ology of Leukemias held last June in Ferrara, under the auspices of the GIMEMA Group. Some selected papers, which have undergone a peer review process will appear in a special section of the Journal (*Guest Editors: Gianluigi Castoldi, Robin Foà, Vincenzo Liso, Estella Matutes*) and may possibly renew multi-faceted interest in the classification of hematologic disorders.

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BASIC, LABORATORY AND CLINICAL ASPECTS OF THROMBOEMBOLIC DISEASES

Last March, the *Second International Winter Meeting on Coagulation* was held in La Thuile (AO), Italy. During the meeting, entitled *Basic, Laboratory and Clinical Aspects of Thromboembolic Diseases*, some relevant topics were discussed. Thrombophilia, ill-defined as prothrombotic state, secondary to the presence of persistent or temporary predisposing factors, was the subject of a large part of the meeting. The various mechanisms of venous and arterial thrombosis, the role of natural anticoagulants and their molecular defects, autoimmunity, inflammation and thrombosis, and chronic thromboembolic pulmonary hypertension were also the subjects of different sessions.

Role of mild hyperhomocysteinemia in venous and arterial thrombosis

A session of the meeting was dedicated to the role of mild homocysteinemia predisposing to venous and arterial thrombosis; the molecular biology of hyperhomocysteinemia, methodological aspects of plasma homocysteine measurement and thrombogenic mechanisms of hyperhomocysteinemia were discussed. In the last decade homocysteine has been confirmed as an independent risk factor in the development of thromboembolic disease. Subjects with mild hyperhomocysteinemia have the same rate of recurrencies as those with other predisposing factors (protein S, C, plasminogen deficiency and activated protein C deficiency). Moderate hyperhomocysteinemia should therefore be included among the inherited disorders causing venous thrombophilia. The relationship between severe hyperhomocysteinemia and arterial disease is well established. Mild hyperhomocysteinemia has also recently been associated with arterial thrombosis. Insufficient levels of folate and vitamin B6 appear to predict this elevated risk.

Deep vein thrombosis and pulmonary embolism: natural history, diagnosis and treatment

Several strategies have been proposed to reduce the need for pulmonary angiography in the diagnosis of pulmonary embolism. The association of plasma D-Dimer measurement (highly sensitive) and venous compression ultrasound of lower limbs (highly specific) appear to be the most rational sequence. With this cost-effective strategy, pulmonary angiography should be performed only in the case of inconclusive results from non-invasive tests.

Low-molecular weight heparin preparations can be administered subcutaneously, without laboratory monitoring. A series of studies is now available that demonstrate how low-molecular weight heparins administered subcutaneously in fixed doses adjusted for body weight and without laboratory monitoring are more effective and safer than adjusted-dose standard heparin in the treatment of symptomatic deep vein thrombosis, and these compounds can be given out of hospital.

New evidence is now growing that suggests it is necessary to re-define the length of anticoagulation in patients with symptomatic deep vein thrombosis. This is particularly true for subjects without

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transient risk factors for deep vein thrombosis, in whom a longer course of anticoagulation may be indicated.

Chronic major vessel thromboembolic pulmonary hypertension

Chronic major vessel thromboembolic pulmonary hypertension, now considered more common than previously suspected, has been shown to be surgically curable over the past decade. Pulmonary thromboendarterectomy (PTE) has emerged as an effective surgical procedure for incapacitating pulmonary hypertension resulting from chronic large-vessel pulmonary embolism. The major goals of diagnostic evaluation are to establish the presence and degree of pulmonary hypertension, to define its chronic thromboembolic basis, and to confirm surgical accessibility. The overall perioperative mortality for thromboendarterectomy is currently around 6%. Post-operative management is essential for a successful outcome following PTE. The improved prognosis is largely the result of increased experience and close interaction among members of a multidisciplinary team, aware of the challenging problems these patients present in the evaluative, surgical, and post-operative phases of their care.

Inflammation, sepsis and coagulation

Inflammation promotes coagulation by leading to intravascular tissue factor expression, eliciting the expression of leukocyte adhesion molecules and down-regulating the fibrinolytic and protein C anticoagulant pathways. This leads to the formation of thrombin, which in turn promotes inflammatory responses. Eventually these reactions produce vascular injury. A novel regulatory/inhibitory mechanism in inflammation involving the protein C pathway has recently been reported. Receptors have been identified on the endothelial cell surface that could modulate the specificity of activated protein C in a manner analogous to the mechanisms by which thrombomodulin modulates thrombin specificity. The protein C pathway may therefore modulate response to injury and inflammation.

Antithrombin III is constantly decreased in conditions associated with disseminated intravascular coagulation, particularly in sepsis and shock. Decreased ATIII plasma concentration may indicate a role for DIC in the pathogenesis of multiple organ failure (MOF). Data are emerging on the possible role of ATIII replacement therapy in reducing mortality in septic shock patients.

These and other topics were largely discussed during the meeting, which was characterized by the remarkable level of the presentations and by the mutual exchange of experiences from different settings and different disciplines. The proceedings of the meeting will be reported as original contributions in a special section of this Journal. The guest Editors (*Armando D'Angelo, Antonio Girolami and Franco Piovella*) wish to take this opportunity to thank all the participants at this "special" meeting and hope that, due to the high quality of the contributions, the particular spirit of the participants and the unique atmosphere of the place, the International Meeting on Coagulation will possibly become a Winter Classic among scientists.

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