typically occur in DIC and Kasabach-Merritt syndrome. • Reticulocytes and nucleated cells are increased in TORCHES infection. • Giant platelets occur in maternal immune thrombocytopaenia, NAIT and Kasabach-Merritt syndrome while the platelets appear dysplastic in TAR and Bernard-Soulier syndrome.
Fibrin degradation product (FDP) and D Dimer	• These are increased in situations of increased cell fragmentation like DIC and Kasabach-Merritt syndrome.
Apt test	• Helps to differentiate between neonatal gastrointestinal haemorrhage and swallowed maternal blood syndrome when neonates present with Malena or pseudo haemorrhage of the gastrointestinal system soon after birth
Bone marrow examination	• This is relevant in cases of bleeding secondary to inadequate platelet production as it may occur in congenital leukaemia and Wiskott Aldrich syndrome where excessive blast cells and dysplastic megakaryocytes respectively are typical.
Liver function test	• Hyperbilirubinaemia, decreased serum albumin and deranged hepatic enzymes (Aspartate transaminase, Alanine transaminase and Alkaline transferase) characterize TORCHES infection and liver diseases generally.
Coagulation profile	• **Normal coagulation profile** - Prothrombin Time (PT) - 11 to15 seconds,Partial Thromboplastin Time (aPTT) - 30 to 40 seconds, Thrombin Time (TT) - 11 to 15 seconds, bleeding time (BT) - 4 to 8 minutes (mostly determined by individual laboratories).

	• **Prolonged PT and PTT with reduced plasma fibrinogen** - DIC, TORCHES infection, Kasabach-Merritt syndrome and liver impairment. • **Prolonged PT and PTT with normal fibrinogen level**- VKDB. • **Normal PT and PTT** - in maternal immune thrombocytopenias, NAIT, conditions of inadequate platelets production like congenital leukaemia, TAR, Trisomy -18 and Wiskott Aldrich syndrome, vonWillebrand disease. • **Normal TT**- VKDB and haemophilia • **Prolonged TT** - DIC, liver disease and TORCHES infection. • **Prolonged aPTT and normal PT** - Hemophilia. • **Prolonged BT** - thrombocytopaenia and in situations of poor platelets function like von Willebrand disease, Bernard Soulier syndrome and Glanzmann thrombasthenia.
Plasma clotting factors deficiency	• This measures the plasma levels of the various clotting factor using individual factor deficient plasmas. However, afibrinogenemia and haemophilia are common clotting factor deficiencies in the neonatal age.
Mixing study	• Used to determine the cause of prolonged PT or aPTT.
Platelet aggregometry	• Activation of platelet-rich plasma from a suspected case of platelet dysfunction with a platelet aggregation agonist like adrenaline or collagen corrects the dysfunction. • Reduced platelets aggregation characterizes conditions of platelets dysfunction like Bernard Soul ier syndrome and Glanzmann thrombasthenia.
USG / MRI	• To exclude intracranial hemorrhage

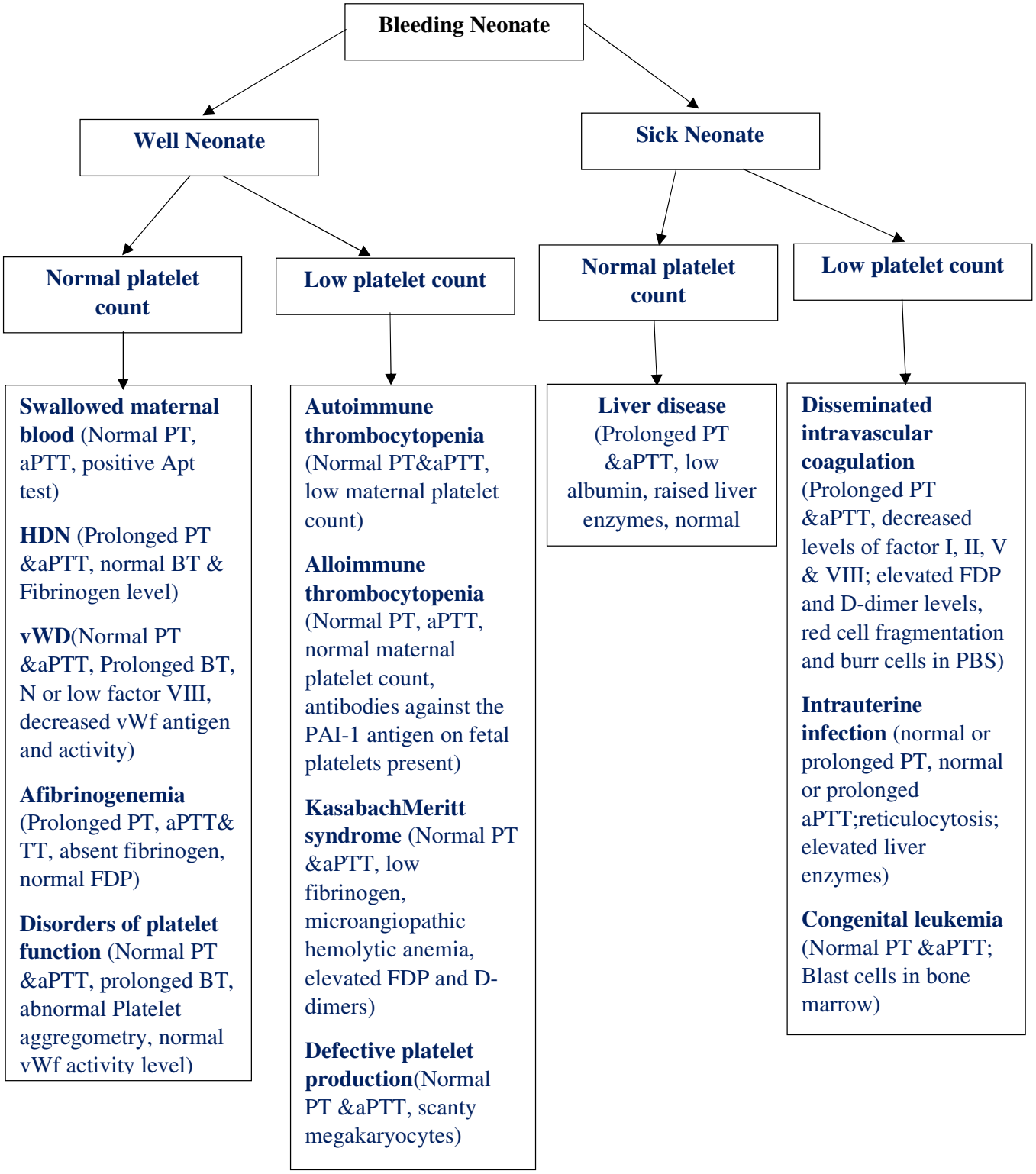

Fig. 1. The differential diagnoses and steps in the laboratory evaluation of neonatal bleeding disorders