4. Guidelines for investigation of a bleeder

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INDEX

CONTENT **PAGE NUMBER**

4.1 Introduction

Normal values for measurement of the haemostatic system can vary according to age and other physiological alterations. In routine practice comparisons are made with adult pooled plasma obtained from young males and females aged 20 to 40 years.

When the clinical history and /or the physical examination indicate that a bleeding tendency should be evaluated, appropriate laboratory tests are performed. These tests, called haemostatic screening tests, are selected and performed as a group, depending on the age and clinical findings of the patient.

4.2 The Haemostatic History Questionnaire

1. Bleeding history -
   a. Ecchymoses or petechiae - location, extent, spontaneous or post trauma.
   b. Prolonged bleeding from injuries and surgeries – delayed or episodic bleeding and poor wound healing. List all operations and significant trauma.
   c. Epistaxis / menorrhagia - without an apparent cause, whether needed to treat with blood transfusions or haematinics.
   d. Soft tissue, joint haemorrhage-unexplained arthritis, joint swelling.
   e. Haematemesis, malaena, haematuria or haemoptysis-without an obvious cause.

2. Family history – immediate and extended
3. General health- evidence of disorders known to cause bleeding
4. Drugs- fixed drug eruptions need to be excluded
5. Physical examination- hepato-splenomegaly, telangiectasia, lymphadenopathy and albinism.

From the questionnaire the patients are categorized into-.

- A. Definite bleeder.
- B. Questionable, need some tests to decide.
- C. Questionable as haemostatically not fully challenged.
- D. Not a bleeder.

All patients except D should be subjected to the first line screening tests. All the tests fall into Grade X unless specified.

4.3 First line screening tests.

- Full blood count + blood picture.
- Bleeding time.
- Activated Partial Thromboplastin Time (APTT).
- Prothrombin Time (PT).
- Thrombin Time(TT).
- Fibrinogen level.

If above tests are normal no further investigations are necessary **except in**: -

- Positive family history.
- Significant bleeding history with normal first line tests.

4.4 Second line screening tests

Selection criteria

- Abnormal first line screening tests.
- Significant bleeding history with normal 1st line tests.
- Positive family history with normal first line tests.

According to the abnormal first line test/s the type of the following second line test/s is/are decided.

1. Low platelets +/- abnormal platelet morphology
   - Bone marrow – if clinically indicated.
   - Platelet function tests.

2. Increased bleeding time
   - Platelet function tests.
   - VW antigen level.
   - Ricof activity.
   - Multimer analysis.

3. Prolonged APTT
- Mixing and correction studies.
- Factor assay.
- Inhibitor screening.
- Exclude heparin effect.

4. Prolonged PT
- Mixing tests.
- Factor assay.
- Liver function tests.

5. Prolonged TT
- Mixing tests
- Toludine blue test

If all above are normal,

- Factor XIII assay / clot solubility test.
- If 1 – 4 above are abnormal with low platelets – D-Dimer, FDP.
- If 1–5 above are prolonged with normal Platelets-dysfibrinogenaemia, fibrinolysis, hypofibrinogenaemia and afibrinogenaemia

4.5 Congenital Bleeding Disorders

1. Haemophilia A / B.
- Positive bleeding history / physical findings.
- Positive / negative family history(FH).
- Prolonged APTT.

  Haemophilia A – Factor VIII deficiency
  Haemophilia B – Factor IX deficiency

2. Other Factor deficiency
- Factor XI – positive bleeding / FH and prolonged APTT.
- Factor X – positive bleeding / FH and prolonged APTT and PT.
- Factor XIII – positive bleeding / FH.
  All screening tests are normal,
  Abnormal clot solubility test.
  Low Factor XIII.

3. VWD
- Prolonged / normal bleeding time.
- Prolonged / normal APTT.
- Low Factor VIII level.
- Abnormal platelet function tests.
- Low VW antigen level. (Grade Y)
- Low Ricof activity. (Grade Y)
- Abnormal multimer analysis. (Grade Y)

4. Thrombasthenia
- Normal platelet count.
- Prolonged bleeding time.
- Abnormal platelet function tests.

5. Bernard Soulier syndrome
- Abnormal platelet morphology.
- Low platelet count.
- Prolonged bleeding time.
- Abnormal platelet functions.

6. Storage pool defects
- Abnormal / normal platelet morphology.
- Prolonged bleeding time.
- Abnormal platelet functions.

7. Hypo, dysfibrinogenaemia and afibrinogenaemia
- Abnormal PT / APTT / TT – corrected with normal plasma.
- Low fibrinogen level (Hypo).
- Abnormal clot (Dys).
- Positive Toludine Blue test(Dys).

8. Factor VII deficiency
- Prolonged PT
- low factor VII

9. Marfan's syndrome, Ehlers – Danlos syndrome
- Prolonged bleeding time.

10. TAR syndrome/congenital megakaryocytic hypoplasia/giant haemangioma
- Prolonged bleeding time and low platelets

- Genetic studies – for congenital bleeding disorders. (Grade Y)

4.6 Acquired Bleeding Disorders

1. Low platelets only –
ITP (Primary or Secondary),bone marrow failure

2. Prolonged PT only –
warfarin, vitamin K deficiency, malabsorption, early liver disease.

3. Prolonged PT / APTT –
vitamin K deficiency, liver disease, long standing warfarin therapy.

4. Prolonged APTT corrected with Protamin Sulphate –
heparin effect.

5. Prolonged APTT not corrected with protamin sulphate, corrected with Toludine Blue – dysfibrinogaenemia of liver disease.

6. Prolonged PT / APTT / TT and low platelets – DIC, acute liver necrosis.

7. Prolonged PT/ APTT and low platelets –
liver cirrhosis, massive blood transfusion.

8. Prolonged bleeding time only –
platelet function and vascular defects.

9. Prolonged TT –
   renal and liver diseases, fibrinolysis.

10. low fibrinogen –
    DIC , systemic fibrinolysis, liver disease-
    (PT/APTT is not sensitive to moderate hypofibrinogenaemia)

11. Short Euglobin lysis time (ELT) –
    systemic fibrinolysis.

Children up to 13 years without any bleeding history have to be screened with the first line tests before any major surgery. They may be potential bleeders hitherto undetected if they are not met with a major haemostatic challenge.

4.7 References

These guidelines are based on the guidelines published by the British Committee for Standards in Haematology.

1. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy *British Journal of Haematology* ***2003; 120:574-596***

2. Goodnight S, Hathaway W.*Disorders in Haemostasis and Thrombosis, A Clinical Guide.*USA:Mc Graw-Hill, 2001.