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Mini Review

Hemostasis factors and aging

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Abstract

With advancing age, an increasing number of healthy individuals have laboratory signs of heightened coagulation enzyme activity. Such biochemical hypercoagulability might be the basis of either the increased thrombotic tendency occurring with age or a harmless manifestation of this process. Centenarians had striking signs of heightened coagulation enzyme activity, accompanied by signs of enhanced formation of fibrin and secondary hyperfibrinolysis. Plasma concentrations of fibrinogen and factor VIII were higher than in controls, whereas other coagulation factors were not elevated. It is of interest that centenarians have a significantly higher frequency than young individuals of the high risk 4G allele of the PAI-1-675 (4G/5G) polymorphism, mutant factor V (Arg506Gln) and prothrombin gene G20210A mutation. Von Willebrand factor (VWF), a well-known independent predictor of atherothrombotic disease, was increased in centenarians, independently of the blood group, confirming the previous results of a state of hypercoagulability.

The finding that the VWF cleaving proteases levels are low when VWF levels are high in centenarians could be a corollary of the previous described paradox of successful aging, adding another marker of increased risk of atherothrombosis to the scenario. Alike, high prevalence of anti-phospholipids antibodies, not associated with an anti-phospholipid syndrome has been described in centenarians.

In conclusion, the data show the oldest old do not escape the state of hypercoagulability associated with aging, but that this phenomenon is compatible with health and longevity. Hence, high plasma levels of the coagulation activation markers in older populations do not necessarily mirror a high risk of arterial or venous thrombosis.

Keywords: Coagulation factors; Endothelial; Centenarians

1. Introduction

Physiological aging is associated with increased plasma levels of many proteins of blood coagulation, with alterations of platelets and fibrinolysis impairment. This may be of great concern in view of the known association between vascular and thromboembolic diseases and advancing age.

1.1. Coagulation factors

Coagulation factors circulate in the plasma as cofactors or as proenzymes, and, when activated supply some of the components needed for clot formation. According to the international nomenclature system, coagulation cofactors and proenzymes were assigned roman numerals in the order of their discovery and do not correspond to their location in the coagulation sequence of activation (Table 1). The coagulation factors are generated in the liver cells, except for the von Willebrand factor, which is produced in multiple organs, possibly the endothelial cells and megakaryocytes. The model generally used to describe the mechanism of coagulation is the cascade system (Fig. 1). The cascade is separated into three areas: the intrinsic system, which is activated by surface contact; the extrinsic system, which is activated by vascular injury, and, the common pathway, which is set into motion by activation from the intrinsic and/or the extrinsic pathway. The fibrinolytic pathway removes the clot from the injured tissue; the end product of this pathway is the enzyme plasmin, a potent

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Table 1
Characterisctics of coagulation factors

Factor	Molecular weight	Functional activity	Biologic half-life	Plasma concentration
Fibrinogen	340,000	–	90 h	300–400 mg/dL
Prothrombin	72,000	Serine protease	60 h	10–15 mg/dL
Factor V	330,000	Cofactor	12–36 h	0.5–1.0 mg/dL
Factor VII	48,000	Serine protease	4–6 h	0.1 mg/dL
Factor VIII:C	70–240,000	Cofactor	12 h	1–2 mg/dL
Factor IX	57,000	Serine protease	20 h	4 μg/mL
Factor X	58,000	Serine protease	24 h	0.75 mg/dL
Factor XI	160,000	Serine protease	40 h	1.2 mg/dL
Factor XII	80,000	Serine protease	48–52 h	0.4 mg/dL
Prekallikrein	80,000	Serine protease	48–52 h	0.29 mg/dL
High molecular weight kininogen	120,000	Cofactor	6.5 days	0.70 mg/dL
Factor XIII	320,000	Trans glutaminase	3–5 days	2.5 mg/dL
Protein C	62,000	Serine protease	8–12 h	4–5 μg/mL
Protein S	84,000	Cofactor	–	25 mg/L

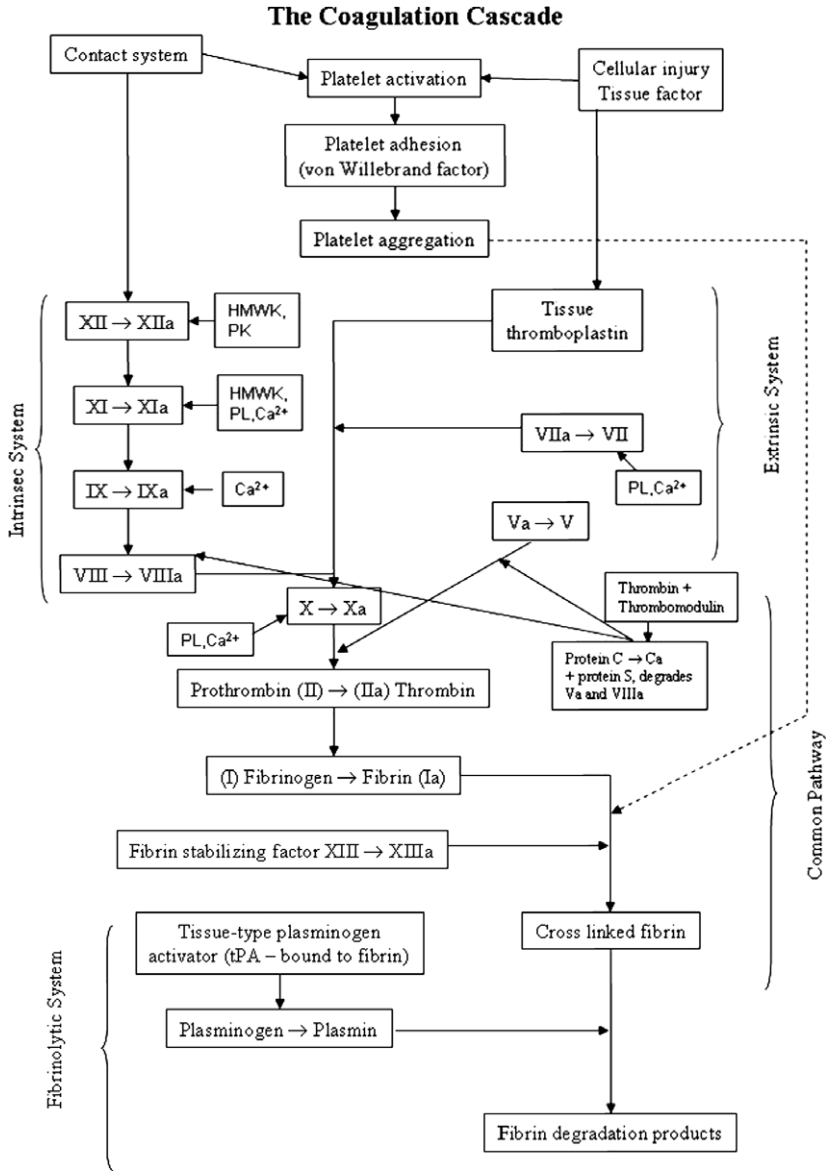

Fig. 1. The coagulation cascade. HMWK, high molecular weight kininogen; PK, prekallikrein; PL, phospholipids from activated platelets, Ca^{2+}.