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Point-of-Care Information About Coagulation Tests and Bleeding Disorders Anytime, Anywhere.

Contents

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Point-of-Care Information About Coagulation Tests and Bleeding Disorders Anytime, Anywhere.

Coagulation Toolkit | **Key concomitant factors that can affect coagulation**

Acidosis

Acidosis interferes with the coagulation of plasma by reducing the activity of various vitamin K–dependent factors. This markedly reduces the activity of coagulation factor complexes. Acidosis occurs when low perfusion leads to insufficient oxygen delivery to tissues.[1]

Reference

1. Zimrin AB, Holcomb JB, Hess JR. Hemorrhage control and thrombosis following severe injury. In: Kitchens CS, Alving BM, Kessler CM, eds. *Consultative Hemostasis and Thrombosis*. 2nd ed. Philadelphia, PA: Saunders Elsevier; 2007:717-722.

Bleeding history

A family history of a bleeding disorder and/or bleeding with prior surgery or trauma are suggestive of an underlying congenital bleeding disorder.[1]

Reference

1. Deloughery TG. Management of acute hemorrhage. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1159-1171.

Cardiopulmonary bypass

Most patients undergoing cardiopulmonary bypass exhibit abnormal platelet function and thrombocytopenia. Postoperatively, bleeding time may be prolonged and platelet aggregation may be abnormal, with decreased aggregation in response to ristocetin and decreased α-granule or δ-granule concentrations.[1]

Reference

1. López JA, Lockhart E. Acquired disorders of platelet function. In: Hoffman R, Benz EJ Jr, Shattil SJ, et al, eds. *Hematology: Basic Principles and Practice.* 5th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:2145-2159.

Contraceptives

Estrogen-containing contraceptives affect clotting by increasing plasma fibrinogen, soluble fibrin, and coagulation factor activity, especially FII, FVII, FVIII, FIX, and FX.[1]

Reference

1. Bonnar J. Coagulation effects of oral contraception. *Am J Obstet Gynecol*. 1987;157(4, pt 2):1042-1048.

Dilution/consumption

In the setting of massive hemorrhage, dilution of the remaining blood by administration of IV fluids and plasma-poor red blood cells can reduce clotting factors and platelets. Consumption of coagulation factors and platelets in response to tissue factor activation can also occur. These disturbances can manifest clinically with abnormal coagulation testing and as a diffuse bleeding diathesis.[1]

Reference

1. Zimrin AB, Holcomb JB, Hess JR. Hemorrhage control and thrombosis following severe injury. In: Kitchens CS, Alving BM, Kessler CM, eds. *Consultative Hemostasis and Thrombosis*. 2nd ed. Philadelphia, PA: Saunders Elsevier; 2007:717-722.

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Dysproteinemia

Dysproteinemias such as immunoglobulin A (IgA) myeloma, Waldenström macroglobulinemia, IgG myeloma, and benign monoclonal gammopathy (less common) can cause platelet dysfunction. All aspects of platelet function, including aggregation, secretion, procoagulant activity, and clot retraction, can be inhibited by myeloma proteins. The platelet function abnormalities associated with paraproteinemia are concentration dependent.[1]

Reference
1. López JA, Lockhart E. Acquired disorders of platelet function. In: Hoffman R, Benz EJ Jr, Shattil SJ, et al, eds. *Hematology: Basic Principles and Practice.* 5th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:2145-2159.

Giant cavernous hemangioma

Giant cavernous hemangioma can be associated with thrombocytopenia due to increased platelet destruction.[1] It was first described as a cause of bleeding by Kasabach and Merritt.[2] Kasabach-Merritt syndrome typically occurs in a neonate or infant and is characterized by hemangioma along with widespread ecchymoses, thrombocytopenia, and a localized consumptive coagulopathy.[3]

References
1. Kuter DJ. General aspects of thrombocytopenia, platelet transfusions, and thrombopoietic growth factors. In: Kitchens CS, Alving BM, Kessler CM, eds. *Consultative Hemostasis and Thrombosis.* 2nd ed. Philadelphia, PA: Saunders Elsevier; 2007:111-122. **2.** Marder VJ, Feinstein DI, Colman RW, Levi M. Consumptive thrombohemorrhagic disorders. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice.* 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1571-1600. **3.** Coller BS, Schneiderman PI. Clinical evaluation of hemorrhagic disorders: the bleeding history and differential diagnosis of purpura. In: Hoffman R, Benz EJ Jr, Shattil SJ, et al, eds. *Hematology: Basic Principles and Practice.* 5th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:1851-1876.

Hypersplenism

Hypersplenism is a syndrome in which splenomegaly is accompanied by 1 or more cytopenias: thrombocytopenia, leukopenia, or anemia. Thrombocytopenia is primarily caused by increased splenic sequestration of platelets. Even though hypersplenism is characterized by splenomegaly, many patients with splenomegaly do not have hypersplenism.[1]

Reference
1. Warkentin TE. Thrombocytopenia due to platelet destruction and hypersplenism. In: Hoffman R, Benz EJ Jr, Shattil SJ, et al, eds. *Hematology: Basic Principles and Practice.* 5th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:2113-2131.

Hypothermia

Hypothermia slows the rates of all enzymatic coagulation reactions and impairs platelet function. It can occur both with exposure to the elements and from resuscitation with cold IV fluids or red blood cells.[1]

At core temperatures of 32°C-34°C, platelet activities, though present, are reduced. At a core temperature of 30°C, an acquired Bernard-Soulier syndrome–like platelet dysfunction may occur. This is associated with a loss of platelet secretion, aggregation, and active surfaces for the assembly of coagulation factor complexes.[1]

Reference
1. Zimrin AB, Holcomb JB, Hess JR. Hemorrhage control and thrombosis following severe injury. In: Kitchens CS, Alving BM, Kessler CM, eds. *Consultative Hemostasis and Thrombosis.* 2nd ed. Philadelphia, PA: Saunders Elsevier; 2007:717-722.

Infection

Infection can be associated with both thrombocytopenia and thrombocytosis. In the absence of DIC, thrombocytopenia (sometimes severe) may occur in septicemia associated with bacterial, fungal, or viral infections. Mild to moderate thrombocytosis is commonly associated with infection (especially chronic infections) and may also occur during recovery from infection.[1]

Reference
1. Marks PW, Rosenthal DS. Hematologic manifestations of systemic disease: infection, chronic inflammation, and cancer. In: Hoffman R, Benz EJ Jr, Shattil SJ, et al, eds. *Hematology: Basic Principles and Practice.* 5th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:2309-2319.

Liver disease

Both platelet number and platelet function are commonly affected by liver disease. Thrombocytopenia (typically mild to moderate) is seen in approximately one-third of patients with chronic liver disease. Platelet function may also be impaired, with abnormalities observed in platelet aggregation in response to ADP, arachidonic acid, collagen, and thrombin.[1]

Reference
1. Senzolo M, Burroughs AK. Hemostatic alterations in liver disease and liver transplantation. In: Kitchens CS, Alving BM, Kessler CM, eds. C*onsultative Hemostasis and Thrombosis.* 2nd ed. Philadelphia, PA: Saunders Elsevier; 2007:647-659.

Lupus autoimmune disease

Systemic lupus erythematosus is associated with an increased risk of developing circulating antibodies to coagulation factors, including FII, FV, FVIII, FIX, FX, and FXI.[1] Lupus anticoagulant is commonly associated with an in vitro elevation of aPTT but clinically associated with an increased risk of clotting.[2,3]

References
1. Hematology. In: Wallach J, ed. *Interpretation of Diagnostic Tests.* 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:368-560. **2.** Kessler CM, Acs P, Mariani G. Acquired disorders of coagulation: the immune coagulopathies. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1061-1084. **3.** Konkle BA. Clinical approach to the bleeding patient. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1147-1158.

Malignancy

In patients with a malignancy, the clotting system can be systemically activated, which leads to consumption of clotting factors, and then fibrinolysis. Fibrinogen and clotting factors (ie, FV, FVIII, FIX, FXI, FXII) may be either elevated or depressed, while both PT and aPTT are either shortened or prolonged.[1] Plasma D-dimers may also be increased.[2]

Prominent thrombocytopenia may occur in several hematologic malignancies as a consequence of underlying marrow replacement or an autoimmune disorder. Myeloproliferative disorders and myelodysplastic syndrome with the 5q- chromosomal abnormality may present with prominent thrombocytosis.[3]

References
1. Dvorak HF, Rickles FR. Malignancy and hemostasis. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:851-873. **2.** Respiratory diseases. In: Wallach J, ed. *Interpretation of Diagnostic Tests.* 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:144-170. **3.** Marks PW, Rosenthal DS. Hematologic manifestations of systemic disease: infection, chronic inflammation, and cancer. In: Hoffman R, Benz EJ Jr, Shattil SJ, et al, eds. *Hematology: Basic Principles and Practice.* 5th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:2309-2319.

Other drugs/foods/supplements

Other drugs[1,2]

- Nonsteroidal anti-inflammatory drugs
- Prostacyclin analogues: epoprostenol, iloprost, beraprost
- Phosphodiesterase inhibitors: methylxanthines (eg, theophylline), sildenafil
- Statins (eg, lovastatin, pravastatin, simvastatin, fluvastatin, atorvastatin)
- Antibiotics: β-lactam antibiotics, penicillins, nitrofurantoin, moxalactam
- Plasma expanders: dextran, hydroxyethyl starch
- Psychotropics: tricyclic antidepressants (eg, imipramine, amitriptyline, nortriptyline), phenothiazines (eg, chlorpromazine, promethazine, trifluoperazine), selective serotonin reuptake inhibitors (eg, fluoxetine, paroxetine, sertraline)

- Cardiovascular drugs: α-adrenergic receptor blockers (eg, propranolol, metoprolol, nebivolol, pindolol), calcium channel blockers (eg, verapamil, diltiazem, nifedipine), angiotensin-converting enzyme (ACE) inhibitors (eg, losartan), quinidine, diuretics (eg, furosemide), nitrites, nitroprusside
- Anesthetics: dibucaine, procaine, cocaine, halothane
- Oncologic drugs: mithramycin, daunorubicin, bis-chloroethyl nitrosourea
- Radiologic contrast agents: Renografin-76®, Renovist II, Conray® 60
- Antihistamines: diphenhydramine, chlorpheniramine
- Miscellaneous: clofibrate, hydroxychloroquine, oral $\alpha_{IIb}\beta_3$ inhibitors, fibrinolytic agents

Foods/supplements[2]

- Omega-3 fatty acids, fish oil, vitamin E, garlic, onion, cumin, turmeric, clove

References
1. López JA, Lockhart E. Acquired disorders of platelet function. In: Hoffman R, Benz EJ Jr, Shattil SJ, et al, eds. *Hematology: Basic Principles and Practice.* 5th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:2145-2159. **2.** Rao AK. Acquired qualitative platelet defects. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice.* 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1045-1060.

Pregnancy

Numerous clotting factors are elevated during pregnancy, including FVII, FVIII, FX, and fibrinogen.[1]
Normal fibrinogen levels during pregnancy are[2]:

- 13 to 28 weeks gravid—8.5-16.8 mcmol/L (289-571 mg/dL)
- 29 to 42 weeks gravid—9.5-19.1 mcmol/L (323-650 mg/dL)

Thrombocytopenia occurs in approximately 7%-12% of pregnancies. Women with gestational thrombocytopenia typically have platelet counts of 70,000-150,000 per mcL, are otherwise healthy, and have no history of ITP.[3]

References
1. Hematology. In: Wallach J, ed. *Interpretation of Diagnostic Tests.* 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:368-560. **2.** Szecsi PB, Jørgensen M, Klajnbard A, Andersen MR, Colov NP, Stender S. Haemostatic reference intervals in pregnancy. *Thromb Haemost*. 2010;103(4):718-727. **3.** Laubach J, Bendell J. Hematologic changes of pregnancy. In: Hoffman R, Benz EJ Jr, Shattil SJ, et al, eds. Hematology: *Basic Principles and Practice.* 5th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:2385-2396.

Sickle cell disease

In sickle cell disease, there is a significant activation of coagulation along with an increase in fibrinolysis.[1] Plasma D-dimers are also elevated with increased fibrinolysis.[2]

References
1. Hagger D, Wolff S, Owen J, Samson D. Changes in coagulation and fibrinolysis in patients with sickle cell disease compared with healthy black controls. *Blood Coagul Fibrinolysis*. 1995;6(2):93-99. **2.** Respiratory diseases. In: Wallach J, ed. *Interpretation of Diagnostic Tests.* 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:144-170.

Uremia

Platelet function may be altered in patients with uremia. Abnormalities include reduced fibrinogen binding, aggregation, and secretion in response to various agonists. Prolonged bleeding time may also occur.[1]

Reference
1. López JA, Lockhart E. Acquired disorders of platelet function. In: Hoffman R, Benz EJ Jr, Shattil SJ, et al, eds. *Hematology: Basic Principles and Practice.* 5th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:2145-2159.

Anticoagulants

Heparin (unfractionated)

Overview

Heparin is a negatively charged glycosaminoglycan obtained from animal or plant sources. It exerts its anticoagulant activity by binding to antithrombin, thrombin, and FXa, inhibiting the ability of FXa and thrombin to initiate clots.[1] Heparin is given to prevent and treat venous thrombosis and for the management of arterial disease.[2]

Monitoring

Heparin effect is traditionally monitored using aPTT. However, an anti-FXa activity assay can also be used to establish a therapeutic range for heparin.[1] A prolonged TT with a normal RT is typical of heparin effect.[3]

Effects on lab values[3-5]

Typical lab values*

Tests	Values
PT	= or ↑
aPTT	↑
TT	↑
Anti-FXa activity	↑
Fibrinogen	=
Platelet aggregation	↓ or = or ↑[a]

Key ↑ Increased ↓ Decreased = No change

[a]Heparin can cause heparin-induced thrombocytopenia type 2, an immune-mediated drug reaction that increases the risk of arterial and venous thrombosis. This disorder is associated with increased platelet activation.[6]

*Values may not represent those seen when additional drugs or confounding illnesses are present.

References

1. Ng VL. Anticoagulation monitoring. *Clin Lab Med*. 2009;29(2):283-304. **2.** Fink LM, Marlar RA, Miller JL. Antithrombotic therapy. In: McPherson RA, Pincus MR, eds. *Henry's Clinical Diagnosis and Management by Laboratory Methods*. 21st ed. Philadelphia, PA: Saunders Elsevier; 2007:778-788. **3.** Hematology. In: Wallach J, ed. *Interpretation of Diagnostic Tests*. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:368-560. **4.** Slaughter TF. Coagulation. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, eds. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:1767-1779.
5. Tran HAM, Ginsberg JS. Anticoagulant therapy for major arterial and venous thromboembolism. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1673-1688. **6.** Warkentin TE. Heparin-induced thrombocytopenia. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1649-1661.

Low-molecular-weight heparin (LMWH)

(eg, tinzaparin, dalteparin, enoxaparin)[1]

Overview

LMWH is a polysaccharide polymer like unfractionated heparin, but it is restricted in size to fragments ≤10,000 daltons. Since LMWH is shorter than unfractionated heparin, it only binds antithrombin and FXa, not thrombin. The primary effect is FXa inhibition.[2] LMWH is typically used to prevent thromboembolism and to treat acute deep venous thrombosis and pulmonary embolism.[1]

Monitoring

Routine lab monitoring is not needed for most patients on LMWH because of its predictable pharmacokinetics. For patients who are pregnant, have renal failure, are of a low weight where weight-based dosing may not be accurate, or are neonates, LMWH therapy is monitored by an anti-FXa activity assay.[2]

Effects on lab values[1,3]

Typical lab values*

Tests	Values
PT	=
aPTT[a]	=
TT	N/A
Anti-FXa activity	↑
Fibrinogen	N/A
Platelet aggregation	N/A

Key ↑ Increased ↓ Decreased = No change

[a]Check with your lab to see if its aPTT reagents have any sensitivity to LMWH.

*Values may not represent those seen when additional drugs or confounding illnesses are present.

References

1. Tran HAM, Ginsberg JS. Anticoagulant therapy for major arterial and venous thromboembolism. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1673-1688. **2.** Ng VL. Anticoagulation monitoring. *Clin Lab Med*. 2009;29(2):283-304. **3.** Slaughter TF. Coagulation. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, eds. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:1767-1779.

Warfarin

Overview

Warfarin is a dicumarol derivative. It exerts an anticoagulatory effect by inhibiting the gamma carboxylation of vitamin K–dependent coagulation factors. This leads to lower levels of active coagulation factors.[1] FVII is affected initially because it has the shortest half-life, while effects on FII, FIX, and FX follow later.[2] As a result, early warfarin effect may present with only a prolongation of the PT/INR, while both PT and aPTT will be prolonged with longer treatment.[3] Warfarin is commonly used for long-term treatment of venous and arterial thrombosis.[2]

Monitoring[4]

Warfarin is typically monitored by the INR.

Effects on lab values[5,6]

Typical lab values*

Tests	Values
PT	↑
aPTT	= or ↑[a]
TT	=
Anti-FXa activity	N/A
Fibrinogen	=
Platelet aggregation	=

Key ↑ Increased ↓ Decreased = No change

[a]Increased with high drug dosage.

*Values may not represent those seen when additional drugs or confounding illnesses are present.

References

1. Ng VL. Anticoagulation monitoring. *Clin Lab Med*. 2009;29(2):283-304. **2.** Tran HAM, Ginsberg JS. Anticoagulant therapy for major arterial and venous thromboembolism. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1673-1688. **3.** Prothrombin time. In: Jacobs DS, DeMott WR, Oxley DK, eds. *Lexi-Comp's Laboratory Test Handbook Concise With Disease Index*. 3rd ed. Hudson, OH: Lexi-Comp; 2004:1116-1121. **4.** Francis CW. Antithrombotic agents. In: Kitchens CS, Alving BM, Kessler CM, eds. *Consultative Hemostasis and Thrombosis*. 2nd ed. Philadelphia, PA: Saunders Elsevier; 2007:449-460. **5.** Hematology. In: Wallach J, ed. *Interpretation of Diagnostic Tests*. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:368-560. **6.** Slaughter TF. Coagulation. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, eds. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:1767-1779.

Direct thrombin inhibitors

(eg, hirudin, lepirudin, argatroban, dabigatran)[1]

Overview

Direct thrombin inhibitors are a class of medicines that directly inhibit the activation of thrombin without the help of antithrombin. Thrombin normally cleaves fibrinogen to fibrin to begin the process of clot formation. The recommended clinical use for these compounds is rapidly evolving.[1] One potential use is in patients with thrombosis who have heparin-induced thrombocytopenia.[2]

Monitoring[3]

Direct thrombin inhibitors are typically monitored by aPTT and activated clotting time.

Effects on lab values[2,4]

Typical lab values*

Tests	Values
PT	= or ↑[a]
aPTT	↑
TT	↑
Anti-FXa activity	N/A
Fibrinogen	N/A
Platelet aggregation	N/A

Key ↑ Increased ↓ Decreased = No change

[a]Argatroban and lepirudin may increase the normal PT 4 to 5 seconds.[4]

*Values may not represent those seen when additional drugs or confounding illnesses are present.

References

1. Ng VL. Anticoagulation monitoring. *Clin Lab Med*. 2009;29(2):283-304. **2.** Tran HAM, Ginsberg JS. Anticoagulant therapy for major arterial and venous thromboembolism. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1673-1688. **3.** Francis CW. Antithrombotic agents. In: Kitchens CS, Alving BM, Kessler CM, eds. *Consultative Hemostasis and Thrombosis*. 2nd ed. Philadelphia, PA: Saunders Elsevier; 2007:449-460. **4.** Slaughter TF. Coagulation. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, eds. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:1767-1779.

Factor Xa (FXa) inhibitors

(eg, fondaparinux)[1]

Overview[1]

FXa inhibitors, such as fondaparinux, are synthetic polysaccharides that specifically inhibit FXa without having any activity against thrombin. They exert their effect by binding to antithrombin. A possible use for fondaparinux includes prevention of venous thromboembolism in high-risk patients, such as those undergoing orthopedic procedures.

Monitoring[2]

Fondaparinux is typically monitored by an anti-FXa assay.

Effects on lab values[1]

Typical lab values*

Tests	Values
PT	=
aPTT	=
TT	N/A
Anti-FXa activity	↑
Fibrinogen	N/A
Platelet aggregation	N/A

Key ↑ Increased ↓ Decreased = No change

*Values may not represent those seen when additional drugs or confounding illnesses are present.

References

1. Tran HAM, Ginsberg JS. Anticoagulant therapy for major arterial and venous thromboembolism. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1673-1688. **2.** Francis CW. Antithrombotic agents. In: Kitchens CS, Alving BM, Kessler CM, eds. *Consultative Hemostasis and Thrombosis*. 2nd ed. Philadelphia, PA: Saunders Elsevier; 2007:449-460.

Oral direct factor Xa (FXa) inhibitors

(eg, rivaroxaban, apixaban)[1]

Overview

Oral direct FXa inhibitors, such as rivaroxaban and apixaban, are a newer class of medicines that are seen as an alternative to vitamin K antagonists for patients at risk for thromboembolism.[1,2] Through direct targeting, these drugs inhibit the activity of both free FXa and prothrombinase-bound FXa, effectively blocking the activity of enzymes that convert prothrombin into thrombin.[1,3] Rivaroxaban and apixaban are oral medicines that are eliminated by both the liver and the kidneys.[1]

Overview

Unlike injectable direct thrombin inhibitors, oral direct FXa inhibitors don't require active laboratory monitoring.[3,4] Though experience is limited, the most reliable test for assessing activity may be the anti-FXa assay.[3,5]

Effects on lab values[1,5-7]

Typical lab values*

Tests	Values
PT	↑[a]
aPTT	↑[a]
TT	=[b]
Anti-FXa activity	↑
Fibrinogen	=[b,c]
Platelet aggregation	↑[b]

Key ↑ Increased ↓ Decreased = No change

[a]Different reagents may cause the effect of rivaroxaban on PT and aPTT to vary. The effect of apixaban on PT and aPTT is slight.[5]

[b]Effect of apixaban not studied.[1,6,7]

[c]Levels may be ≈10% lower compared with baseline with increasing doses of rivaroxaban.[7]

*Values may not represent those seen when additional drugs or confounding illnesses are present.

References

1. Garcia D, Libby E, Crowther MA. The new oral anticoagulants. *Blood.* 2010;115(1):15-20. **2.** Granger CB, Alexander JH, McMurray JJV, et al; ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med.* 2011;365(11):981-992. **3.** Tsiara S, Pappas K, Boutsis D, Laffan M. New oral anticoagulants: should they replace heparins and warfarin? *Hellenic J Cardiol.* 2011;52(1):52-67. **4.** Warkentin TE. HIT: treatment easier, prevention harder [comment]. *Blood.* 2012;119(5):1099-1100. **5.** Tripodi A, van den Besselaar A. Laboratory monitoring of anticoagulation: where do we stand? *Semin Thromb Hemost.* 2009;35(1):34-41. **6.** Kubitza D, Becka M, Mueck W, Zuehlsdorf M. Rivaroxaban (BAY 59-7939)—an oral, direct factor Xa inhibitor—has no clinically relevant interaction with naproxen. *Br J Clin Pharmacol.* 2007;63(4):469-476. **7.** Hillarp A, Baghaei F, Fagerberg Blixter I, et al. Effects of the oral, direct factor Xa inhibitor rivaroxaban on commonly used coagulation assays. *J Thromb Haemost.* 2011;9(1):133-139.

Platelet antagonists

Adenosine diphosphate (ADP) receptor inhibitors

(eg, clopidogrel, ticlopidine)[1]

Overview

ADP receptor inhibitors stop the clumping of platelets and block the binding of ADP to the $P2Y_{12}$ component, inhibiting ADP-induced platelet activation.[2] This class of agents is used in the treatment of vascular diseases such as symptomatic peripheral vascular disease.[1]

Effects on lab values[3,4]

Typical lab values*

Tests	Values
PT	=
aPTT	=
TT	N/A
Anti-FXa activity	N/A
Fibrinogen	N/A
Platelet aggregation	↓

Key ↑ Increased ↓ Decreased = No change

*Values may not represent those seen when additional drugs or confounding illnesses are present.

References

1. Roth GJ. Antiplatelet therapy. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1725-1737. **2.** Gelfand EV, Cannon CP. Acute coronary syndromes. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1387-1404. **3.** Slaughter TF. Coagulation. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, eds. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2009:1767-1779. **4.** Rao AK. Acquired qualitative platelet defects. In: Colman RW, Marder VJ, Clowes AW, George JN, Goldhaber SZ, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1045-1060.

Cyclooxygenase (COX) inhibitors

(eg, aspirin)[1]

Overview

COX inhibitors decrease overall platelet aggregation at the site of thrombosis by blocking thromboxane A_2 production. This action permanently acetylates COX-1, which lasts for the lifetime of the platelets (7-10 days).[2] Aspirin has been extensively studied and is considered a fundamental part of managing arterial thrombosis.[1]

Effects on lab values[3,4]

Typical lab values*

Tests	Values
PT	= or ↑[a]
aPTT	=
TT	=
Anti-FXa activity	N/A
Fibrinogen	=
Platelet aggregation	↓

Key ↑ Increased ↓ Decreased = No change

[a]Increased with high drug dosage.

*Values may not represent those seen when additional drugs or confounding illnesses are present.

References

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Phosphodiesterase inhibitors

(eg, dipyridamole, cilostazol)[1,2]

Overview

Dipyridamole is a weak phosphodiesterase inhibitor that slows adenosine uptake by platelets, which triggers an accumulation of cyclic adenosine monophosphate (cAMP) and inhibits platelet aggregation. It does not inhibit aggregation responses to collagen, epinephrine, or ADP at usual doses.[1,3] Modified-release dipyridamole can be used with low-dose aspirin.[4]

Cilostazol exhibits antiplatelet properties, vasodilatory properties, and in vitro inhibition of vascular smooth muscle cells. It can be used for the treatment of intermittent claudication in patients who have peripheral arterial disease.[2]

Effects on lab values[5]

Typical lab values*

Tests	Values[a]
PT	=
aPTT	=
TT	=
Anti-FXa activity	N/A
Fibrinogen	=
Platelet aggregation	=

Key ↑ Increased ↓ Decreased = No change

[a]Values shown for dipyridamole.

*Values may not represent those seen when additional drugs or confounding illnesses are present.

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Glycoprotein IIb/IIIa (GPIIb/IIIa) inhibitors

(IV use only; eg, abciximab, eptifibatide, tirofiban)[1]

Overview

GPIIb/IIIa inhibitors act as pharmacologic antiplatelet strategies against the "final common pathway" of platelet aggregation. They inhibit the binding of fibrinogen or vWF and other adhesive proteins that connect nearby proteins.[2] These drugs are used in acute coronary interventions such as percutaneous coronary intervention.[1]

Effects on lab values[3,4]

Typical lab values*

Tests	Values
PT	=
aPTT	=
TT	N/A
Anti-FXa activity	N/A
Fibrinogen	N/A
Platelet aggregation	↓

Key ↑ Increased ↓ Decreased = No change

*Values may not represent those seen when additional drugs or confounding illnesses are present.

References

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Thrombolytics

Plasminogen activators

(eg, urokinase, streptokinase)[1]

Overview[1]

Plasminogen activators comprise all of the currently used thrombolytic agents. These activators bind plasminogen with fibrin and induce plasmin action, which then degrades the fibrin into fibrin degradation products that reduce thrombus size. These agents are used to dissolve clots in a variety of clinical situations.

Effects on lab values[2]

Typical lab values*

Tests	Values
PT	↑
aPTT	↑
TT	↑
Anti-FXa activity	N/A
Fibrinogen	↓
Platelet aggregation	↓

Key ↑ Increased ↓ Decreased = No change

*Values may not represent those seen when additional drugs or confounding illnesses are present.

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