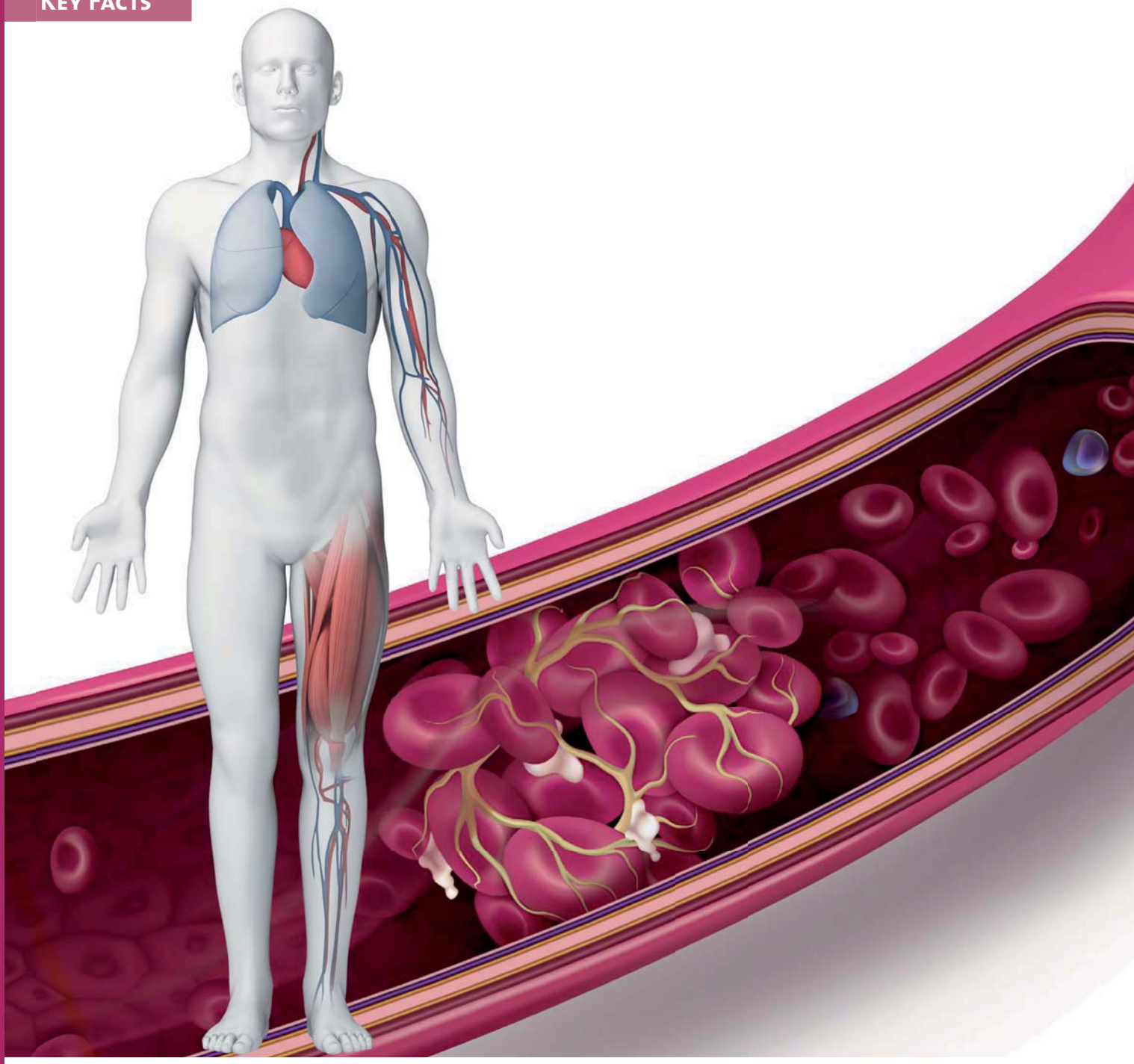
Hemostasis

PT and aPTT

First-line coagulation assays

- Pre-operative screening for a bleeding risk
- Monitoring of medical treatment with anticoagulants
- Initial assessment of thrombotic- or bleeding -abnormalities

Key Facts



Human

Diagnostics Worldwide

activated Partial Thromboplastin Time (aPTT)

Evaluation of the intrinsic pathway

The activated partial thromboplastin time (aPTT) is a global coagulation assay. A prolongation of the aPTT clotting time indicates an abnormality of the intrinsic and final common coagulation pathway.

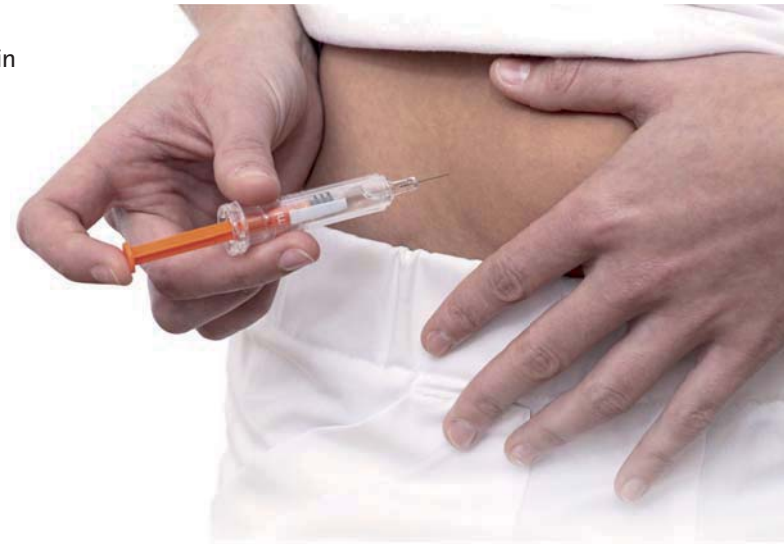
aPTT results are reported in seconds. Until now, there is no global standardization.
The results are specific to the aPTT reagent of a manufacturer.

Clinical relevance	› Monitoring of therapy with unfractionated heparin (UFH) › Hemophilia A, B and C › Coagulation factor inhibitors › Phospholipid antibodies (lupus anticoagulants)

Monitoring of anticoagulant therapy with UFH

Unfractionated heparin is commonly used for anticoagulant prophylaxis and treatment of venous thromboembolism (VTE), acute coronary syndromes or atrial fibrillation. It is either administered intravenously or subcutaneously.
The short half-life of UFH provides flexibility in medical treatment.

Monitoring the therapeutic dosage of unfractionated heparin is mandatory to prevent over- or under -anticoagulation levels in the blood plasma.
The most common method for monitoring UFH is the activated partial thromboplastin time (aPTT).[1]

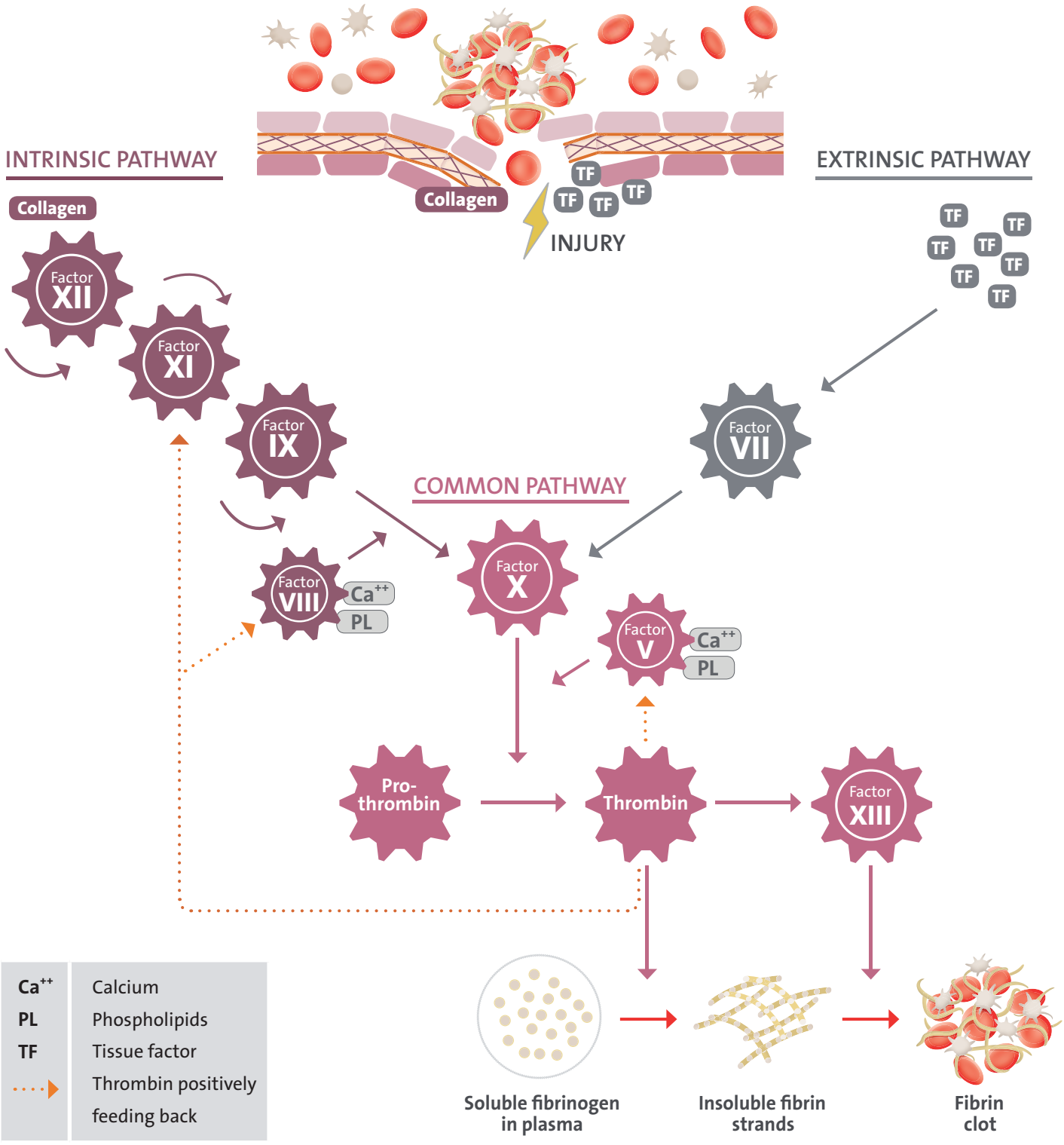


Plasmatic Coagulation Cascade

Coordinating the formation of a fibrin clot

For coagulation, soluble fibrinogen of the blood plasma is converted into insoluble fibrin strands which form a mesh that traps thrombocytes and erythrocytes, producing a solid blood clot. This is coordinated by enzymatic coagulation factors present in the blood plasma. There are basically two pathways that both end in a final common pathway that leads to the formation of a fibrin clot.

- **Intrinsic Pathway:** triggered by thrombin, collagen and negatively charged surfaces. The corresponding assay is aPTT.
- **Extrinsic Pathway:** triggered by tissue factor (TF) that is released by injured tissue. The corresponding assay is PT.



Prothrombin Time (PT)

Evaluation of the extrinsic pathway

The prothrombin time (PT) is a global coagulation assay. A prolongation of the PT clotting time evaluates the integrity of the extrinsic and final common coagulation pathway.

PT results are reported in seconds, in the prothrombin ratio, % activity or as International Normalized Ratio (INR).

Clinical relevance	› Monitoring of oral anticoagulant therapy with vitamin K antagonists (VKAs) e.g. warfarin › Decreased or defective factors e.g. VII › Coagulation factor inhibitors › Vitamin K deficiency › Liver synthetic function › Disseminated intravascular coagulation (DIC)

Prothrombin Time (PT)

Monitoring of oral anticoagulant therapy with VKAs

VKAs e.g. warfarin are commonly used for oral prophylaxis and treatment of venous thromboembolism and for patients with a high risk for myocardial infarction or stroke. The anticoagulant effect of warfarin depends strongly on the individual patient and the living conditions (e.g. genetics, metabolism, diet). Thus, it is required to adjust and monitor the warfarin dosage on a regular base.

A typical therapeutic target value of the PT is an INR of 2.0 – 3.0. Individual INR target ranges vary based on disease state, age and advising doctor's treatments.

Thromboembolism
INR values below the therapeutic window indicate a possible underdose of VKAs. The risk of thromboembolic events is increased.

Hemorrhage
INR values above the therapeutic window indicate a possible overdose of VKAs. The risk for bleeding is increased.[2,3]

Example of a therapeutic window in INR

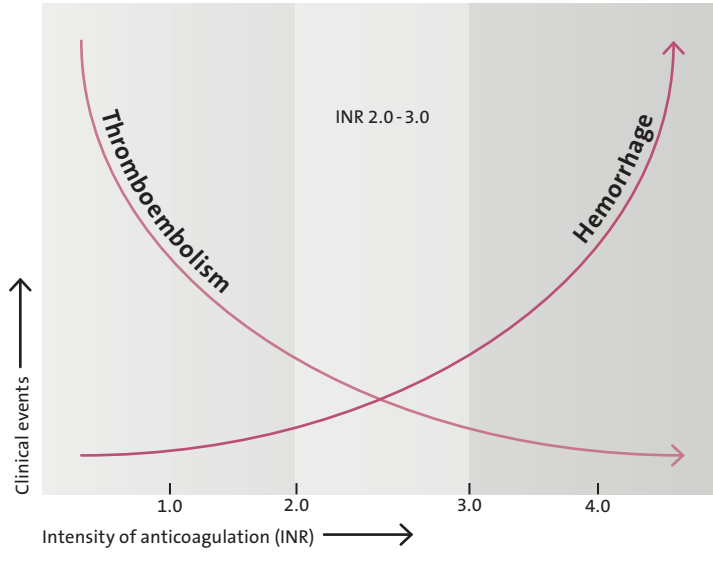


Figure 1:
Balancing the risk of anticoagulant therapy (adapted from Blann, 2003)[3]

Result Interpretation of aPTT and PT

Evalulation of the hemostasis status

The interpretation of results must always to be performed in conjunction with a full clinical assessment.* This may require further tests. For a prolonged PT and aPTT above the reference range, it is especially important to consider if and what kind of bleeding symptoms are observed.[4]

Normal aPTT → **Prolonged PT ↑**	› Decreased or defective factor VII › Coagulation factor inhibitors › Liver disease › Vitamin K deficiency › Chronic disseminated intravascular coagulation (DIC) › Anticoagulants (e.g. antagonists of vitamin K like warfarin)
Prolonged aPTT ↑ **Normal PT →**	› Hemophilia A (decreased or defective factor VIII) › Hemophilia B (decreased or defective factor IX) › Hemophilia C (decreased or defective factor XI) › Factor XII deficiency › Coagulation factor inhibitors e.g. acquired hemophilia A or alloantibodies following exposure of factor VIII concentrates › von Willebrand disease (severe form) › Phospholipid antibodies (lupus anticoagulants) › Anticoagulants e.g. UFH
Prolonged aPTT ↑ **Prolonged PT ↑**	› Vitamin K deficiency › Severe liver disease › Acute disseminated intravascular coagulation (DIC) › Combined deficiency of clotting factors e.g. factor V and factor VII › Common pathway factor deficiencies: thrombin, factor V, factor X and fibrinogen › Anticoagulants (high doses of UFH, direct thrombin inhibitors e.g. Hirudin)
Shortened aPTT ↓	› In some cases this may indicate a hypercoagulable state[6]

Table 1: Result interpretation [4, 5]

Mixing Studies: Distinguishing factor deficiency from inhibitors

A mixing study is used to further investigate the cause of a prolonged PT and aPTT. Normal plasma is mixed with the patient‘s sample typically in a 1:1 proportion. If the addition of normal plasma corrects the result the cause is likely a disfunction or deficiency of a required coagulation factor. The added plasma counterbalances the deficiency.
If the addition of normal plasma fails to correct the result the cause of the abnormal test is likely an inhibitor, e.g. coagulation factor inhibitor or antiphospholipid antibody (e.g. a lupus anticoagulant).[7]

* Please note: the content is not intended to be a substitute for professional medical advice, diagnosis, or treatment.

HEMOSTAT Reagents

High quality coagulation assessment with aPTT and PT

HUMAN hemostasis solutions

HUMAN offers laboratories integrated test solutions for hemostasis with HEMOSTAT reagents and HumaClot analyzers. Semi-automated and fully-automated HumaClot analyzers support an accurate assessment of coagulation. Validated applications for all HEMOSTAT reagents are pre-programmed on HumaClot analyzers. For an overview of our coagulation portfolio please refer to www.human.de/products/hemostasis.

Ordering Information

HEMOSTAT THROMBOPLASTIN[liquid]

REF	Format	Unit/Size
31012	Complete kit	6 x 2 ml

- Liquid, ready-to-use reagent
- No preparation step needed, freeing up lab technician's time for more important tasks
- Heparin-insensitive up to 0.6 IU/ml: Thromboplastin can be used for heparinized patients up to 0.6 IU/ml
- High factor-sensitivity: for reliable detection of factor deficiency

HEMOSTAT THROMBOPLASTIN-SI

REF	Format	Unit/Size
31002	Reagent kit	6 x 2 ml
31003		6 x 10 ml

- Lyophilized reagent
- Ready-to-use reconstitution medium included, thereby reducing the risk of errors with reconstitution
- Heparin-insensitive up to 0.6 IU/ml: Thromboplastin can be used for heparinized patients up to 0.6 IU/ml
- High factor-sensitivity: for reliable detection of factor deficiency

HEMOSTAT aPTT-EL

REF	Format	Unit/Size
33002	Complete kit	6 x 4 ml
33012	aPTT reagent	6 x 4 ml
33013	aPTT reagent	6 x 10 ml
33022	$CaCl_2$	4 x 30 ml

- Liquid, ready-to-use reagent
- Sensitive to heparin and lupus anticoagulants
- High factor-sensitivity: for reliable detection of factor deficiencies

Your local distribution partner

1. Israfil Baluwala, Emmanuel J. Favaloro & Leonardo Pasalic, (2017) Therapeutic monitoring of unfractionated heparin – trials and tribulations, Expert Review of Hematology, 10:7, 595-605.
2. British Columbia (04/2015): Warfarin Therapy Management. URL: https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/warfarin-therapy.
3. Blann AD, Fitzmaurice DA, Lip GYH. Anticoagulation in hospitals and general practice. BMJ 2003;326:153-6.
4. Kamal, Arif H. et al., How to Interpret and Pursue an Abnormal Prothrombin Time, Activated Partial Thromboplastin Time, and Bleeding Time in Adults, Mayo Clinic Proceedings, Volume 82, Issue 7, 864 - 8735.
5. AACC Lab Tests Online (11/2019): Partial Thromboplastin Time (PTT, aPTT). URL: https://labtestsonline.org/tests/partial-thromboplastin-time-ptt-aptt.
6. Abdullah, Wan Zaidah et al., Shortened activated partial thromboplastin time, a hemostatic marker for hypercoagulable state during acute coronary event, Translational Research, Volume 155, Issue 6, 315 - 319.
7. Rebecca Kruse-Jarres, Tammuella C. Singleton & Cindy A. Leissinger, Identification and Basic Management of Bleeding Disorders in Adults, The Journal of the American Board of Family Medicine July 2014, 27 (4) 549-564.
8. Pictures source: 1. studiovin / shutterstock, 2. TunedIn by Westend61 / shutterstock

HUMAN Gesellschaft für Biochemica und Diagnostica mbH
Max-Planck-Ring 21 · 65205 Wiesbaden · Germany
Tel. +49 6122-9988-0 · Fax +49 6122-9988-100 · e-mail: human@human.de · www.human.de

Human
Diagnostics Worldwide