1

ANTICOAGULATION ET ANESTHÉSIE RÉGIONALE

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20 février 2025

1

2

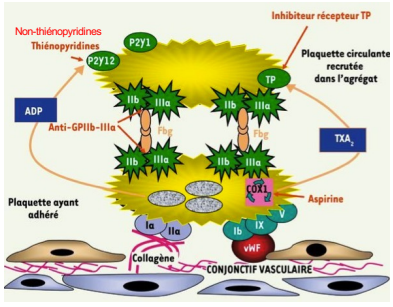
Plan

- Coagulation revisitée
- Anticoagulants courants – Lignes directrice ASRA 2025
  - Mécanisme d'action
  - Pharmacocinétique
  - **Recommandations**
- Blocs nerveux périphériques
- Application

2

3

Activation plaquettaire



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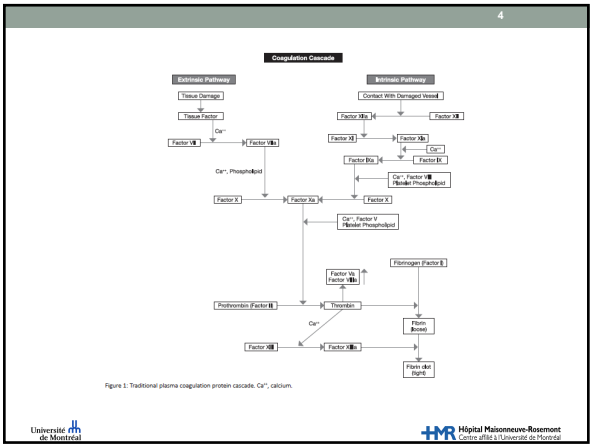
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Coagulation Cascade
Extrinsic Pathway
Intrinsic Pathway
Tissue Damage
Tissue Factor
Factor VII
Factor VIIa
Contact With Damaged Vessel
Factor XII
Factor XIIa
Factor XI
Factor XIa
Factor IX
Factor IXa
Factor X
Factor Xa
Factor V
Prothrombin (Factor II)
Thrombin
Fibrinogen (Factor I)
Fibrin (loose)
Factor XIII
Factor XIIIa
Fibrin clot (tight)
Figure 1: Traditional plasma coagulation protein cascade. Ca2+, calcium.
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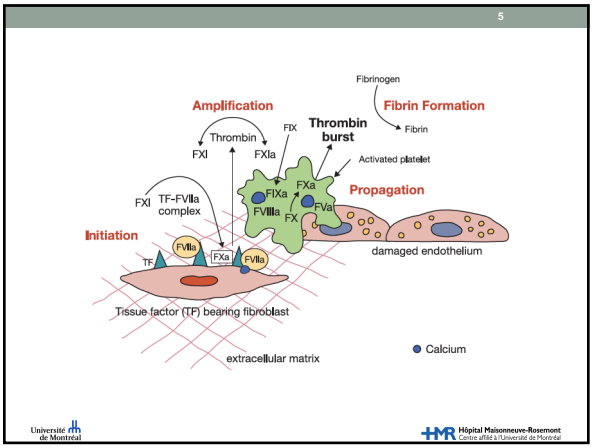
4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Fibrinogen
Amplification
Fibrin Formation
Thrombin
FXI
FXIa
FIX
Thrombin burst
Fibrin
Activated platelet
FXI
TF-FVIIa complex
FIXa
FVIIIa
FXa
FVa
FX
Propagation
Initiation
FVIIa
TF
FXa
FVIIa
damaged endothelium
Tissue factor (TF) bearing fibroblast
extracellular matrix
Calcium
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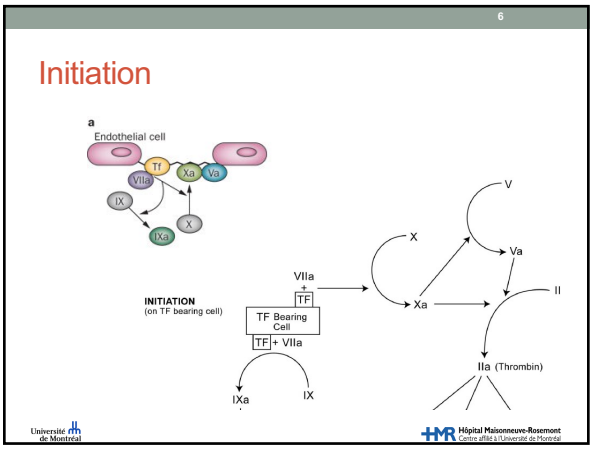
5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Initiation
a
Endothelial cell
Tf
VIIa
Xa
Va
IX
X
IXa
INITIATION
(on TF bearing cell)
VIIa
TF
TF Bearing Cell
TF + VIIa
IXa
IX
X
Xa
V
Va
II
IIa (Thrombin)
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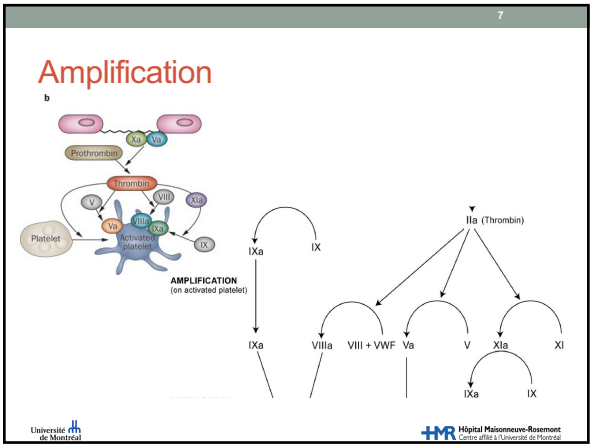
6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Amplification
b
Xa
Va
Prothrombin
Thrombin
V
VIII
XIa
Platelet
Va
VIII
IXa
Activated platelet
IX
AMPLIFICATION
(on activated platelet)
IXa
IX
IIa (Thrombin)
IXa
VIIIa
VIII + VWF
Va
V
XIa
XI
IXa
IX
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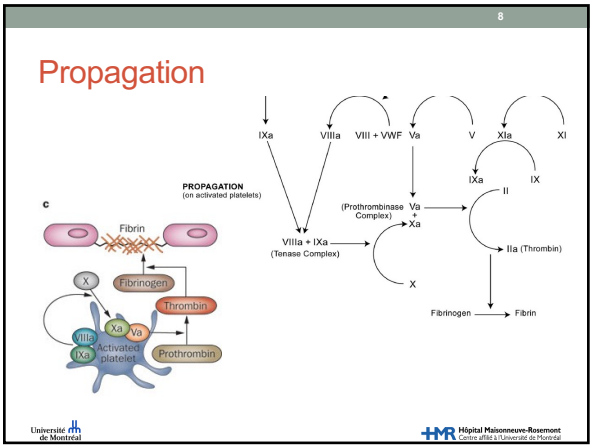
7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Propagation
c
Fibrin
X
Fibrinogen
Thrombin
Xa
Va
VIIIa
IXa
Activated platelet
Prothrombin
PROPAGATION
(on activated platelets)
IXa
VIIIa
VIII + VWF
Va
V
XIa
XI
IXa
IX
(Prothrombinase Complex)
Va
+
Xa
II
IIa (Thrombin)
VIIIa + IXa
(Tenase Complex)
X
Fibrinogen
Fibrin
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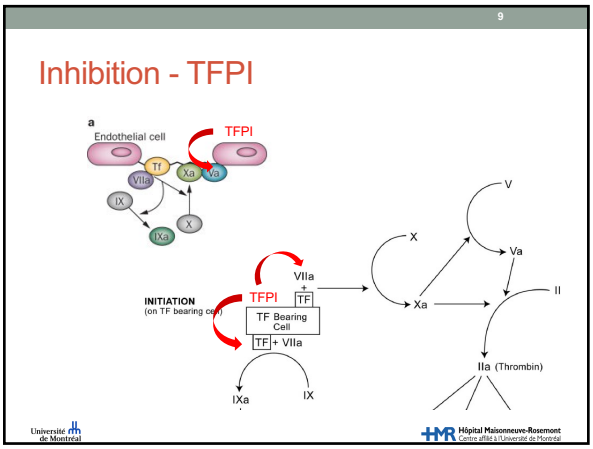
8


9
Inhibition - TFPI
a
Endothelial cell
TFPI
Tf
Xa
Va
VIIa
IX
X
IXa
INITIATION
(on TF bearing cell)
TFPI
VIIa
+
TF
TF Bearing Cell
TF + VIIa
IXa
IX
X
V
Va
Xa
II
IIa (Thrombin)
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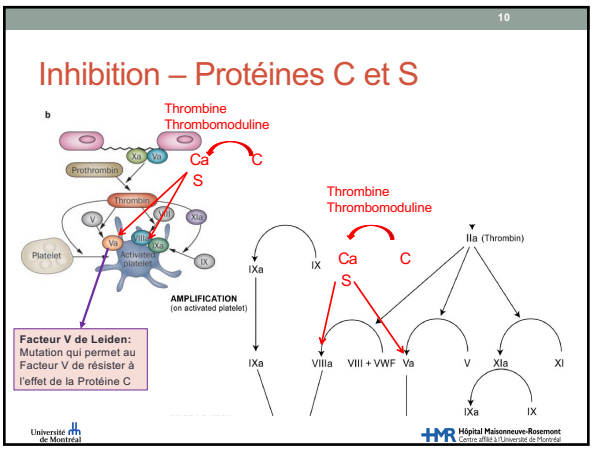
9


10
Inhibition – Protéines C et S
Thrombine
Thrombomoduline
Ca
C
S
Prothrombin
Thrombin
Platelet
Activated platelet
AMPLIFICATION
(on activated platelet)
Facteur V de Leiden:
Mutation qui permet au Facteur V de résister à l'effet de la Protéine C
IIa (Thrombin)
IXa
IX
VIIIa
VIII + VWF
Va
V
XIa
XI
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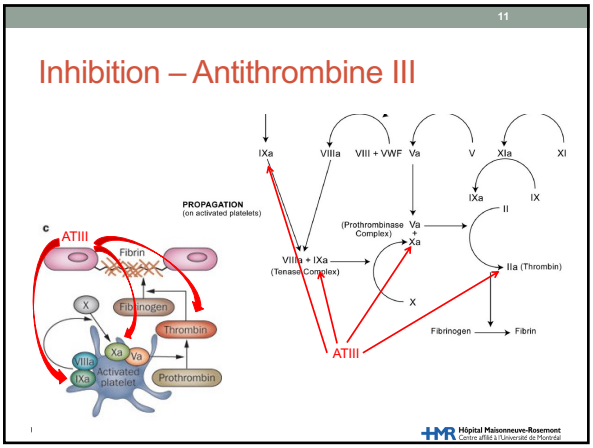
10


11
Inhibition – Antithrombine III
PROPAGATION
(on activated platelets)
ATIII
Fibrin
Fibrinogen
Thrombin
Prothrombin
Activated platelet
(Prothrombinase Complex)
(Tenase Complex)
IIa (Thrombin)
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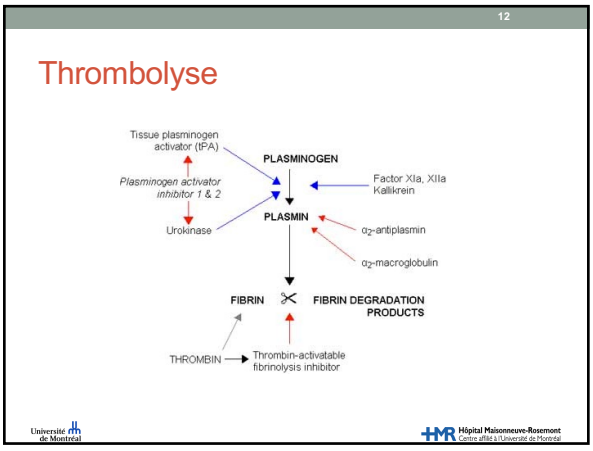
11


12
Thrombolyse
Tissue plasminogen activator (tPA)
PLASMINOGEN
Plasminogen activator inhibitor 1 & 2
Factor XIa, XIIa Kallikrein
Urokinase
PLASMIN
α2-antiplasmin
α2-macroglobulin
FIBRIN
FIBRIN DEGRADATION PRODUCTS
THROMBIN
Thrombin-activatable fibrinolysis inhibitor
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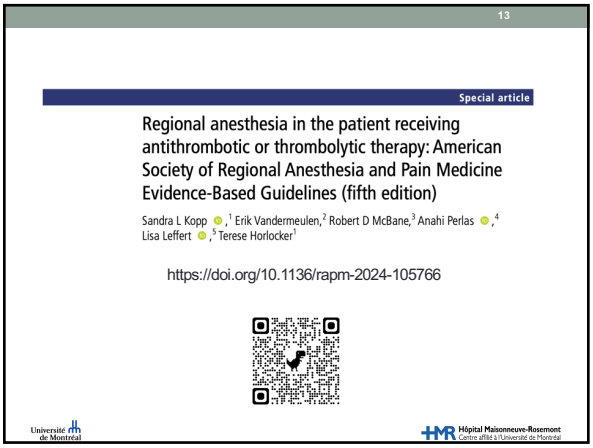
12


13
Special article
Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (fifth edition)
Sandra L Kopp ,[1] Erik Vandermeulen,[2] Robert D McBane,[3] Anahi Perlas ,[4] Lisa Leffert ,[5] Terese Horlocker[1]
https://doi.org/10.1136/rapm-2024-105766
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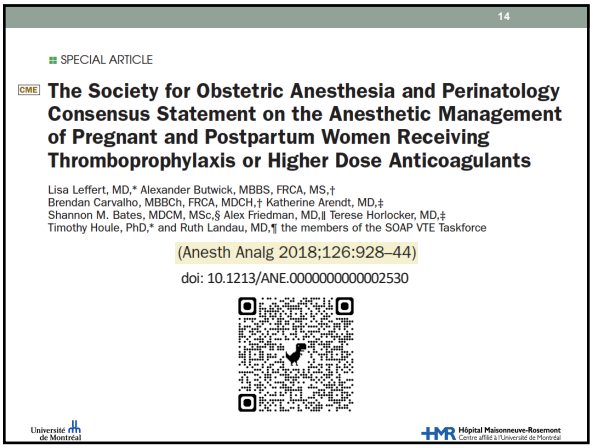
13


14
SPECIAL ARTICLE
CME
The Society for Obstetric Anesthesia and Perinatology Consensus Statement on the Anesthetic Management of Pregnant and Postpartum Women Receiving Thromboprophylaxis or Higher Dose Anticoagulants
Lisa Leffert, MD,* Alexander Butwick, MBBS, FRCA, MS,† Brendan Carvalho, MBBCh, FRCA, MDCH,† Katherine Arendt, MD,‡ Shannon M. Bates, MDCM, MSc,§ Alex Friedman, MD,‖ Terese Horlocker, MD,‡ Timothy Houle, PhD,* and Ruth Landau, MD,¶ the members of the SOAP VTE Taskforce
(Anesth Analg 2018;126:928–44)
doi: 10.1213/ANE.0000000000002530
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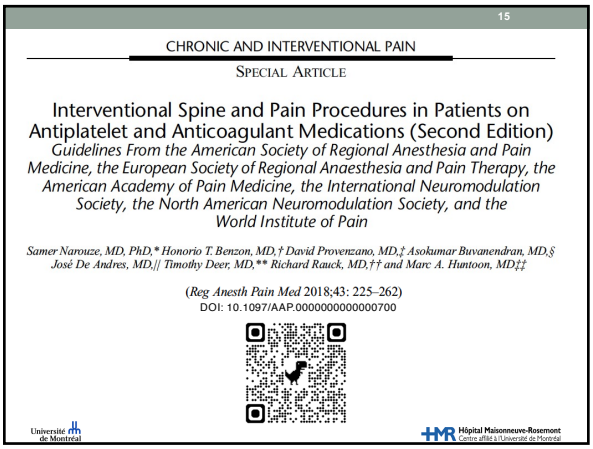
14


15
CHRONIC AND INTERVENTIONAL PAIN
SPECIAL ARTICLE
Interventional Spine and Pain Procedures in Patients on Antiplatelet and Anticoagulant Medications (Second Edition)
Guidelines From the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain
Samer Narouze, MD, PhD,* Honorio T. Benzon, MD,† David Provenzano, MD,‡ Asokumar Buvanendran, MD,§ José De Andres, MD,|| Timothy Deer, MD,** Richard Rauck, MD,†† and Marc A. Huntoon, MD‡‡
(Reg Anesth Pain Med 2018;43: 225–262)
DOI: 10.1097/AAP.0000000000000700
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15

16

Table 2 VTE risk scoring tools: medical patients

Risk factor	Points PADUA score[14]	IMPROVE score[26]
Active cancer	3	2
Prior VTE	3	3
Reduced mobility	3	Limb paresis (2 points)
		Immobility ≥ 7 days (1 point)
Thrombophilia	3	2
Recent trauma/surgery (≤1 month)	2	–
Age ≥70 years	1	1 (age >60 years)
Heart or respiratory failure	1	–
Acute MI or ischemic stroke	1	ICU stay (1 point)
Acute infection/rheumatological disorder	1	–
Obesity (BMI >30)	1	–
Hormonal therapy	1	–
High thrombosis risk	≥4 points	≥4 points

BMI, body mass index; ICU, intensive care unit; IMPROVE, International Medical Prevention Registry on Venous Thromboembolism; MI, myocardial infarction; PADUA, from University of Padua, Padova Italy; VTE, venous thromboembolism.


TABLE 1. Risk Factors for Venous Thromboembolism

Adapted from Geerts et al,[27] with permission.

17

2025

Table 3 Suggested risk stratification for patient-specific periprocedural thromboembolism*

Risk category	Mechanical heart valve	Atrial fibrillation	VTE
High (>10%/y risk of ATE or >10%/mo risk of VTE)	Mitral valve with major risk factors for stroke† Caged ball or tilting disc mitral valve in mitral/aortic position Recent (<3 mo) stroke or TIA	CHADS2/ASSc score ≥7 or CHADS2 score of 5 or 6; recent (<3 mo) stroke or TIA; rheumatic valvular heart disease	Recent (< 3 month and especially < 1 month) VTE Severe thrombophilia (deficiency of protein C, protein S, or antithrombin; homozygous factor V Leiden or prothrombin gene G20210A mutation or double heterozygous for each mutation, multiple thrombophilias) Antiphospholipid antibodies Active cancer associated with high VTE risk‡
Moderate (4%–10%/y risk of ATE or 4%–10%/mo risk of VTE)	Mitral valve without major risk factors for stroke Bileaflet AVR with major risk factors for stroke	CHA2DS2 score of 5 or 6 or CHADS2 score of 3 or 4	VTE within past 3–12 mo Recurrent VTE Non-severe thrombophilia (heterozygous factor V Leiden or prothrombin gene G20210A mutation) Active cancer or recent history of cancer
Low (<4%/y risk of ATE or <2%/mo risk of VTE)	Bileaflet AVR without major risk factors for stroke‡	CHA2DS2-Vasc score of 1–4 or CHADS2 score of 0–2 (and no prior stroke or TIA)	VTE >12 mo ago

Adapted from Doeksters et al.[29]
*Empiric risk stratification that is a starting point for assessing perioperative thromboembolism risk; should be combined with clinical judgment that incorporates individual patient-related and surgery/procedure-related factors.
†Includes AF, prior stroke/TIA during anticoagulant interruption or other prior stroke/TIA, prior valve thrombosis, rheumatic heart disease, hypertension, diabetes, congestive heart failure, age ≥75 y.
‡Includes pancreatic cancer, myeloproliferative disorders, primary brain cancer, gastric cancer, and esophageal cancer.
AF, atrial fibrillation; ATE, arterial thromboembolism; AVR, aortic valve replacement; CHADS2, congestive heart failure, hypertension, age ≥75 y, diabetes mellitus, prior stroke or TIA; CHA2DS2VASc, congestive heart failure, hypertension, age ≥75 y, diabetes mellitus, prior stroke or TIA, vascular disease history, age ≥65 y, female sex; mo, months; TIA, transient ischemic attack; VTE, venous thromboembolism; y, years.

IMPROVE Bleeding score (≥7)
- Ulcus duodénal actif
- ATCD hémorragie
- Thrombopénie
- *Âge avancé*
- *Insuf. hépat./rénale*
- *USI*
- *TVC*
- *Mx rhumatique*
- *Néoplasie*
- *hommes*

http://dx.doi.org/10.1378/chest.09-3081

2018

TABLE 2. Recommendations for Thromboprophylaxis in Nonorthopedic Surgical Patients

Risk of Symptomatic VTE	Risk of Major Bleeding Complications: Average Risk (<1%)	High Risk (~2%) or Severe Consequences
Very low (<0.5%)	No specific prophylaxis	
Low (~1.5%)	Mechanical prophylaxis, preferably with IPC	
Moderate (~3.0%)	LDUH, LMWH, *or* mechanical prophylaxis, preferably with IPC	Mechanical prophylaxis, preferably with IPC
High (~6.0%)	LDUH *or* LMWH *plus* mechanical prophylaxis with ES *or* IPC	Mechanical prophylaxis, preferably with IPC; until risk of bleeding diminishes and pharmacologic prophylaxis can be added
High-risk cancer surgery	LDUH *or* LMWH *plus* mechanical prophylaxis with ES *or* IPC *and* extended-duration prophylaxis with LMWH postdischarge	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added
High risk, LDUH, and LMWH contraindicated or not available	Fondaparinux *or* low-dose aspirin (160 mg/d; mechanical prophylaxis, preferably with IPC; or both	Mechanical prophylaxis, preferably with IPC; until risk of bleeding diminishes and pharmacologic prophylaxis can be added

ES indicates elastic stockings; IPC, intermittent pneumatic compression; LDUH, low-dose UFH.
Adapted from Gould et al,[28] with permission.

18

Hématome péridural

PAIN AND REGIONAL ANESTHESIA

Severe Neurological Complications after Central Neuraxial Blockades in Sweden 1990–1999

Complication permanentes :
- Épidurales : ≈ 5-28 : 100 000
- Rachidiennes: ≈ 1,6-5 : 100 000
- Combinées : ≈ 12-18 : 100 000

Parturientes : 1 : 200 000

Severe complications associated with epidural and spinal anaesthesias in Finland 1987–1993. A study based on patient insurance claims

BJA

SPECIAL ARTICLE

Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists

Table 1 Complications sought in the audit process

Complication	Example
Spinal infections	Epidural abscess, meningitis
Spinal bleeding	Vertebral canal haematoma
Major nerve damage	Spinal cord damage, spinal cord infarction, paraplegia, major neuropathy
Wrong route injection errors	Epidural/intrathecal drugs given i.v. or *vice versa*
Death where the anaesthetic/ analgesic procedure is implicated as causal	Cardiovascular collapse, other

19

Hématome péridural

TABLE 6. Risk Factors and Estimated Incidence for Spinal Hematoma and Neuraxial Anesthesia

	Relative Risk of Spinal Hematoma	Estimated Incidence for Epidural Anesthesia	Estimated Incidence for Spinal Anesthesia
No heparin			
Atraumatic	1.00	1:220,000	1:320,000
Traumatic	11.2	1:20,000	1:29,000
With aspirin	2.54	1:150,000	1:220,000
Heparin anticoagulation following neuraxial procedure			
Atraumatic	3.16	1:70,000	1:100,000
Traumatic	112	1:2000	1:2900
Heparin >1 h after puncture (Héparine IV)	2.18	1:100,000	1:150,000
Heparin <1 h after puncture	25.2	1:8700	1:13,000
With aspirin	26	1:8500	1:12,000

Data from Stafford-Smith,[45] with permission.

- < 1 heure
- Traumatique
- AAS

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20

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TABLE 8. Patient, Anesthetic, and LMWH Risk Factors* Associated With Spinal Hematoma

	n
Patient factors	
Female sex	72
Elderly (≥65 y)	70
Abnormalities of spinal cord or vertebral column	20
Patients at increased risk of hemorrhage†	47
Renal insufficiency	7
Anesthetic factors	
Traumatic needle/catheter placement	26
Epidural technique	54
Indwelling epidural catheter during LMWH administration	36
LMWH dosing factors	
Immediate preoperative administration (<12 h)	5
Intraoperative administration	7
Early postoperative administration (<12 h)	17
Administration close to indwelling catheter removal (<12 h)	1
Twice-daily administration (vs once daily administration)	48
Higher LMWH dose than that in the label	1
Concomitant medications affecting hemostasis	43

*More than 1 risk factor may have been present in a single case.
Adapted from the FDA Drug Safety Communication.[59]

U.S. Food and Drug Administration — Protecting and Promoting Your Health — Drug Safety Communications

Updated recommendations to decrease risk of spinal column bleeding and paralysis in patients on low molecular weight heparins

12. Horlocker TT, Wedel DJ. Neuraxial block and low–molecular-weight heparin: balancing perioperative analgesia and thromboprophylaxis. *Reg Anesth Pain Med.* 1998;23:164–177.

33. Moen V, Dahlgren N, Irestedt L. Severe neurological complications after central neuraxial blockades in Sweden 1990–1999. *Anesthesiology.* 2004;101:950–959.

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21

Résumé facteurs de risque d'hématome péridural

- Âge avancé
- Anomalies spinales / vertébrales
- Coagulopathie sous-jacente
- Technique neuraxiale difficile / traumatique
- Cathéter *in situ* et anticoagulation continue

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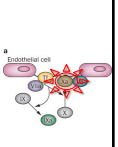
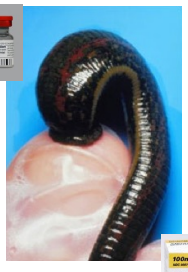
Inhibiteurs sélectifs X_a et II_a



24

Inhibiteurs directs de la thrombine



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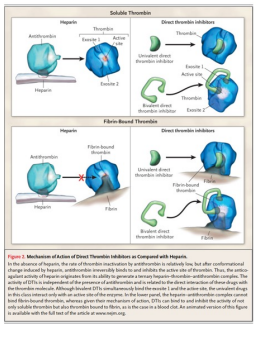
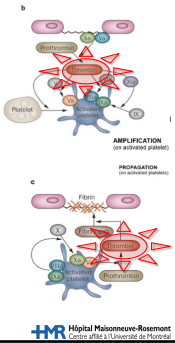
Inhibiteurs directs de la thrombine





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27

Inhibiteurs directs de la thrombine

Table 1. Main Properties and Pharmacokinetic Characteristics of Direct Thrombin Inhibitors.

Characteristic	Recombinant Hirudins*	(Angiomax) Bivalirudin (Hirulog)	(Anticoagulation patients HIT) Argatroban (Novastan)	Ximelagatran and Melagatran (Exanta)	(Pradaxa) Dabigatran
Route of administration	Intravenous, subcutaneous	Intravenous	Intravenous	Intravenous, subcutaneous (melagatran), oral (ximelagatran)	Oral
Plasma half-life	Intravenous, 60 min; subcutaneous, 120 min	25 min	45 min	Intravenous and subcutaneous, 2–3 hr; oral, 3–5 hr	12 hr
Main site of clearance	Kidney	Kidney, liver, other sites	Liver	Kidney	Kidney

* Recombinant hirudins include lepirudin (Refludan) and desirudin (Iprivask).

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28

Inhibiteurs sélectifs X_a

The anticoagulant effect of DXAs can be reliably measured using drug-specific, calibrated anti-X activity (aXa) assays.[57–60] A non-detectable anticoagulant effect is defined as a drug-specific threshold plasma level <30 ng/mL.[57 59] If drug-specific calibrated aXa assays are not available, a clinically relevant DXA effect can be ruled out by the use of UFH-calibrated or LMWH-calibrated chromogenic aXa assays.[58 61] In these cases, an aXa activity of 0.1 IU/mL or less is considered to be an undetectable anticoagulant effect.[57–60] Chromogenic drug-specific calibrated aXa assays are very sensitive to the presence of DXA, especially

Prior to neuraxial block or deep plexus/peripheral block we suggest that a residual dabigatran plasma level <30 ng/mL is acceptable (grade IIC)

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29

Recommandations: Inhibiteurs sélectifs X_a

MANAGEMENT OF NEURAXIAL BLOCK OR DEEP PLEXUS/ PERIPHERAL BLOCK IN THE PATIENT RECEIVING A HIGH DOSE OF APIXABAN, EDOXABAN, RIVAROXABAN

We suggest that a high dose of apixaban be discontinued at least 72 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking apixaban or aXa plasma level if <72 hours (grade IIC)

Remarks: there is no change in this recommendation.

We suggest that a residual apixaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL is acceptable prior to neuraxial block or deep plexus/peripheral block (grade IIC)

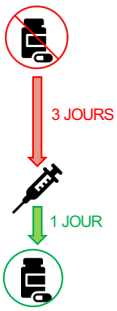
Remarks: this new recommendation includes acceptable plasma levels and aXa levels.

We suggest that needle placement/catheter removal occurs at least 24 hours prior to the first postoperative dose (grade IIC)

Remarks: this is a new recommendation in the setting of high-dose administration.

With the unanticipated administration of high dose of apixaban with a neuraxial catheter in situ, we suggest that apixaban dosing be withheld for at least 72 hours, or a residual apixaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL before the catheter is removed (grade IIC)

Remarks: this is a new recommendation in the setting of high-dose administration and recommendations for acceptable plasma levels and aXa levels.



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Recommandations: Inhibiteurs sélectifs X_a

MANAGEMENT OF NEURAXIAL BLOCK OR DEEP PLEXUS/ PERIPHERAL BLOCK IN THE PATIENT RECEIVING A LOW DOSE OF APIXABAN

We suggest that a low dose of apixaban be discontinued for at least 36 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking apixaban or aXa plasma level if <36 hours (grade IIC)

Remarks: this is a new recommendation in the setting of low-dose administration.

We suggest that a residual apixaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL is acceptable prior to neuraxial block or deep plexus/peripheral block (grade IIC)

Remarks: this new recommendation includes acceptable plasma levels and aXa levels.

We suggest that needle placement/catheter removal occurs at least 6 hours prior to the first postoperative dose (grade IIC)

Remarks: there is no change in this recommendation.

With the unanticipated administration of low dose of apixaban with a neuraxial catheter in situ, we suggest that apixaban dosing be withheld for at least 36 hours, or a residual apixaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL before the catheter is removed (grade IIC)

Remarks: this is a new recommendation in the setting of low-dose administration and recommendations for acceptable plasma levels and aXa levels.

RIVAROXABAN
- 24 h;
- 30 h si ClCr < 30

EDOXABAN :
?

Eliquis :
1-1/2 JOURS
Xarelto :
24-30 HEURES

6 HEURES

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30

Recommandations : inhibiteur direct de la thrombine ORAL : Dabigatran (Pradaxa)

MANAGEMENT OF NEURAXIAL BLOCK OR DEEP PLEXUS/ PERIPHERAL BLOCK IN THE PATIENT RECEIVING A HIGH DOSE OF DABIGATRAN

We suggest that a high dose of dabigatran be discontinued for at least 72 hours in patients with a CrCl ≥50 mL/min prior to neuraxial block or deep plexus/peripheral block. Consider checking dabigatran plasma level if <72 hours (grade IIC)

We suggest that a high dose of dabigatran be discontinued for 120 hours in patients with a CrCl 30–49 mL/min prior to neuraxial block or deep plexus/peripheral block. Consider checking dabigatran plasma level if <120 hours (grade IIC)

We suggest against the performance of neuraxial or deep plexus/ peripheral blocks in patients with a CrCl <30 mL/min unless a dabigatran plasma level is obtained and <30 ng/mL (grade IIC)

Prior to neuraxial block or deep plexus/peripheral block we suggest that a residual dabigatran plasma level <30 ng/mL is acceptable (grade IIC)

We suggest that needle placement/catheter removal occurs at least 24 hours prior to the first postoperative dose (grade IIC)

With the unanticipated administration of high-dose dabigatran with a neuraxial catheter in situ, we suggest that dabigatran dosing be withheld for at least 72 hours (120 hours if CrCl 30–49 mL/min) or a residual dabigatran plasma level <30 ng/mL before the catheter is removed (grade IIC)

3 JOURS ou 5 JOURS ou NON

2 JOURS

1 JOUR

6 heures

MANAGEMENT OF NEURAXIAL BLOCK OR DEEP PLEXUS/ PERIPHERAL BLOCK IN THE PATIENT RECEIVING A LOW DOSE OF DABIGATRAN

We suggest that a low dose of dabigatran be discontinued for at least 48 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking dabigatran plasma level if <48 hours (grade IIC)

We suggest that a residual dabigatran plasma level <30 ng/mL is acceptable prior to neuraxial block or deep plexus/peripheral block (grade IIC)

We suggest against the performance of neuraxial or deep plexus/ peripheral blocks in patients with a CrCl <30 mL/min unless a dabigatran plasma level is obtained and <30 ng/mL (grade IIC)

We suggest that needle placement/catheter removal occurs at least 6 hours prior to the first postoperative dose (grade IIC)

With the unanticipated administration of low dose of dabigatran with a neuraxial catheter in situ, we suggest that dabigatran dosing be withheld for at least 48 hours, or a residual dabigatran plasma level <30 ng/mL before the catheter is removed (grade IIC)

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31

Recommandations : inhibiteurs directs de la thrombine INTRAVEINEUX :

MANAGEMENT OF NEURAXIAL BLOCK OR DEEP PLEXUS/ PERIPHERAL BLOCK IN THE PATIENT TAKING PARENTERAL THROMBIN INHIBITORS (ARGATROBAN, BIVALIRUDIN, AND DESIRUDIN)

In patients receiving parenteral thrombin inhibitors, we suggest against the performance of neuraxial techniques (grade IIC)

Remarks: there is no change in this recommendation.

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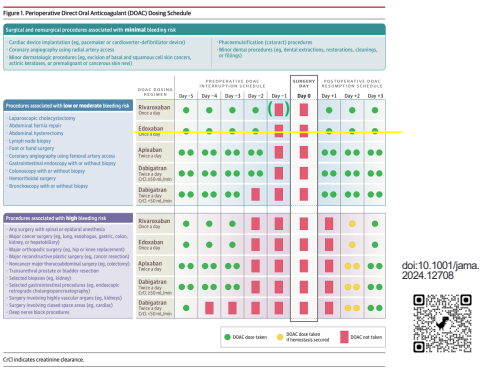
32

Figure 1. Perioperative Direct Oral Anticoagulant (DOAC) Dosing Schedule



doi:10.1001/jama.2024.12708

33

Inhibiteurs sélectifs X_a: antidote

Drugs (2018) 78:1049–1055
https://doi.org/10.1007/s40265-018-0940-4

ADISINSIGHT REPORT

Andexanet Alfa: First Global Approval

Young-A Heo[1]

Published online: 20 June 2018

Abstract
Intravenous andexanet alfa [coagulation factor Xa (recombinant), inactivated-zhzo; Andexxa®] is a first-in-class recombinant modified factor Xa protein that has been developed by Portola Pharmaceuticals as a universal antidote to reverse anticoagulant effects of direct or indirect factor Xa inhibitors. In May 2018, andexanet alfa received its first global approval in the USA for use in patients treated with rivaroxaban and apixaban, when reversal of anticoagulant effects is required in life-threatening or uncontrolled bleeding. Intravenous andexanet alfa is under regulatory review in the EU and is undergoing clinical development in Japan. This article summarizes the milestones in the development of andexanet alfa leading to this first global approval for reversing anticoagulation of rivaroxaban and apixaban in adults.

34

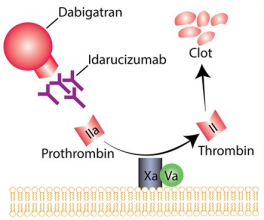
ANDRAXENET ALFA

- FDA
  - Approbation : antidote APIXABAN et RIVAROXABAN pour hémorragie non-contrôlée ou mettant la vie en danger.
  - NON APPROUVÉ : pré-chirurgie urgentes et procédures neuraxiales

35

36

Inhibiteurs directs de la thrombine : antidote



Praxbind® idarucizumab INJECTION 5g

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36

37

PRAXBIND

- FDA
  - Approbation : antidote DABIGATRAN pour hémorragie non-contrôlée ou mettant la vie en danger ou pour situations urgentes.
  - NON APPROUVÉ : procédures neuraxiales

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37

38

Inhibiteurs sélectifs X_a: antidote

Ciraparantag : toujours à l'étude

- Rivaroxaban
- Apixaban
- Edoxaban
- HBPM
- HNF
- Dabigatran

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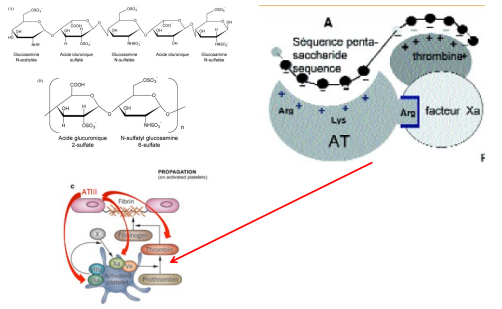
38

39

Héparine non-fractionnée (HNF)



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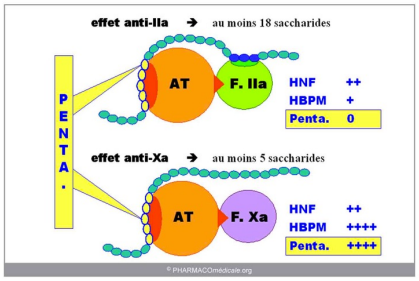
40

HBPM



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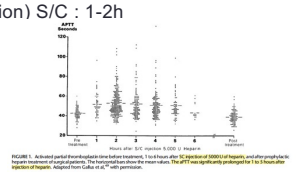
41

Héparine non-fractionnée

- Métabolisme : hépatique, CYP 450, syst réticulo-endothélial.
- Excrétion : urinaire : $T_{1/2}$ 1,5h
- Pic plasmatique (et d'action) IV : immédiat
- Pic plasmatique (et d'action) S/C : 1-2h
- Monitoring : aPTT



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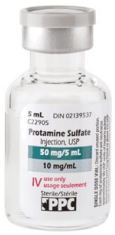
42

Héparine non-fractionnée

- Antagonisme (IV)
- 1mg prot. : 100 U hép.
- 25mg prot. : 1200 U/h hép.



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42

43

Recommandations - HNF

- Héparine 5000 U SC
  - OK BID **et TID**
  - Technique 4-6 heures après la dose
  - +/- test
  - 1 h après le retrait (mise en place ?)
  - OK KT *in situ*
- CF guidelines pour doses plus élevées

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43

44

Recommandations - HNF

- Héparine IV et chirurgie vasculaire
  - Technique 4-6 heures post-dose + test
  - Dose 1 heure post-technique
  - Idem pour mise en place et retrait
  - Pas de KT *in situ*
  - Pas d'annulation systématique :
    - Technique difficile
    - Traumatique

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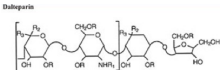
44

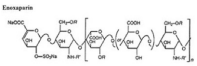
45

Héparines de bas poids moléculaire (HBPM)

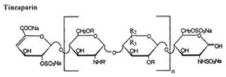
Dalteparin



Enoxaparin



Tinzaparin



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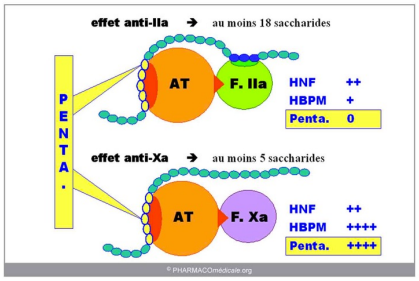
45

46

HBPM



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46

47

Héparines de bas poids moléculaire (HBPM)

- Antidote : protamine pour l'activité anti-II_a seulement

	LMWH	Average molecular weight	Ratio anti-Xa/anti-IIa activity
	Bemiparin	3600	9.7
	Certoparin	5400	2.4
Fragmin	Dalteparin	6000	2.5
Lovenox	Enoxaparin	4500	3.9
	Nadroparin	4300	3.3
	Parnaparin	5000	2.3
	Reviparin	4400	4.2
Innohep	Tinzaparin	6500	1.6

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47

48

HBPM

- Pic d'action (act. anti-X_a) : 3-5 heures
- $T_{1/2}$: 3-4 X HNF (↑insuffisance rénale)
- Activité présente 12h post administration

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48

49

Recommandations - HBPM

Thérapie en cours

- Dose prophylactique (LOW DOSE) :
  - Technique 12h post-dose
- Dose thérapeutique (HIGH DOSE):
  - Technique 24h post-dose

- Dans les deux cas :
  - PRN : Activité aXa : ≤ 0,1 UI/mL

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49

50

Recommandations – HBPM

Thérapie débutée en post-opératoire

- Prophylaxie die :
  - 1ère Dose 12h post-technique
  - OK cathéter continu
  - Retrait de kt 12h post-dose
  - Dose 4h post retrait de kt

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50

51

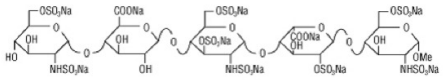
Recommandations – HBPM

- Prophylaxie bid :
  - Dose le lendemain
    - min 12h post-technique
  - PAS de cathéter continu
  - Si kt en place :
    - Dose 4h post retrait de kt

51

52

Fondaparinux



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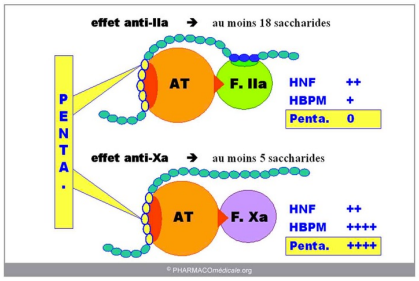
53

HBPM



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54

Fondaparinux

MANAGEMENT OF NEURAXIAL BLOCK OR DEEP PLEXUS/ PERIPHERAL BLOCK IN THE PATIENT RECEIVING FONDAPARINUX

Low-dose fondaparinux (2.5 mg once per day)

We suggest holding low-dose fondaparinux (2.5 mg once per day) for 36 hours (young patients) to 42 hours (elderly patients) in healthy patients with normal renal function (grade IIC)

Remarks: these are new recommendations in the setting of low-dose administration and aXa level suggestions.

We suggest holding fondaparinux for a minimum of 58 hours in patients with moderate renal insufficiency (CrCl 30–50 mL/min) (grade IIC)

Remarks: these are new recommendations in the setting of low-dose administration and aXa level suggestions.

We suggest not performing neuraxial or deep plexus/peripheral blocks in patients with severe renal impairment (CrCl <30 mL/min) due to the 72 hours half-life (grade IIC)

Remarks: these are new recommendations in the setting of low-dose administration and aXa level suggestions.

We suggest testing aXa activity calibrated to fondaparinux if placing the needle prior to these recommended times is considered (aXa ≤0.1 IU/mL) (grade IIC)

Remarks: these are new recommendations in the setting of low-dose administration and aXa level suggestions.

High-dose fondaparinux (5–10 mg once per day)

We suggest holding fondaparinux for a minimum of 70 hours in young patients with normal renal function (grade IIC)

Remarks: these are new recommendations in the setting of high-dose administration and aXa level suggestions.

We suggest holding fondaparinux for a minimum of 105 hours in elderly patients with normal renal function (grade IIC)

Remarks: these are new recommendations in the setting of high-dose administration and aXa level suggestions.

We suggest testing aXa activity calibrated to fondaparinux if placing needle prior to the recommended times is considered (aXa ≤0.1 IU/mL) (grade IIC)

Remarks: these are new recommendations in the setting of high-dose administration and aXa level suggestions.

We suggest that neuraxial catheters be removed at least 6 hours *prior* to the first postoperative dose (grade IIC)

Remarks: there is no change in this recommendation.

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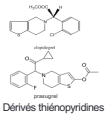
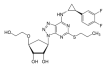
56

Antiplaquettaires

Anti-inflammatoires non stéroïdiens et AAS



Dérivés thiénopyridines



Non-thiénopyridines

Anti gp2b3a

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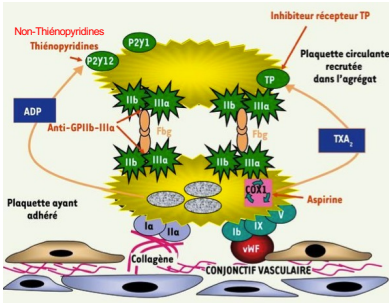
57

Antiplaquettaires



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57

58

Recommandations - Thiénopyridines

Cesser avant la technique :
- Clopidogrel : 5-7 jours
- Prasugrel : 7-10 jours
- Ticlodipine : discontinuée

- Reprise après retrait kt :
  - Pas de dose de charge : immédiat
  - Dose de charge : 6h

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58

59

Recommandations – inhibiteurs P2Y12

- Cesser avant la technique :
  - Ticagrelor : 5 jours
  - Cangrelor : 3 *heures*
- Reprise après retrait kt :
  - Ticagrelor:
    - Pas de dose de charge : immédiat
    - Dose de charge : 6h
  - Cangrelor:
    - 8h

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59

60

Recommandations - AINS

- Neuraxiale ok si monothérapie
- Attention si thromboprophylaxie
  - Favoriser anti-COX II

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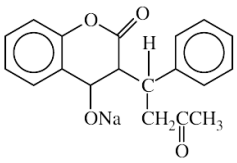
60

61

Warfarin



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61

62

Warfarine

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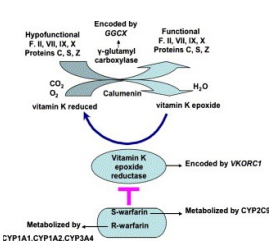
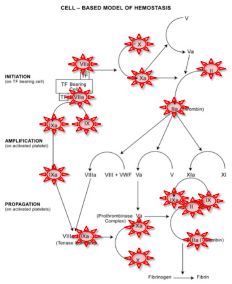
62

63

Warfarine





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63

64

Warfarine

Factor	Half-Life, hrs
Factor VII	6–8
Factor IX	24
Factor X	25–60
Factor II	50–80

- 40% de chaque facteur pour coag. normale
- INR associé à F_{VII} >>> F_{II}
- INR = 1,2 : F_{VII} = 55%
- INR = 1,5 : F_{VII} = 40 %
- À l'arrêt : INR ↓ mais F_{II} encore inhibé

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64

65

Warfarine

- Métabolisme hépatique : CYP 2C9 et autres
- Excrétion urinaire
- Pic action 72-96 heures
- $T_{1/2}$ 20 à 90 heures selon énantiomère
- Monitoring : PT / INR
- Activité thérapeutique affectée par
  - Apport en Vit K_1 / diète
  - Âge avancé
  - Insuffisance hépatique
  - Inducteurs ou inhibiteurs enzymatiques
  - (cf monographie)

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65

66

Recommandations - warfarine

12.1 Caution should be used when performing neuraxial techniques in patients recently discontinued from chronic warfarin therapy. In the first 1 to 3 days after discontinuation of warfarin therapy, the coagulation status (reflected primarily by factors II and X levels) may not be adequate for hemostasis despite a decrease in the INR (indicating a return of factor VII activity). Adequate levels of II, VII, IX, and X may not be present until the INR is within normal limits. We recommend that the anticoagulant therapy must be stopped (ideally 5 days prior to the planned procedure), and the INR normalized prior to initiation of neuraxial block (grade 1B).

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66

67

Recommandations - warfarine

12.7 As thromboprophylaxis with warfarin is initiated, we suggest that neuraxial catheters be removed when the INR is less than 1.5. While removal of epidural catheters 12 to 24 hours after warfarin was given does not appear to represent increase risk, the risk of removing epidural catheters at 48 hours is not guaranteed.

We suggest that neuraxial catheters be removed when the INR is <1.5 (grade IIC)

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67

68

Recommandations - warfarine

12.8 In patients with INR of greater than 1.5 but less than 3, the increase in risk with progressive INR prolongation remains unknown. We suggest indwelling catheters may be maintained with caution, based on INR and duration of warfarin therapy (grade 2C).

In patients with an INR >3, we recommend that the warfarin dose be held or reduced in patients with indwelling neuraxial catheters (grade IA)

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68

69

Les 3G



Table 6 Three herbal medications with the greatest impact on hemostasis*

	Important effects	Perioperative concerns	Time to normal hemostasis after discontinuation
Garlic	Inhibition of platelet aggregation (may be irreversible) Increased fibrinolysis Equivocal antihypertensive activity	Potential to increase bleeding, especially when combined with other medications that inhibit platelet aggregation	7 days
Ginko	Inhibition of platelet-activating factor	Potential to increase bleeding, especially when combined with other medications that inhibit platelet aggregation	36 hours
Ginseng	Lowers blood glucose Increased prothrombin and activated partial prothrombin times in animals Other diverse effects	Hypoglycemia Potential to increase risk of bleeding Potential to decrease anticoagulant effect of warfarin	24 hours

Adapted from Horlocker *et al*[3]
*At this time, it is not deemed necessary to discontinue herbal medications and allow resolution of their effects on hemostasis prior to surgery or anesthesia.

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69

70

Recommandations – Les 3G

Pas de contre-indication

70

71

Blocs nerveux périphériques

Anaesthesia Critical Care & Pain Medicine
Available online 23 December 2018
In Press, Corrected Proof

Review article

Bleeding complications following peripheral regional anaesthesia in patients treated with anticoagulants or antiplatelet agents: A systematic review

F. Joubert [a], P. Gillois [b], H. Bouaziz [c], E. Marret [d], G. Iohom [e], P. Albaladejo [a]

71

72

Blocs nerveux périphériques

- 9738 blocs chez 5876 patients recevant anti-PLQ ou AC
- Incidence de complications hémorragiques :
  - 0,67 % (0,51%-0,83%)
  - Hématomes sites de ponction
  - Pas de neuropathie associée aux saignements

https://doi.org/10.1016/j.accpm.2018.12.009

- Sévérité des complications associées à :
  - Impossibilité de compression du site
  - Proximité de gros vaisseaux
  - Absence d'hématome cutané (saignement occulte)
  - Proximité de la colonne vertébrale (bloc paravertébraux)

72

73

Blocs nerveux périphériques

MANAGEMENT OF DEEP PLEXUS/PERIPHERAL BLOCK IN THE ANTICOAGULATED PATIENT

For patients undergoing deep plexus or deep peripheral block, we recommend that guidelines for neuraxial block be similarly applied (grade IC)

Remarks: there is no change in this recommendation.

For patients undergoing other plexus or peripheral techniques, we suggest performance, catheter maintenance, and catheter removal be based on site compressibility, vascularity, and consequences of bleeding, should it occur (grade IIC)

Remarks: there is no change in this recommendation.

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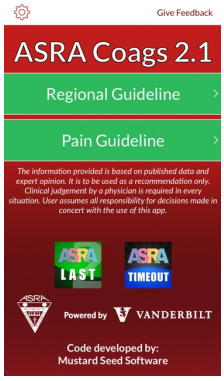
73

74



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74

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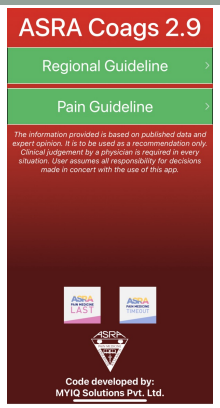

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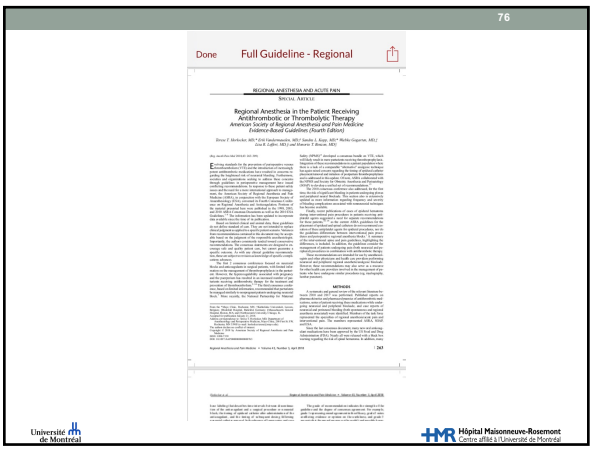
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Done
Full Guideline - Regional
Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy
American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition)
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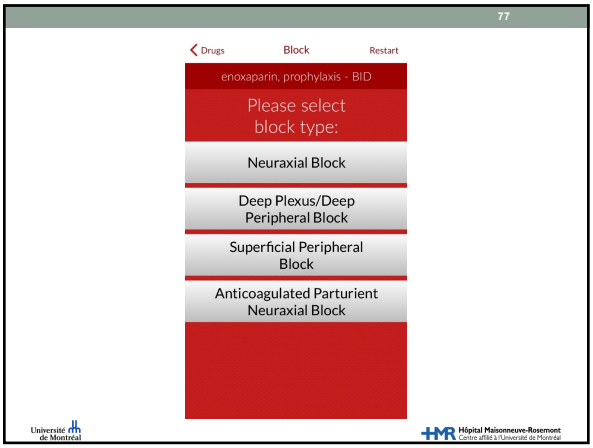
76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Drugs
Block
Restart
enoxaparin, prophylaxis - BID
Please select block type:
Neuraxial Block
Deep Plexus/Deep Peripheral Block
Superficial Peripheral Block
Anticoagulated Parturient Neuraxial Block
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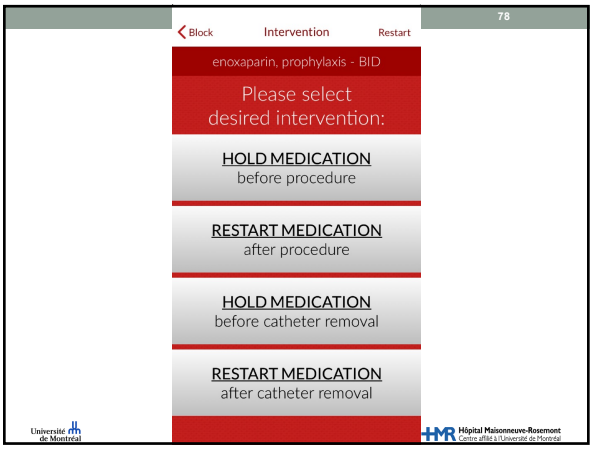
77


78
Block
Intervention
Restart
enoxaparin, prophylaxis - BID
Please select desired intervention:
HOLD MEDICATION before procedure
RESTART MEDICATION after procedure
HOLD MEDICATION before catheter removal
RESTART MEDICATION after catheter removal
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78

79

Intervention Regional Recs. Restart

enoxaparin, prophylaxis - BID

Place Neuraxial Block?

12 hours

We recommend that needle placement should occur at least 12 hours after a prophylactic LMWH dose.

In patients administered a dose of LMWH 2 hours preoperatively (general surgery patients), we recommend against neuraxial techniques because needle placement would occur close to peak anticoagulant activity.

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79

80

- Questions
- Commentaires

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80