

# Milestones in Anticoagulation

	1930s	1940s	1980s	1990s	2000s	2008...
CLASS	Heparin	Vitamin K Antagonists	Low-molecular weight Heparin	Direct Thrombin Inhibitors	Indirect Xa Inhibitors	Oral Direct Factor Xa & Thrombin Inhibitors
TARGET	AT + Xa + IIa (1:1 ratio)	II, VII, IX, X (Protein C, S)	AT + Xa + IIa (Xa > IIa)	Thrombin (II)	AT + Xa	Factor Xa Thrombin (II)
ROUTE	Parenteral	Oral	Parenteral	Parenteral	Parenteral	Oral
HISTORIC PERSPECTIVES	Anticoagulation widely available	First oral anticoagulants	Efficacy and safety with improved convenience	Anticoagulant options that target a single clotting factor	Efficacy, safety, convenience	Efficacy, safety, convenience

- Hirsh J, Anand S, Halperin J, Fuster V. Guide to anticoagulant therapy: heparin: a statement for healthcare professionals from the American Heart Association. *Circ*. 2001;103: 2994-3018. <http://circ.ahajournals.org/cgi/content/full/103/24/2994>. Accessed May 31, 2011.
- Hirsh J, Raschke R. Heparin and low-molecular-weight heparin: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest*. 2004;126:188S-203S. [http://chestjournal.chestpubs.org/content/126/3\\_suppl/188S.full.html](http://chestjournal.chestpubs.org/content/126/3_suppl/188S.full.html). Accessed May 31, 2011.
- Best CH. Preparation of heparin and its use in the first clinical cases. *Circ*. 1959;19:79-86. <http://circ.ahajournals.org>. Accessed May 31, 2011.
- Ansell J, Hirsh J, Poller L, Bussey H, Jacobson A, Hylek E. The pharmacology and management of the vitamin K antagonists: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest*. 2004;126:204-233. [http://www.chestjournal.org/cgi/content/full/126/3\\_suppl/204S](http://www.chestjournal.org/cgi/content/full/126/3_suppl/204S). Accessed May 31, 2011.
- Turpie AGG. Oral, direct factor Xa inhibitors in development for the prevention and treatment of thromboembolic diseases. *Arterioscler Thromb Vasc Biol*. 2007;27:1238-1247. <http://atvb.ahajournals.org/cgi/content/full/27/6/1238>. Accessed May 31, 2011.
- Turpie AGG, Bauer KA, Eriksson BI, Lassen MR, for the Steering Committees of the Pentasaccharide Orthopedic Prophylaxis Studies. Fondaparinux vs enoxaparin for the prevention of venous thromboembolism in major orthopedic surgery. *Arch Intern Med*. 2002;162:1833-1840.
- Weitz J, Hirsch J. New anticoagulant drugs. *Chest*. 2001;119:95S-107S. [http://chestjournal.chestpubs.org/content/119/1\\_suppl/95S.full.html](http://chestjournal.chestpubs.org/content/119/1_suppl/95S.full.html). Accessed May 31, 2011.
- US Department of Health and Human Services. FDA.gov. Drugs@FDA. <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>. Accessed May 22, 2011.
- Xarelto.com. Press resources. Aug-Oct 2008. <http://www.xarelto.com/en/resources/newsticker/index.php>. Accessed May 22, 2011.
- Population Health Research Institute. The Michelangelo studies: oasis 5. Study drug. <http://www.phri.ca/oasis5/enox.htm>. Accessed May 31, 2011.
- Hirsh J, Bauer KA, Donati MB, Gould M, Samama MM, Weitz JI. Parenteral anticoagulants: American College of Chest Physicians evidence-based clinical practice guidelines (8th Edition). *Chest*. 2008;133:141S-159S. [http://chestjournal.chestpubs.org/content/133/6\\_suppl/141S.full.html](http://chestjournal.chestpubs.org/content/133/6_suppl/141S.full.html).