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
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.*

<table>
<thead>
<tr>
<th>Clinical relevance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring of therapy with unfractionated heparin (UFH)</td>
</tr>
<tr>
<td>Hemophilia A, B and C</td>
</tr>
<tr>
<td>Coagulation factor inhibitors</td>
</tr>
<tr>
<td>Phospholipid antibodies (lupus anticoagulants)</td>
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</tbody>
</table>

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.

![Diagram of the Plasmatic Coagulation Cascade]

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**Ca**²⁺ | Calcium  
---|---
**PL** | Phospholipids  
**TF** | Tissue factor  
---|---
**TF** | Thrombin positively feeding back

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**Soluble fibrinogen in plasma** → **Insoluble fibrin strands** → **Fibrin clot**
# 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).*

<table>
<thead>
<tr>
<th>Clinical relevance</th>
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</thead>
<tbody>
<tr>
<td>Monitoring of oral anticoagulant therapy with vitamin K antagonists (VKAs) e.g. warfarin</td>
</tr>
<tr>
<td>Decreased or defective factors e.g. VII</td>
</tr>
<tr>
<td>Coagulation factor inhibitors</td>
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<tr>
<td>Vitamin K deficiency</td>
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<tr>
<td>Liver synthetic function</td>
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<tr>
<td>Disseminated intravascular coagulation (DIC)</td>
</tr>
</tbody>
</table>

## 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.²³

![Example of a therapeutic window in INR](image_url)

*Figure 1: Balancing the risk of anticoagulant therapy (adapted from Blann, 2003)²¹*
# Result Interpretation of aPTT and PT

**Evaluation of the hemostasis status**

The interpretation of results must always 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

<table>
<thead>
<tr>
<th>Normal aPTT</th>
<th>Prolonged PT</th>
</tr>
</thead>
</table>
| › 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) |

<table>
<thead>
<tr>
<th>Prolonged aPTT</th>
<th>Normal PT</th>
</tr>
</thead>
</table>
| › 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 |

<table>
<thead>
<tr>
<th>Prolonged aPTT</th>
<th>Prolonged PT</th>
</tr>
</thead>
</table>
| › 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) |

<table>
<thead>
<tr>
<th>Shortened aPTT</th>
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<tbody>
<tr>
<td>› In some cases this may indicate a hypercoagulable state6</td>
</tr>
</tbody>
</table>

### 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

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* 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

<table>
<thead>
<tr>
<th>REF</th>
<th>Format</th>
<th>Unit/Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>31012</td>
<td>Complete kit</td>
<td>6 x 2 ml</td>
</tr>
</tbody>
</table>

- 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

<table>
<thead>
<tr>
<th>REF</th>
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<tr>
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<tr>
<td>31003</td>
<td></td>
<td>6 x 10 ml</td>
</tr>
</tbody>
</table>

- 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 Thromboplastin-SI

<table>
<thead>
<tr>
<th>REF</th>
<th>Format</th>
<th>Unit/Size</th>
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<tr>
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<tr>
<td>33012</td>
<td>aPTT reagent</td>
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<tr>
<td>33013</td>
<td>aPTT reagent</td>
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<tr>
<td>33022</td>
<td>CaCl₂</td>
<td>4 x 30 ml</td>
</tr>
</tbody>
</table>

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

Your local distribution partner

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2. British Columbia (04/2015): Warfarin Therapy Management. URL: https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/warfarin-therapy
8. Pictures source: 1. studiovin / shutterstock, 2. TunedIn by Westend61 / shutterstock