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Guidelines

Regional anaesthesia and patients with abnormalities of coagulation

The Association of Anaesthetists of Great Britain & Ireland
The Obstetric Anaesthetists' Association
Regional Anaesthesia UK

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Summary

Concise guidelines are presented that relate abnormalities of coagulation, whether the result of the administration of drugs or that of pathological processes, to the consequent haemorrhagic risks associated with neuraxial and peripheral nerve blocks. The advice presented is based on published guidelines and on the known properties of anticoagulant drugs. Four separate Tables address risks associated with anticoagulant drugs, neuraxial and peripheral nerve blocks, obstetric anaesthesia and special circumstances such as trauma, sepsis and massive transfusion.

This is a consensus document produced by expert members of a Working Party established by the Association of Anaesthetists of Great Britain & Ireland, the Obstetric Anaesthetists' Association and Regional Anaesthesia UK. It has been seen and approved by the elected Councils/Committees of all three organisations.
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- *What other statements are available on this topic?*
  Guidance publications on regional anaesthesia in patients taking anticoagulant or thromboprophylactic drugs are widely available, two well-known guidelines having been published by the American Society of Regional Anesthesia and Pain Medicine (ASRA) [1] or adopted by the European Society of Regional Anaesthesia and Pain Therapy (ESRA) [2].
- *Why was this guideline developed?*
  The available published guidance focuses on neuraxial blockade in patients receiving drug therapy specifically aimed at modifying coagulation, but does not address non-neuraxial regional blockade or patients with abnormalities of coagulation for other reasons. Currently available guidelines are lengthy and discursive, and do not lend themselves to use in the acute clinical setting. The remit of the Working Party that produced these guidelines was to create a concise document that considered regional anaesthesia of all forms and abnormalities of coagulation of both therapeutic and pathological origins.

- *How does this statement differ from existing guidelines?*
  Although based on the available guidance and on published pharmacokinetic and pharmacodynamic data pertaining to anticoagulant drugs, this guidance is considerably more concise.
- *Why does this statement differ from existing guidelines?*
  These guidelines were developed in order to make useful and concise guidance available to anaesthetists in the clinical setting.

Anaesthetists are often faced with the question of whether the risks of regional anaesthetic techniques are increased when performed on patients with abnormalities of coagulation and, if so, whether they are so increased that the techniques should be modified or avoided. This is not only because the popularity of regional anaesthesia is on the rise but also because the use of anticoagulant drugs in the prevention of venous thromboembolism is expanding, as is the number of different drugs in use. The serious complications of regional anaesthesia in patients without abnormalities of coagulation are very rare indeed [3]. For example, in the third National Audit Project (NAP3), the incidence of vertebral canal haematoma after neuraxial blockade was 0.85 per 100 000 (95% CI 0–1.8 per 100 000). The extent to which the risk of haemorrhagic complications is increased in patients with abnormalities of coagulation is unquantifiable, but likely to be small. The rarity of the complications means that it is difficult to make accurate estimates of the incidence of complications related to abnormalities of coagulation, and therefore offering patients and clinicians advice on the basis of 'hard data' is not possible, and is unlikely ever to become possible. We are therefore reliant on expert opinion, case reports, case series, cohort studies and extrapolations from drug properties such as the time taken to achieve peak plasma levels and the known half-lives of drugs.

Published clinical guidance in relation to the risk associated with regional anaesthesia in patients with abnormalities of coagulation is often binary. For instance, it is often said that the performance of neuraxial block in a patient with $< 75 \times 10^9.l^{-1}$ platelets is not acceptable, whereas its performance in the presence of $> 75 \times 10^9.l^{-1}$ platelets is acceptable. However, there can be no relevant difference in risk or outcome after neuraxial blockade in two patients, one of whom has a platelet count of $74 \times 10^9.l^{-1}$ and the other $76 \times 10^9.l^{-1}$. Risk is a continuum that runs from 'normal risk' to 'very high risk', and this guidance seeks to emphasise this point. This guidance must be interpreted and used after consideration of an individual patient's circumstances. None of the advice in this guidance should be taken as being prohibitive or indicative. An abnormality of coagulation – however severe – is always a *relative* contraindication to the use of a regional anaesthetic technique. However, there may be circumstances in which, although the use of a regional technique for a patient with abnormal coagulation may put the patient at significant risk as a result, the alternative for this patient (often a general anaesthetic) may expose them to even greater risk. Experienced clinicians should be involved in decisions about whether or not to perform a regional anaesthetic technique on a patient with abnormal coagulation, and the patient with capacity should be given all the information he/she needs to make an informed choice.

Advice is often offered that if regional anaesthesia is to be considered in a patient with a known abnormality of coagulation, an 'experienced anaesthetist' should perform the procedure. There are, of course, no hard data to support this suggestion. However, it is advice that the Working Party supports. It is likely that an experienced regional anaesthetist will need fewer attempts to gain block success, and it is likely that the complications related to bleeding are in part related to the number of attempts at a block. It is reasonable to ask novices to perform their blocks on patients at 'normal risk', reserving attempts in patients at 'increased risk' for experienced clinicians.

Guidance is offered here in the form of four Tables, each with explanatory notes: Table 1 contains recommendations related to drugs used to modify coagulation; Table 2 suggests the relative risk related to the performance of neuraxial and peripheral nerve blocks in patients with abnormalities of coagulation; Table 3 indicates relative risks related to obstetric patients; and Table 4 describes risks of regional anaesthesia in special circumstances.

Table 1 Recommendations related to drugs used to modify coagulation. Recommended minimum times are based in most circumstances on time to peak drug effect + (elimination half-life × 2), after which time < ¼ of the peak drug level will be present. For those drugs whose actions are unrelated to plasma levels, this calculation is not relevant. Data used to populate this Table are derived from ASRA and ESRA guidelines [1, 2] and information provided by drug manufacturers. These recommendations relate primarily to neuraxial blocks and to patients with normal renal function except where indicated.

Drug	Time to peak effect	Elimination half-life	Acceptable time after drug for block performance	Administration of drug while spinal or epidural catheter in place[1]	Acceptable time after block performance or catheter removal for next drug dose
Heparins					
UFH sc prophylaxis	< 30 min	1–2 h	4 h or normal APTTR	Caution	1 h
UFH iv treatment	< 5 min	1–2 h	4 h or normal APTTR	Caution[2]	4 h
LMWH sc prophylaxis	3–4 h	3–7 h	12 h	Caution[3]	4 h[3]
LMWH sc treatment	3–4 h	3–7 h	24 h	Not recommended	4 h[4]
Heparin alternatives					
Danaparoid prophylaxis	4–5 h	24 h	Avoid (consider anti-Xa levels)	Not recommended	6 h
Danaparoid treatment	4–5 h	24 h	Avoid (consider anti-Xa levels)	Not recommended	6 h
Bivalirudin	5 min	25 min	10 h or normal APTTR	Not recommended	6 h
Argatroban	< 30 min	30–35 min	4 h or normal APTTR	Not recommended	6 h
Fondaparinux prophylaxis[5]	1–2 h	17–20 h	36–42 h (consider anti-Xa levels)	Not recommended	6–12 h
Fondaparinux treatment[5]	1–2 h	17–20 h	Avoid (consider anti-Xa levels)	Not recommended	12 h
Antiplatelet drugs					
NSAIDs	1–12 h	1–12 h	No additional precautions	No additional precautions	No additional precautions
Aspirin	12–24 h	Not relevant; irreversible effect	No additional precautions	No additional precautions	No additional precautions
Clopidogrel	12–24 h		7 days	Not recommended	6 h
Prasugrel	15–30 min		7 days	Not recommended	6 h
Ticagrelor	2 h	8–12 h	5 days	Not recommended	6 h
Tirofiban	< 5 min	4–8 h[6]	8 h	Not recommended	6 h
Eptifibatide	< 5 min	4–8 h[6]	8 h	Not recommended	6 h
Abciximab	< 5 min	24–48 h[6]	48 h	Not recommended	6 h
Dipyridamole	75 min	10 h	No additional precautions	No additional precautions	6 h
Oral anticoagulants					
Warfarin	3–5 days	4–5 days	INR ≤ 1.4	Not recommended	After catheter removal
Rivaroxaban prophylaxis[5] (CrCl > 30 ml.min^{-1})	3 h	7–9 h	18 h	Not recommended	6 h
Rivaroxaban treatment[5] (CrCl > 30 ml.min^{-1})	3 h	7–11 h	48 h	Not recommended	6 h
Dabigatran prophylaxis or treatment[7]					
(CrCl > 80 ml.min^{-1})	0.5–2.0 h	12–17 h	48 h	Not recommended	6 h
(CrCl 50–80 ml.min^{-1})	0.5–2.0 h	15 h	72 h	Not recommended	6 h
(CrCl 30–50 ml.min^{-1})	0.5–2.0 h	18 h	96 h	Not recommended	6 h
Apixaban prophylaxis	3–4 h	12 h	24–48 h	Not recommended	6 h
Thrombolytic drugs					
Alteplase, anistreplase, reteplase, streptokinase	< 5 min	4–24 min	10 days	Not recommended	10 days

UFH, unfractionated heparin; sc, subcutaneous; APTTR, activated partial thromboplastin time ratio; iv, intravenous; LMWH, low molecular weight heparin, NSAIDs, non-steroidal anti-inflammatory drugs; INR, international normalised ratio; CrCl, creatinine clearance.

Notes to accompany Table 1

1 The dangers associated with the administration of any drug that affects coagulation while a spinal or epidural catheter is in place should be considered carefully. There are limited data on the safety of the use of the newer drugs in this Table, and they are therefore not recommended until further data become available. The administration of those drugs whose entry in this column is marked as 'caution' may be acceptable, but the decision must be based on an evaluation of the risks and benefits of administration. If these drugs are given, the times identified in the column to the left ('Acceptable time after drug for block performance') should be used as a guide to the minimum time that should be allowed between drug administration and catheter removal.

2 It is common for intravenous unfractionated heparin to be given a short time after spinal blockade or insertion of an epidural catheter during vascular and cardiac surgery. Local clinical governance guidelines should be followed and a high index of suspicion should be maintained if any signs attributable to vertebral canal haematoma develop.

3 Low molecular weight heparins are commonly given in prophylactic doses twice daily after surgery, but many clinicians recommend that only one dose be given in the first 24 h after neuraxial blockade has been performed.

4 Consider increasing to 24 h if block performance is traumatic.

5 Manufacturer recommends caution with use of neuraxial catheters.

6 Time to normal platelet function rather than elimination half-life.

7 Manufacturer recommends that neuraxial catheters are not used.

Table 2 Relative risk related to neuraxial and peripheral nerve blocks in patients with abnormalities of coagulation.

	Block category	Examples of blocks in category
Higher risk	Epidural with catheter	
	Single-shot epidural	
	Spinal	
	Paravertebral blocks	Paravertebral block Lumbar plexus block Lumbar sympathectomy Deep cervical plexus block
	Deep blocks	Coeliac plexus block Stellate ganglion block Proximal sciatic block (Labat, Raj, sub-gluteal) Obturator block Infraclavicular brachial plexus block Vertical infraclavicular block Supraclavicular brachial plexus block
	Superficial perivascular blocks	Popliteal sciatic block Femoral nerve block Intercostal nerve blocks Interscalene brachial plexus block Axillary brachial plexus block
	Fascial blocks	Ilio-inguinal block Ilio-hypogastric block Transversus abdominis plane block Fascia lata block
	Superficial blocks	Forearm nerve blocks Saphenous nerve block at the knee Nerve blocks at the ankle Superficial cervical plexus block Wrist block Digital nerve block Bier's block
Normal risk	Local infiltration	

Notes to accompany Table 2

There have only been 26 published reports of significant haemorrhagic complications of peripheral nerve and plexus blocks [1]. Half of these occurred in patients being given anticoagulant drugs and half in patients with normal coagulation. Patient harm has derived from:

- Spinal haematoma after accidental entry into the spinal canal during attempted paravertebral blocks as defined in the Table.
- Exsanguination.
- Compression of other structures, e.g. airway obstruction, occlusion of major blood vessels or tissue ischaemia.

The one death in this series was that of a patient on clopidogrel who underwent a lumbar plexus block and subsequently exsanguinated. The majority of the 26 cases underwent deep blocks or superficial perivascular blocks. From these data, and from other data relating to neuraxial blocks, we have placed blocks in the order of relative risk shown in the Table.

Catheter techniques may carry a higher risk than single-shot blocks. The risk at the time of catheter removal is unlikely to be negligible.

Ultrasound-guided regional anaesthesia, when employed by clinicians experienced in its use, may decrease the incidence of vascular puncture, and may therefore make procedures such as supraclavicular blocks safer in the presence of altered coagulation.

Some readers may question the absence of a section on haematological conditions associated with abnormalities of coagulation – why do we not mention Christmas disease or other forms of haemophilia? Most of these diseases are the result of the absence or shortage in the body of a particular clotting factor or group of factors. Most of the patients with haematological diseases such as these reach surgery in the full knowledge that they have the disease. The standard treatment of bleeding resulting from a deficiency of a clotting factor or other

Table 3 Relative risks related to neuraxial blocks in obstetric patients with abnormalities of coagulation.

Risk factor	Normal risk	Increased risk	High risk	Very high risk
LMWH – prophylactic dose	> 12 h	6–12 h	< 6 h	< 6 h
LMWH – therapeutic dose	> 24 h	12–24 h	6–12 h	
UFH – infusion	Stopped > 4 h and APTTR ≤ 1.4			APTTR above normal range
UFH – prophylactic bolus dose	Last given > 4 h	Last given < 4 h		
NSAID + aspirin	Without LMWH	With LMWH dose 12–24 h	With LMWH dose < 12 h	
Warfarin	INR ≤ 1.4	INR 1.4–1.7	INR 1.7–2.0	INR > 2.0
General anaesthesia*	Starved, not in labour, antacids given		Full stomach or in labour	
Pre-eclampsia	Platelets > 100 × 10^9.l^{-1} within 6 h of block	Platelets 75–100 × 10^9.l^{-1} (stable) and normal coagulation tests	Platelets 75–100 × 10^9.l^{-1} (decreasing) and normal coagulation tests	Platelets < 75 × 10^9.l^{-1} or abnormal coagulation tests with indices ≥ 1.5 or HELLP syndrome
Idiopathic thrombocytopenia	Platelets > 75 × 10^9.l^{-1} within 24 h of block	Platelets 50–75 × 10^9.l^{-1}	Platelets 20–50 × 10^9.l^{-1}	Platelets < 20 × 10^9.l^{-1}
Intra-uterine fetal death	FBC and coagulation tests normal within 6 h of block	No clinical problems but no investigation results available		With abruption or overt sepsis
Cholestasis	INR ≤ 1.4 within 24 h	No other clinical problems but no investigation results available		

LMWH, low molecular weight heparin; UFH, unfractionated heparin; APTTR, activated partial thromboplastin time; NSAID, non-steroidal anti-inflammatory drug; INR, international normalised ratio.

*Although general anaesthesia is not a risk factor per se for coagulation complications, it is included in this Table to highlight that the alternatives to regional anaesthesia are not free of risk; thus a risk–benefit comparison is required when choosing one over the other. See notes below.

Notes to accompany Table 3

Risks: The risks are primarily those of vertebral canal haematoma with subsequent cord compression and permanent damage. Realistic alternatives to epidural analgesia exist in labour, but, for caesarean section, the choice is that of general or neuraxial anaesthesia, and the risks of spinal haematoma in patients with abnormal coagulation must be weighed against those of general anaesthesia, especially in patients who are in labour and have a full stomach. These risks include hypoxaemia associated with difficulties maintaining the airway, pulmonary aspiration and thromboembolic complications.

Low platelets: The debate regarding the safety of neuraxial blockade in women with thrombocytopenia is guided by expert consensus opinion in the absence of clinical trials; it is not therefore possible to give definitive values for a lower limit at which there is an increased risk of haematoma. For normal healthy women, there is no increased risk of complications with platelet counts > 100 × 10^9.l^{-1} [4]. A count of > 75 × 10^9.l^{-1} has been proposed as an adequate level for regional blocks when there are no risk factors and the count is not decreasing [5]. In pre-eclampsia, a decreasing platelet count is accompanied by other coagulation abnormalities, and this is assumed to be the case once the platelet count decreases to below 100 × 10^9.l^{-1}. If the platelet count is below this value, a coagulation screen should be performed – if this is normal, it would be reasonable to perform a regional block down to a level of 75 × 10^9.l^{-1}, depending on the rate of decrease in platelet count [6]. In idiopathic thrombocytopenic purpura and gestational thrombocytopenia, there are reduced platelet numbers, but normal function. In these situations, expert opinion is that an experienced anaesthetist might reasonably perform a neuraxial blockade providing the platelet count is > 50 × 10^9.l^{-1} and stable, but an individual risk–benefit assessment should be made [7–11]. It is possible that spinal anaesthesia with platelet counts below this level may be safe if data are extrapolated from that derived from lumbar punctures in non-pregnant patients performed by haematologists using needles considerably larger than those used by obstetric anaesthetists [9]. A stable level of 40 × 10^9.l^{-1} may be safe for lumbar puncture in the absence of other coagulation abnormalities.

The platelet count should be checked before any neuraxial procedure if there is any suspicion of decreasing platelet numbers during routine antenatal testing, signs of the development of pre-eclampsia, e.g. proteinuria or hypertension, or other clinical features suggesting coagulopathy, placental abruption or if the patient has been given recent anticoagulant therapy. Platelet numbers can decrease in patients treated with regular heparin for > 4 days. Otherwise, it would not be routine to check platelet numbers and delay neuraxial block whilst these results are awaited. It would be standard practice to perform a neuraxial procedure within 6 h of the last platelet count and clotting studies in patients with mild or moderate pre-eclampsia. However, if the patient has severe or fulminating pre-eclampsia or HELLP syndrome, a platelet count and clotting studies should be checked immediately before performing the procedure, as decreases in platelet count can occur rapidly in these circumstances.

Low molecular weight heparins with aspirin: Treatment with daily LMWH and aspirin 75 mg may be encountered when following NICE guidelines, which recommend low-dose aspirin for obesity or hypertension. Provided the LMWH is stopped for > 12 h, the platelet count is > 75 × 10^9.l^{-1} and normal coagulation is confirmed, neuraxial blocks can be categorised as 'increased risk' only.

Intra-uterine fetal death: After intra-uterine death, there is an increased risk of coagulopathy and sepsis, especially in the second week after fetal demise. Coagulation abnormalities can occur on presentation in about 3% of women with apparently uncomplicated intra-uterine death, and this increases in the presence of abruption or uterine perforation to around 13% [12]. It is therefore prudent to check coagulation status before any regional procedure. The onset of coagulopathy is variable, but can be rapid.

Cholestasis: In obstetric cholestasis, coagulopathy may develop as a result of decreased absorption of vitamin K essential for activation of clotting factors. It is important to check coagulation before regional blockade, but changes do not occur rapidly.

Removal of epidural catheters: The recommendations given in Table 1 for the removal of epidural catheters should be noted.

Table 4 Risks of regional anaesthesia in patients with abnormalities of coagulation – special circumstances.

Trauma	The coagulopathy of trauma is precipitated by tissue trauma, shock, haemodilution, hypothermia, acidaemia and inflammation. Following major trauma, it is recommended that an assessment of potential coagulopathy be made before performing any regional anaesthetic technique.
Sepsis	Severe sepsis is associated with a procoagulant state. Guidelines support the use of chemoprophylaxis against deep venous thrombosis. For advice on regional anaesthesia with intercurrent thromboprophylaxis, refer to Table 1. Septic shock may be associated with the development of a consumptive coagulopathy. Clinically significant systemic sepsis remains a relative contraindication to central neuraxial anaesthesia due to the presumed increased incidence of epidural abscess and meningitis.
Uraemia	Uraemia may lead to coagulopathy secondary to thrombocytopenia. It is recommended that all patients with significant uraemia undergo assessment of platelet number and function before regional anaesthesia. Platelet function may be improved by the administration of DDAVP. Patients with chronic renal impairment may be managed with regular dialysis. The presence of residual anticoagulation after heparin administration must be considered in patients after dialysis, and heparin reversed if indicated. If regional anaesthesia is performed, the safety of catheter removal must be considered in patients likely to receive heparin during further dialysis.
Liver failure	All coagulation factors except factor VIII are synthesised in the liver. Liver failure is associated with haemostatic abnormality, the extent of which must be assessed before regional anaesthetic techniques are performed. There may be thrombocytopenia and abnormal platelet function due to associated hypersplenism. Patients in liver failure represent a high-risk group for general anaesthesia. When regional anaesthesia is considered as an alternative, coagulopathy must be assessed and corrected when indicated.
Massive transfusion	Massive transfusion is associated with altered haemostasis, with dilution and consumption of coagulation factors being the primary causes in this pathophysiological change. In assessing the degree of coagulopathy before regional anaesthetic techniques, it is recognised that coagulopathy in massive transfusion is a dynamic situation. Assessment should be made when haemorrhage is controlled and the patient is cardiovascularly stable. An assessment of platelet function should ideally occur in patients who have been given platelet transfusions.
Disseminated intravascular coagulopathy	Disseminated intravascular coagulopathy (DIC) is the pathological activation of coagulation mechanisms in response to a disease process leading to a consumptive coagulopathy. A diagnosis of DIC is incompatible with safe neuraxial blockade. When peripheral blocks are considered, they should be at compressible sites.

Notes to accompany Table 4
All of the conditions discussed can, in their 'active' state, be associated with significant coagulopathy. When regional anaesthesia is thought to be of potential value, e.g. for postoperative analgesia, it should be conducted with reference to the guidelines outlined in the rest of this publication.

contributor to normal coagulation when faced with surgery is the administration of that factor or other contributor after guidance from a haematologist. Therefore, for elective surgery, the solution is almost always the performance of the regional technique after acceptable normalisation of coagulation on the advice of a haematologist. In the emergency situation, urgent advice should be sought from on-call haematologists.

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