DRUGS ACTING ON THE COAGULATION SYSTEM

ANTICOAGULANTS

HEPARINS

HEPARIN - structure

- polymeric mixture of sulfated mucopolysaccharides
- contains 8 – 15 repeats of

  D – glycosamine – L – iduronic acid and

  D – glycosamine – D – glucuronic acid
- synthesized as a normal product of many tissues, including the lung, intestine and liver

HEPARIN - structure

- **Unfractionated Heparin (UFH) includes average of 40-50 sugar units (monomers) and has a molecular weight of 3-30 kD**
- **Low Molecular Weight Heparins (LMWH) (deltaparin, enoxaparin, nadroparin) are obtained by depolymerizing UFH, have an average weight of 5 kD and are composed of less than 18 monomers**

HEPARIN - actions

1. **Increases the activity of antithrombin III by 1000-fold:**
   - **antithrombin III inhibits activated serine proteases in the clotting cascade, including Xa, IIa (thrombin), IXa, XIa, XIIa and XIIIa**
   - **inhibits the process of converting prothrombin to thrombin**
   - **LMWHs differ from standard heparin that mainly inhibit factor Xa, having only a small effect on thrombin**

HEPARIN - actions

2. **Has a direct anticoagulant activity – can inhibit clotting *in vitro***
3. **Releases lipoprotein lipase from vascular beds, which accelerates postprandial clearing of lipoproteins from the plasma**

Heparin does not have fibrinolytic activity and does not dissolve existing fibrinous clot.

HEPARIN – pharmacologic properties

- must be given parenterally – by slow infusion or deep subcutaneous injection
- the half-life is dose - dependent
- metabolized in the liver by heparinase to smaller molecular - weight compounds, which are excreted in the urine

HEPARIN – therapeutic uses

- preoperative prophylaxis against deep vein thrombosis
- prevention and treatment of venous thromboembolism (pulmonary embolism and deep vein thrombosis)
- treatment of acute coronary syndromes
- coronary angioplasty and implantation of vascular stents
- treatment of acute peripheral arterial emboli
- operations with extracorporeal circulation
- hemodialysis

HEPARIN – adverse effects

- bleeding, especially in older women and in patients with renal disease

  (protamine sulfate can be administered iv if bleeding does not abate after the cessation of heparin therapy)
- heparin induced thrombocytopenia (HIT) type I and II
  - ✓ thrombocytopenia in 25% of patients, but severe platelet reductions in 5% of patients (may induce antiplatelet antibodies and may also induce platelet aggregation and lysis)

HEPARIN – adverse effects

- hypersensitivity reactions, including chills, fever, urticaria and anaphylaxis
- reversible alopecia
- osteoporosis and predisposition to fracture with long - term use

HEPARIN – contraindications

- in patients who are bleeding (internally or externally)
- in high risk of bleeding (gastric ulcer, esophageal varices, uncontrolled severe hypertension)
- extensive injuries
- endocarditis
- current or past history of thrombocytopenia (especially HIT type II!!!)
- hemophilia, thrombocytopenia or purpura
- extreme caution is advised in the treatment of pregnant women; however, alternative agents (coumarin derivatives) are teratogenic

HEPARIN

- efficacy of UFH therapy must be controlled by checking APTT (Activated Partial Thromboplastin Time)
- this parameter should be prolonged 1.5 – 2.5 times than normal
- LMWHs does not affect APTT, so that it is not necessary to check it
- platelet count should be checked, too

HEPARIN

CAUTION!!!

- **in case of massive bleeding into the CNS or gastrointestinal tract heparin treatment absolutely must be stopped and should be started administration of 1.5 mg protamine sulfate per 100 IU heparin in slow infusion**
- **does not remove completely the low molecular weight heparins action**

HEPARINS - differences

- indications for UFH and LMWHs are no different essentially because they have similar clinical efficacy
- LMWHs have a more favorable pharmacokinetic properties (longer half-life, binding to a lesser extent to plasma proteins, thrombocytes and vascular endothelium - better predictability of the blood clotting inhibitory effect)
- administration of UFH requires monitoring of aPTT

COUMARIN DERIVATIVES

COUMARIN DERIVATIVES - structure

- derived from 4 – hydroxycoumarin
- include dicumarol, warfarin sodium and phenprocoumon
- warfarin has the best bioavailability and the least severe adverse effects

COUMARIN DERIVATIVES - actions

- interfere with γ – carboxylation of glutamate residues in clotting factors II (prothrombin), VII, IX and X, which is coupled to the oxidation of vitamin K
- continued production of functional clotting factors requires replenishment of reduced vitamin K from the oxidized form – this reduction is catalyzed by vitamin K epoxide and is blocked by coumarin derivatives

COUMARIN DERIVATIVES - actions

Clotting factors are still synthesized and cleaved to active forms, but they cannot bind Ca^{2+} and thus cannot bind to platelet membranes

COUMARIN DERIVATIVES – therapeutic uses

- state after implantation of artificial valve
- prophylaxis and treatment of venous thrombosis and pulmonary embolism
- atrial fibrillation
- presence of thrombus in the cardiac cavities
- some cases of thrombophilia

COUMARIN DERIVATIVES – adverse effects

- bleeding - the most dangerous adverse effect
- allergy, skin necrosis, alopecia
- warfarin causes: hemorrhagic infarction in the breast, intestine, and fatty tissue;

  it also readily crosses the placenta and can cause hemorrhage in the fetus; defects in normal fetal bone formation (its teratogenic potential is high)

COUMARIN DERIVATIVES – adverse effects

- in case of overdosing (bleeding) the administration of c.d. must be discontinued
- vitaminum K (in dose of 0.02 – 0.2) intravenously
- administration of fresh frozen plasma (FFP)

COUMARIN DERIVATIVES – drug and food interaction

- aspirin and NSAID increase c. d. action
- antibiotics decrease microbial vitamin K production in the intestine so increase c. d. action
- oral contraceptives decrease c. d. effectiveness by increasing plasma clotting factors and decreasing antithrombin III
- foods rich in vit. K e.g.: cabbage, cauliflower, broccoli, lettuce, spinach, parsley, green peas, soybeans, pistachios, avocado, kiwi, olive oil, green tea decrease c. d. effectiveness
- grapefruit juice and cranberry inhibit the metabolism of c. d. thereby intensifying their activity and increase the risk of bleeding complications

COUMARIN DERIVATIVES – dosage

- there is always individual
- therapy begins with a higher loading dose, that decreases after 1 - 2 days

COUMARIN DERIVATIVES

- we have to control efficacy of coumarin derivatives (check INR systematically)
- the indicated value from 2.1 to 3.0 (2.5 – 3.5)

Coumarin derivatives and procedures

- thromboembolism risk assesment in relation to bleeding risk (serious)
- discontinue of c.d. therapy is not recommended during procedures with small risk of bleeding, especially if thromboembolism risk is high

Coumarin derivatives and procedures

Procedures with small risk of bleeding:

- ✓ operations in oral cavity
- ✓ small procedures in the skin
- ✓ coronarography
- ✓ diagnostic endoscopy
- ✓ arthrocentesis
- ✓ hernioplasty
- ✓ scrotum surgery
- ✓ cataract operation

➢ **risk of local bleeding occurs in <10% of patients**

- ✓ only 1% cases require different from local intervention
- ✓ not correlate with INR between 1.5 to 4.0

Coumarin derivatives and procedures

Procedures with high risk of bleeding:

- ✓ abdominal cavity and chest surgery
- ✓ great vascular and orthopaedic operation
- ✓ cardiosurgical and neurosurgical operation
- ✓ urinary bladder and prostate surgery
- ✓ pacemaker and cardioverter implantation
- ✓ biopsy of tissues impossible to pressure

➢ **substitution c.d. by low molecular weight heparin in prophylactic or therapeutic dose about a week earlier (the INR should be normal: 0.8 – 1.2)**

FACTOR XA INHIBITORS

FONDAPARINUX

- indirectly inhibits FXa via a co-factor - antithrombin
- increases the activity of antithrombin III by 300-fold
- administered s.c. and i.v.
- in NSTEMI lower risk of bleeding than with enoxaparin

FONDAPARINUX - indications

- myocardial infarction without ST segment elevation and with ST-segment elevation not treated with primary PCI
- prevention of venous thromboembolism (VTE) in patients undergoing surgery in the abdomen
- prevention of VTE in patients with internal diseases with a high risk of its occurrence, immobilized for reasons acute illness
- prevention of VTE in patients undergoing hip or knee replacement

RIVAROXABAN and APIXABAN

- highly selective, direct factor Xa inhibitors (without using antithrombin as a mediator)
  - ✓ interrupt the intrinsic and extrinsic pathway of the blood coagulation cascade, inhibit both thrombin formation and as thrombus formation
- not inhibit thrombin neither affect platelets
- administered orally

RIVAROXABAN - indications

- **prevention of VTE in patients after hip or knee replacement**
- **prevention of stroke and systemic embolism in adults patients with non-valvular atrial fibrillation (NVAF) (**with one or more of the risk factors such as prior stroke or transient ischemic attack (TIA), congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus**)**
- **treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and secondary prevention of DVT and PE in adults**
- **prevention of thrombotic events on the atherosclerosis substrate after an acute coronary syndrome (ACS) with elevated cardiac biomarkers (with ASA or ASA and clopidogrel)**

APIXABAN - indications

- **prevention of VTE in patients after hip or knee replacement**
- **prevention of stroke and systemic embolism in adults patients with non-valvular atrial fibrillation (NVAF)** (with one or more of the risk factors such as: prior stroke or transient ischemic attack (TIA), symptomatic heart failure (NYHA ≥ II), hypertension, age ≥ 75 years, diabetes mellitus)
- **treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and secondary prevention of DVT and PE in adults**

RIVAROXABAN - proceedings periprocedural

Manufacturer recommendation:

- **should be discontinued at least 24 hours prior to elective surgery or invasive procedures**
- **should be restarted as soon as possible provided the clinical situation allows and adequate haemostasis has been established – usually six hours after the invasive procedure**

APIXABAN - proceedings periprocedural

Manufacturer recommendation:

- **should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding**
- **should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of bleeding**
- **should be restarted as soon as possible provided the clinical situation allows and adequate haemostasis has been established**

DIRECT THROMBIN INHIBITORS

DIRECT THROMBIN INHIBITORS

- block the catalytic site and the substrate recognition site in thrombin molecule
- block its interaction with its substrates (fibrinogen, factors V, VIII, XI etc.)
- prevent the development of thrombus
- activity does not depend on the presence of antithrombin

DIRECT THROMBIN INHIBITORS

- dabigatran – administered orally
- recombinant hirudins – lepirudin, desirudin – administered i.v.
- synthetic analogs of hirudin - bivalirudin, argatroban – administered i.v.

BIVALIRUDIN - indications

- treatment of HIT type II
- artery angioplasty in patients with a history of HIT II
- coronary angioplasty urgently (ACS) and planned , especially in people with high risk of bleeding complications

DABIGATRAN - indications

- **prevention of VTE in patients after hip or knee replacement**
- **prevention of stroke and systemic embolism in adults patients with non-valvular atrial fibrillation (NVAF)** (with one or more of the risk factors such as: prior stroke or transient ischemic attack; symptomatic heart failure (NYHA II-IV), age> = 75 years , diabetes mellitus, hypertension)
- **treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults**

DABIGATRAN
- proceedings periprocedural

Manufacturer recommendation (proceedings in the perioperative period in patients receiving dabigatran is not established because no published studies describing results of treatment of such patients requiring elective surgeries):

- **should be discontinued 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding**
- **should be discontinued 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of bleeding**
- **should be restarted as soon as possible provided the clinical situation allows and adequate haemostasis has been established**
- **it is not clear whether treatment with dabigatran can continue without interruption during minor dental, ophthalmic and dermatological procedures**

ANTITHROMBOTICS

ASPIRIN – mechanism of action

- inhibition of platelet aggregation by inhibiting the release of ADP and thromboxane A2
- inhibition of the biosynthesis of thromboxane A2 is a consequence of blocking the enzyme cyclooxygenase (COX-1) as a result of irreversible acetylation
- process lasts until the end of life platelets (cells without a nucleus do not synthesize new enzymes)

ASPIRIN

- in order to block the cyclooxygenase in platelets should be used 0.075 - 0.3 g of acetylsalicylic acid per day
- the drug is administered every day or every other day in double dose
- higher doses of the drug causing blockage of endothelial cell cyclooxygenase and consequently it inhibits the synthesis of prostacyclin (PGI2), that has antagonistic action to thromboxane A2

ASPIRIN - indications

Prophylaxis of:

- **myocardial infarction**
- **stroke**
- **thrombotic complications after grafting of artificial valve or coronary bypass**

ASPIRIN – adverse effects

- in cardiological dose is well tolerated
- hypersensitivity
- gastrointestinal disturbances

ASPIRIN - procedures

The administration of aspirin should not be discontinued before dentistry operation

Derivatives of thienopyridine

- ticlopidine
- clopidogrel
- prasugrel
- ticagrelor

Derivatives of thienopyridine - mechanism of action

- inhibition of platelet activation dependent on adenosine diphosphate (ADP)
  - modification of the structure of the platelet ADP receptor
  - inhibition the activation of complex glycoprotein GPIIb / IIIa
- impaired platelet aggregation induced by collagen and TXA2
- antiaggregation potency of clopidogrel is 10 times greater than ticlopidine

Derivatives of thienopyridine - indications

- acute coronary syndrome with and without ST elevation - together with aspirin
- thrombosis prevention after percutaneous coronary intervention with stent implantation (BMS and DES) - together with aspirin
- subacute stent thrombosis prevention - together with aspirin
- secondary prevention of cerebral thrombosis - together with aspirin
- conditions that are indicating the use of aspirin in case of hypersensitivity to aspirin

Derivatives of thienopyridine – adverse effects

- bleeding
- disturbances of the gastrointestinal tract (vomiting, diarrhea)
- angioedema
- resistance to clopidogrel
- myelosuppression (leucopenia, agranulocytosis, thrombocytopenia, pancytopenia) - ticlopidine

Derivatives of thienopyridine - dosage

- clopidogrel – 1 x 75 mg per day, orally
- prasugrel – 1 x 5-10 mg per day, orally
- ticagrelor – 2 x 90 mg per day, orally
- ticlopidine – 2 x 250 mg per day, orally

Derivatives of thienopyridine - procedures

- single antiplatelet therapy - should not be discontinued
- dual antiplatelet therapy:
  - ✓ elective surgery should be postponed, so that had passed at least six months from implantation stent in the case of a drug-eluting stent, six weeks of metal stents and twelve months from an acute coronary syndrome
    - if this is impossible - only aspirin or clopidogrel (prasugrel, ticagrelor) should be discontinued five days before surgery

GP IIb/IIIa inhibitors

- prevent platelet aggregation and thrombus formation
- inhibit the glycoprotein IIb/IIIa receptor on the surface of the platelets - inhibit the process of connecting the individual platelets through the bridges of fibrinogen

GP IIb/IIIa inhibitors

- **abciximab - percutaneous coronary interventions – patients with high risk of MI or death**
- **eptifibatide and tirofiban – acute coronary syndrome NSTE – patients with intermediate and high risk of MI and death - especially with ST segment depression or diabetes**

THROMBOLYTIC DRUGS/ FIBRINOLYTICS

Thrombolytic drugs/ fibrinolytics

- streptokinase
- anistreplase
- alteplase
- reteplase
- tenecteplase

Thrombolytic drugs/ fibrinolytics

- convert plasminogen to the active plasmin
- plasmin degrades many blood plasma proteins (clotting factors) – consequently causing dissolve the thrombus

Thrombolytic drugs/ fibrinolytics

Indications:

- **STEMI**
- **massive pulmonary embolism**
- **arterial embolism and thrombosis (extremities)**
- **ischemic stroke**

ANTIHEMORRHAGIC AGENTS

VITAMIN K

- essential cofactor for a carboxylase that catalyzes carboxylation of glutamic acid residues on vitamin K-dependent proteins:
  - factors II (prothrombin), VII, IX and X
  - proteins C and S
- these proteins have in common the requirement to be post-translationally modified by carboxylation of glutamic acid residues (forming gamma-carboxyglutamic acid) in order to become biologically active

VITAMIN K

- deficiency of vitamin K: biliary obstruction, celiac disease or sprue, ulcerative colitis, regional enteritis, cystic fibrosis etc.
- liver disfunction
- overdosing of coumarin derivatives

VITAMIN K

- **in non-emergency situations:**
  - **can be given in a daily dose of 5-10 milligrams orally**
- **in emergency situations:**
  - **can be injected at a dose of 10 milligrams, repeated after 8-12 hours**

ANTIFIBRINOLYTIC AGENTS

- competitively inhibit the activation of plasminogen to plasmin (responsible for the degradation of fibrin)
- used to treat serious bleeding, especially when the bleeding occurs after dental surgery
- sometimes given before an operation to prevent serious bleeding in patients with medical problems that increase the chance of serious bleeding

ANTIFIBRINOLYTIC AGENTS - Tranexamic Acid (Cyklokapron)

- **orally (tablets):**
  - **usually 25 mg/kg of body weight every six to eight hours, beginning one day before surgery**
  - **after surgery, the dose is usually 25 mg/kg every six to eight hours for two to eight days**

ANTIFIBRINOLYTIC AGENTS - Tranexamic Acid (Cyklokapron)

- **parenterally:**
  - **usually 10 mg/kg, injected into a vein just before surgery**
  - **after surgery, usually 10 mg/kg, injected into a vein every six to eight hours for seven to ten days**

ANTIFIBRINOLYTIC AGENTS
- Aminocaproic Acid

- **orally**
  - **adults – initial dose 5 g; then 1 g every six to eight hours**
  - **children – initial dose 100 mg/kg; then 33.3 mg/kg of body weight every six to eight hours**

ANTIFIBRINOLYTIC AGENTS - Aminocaproic Acid

- **parenterally**
  - **adults – at first, 4 to 5 g iv over a period of one hour; then 1 g/h iv over a period of eight hours**
  - **children – at first, 100 mg/kg iv over a period of one hour; then 33.3 mg/kg/h iv over a period of eight hours**

Natural inhibitor of fibrinolysis

Aprotinin

Aprotinin – action

- prevents excessive blood loss by:
  - ✓ competitive inhibition of plasmin
  - ✓ inhibition of plasminogen activation
  - ✓ inhibition of the proteolytic degradation of fibrin and fibrinogen
  - ✓ inactivation of kallikrein, trypsin and chymotrypsin

Aprotinin - indication

- acute fibrinolytic defect
- hemorrhagic, posttraumatic, endotoxin shock - disseminated intravascular coagulation with increased fibrinolysis
- component of fibrin tissue adhesives

TOPICAL HEMOSTATICS

Used to inhibition of local bleeding of various origins especially in small surgical and dental procedures.

TOPICAL HEMOSTATICS - Thrombin

- converts fibrinogen into fibrin by hydrolyzing peptides (and amides and esters) of L-arginine
- causes clotting of whole blood
- used as a topical hemostatic for capillary bleeding with or without fibrin foam

IT'S NOT ALLOWED TO ADMINISTER INTRAVENOUSLY!!!

TOPICAL HEMOSTATICS – Gelatin sponge

- sterile, absorbable, water-insoluble
- indicated for use in oral or dental surgery as an aid in providing hemostatis
- controls capillary and venous bleeding, forming a stable adherent coagulum
- traps platelets thereby activates the clotting cascade as well absorbs fluid 45x exceeding its weight, thus presses mechanically bleeding vessels
- can be moistened with sterile thrombin solution, physiological saline, antibiotics
- completely absorbed in 3-6 weeks

FIBRIN TISSUE ADHESIVES

- **Tacho-Comb**
  - dry substance collagen-fibrin, resembling a honeycomb
  - dressing contains: collagen, fibrinogen, thrombin, aprotinin, riboflavin
- **Tissucol**
  - fibrin glue, in the form of a set of four vials containing lyophilized and liquid substances
  - composition: fibrinogen, fibronectin, factor XII, plasminogen, aprotinin, thrombin, calcium chloride

Used to inhibit after tooth extraction bleeding in patients with plasma bleeding disorder.

Etamsylate

- synthetic antihemorrhagic and angioprotective medicine, acting on the first phase of hemostasis (interaction between endothelium of the small vessels and platelets)
- does not increase the risk of intravasal blood coagulation and does not change pathologically the prothrombine index

Etamsylate

The preparation is used for prevention and control of small vessel hemorrhage in well-perfused tissues during surgery, including: obstetrics and gynecology, urology, ophtalmology, dentistry, etc.

Etamsylate

1) **Preventively (1–2 hours before surgery intervention):**
   - **intramuscularly or intravenously: 250-500 mg**
   - **orally: 500-750 mg (2-3 tablets)**

Etamsylate

2) Treatment of hemorrhages:

- initial dose: 250-500 mg intramuscularly or intravenously
- 250-500 mg orally every 4-6 hours

Dental interventions in hemophiliacs

Hemophilia

- inherited bleeding disorder
- low level or absence of one of clotting factors in blood
- the main problem for people with hemophilia is bleeding internally, mainly into muscles and joints

Hemophilia

1) **Hemophilia A (sometimes called classical hemophilia)**
   - **deficiency of factor VIII**
2) **Hemophilia B (sometimes called Christmas disease)**
   - **deficiency of factor IX**
3) **Hemophilia C**
   - **deficiency of factor XI**

There is no difference between the types of hemophilia, except that hemophilia B and C are less common than hemophilia A.

Guidelines for regular dental treatment of persons with hemophilia

- dental appointments for children, as well as education in preventive dentistry and caregivers, should be started when the baby teeth begin to erupt
  - frequent visits to the dentist
  - self maintenance of oral hygiene
  - prevention of tooth decay
  - proper implementation of fluor prophylaxis

Guidelines for regular dental treatment of persons with hemophilia

- oral infections should be treated with antibiotics before any surgical procedure is performed
- deep injections, surgical procedures – particularly those involving bone (extractions, dental implants) – or regional local anesthetic blocks should be performed only after clotting factor level has been appropriately increased

Guidelines for regular dental treatment of persons with hemophilia

- in mild or moderate hemophilia, non-surgical dental treatment can be carried out under antifibrinolytic cover (tranexamic acid or epsilon aminocaproic acid), but a hematologist must be consulted before other procedures are done
- in mild hemophilia A (FVIII > 5%), scaling and some minor surgery may be possible under desmopressin (DDAVP) cover
- in severe hemophilia, factor replacement is necessary before surgery or regional block injections or scaling

Guidelines for regular dental treatment of persons with hemophilia

- local use of fibrin glue and swish-and-swallow rinses of tranexamic acid before and after dental extractions are safe and cost-effective methods to help control bleeding
- tranexamic acid used topically significantly reduces bleeding
- 10 ml of a 5% solution used as a mouth rinse for two minutes, four times daily for seven days is recommended
- it may be used in combination with oral tranexamic acid tablets for up to five days

Guidelines for regular dental treatment of persons with hemophilia

- bleeding can be aggravated by painkillers (analgesics) such as ASA or other NSAIDs
- paracetamol/acetaminophen and codeine are safe alternative analgesics

Guidelines for regular dental treatment of persons with hemophilia

- after tooth extraction, a diet of cold liquid and minced solids should be taken for 5-10 days; smoking should be avoided
- any swelling, difficulty swallowing (dysphagy), or hoarseness must always be reported to the dentist/hematologist immediately

In case of need to carry out the extraction or another, even minor surgical procedure in the oral cavity, the patient should be hospitalized and protected substitution treatment (missing clotting factors).

The proceedings before the extraction or other surgical procedure in the oral cavity

1. **Classical hemophilia A:**
   - **plasma-derived preparations - antihaemophilic factor VIII**

[by the formula: dose of factor VIII (IU) = plasma volume (ml) x (A – B)/100; where: A – expected level of factor VIII; B – current level of factor VIII; plasma volume – 40 ml/kg x body weight (kg)];

   - **fresh frozen plasma (FFP)**
   - **ε – aminocaproic acid intravenously at a dose up to 4 g**

The proceedings before the extraction or other surgical procedure in the oral cavity

2. **Mild form of hemophilia A:**
   - **one hour before extraction: desmopressin (ADIURETIN SD MINIRIN) intravenously together with an ε - aminocaproic acid (it causes increment the antihaemophilic globulin (AHG) in serum);**

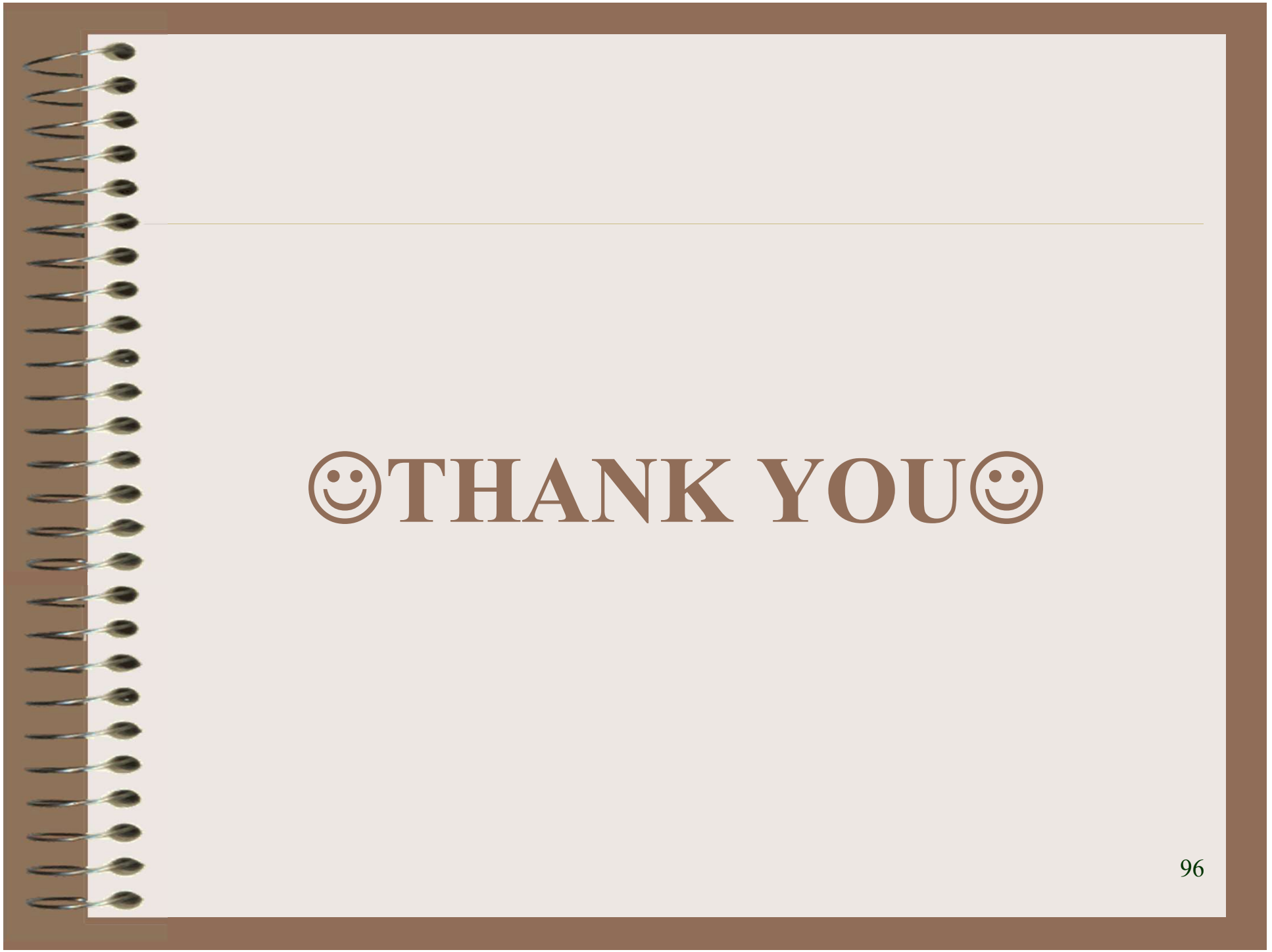
The proceedings after the extraction or other surgical procedure in the oral cavity

1. Continuation of administration of aminocaproic acid at a dose of 0.05 - 0.1 g / kg, orally, in four divided doses for at least one week;
2. Topical application of TAMCHA - rinse the oral cavity
3. Gelatin sponge - directly on the wound
4. Fibrin tissue adhesives - Tissucol, Tacho Comb - applied directly on the wound
5. Application of preparation of factor VIII in case of post extraction bleeding;

Procedures in case of other forms of hemophilia

1. **Hemophilia B:**
   - **PCC – Prothrombin Complex Concentrate**
   - **factor IX concentrate (according to indications)**
   - **fresh frozen plasma (FFP) at a dose of 10 – 30 ml/kg body weight**
2. **Hemophilia C:**
   - **fresh frozen plasma (FFP) at a dose of 10 – 30 ml/kg body weight**

People with hemophilia or congenital bleeding tendencies are a priority group for dental and oral health care, since bleeding after dental treatment may cause severe or even fatal complications. Maintenance of a healthy mouth and prevention of dental problems is of great importance, not only to quality of life and nutrition but also to avoid the dangers of surgery.


☺THANK YOU☺