BJA
British Journal of Anaesthesia
Volume 106, Number 1, January 2011

British Journal of Anaesthesia **106** (1): 1–3 (2011)
doi:10.1093/bja/aeq357

EDITORIAL I

Routine preoperative coagulation tests: an outdated practice?

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Routine coagulation tests have been used for many years in the preoperative setting in the belief that they identify patients who may have acquired or congenital bleeding disorders, and on the assumption that testing will predict perioperative bleeding allowing treatment to be given and prevent it. Coagulation 'screens' typically include the prothrombin time (PT) and the activated partial thromboplastin time (APTT). Both tests were originally developed to aid in the diagnosis of inherited bleeding disorders such as haemophilia and were not intended as screening tests.

Activation of coagulation can be achieved through the intrinsic or the extrinsic pathway leading to activation of the common pathway and conversion of fibrinogen to fibrin leading to clot formation. Although the cascade model of coagulation is not physiological, it is useful as a means to understand the mechanism by which traditional coagulation tests detect coagulopathies. The APTT activates plasma typically with substances such as kaolin or silica which cause activation of the contact pathway and, subsequently, the intrinsic and common coagulation pathways. A deficiency in any of these pathways will therefore prolong the APTT. The PT is activated with supraphysiological concentrations of tissue factor and detects FVII deficiency and also deficiencies in the common pathway. Both tests can also be prolonged by the presence of a lupus anticoagulant, inhibitors such as anticoagulants, and acute conditions associated with an acquired bleeding state.

Inherited coagulation defects are rare. The incidence of haemophilia A and B is estimated at 1:5000[1 2] and 1:30 000[3] male births, respectively. Severe, clinically relevant, deficiencies of FII, FV, FVII, FX, and fibrinogen are even rarer with an incidence varying between 1:300 000 and 1:2 000 000,[4] although this may be higher in populations where consanguineous marriages are more common. FXI deficiency is common in Ashkenazi Jews with a prevalence of 8%[5] but rare in a general population.[4] The majority of patients with these bleeding disorders will be aware of their diagnosis through either a personal or family history of bleeding and will be registered at specialized haemophilia centres. Indiscriminate screening by routine coagulation testing will therefore only very rarely identify previously undetected individuals. In contrast, prolongation of the APTT is a common occurrence with the most common reasons being mild FXII deficiency and the presence of a lupus anticoagulant, neither of which is associated with a bleeding tendency. Moderate and severe FXII deficiency was found in 2.3% of otherwise healthy Austrian blood donors[6] and in 10.3% of patients undergoing cardiac surgery.[7] Lupus anticoagulant can be found in 1.2–3.8% of healthy individuals, but the incidence increases with age and chronic disease, and was found in up to 30% of patients with systemic lupus erythematosus.[8] The ability of a lupus anticoagulant to prolong the APTT or PT depends on the combination of reagents and analysers used and may therefore vary between laboratories. Other causes of a prolonged APTT not associated with a bleeding tendency include high molecular weight kininogen deficiency and prekallikrein deficiency. Finally, a normal range is calculated by the mean ± 2 standard deviations of measurements in healthy, non-bleeding subjects and by definition 2.5% of measurements in normal individuals will show a prolonged clotting time. Therefore, if routine coagulation testing is done to identify previously undiagnosed bleeding disorders, it is much more likely to identify a prolonged routine coagulation test that is not associated with a bleeding tendency. In practice, this can lead to further unnecessary

testing and postponement or delay of the surgery. To further compound the situation, a normal routine test does not exclude the presence of, sometimes severe, bleeding disorders. The most common of these is mild von Willebrand disease. Deficiency of von Willebrand factor can occur in up to 1% of the population, but only 1:10 000 are estimated to have a clinically significant bleeding disorder.[9] Although FVIII may be reduced in patients with von Willebrand disease who therefore will have a prolonged APTT, in milder forms FVIII may be normal and patients may not be detected by routine testing. Mild haemophilia A or B may also be missed if an insensitive reagent/analyser combination is used, or during an acute phase response where a temporarily high FVIII level may lead to shortening of the APTT. Other conditions that cannot be detected by routine coagulation testing but may be associated with clinically significant bleeding include the rare inherited bleeding disorders such as FXIII and alpha 2 antiplasmin deficiency and platelet function disorders.

The British Committee for Standards in Haematology (BCSH) has recently published guidelines on the use of the PT and APTT in the preoperative setting based on a systematic review of the literature.[10] They included studies that enabled the calculation of predictive values (PV) and likelihood ratios (LR) of the coagulation tests and bleeding history for perioperative bleeding in paediatric ENT (six studies), general surgery (two studies), and one study in adult ENT surgery. Three studies were prospective and in total measurements of more than 12 000 patients were included. They found poor positive PV and low LR for bleeding with an abnormal coagulation test, whereas the perioperative bleeding rates were similar in patients with and without abnormal coagulation tests. A similar conclusion was reached in a review of studies of patients undergoing bronchoscopy, central vein cannulation, angiography, liver and kidney biopsy, and paracentesis.[11] The BCSH guideline does not recommend the use of routine coagulation tests to predict perioperative bleeding risk in unselected patients before surgery or other invasive procedures.[10] The systematic review did not include studies of intracranial, neurosurgical, or ophthalmic surgery due to a paucity of data, and although testing may be more justified in procedures with a higher risk from bleeding, the arguments regarding poor sensitivity and specificity of these tests remain.

A bleeding history is subjective and common symptoms are found in up to 25% of a healthy population without bleeding disorders including epistaxis, gum bleeding, and post-partum haemorrhage.[9] The use of a standardized bleeding questionnaire has been suggested as being better than indiscriminate coagulation testing as a screening tool for perioperative bleeding,[12] and there are suggestions that in patients with congenital bleeding disorders, a structured history is at least as informative as laboratory testing to predict bleeding.[13 14] The BCSH guideline recommends that a bleeding history, including family history, evidence of excessive post-traumatic or post-surgical bleeding, and use of antithrombotic drugs should be taken in all patients before surgery or invasive procedures.[10]

Therefore, based on the available evidence, a reasonable approach to assessing the perioperative bleeding risk is that a structured bleeding history is taken and coagulation testing is undertaken only if there is concern about a bleeding tendency arising from the history. This may then also include referral to haematology to investigate disorders that are not detected by routine testing. Testing, however, should be considered in patients with acute conditions potentially associated with a haemorrhagic tendency such as liver disease, sepsis, diffuse intravascular coagulation, pre-eclampsia, cholestasis, and poor nutritional states leading to vitamin K deficiency.

Coagulation testing is often routinely undertaken in anticoagulated patients or patients to be started on anticoagulants. The APTT is used to monitor unfractionated heparin, lepirudin, bivalirudin, and argatroban whereas the INR is used for the monitoring of coumarin anticoagulants. The APTT and PT are insensitive to low molecular weight heparins, fondaparinux and danaparoid. Although prolongation of the APTT can occur at therapeutic doses of these agents, specific anti-Xa measurements should be used to assess the degree of anticoagulation, if necessary. Recently, two new oral anticoagulants, rivaroxaban and dabigatran, were licensed for thromboprophylaxis after total hip and knee replacement and they do not require routine monitoring. Rivaroxaban is a direct anti-Xa inhibitor that can prolong both the PT and APTT (PT more than APTT). Neither test is suitable to monitor the degree of anticoagulation, although a specifically calibrated PT assay has been suggested, and also more specialized assays that are not generally available.[15] Dabigatran is a direct thrombin inhibitor that can also prolong both the PT and APTT (APTT more than PT). Again, neither of these tests is suitable for monitoring the degree of anticoagulation, and although a normal APTT may indicate that no or low plasma concentrations of dabigatran are present, this depends on the reagent/analyser combination used. A normal thrombin time is more likely to indicate that no dabigatran is present and other more specialized, but not generally available, tests such as the ecarin clotting time have also been proposed.[16]

Finally, there is increasing interest in the possibility of perioperative monitoring of the effect of antiplatelet agents such as aspirin and clopidogrel. Although various point-of-care tests have been developed, there remain significant questions about their sensitivity, specificity, and ability to predict bleeding,[17] and none of these tests are therefore currently routinely recommended in the preoperative setting but are the subject of ongoing studies.

In conclusion, we feel that indiscriminate use of routine coagulation testing in the preoperative setting is not helpful and may cause unnecessary further testing and delay of surgery. Coagulation testing should be restricted to well-defined circumstances:

- Patients with a family history of known inherited bleeding disorders.
- Patients with a personal history of bleeding identified by structured history taking or a family history of bleeding. Ideally, these individuals should be investigated

electively by a haematologist before any surgery or invasive procedure.
- Patients with acute illnesses such as sepsis or conditions that can be associated with a coagulopathy such as chronic liver disease.
- Patients on some anticoagulants. As anticoagulants, but not necessarily antiplatelet drugs,[18] are stopped before operation for elective surgery, coagulation testing should only be required for emergency surgery. When surgery is performed on anticoagulated patients, appropriate testing can be useful in excluding over-anticoagulation at the time of surgery.

Conflict of interest

The authors have declared no conflicts of interest related to this editorial. Dr D.R. Spahn has provided a full declaration of interests that was published in *Br J Anaesth* 2010; **105**: 103–5, doi: 10.1093/bja/aeq166.

References

1 Fukutake K. Current status of hemophilia patients and recombinant coagulation factor concentrates in Japan. *Semin Thromb Hemost* 2000; **26**: 29–32

2 Smit C, Rosendaal FR, Varekamp I, *et al.* Physical condition, longevity, and social performance of Dutch haemophiliacs, 1972–85. *Br Med J* 1989; **298**: 235–8

3 Giannelli F, Green PM, Sommer SS, *et al.* Haemophilia B: database of point mutations and short additions and deletions—eighth edition. *Nucleic Acids Res* 1998; **26**: 265–8

4 Bolton-Maggs PH, Perry DJ, Chalmers EA, *et al.* The rare coagulation disorders—review with guidelines for management from the United Kingdom Haemophilia Centre Doctors' Organisation. *Haemophilia* 2004; **10**: 593–628

5 Asakai R, Chung DW, Davie EW, Seligsohn U. Factor XI deficiency in Ashkenazi Jews in Israel. *N Engl J Med* 1991; **325**: 153–8

6 Halbmayer WM, Haushofer A, Schon R, *et al.* The prevalence of moderate and severe FXII (Hageman factor) deficiency among the normal population: evaluation of the incidence of FXII deficiency among 300 healthy blood donors. *Thromb Haemost* 1994; **71**: 68–72

7 Halbmayer WM, Haushofer A, Radek J, Schon R, Deutsch M, Fischer M. Prevalence of factor XII (Hageman factor) deficiency among 426 patients with coronary heart disease awaiting cardiac surgery. *Coron Artery Dis* 1994; **5**: 451–4

8 Petri M. Epidemiology of the antiphospholipid antibody syndrome. *J Autoimmun* 2000; **15**: 145–51

9 Sadler JE, Mannucci PM, Berntorp E, *et al.* Impact, diagnosis and treatment of von Willebrand disease. *Thromb Haemost* 2000; **84**: 160–74

10 Chee YL, Crawford JC, Watson HG, Greaves M. Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures. British Committee for Standards in Haematology. *Br J Haematol* 2008; **140**: 496–504

11 Segal JB, Dzik WH. Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review. *Transfusion* 2005; **45**: 1413–25

12 Koscielny J, Ziemer S, Radtke H, *et al.* A practical concept for preoperative identification for patients with impaired primary hemostasis. *Clin Appl Thromb Hemost* 2004; **10**: 195–204

13 Sramek A, Eikenboom JC, Briet E, Vandenbroucke JP, Rosendaal FR. Usefulness of patient interview in bleeding disorders. *Arch Intern Med* 1995; **155**: 1409–15

14 Tosetto A, Rodeghiero F, Castaman G, *et al.* A quantitative analysis of bleeding symptoms in type 1 von Willebrand disease: results from a multicenter European study (MCMDM-1 VWD). *J Thromb Haemost* 2006; **4**: 766–73

15 Samama MM, Martinoli JL, LeFlem L, *et al.* Assessment of laboratory assays to measure rivaroxaban—an oral, direct factor Xa inhibitor. *Thromb Haemost* 2010; **103**: 815–25

16 van Ryn J, Stangier J, Haertter S, *et al.* Dabigatran etexilate—a novel, reversible, oral direct thrombin inhibitor: interpretation of coagulation assays and reversal of anticoagulant activity. *Thromb Haemost* 2010; **103**: 1116–27

17 Lippi G, Favaloro EJ, Salvagno GL, Franchini M. Laboratory assessment and perioperative management of patients on antiplatelet therapy: from bench to bedside. *Clin Chim Acta* 2009; **405**: 8–16

18 Chassot PG, Delabays A, Spahn DR. Perioperative antiplatelet therapy: the case for continuing therapy in patients at risk for myocardial infarction. *Br J Anaesth* 2007; **99**: 316–28

British Journal of Anaesthesia **106** (1): 3–5 (2011)
doi:10.1093/bja/aeq358

EDITORIAL II

Nerve location in regional anaesthesia: finding what lies beneath the skin

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