Introduction

Laboratory analysis of blood samples are essential for diagnostics and therapy monitoring of patients with bleeding and thromboembolic diseases. The International Society on Thrombosis and Haemostasis (ISTH) developed an evidence based Laboratory Core Curriculum to outline the minimal level of skills and core competencies required by a thrombosis and hemostasis laboratory specialist.

The Core Curriculum provides a framework for laboratory professionals training in this field, enables harmonization of training and accreditation and informs the structuring of continuous professional development. It will help clarify the competencies needed for a thrombosis and hemostasis laboratory specialist. The Curriculum focuses on the competencies considered to be required for the laboratory professional who has completed their training and is ready to practice independently in the thrombosis and hemostasis laboratory. Regional adaptations to this curriculum may be required to respond to availability of specialized laboratory services in different jurisdictions and testing availability. A global survey was developed and used to determine consensus on the minimum competencies required for a thrombosis and hemostasis laboratory specialist.
Competency Levels

Knows how: able to explain how and why they do something or understand the principles.

Laboratory professionals are aware of the important issues and able to describe the use of tests but they may not have direct experience in this activity. The laboratory specialist has developed the skill of acquiring information, analyze and interpret these data, and to communicate the finding into a diagnostic plan.

Shows how: able to identify competence in a simulated scenario or artificial situation.

Laboratory professionals demonstrate an understanding of the laboratory test principles and are able to demonstrate competence in this skill. Laboratory specialists correctly administer tests related to thrombosis and hemostasis and their clinical utility. Understanding of and provision of a detailed interpretation of the test results is also required.

Does: able to demonstrate mastery in a real clinical situation/does this consistently.

A thrombosis and hemostasis laboratory specialist conducts and interprets the laboratory tests related to thrombosis and hemostasis routinely. The laboratory specialist is able to communicate the findings / interpretations to the ordering clinician in a timely and meaningful way.
### Specialties

1. The role of the laboratory specialist in thrombosis and hemostasis
2. Basic laboratory principles
3. Pre-analytical variables
4. Initial assessment of hemostasis
5. Specialized testing for bleeding disorders
6. Specialized testing for thrombotic disorders
7. Apply understanding of the changes to coagulation, including laboratory testing and monitoring therapeutic management, in the following special situations
## The role of the laboratory specialist in thrombosis and hemostasis

1. Apply knowledge of the biochemistry, physiology and pathophysiology of the coagulation, fibrinolytic, platelet and vascular systems.

2. Demonstrate competencies in areas with implications for thrombosis and hemostasis such as inflammation, imaging and genetics.

3. Recommend appropriate tests in the thrombosis and hemostasis laboratory and point of care testing for diagnosis or therapeutic monitoring in clinical settings.

4. Provide a clinically useful interpretation of the laboratory and point of care results.

5. Provide an interface between the laboratory and the clinical coagulation service.

6. Provide leadership, training and mentorship service.
7 Undertake basic, applied and/or diagnostic research related to the scope of a clinical thrombosis and hemostasis laboratory.

8 Manage a diagnostic laboratory including budget, prioritization of testing and resources, laboratory workflow.

2 Basic laboratory principles

1 Incorporate and manage an internal quality control system of a laboratory.

2 Incorporate and manage an external quality control/assessment (proficiency testing) program of a laboratory.

3 Manage the development of, implementation of, and adherence to laboratory standard operating procedures.

4 Seek and maintain laboratory accreditation.

5 Manage health and safety in laboratory practice.
6 Develop and apply appropriate reference intervals, to include pediatric, adult and gender specific as appropriate for thrombosis and hemostasis laboratory testing.

7 Demonstrate understanding of the strengths and limitations, including approaches for troubleshooting, of laboratory tests in the diagnosis and therapeutic monitoring in patients with thrombotic and hemostatic disorders.

8 Manage the installation and validation of new diagnostic instruments.

9 Manage the installation and validation of new diagnostic tests including evaluations of new reagent charges.

10 Perform appropriate validation studies to ensure clinically relevant reagent sensitivities such as activated partial thromboplastin time (APTT) reagent with sensitivity to intrinsic factors and Lupus Anticoagulant and monitoring heparin; prothrombin time (PT) reagent for accurate international sensitivity index (ISI) determination and geometric mean calculation (mean normal PT).
3 Pre-analytical variables

1. Apply an understanding of the impact of how conditions of sample collection (e.g. sample type, appropriate anticoagulant, venipuncture procedure, sampling time, sequence of sampling and contamination issues, tube volume, effects of hematocrit) and transport (temperature, time, activation) influence laboratory tests.

2. Apply an understanding of how factors that impact sample preparation and storage prior to analysis (e.g. stability of analyte, centrifugation, impact of temperature on storage) influence laboratory tests.

3. Apply an understanding of the patient factors that influence laboratory testing (e.g. age, gender, race, blood group, pregnancy, fasting, exercise, storage time, impact of/effect of medication, time from event such as deep vein thrombosis or bleeding).
4 Initial assessment of hemostasis

1 Use baseline laboratory tests including full/complete blood count (FBC/CBC), platelet count (PC), blood film, PT, APTT, fibrinogen, and thrombin time (TT) to screen for coagulation disorders.

2 Perform a basic laboratory assessment of primary hemostasis (e.g. bleeding time or platelet function assay).

3 Demonstrate understanding of the limitations for clinical use of the hemostasis analyses results, e.g. the limitations of the derived fibrinogen.

4 Explain screening test results and advise on further testing if appropriate.
5 Specialized testing for bleeding disorders

1 Refer to the International Society on Thrombosis and Haemostasis (ISTH) Scientific and Standardization Committee (SSC) for recommendations for all specialized hemostasis testing for inherited and acquired bleeding disorders.

2 Formulate follow-up testing as appropriate based on the results of specialized testing for bleeding disorders.

3 Perform appropriate and validated mixing studies in patients with a prolonged PT, APTT, and/or TT to distinguish between factor deficient state or the presence of an inhibitor.

4 Carry out appropriate tests to distinguish between a specific or non-specific inhibitor (e.g. Lupus Anticoagulant) and quantify a Bethesda titre.
5 Investigate for specific factor deficiencies using a systematic approach that takes into consideration reagent factor and Lupus Anticoagulant sensitivities (e.g. elevated APTT, normal PT).

6 Apply understanding of the difference between one-stage and chromogenic (or two-stage) factor (F) VIII and FIX assays in the diagnosis and monitoring of patients with a deficiency state and substitution therapies.

7 Determine activity and antigen level in the setting of fibrinogen or FII deficiency.

8 Test for rare bleeding disorders and abnormalities not detected during screening (e.g. FXIII deficiency, FXI deficiency/Hemophilia C or fibrinolytic abnormalities) in patients with clinically significant bleeding.

9 Perform and interpret comprehensive qualitative and quantitative testing for von Willebrand disease (VWD), including antigen and activity analyses (e.g. Ristocetin-dependent and independent functional von Willebrand factor assays).
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<td>10</td>
<td>Perform appropriate aggregation mixing studies to differentiate between type 2B VWD and platelet type VWD.</td>
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<td>11</td>
<td>Assess platelet function (aggregation, secretion, flow cytometry analysis).</td>
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<td>12</td>
<td>Carry out appropriate tests for monitoring of platelet inhibitor therapies.</td>
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<td>13</td>
<td>Apply understanding of genetic testing in diagnosis of bleeding disorders (e.g. congenital hemophilia, VWD).</td>
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<td>14</td>
<td>Apply understanding of the function, limitations and applications of global tests for bleeding states (e.g. thromboelastography/-metry, thrombin generation).</td>
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**6 Specialized testing for thrombotic disorders**

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<tr>
<td>1</td>
<td>Refer and employ, where appropriate, ISTH-SSC and other international guidelines and recommendations for all specialized coagulation testing for thrombotic disorders.</td>
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2. Identify the limitations (e.g. strengths, weaknesses) of specialized testing for thrombotic disorders.

3. Formulate follow-up testing as appropriate based on the results of specialized testing for initial and recurrent thrombotic events.

4. Interpret functional and genetic tests used for the diagnosis of acquired and congenital inhibitor deficiencies (e.g. antithrombin, protein C, protein S, tissue factor pathway inhibitor).

5. Perform functional and genetic testing of congenital and acquired prothrombotic factors (e.g. FV Leiden, Prothrombin G20210A, JAK2).

6. Interpret functional and genetic testing of congenital and acquired prothrombotic factors.

7. Perform and interpret laboratory tests used for the diagnosis of the antiphospholipid syndrome.
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<td>8</td>
<td>Perform and interpret laboratory tests used for the therapeutic monitoring in patients taking vitamin K antagonists, heparins, antiplatelet drugs and direct oral anticoagulants (DOACs).</td>
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<td>Apply knowledge on the use and limitations of tests for activated coagulation status (e.g. D-Dimer, prothrombin fragment 1+2, Thrombin-Antithrombin complex).</td>
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<tr>
<td>10</td>
<td>Apply understanding of the function, limitations and applications of global tests for thrombotic and fibrinolytic disorders (e.g. thromboelastography/metry, thrombin generation).</td>
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<td>11</td>
<td>Perform and interpret laboratory tests for the assessment of the fibrinolytic system (e.g. plasminogen, plasminogen activator inhibitor-1, alpha-2-antiplasmin, thrombin activatable fibrinolysis inhibitor), and for monitoring fibrinolytic therapy.</td>
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<td>Apply knowledge of new developments e.g. flow-based systems, flow cytometry, to diagnostic practice in thrombosis and hemostasis.</td>
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1. Liver disease.

2. Autoimmune diseases that impact on thrombosis and hemostasis, e.g. Lupus Anticoagulants, Systemic Lupus Erythematosus.

3. Trauma associated coagulopathies and massive transfusion.

4. Heparin Induced Thrombocytopenia (HIT; 4 T-score, screening and confirmation tests).

5. Pregnancy (during the pregnancy and postpartum).


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<td>9</td>
<td>Thrombotic microangiopathies.</td>
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<td>Inflammation, infection associated coagulopathies, disseminated intravascular coagulation.</td>
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<td>Acquired coagulopathies including heart valve diseases, Extracorporeal Membrane Oxygenation or acquired specific factor inhibitors (e.g. anti-FVIII antibodies).</td>
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<td>Perioperative management of thrombotic and hemostatic disorders.</td>
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<td>Renal disorders.</td>
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About the ISTH Laboratory Core Curriculum

The Laboratory Core Curriculum provides a foundation and should be used as a framework for international governing bodies, national and regional thrombosis and hemostasis societies to map their own curricula. This Core Curriculum provides a template for the development of training programs specific to local and regional needs and resources. National and regional groups can then determine and develop the formal methods of assessment for these competencies across jurisdictions.

The Curriculum was developed and reviewed by an international body of laboratory experts and engaged the global thrombosis and hemostasis community. This encourages a sense of ownership of the Curriculum amongst its members. It will be reviewed and updated periodically by the ISTH Education Committee as advancements in this laboratory subspecialty will continue to develop and evolve moving forward.


For more information, please visit www.isth.org.