THE NOVEL ANTICOAGULANTS: ENTERING A NEW ERA
(ARTIGO DE REVISÃO)

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During the past five decades, anticoagulant therapy has consisted of rapidly acting parenteral drugs (unfractionated heparin [UFH] low-molecular-weight heparins [LMWH]) for prevention of venous thromboembolism and initial treatment of arterial and venous thromboembolism, whereas vitamin K antagonists (VKA) are used for longer term oral treatment. These drugs act by indirectly inhibiting several activated plasma clotting factors (UFH, LMWH) or by blocking the synthesis of some of them (VKA). In recent years, compounds that specifically block activated coagulation factor X (FXa) or thrombin have been developed. Thus, fondaparinux, and its long-acting derivative idraparinux, are administered subcutaneously. These substances inhibit F Xa indirectly via antithrombin. Small molecules have also been developed that directly block FXa (rivaroxaban, apixaban) or thrombin (dabigatran etexilate) following oral administration. In the present review we discuss the currently available evidence supporting the use of these new anticoagulants, in particular rivaroxaban and dabigatran etexilate, in the setting of thromboprophylaxis following major orthopaedic surgery, and the broader perspectives that these new drugs may open up in the next few years. **[Swiss Med Wkly. 2009 Feb 7;139(5-6):60-4]**

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PLATELET ADHESION UNDER FLOW

(ARTIGO DE REVISÃO)

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Platelet-adhesive mechanisms play a well-defined role in hemostasis and thrombosis, but evidence continues to emerge for a relevant contribution to other pathophysiological processes, including inflammation, immune-mediated responses to microbial and viral pathogens, and cancer metastasis. Hemostasis and thrombosis are related aspects of the response to vascular injury, but the former protects from bleeding after trauma, while the latter is a disease mechanism. In either situation, adhesive interactions mediated by specific membrane receptors support the initial attachment of single platelets to cellular and extracellular matrix constituents of the vessel wall and tissues. In the subsequent steps of thrombus growth and stabilization, adhesive interactions mediate platelet-to-platelet cohesion (i.e., aggregation) and anchoring to the fibrin clot. A key functional aspect of platelets is their ability to circulate in a quiescent state surveying the integrity of the inner vascular surface, coupled to a prompt reaction wherever alterations are detected. In many respects, therefore, platelet adhesion to vascular wall structures, to one another, or to other blood cells are facets of the same fundamental biological process. The adaptation of platelet-adhesive functions to the effects of blood flow is the main focus of this review. **[Microcirculation. 2009 Jan;16(1):58-83]**

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FLUID SHEAR ATTENUATES ENDOTHELIAL PSEUDOPODIA FORMATION INTO THE CAPILLARY LUMEN

(ARTIGO ORIGINAL)

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Objective: Endothelial cells have the ability to undergo morphological shape changes, including projection of cytoplasmic pseudopodia into the capillary lumen. These cytoplasmic projections significantly influence the hemodynamic resistance to blood flow. To examine mechanotransduction mechanisms, we investigated in vivo the hemodynamic conditions in capillaries that control endothelial pseudopod formation. **Materials and methods:** Capillaries in rat skeletal muscle were fixed under carefully controlled perfusion conditions. The formation of endothelial pseudopodia were observed in cross-sections with electron microscopy and quantified with differential interference contrast microscopy under physiological, stasis, and reperfusion flow conditions. **Results:** Application of physiological levels of fluid flow prevents capillary endothelium to project pseudopodia into the capillary lumen. Reduction of fluid flow to near zero promotes the incidence of pseudopod projection from 5% to 55% of capillaries. After capillary pseudopodia have formed under static conditions, about one-half retract upon restoration of fluid flow. The presence of red blood cells in the capillary lumen prevents pseudopod formation. **Conclusions:** The results suggest that there is a mechanism that serves to control cytoplasmic projections in capillary endothelium that is under the control of hemodynamic fluid stress. Investigation of pseudopodia growth on endothelial cells may be significant in understanding capillary obstruction in cardiovascular diseases. **[Microcirculation. 2008 Aug; 15(6):531-42]**

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COGNITIVE IMPAIRMENT IS RELATED TO INCREASED ARTERIAL STIFFNESS AND MICROVASCULAR DAMAGE IN PATIENTS WITH NEVER-TREATED ESSENTIAL HYPERTENSION

(ARTIGO ORIGINAL)

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Background: It is known that essential hypertension may be implicated in the development of cognitive impairment that is associated to microvascular disease of the brain. It has been hypothesized that increased arterial stiffness of the large arteries may lead to microvascular changes due to increased pulsatile flow. Our study tests the hypothesis that large artery stiffness and microvascular damage are related to brain microcirculation changes as reflected by impaired cognitive function. **Methods:** We studied 110 nondiabetic patients aged 40-80 years (mean age 53.8 +/- 11.2 years, 57 men) with recently diagnosed stage I-II essential hypertension. Mini-Mental State Examination (MMSE) was used as a screening test for global cognitive impairment. We performed both 2-D echocardiography and carotid-femoral pulse wave velocity (PWV) in order to evaluate arterial stiffness. Twenty-four hour urine microalbumin excretion was measured as a marker of microvascular damage. **Results:** In the entire population, MMSE was negatively correlated with age (r = -0.42, P < 0.001), 24-h pulse pressure (PP) (r = -0.18, P < 0.05), and PWV (r = -0.3, P = 0.003). Additionally, MMSE was not independently correlated with microalbuminuria in patients aged over 65 years (r = -0.58, P = 0.003). **Conclusions:** Impaired cognitive function is associated with increased large artery stiffness and microalbumin excretion in newly diagnosed, untreated hypertensive patients. These findings support the hypothesis that cognitive impairment induced by impaired microcirculation is linked to large artery stiffness and microvascular damage. **[Am J Hypertens. 2009 May;22(5):525-30]**

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