PROTOCOL

BLEEDING MANAGEMENT
WITHOUT ALLOGENEIC BLOOD TRANSFUSION

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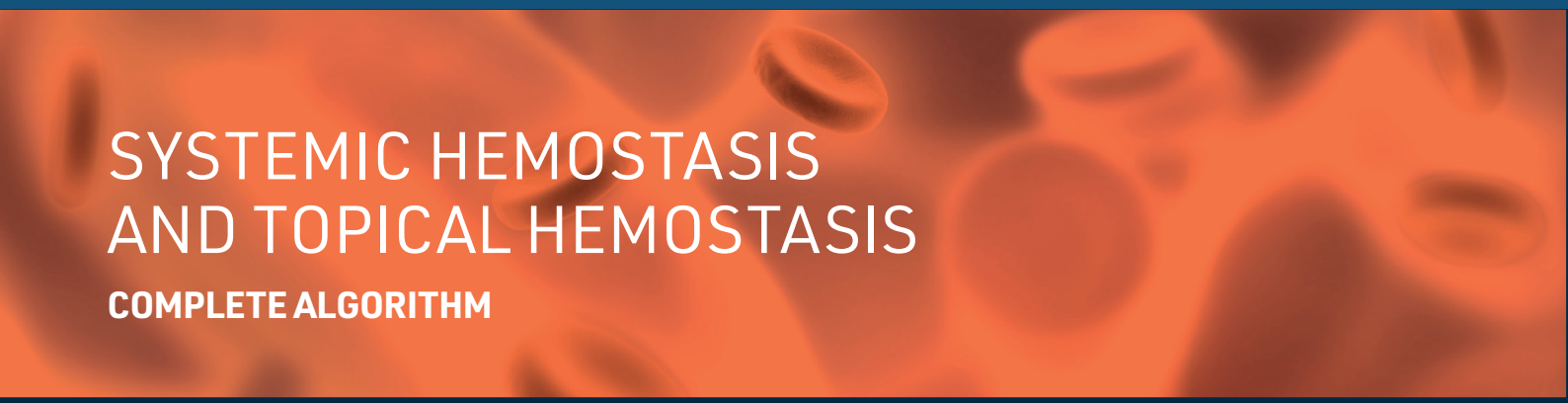


SYSTEMIC HEMOSTASIS AND TOPICAL HEMOSTASIS
COMPLETE ALGORITHM

1. CELL SAVER
   - ☆ AUTOTRANSFUSION BEST PRACTICES
2. ACUTE NORMOVOLEMIC HEMODILUTION
   - ☆ SAME DNA TRANSFUSION
3. ACUTE HEMORRHAGE AND SHOCK
   - 10 STEPS TO SAVE LIVES

PHARMACEUTICAL GUIDE FOR HEMOSTATICS:
DOSAGE, DILUTION, ADMINISTRATION AND COUNTERINDICATION

BLEEDING RISKS EVALUATION
PRE-OPERATIVE

QUESTIONNAIRE: CLINICAL HISTORY – HEMSTOP[10]

1. Have you consulted a doctor or have been treated for prolonged or unusual bleeding (such as nasal bleeding or minor wounds)?
2. Any ocurrence of ecchymosis/hematoma larger than 2 cm without trauma or severe ecchymosis/hematoma after a minor trauma?
3. Have you ever had a prolonged bleeding after a dental extraction, that required medical/odontological attention?
4. Have you ever had excessive bleeding during or after surgery?
5. Is there anyone in your family that suffers from a coagulation disorder (such as hemophilia, von Willebrand disease, etc.)?

FOR WOMEN:

6. Have you consulted a doctor or have been treated for intense or prolonged menstrual cycles (oral anticonceptives, iron, etc.)?
7. Have you ever had postpartum prolonged or excessive bleeding?

TABLE OF MEDICATIONS AND SUSPENTION PERIOD BEFORE SURGERY [11]

SUSPEND	MEDICATION		
10 DAYS BEFORE	☑ PRASUGREL		
7 DAYS BEFORE	☑ CLOPIDOGREL		
6 DAYS BEFORE	☑ DABIGATRAN	☑ ACETYLSALICYLIC ACID	
5 DAYS BEFORE	☑ APIXABAN	☑ TICAGRELOR	☑ WARFARIN (If possible, surgery with normal INR)
3 DAYS BEFORE	☑ RIVAROXABAN	☑ EDOXABAN	

NOTE: In patients with mechanical valve prosthesis, atrial fibrillation and/or previous thromboembolic event, weigh the risk and benefit of anticoagulant discontinuation. In patients with chronic renal failure, evaluate a longer suspension period of antiplatelet and/or anticoagulant agents before a surgery or invasive procedure.

INICIAL LAB TESTS

- Hemogram / Platelets
- Prothrombin Time (PT) or International Normalized Ratio (INR)
- Activated Parcial Thromboplastin Time (APTT)
- Fibrinogen
- Activated Clotting Time (ACT) if Heparin was used
- Calcium
- Arterial Gasometry
- Thromboelastography ou Rotational Thromboelastomery (when available)
- Platelet funcion test (platelet aggregation)

IMPORTANT TO MONITOR REGULARLY

Temp > 35°C/95°F
pH > 7,2
Ca > 1,0 mmol/L
Fibrinogen > 3 g/L
INR < 1,3
Platelets > 80.000/mm^3

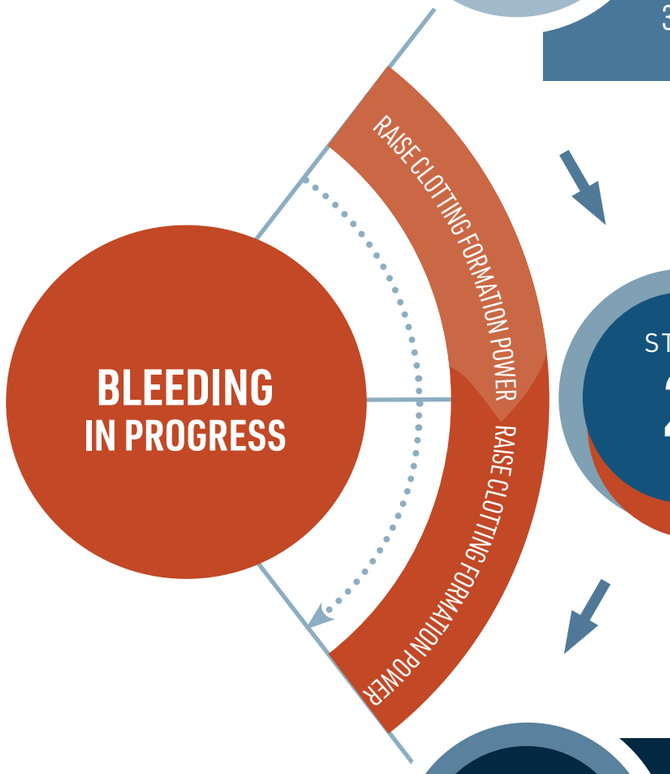
HEMOSTATIC SURGICAL INSTRUMENTS

- Electrocautery
- Ultrassonic or harmonic scalpel
- Advanced hemostasis scissors: HARMONIC® scissors
- Argon plasma coagulation (APC)
- Radio frequency termal ablation
- Microwave devices (microwave ablation)
- Laser

BLEEDING MANAGEMENT
WITHOUT ALLOGENEIC BLOOD TRANSFUSION

ALGORITHM

SYSTEMIC HEMOSTASIS 3 STAGES



STAGE 1

ACT > 130 seg.	INR > 1,4 or APTT > 50 sec	HIPERFIBRINOLYSIS (trauma: ISS > 25)	FIBRINOGEN < 1,5 g/L	PLATELET DYSFUNCTION With or without anti-platelet aggregation agents	PLATELETS < 80.000/mm³
PROTAMIN 30 UI /kg EV	**PROTHROMBIN COMPLEX CONCENTRATES** 25 UI / kg EV (initial dose) and/or **VITAMIN K (PHYTONADIONE)** 10 - 20 mg EV max 50 mg/day	**TRANEXAMIC ACID** 50 mg /kg EV (initial dose)	**FIBRINOGEN CONCENTRATES** 30 mg/ kg EV (initial dose)	**DESMOPRESSIN (DDAVP)** 0,3 mcg / kg EV	**ELTROMBOPAG** 50 - 100 mg /day oral intake or **ROMIPLOSTIM** 2-7 mcg/kg/week SC or **HUMAN IMUNOGLOBULIN** 200-400 mg /kg /day EV for 2 to 5 days

CONSIDER ON EVERY STAGE: SURGICAL HEMOSTASIS STAGE

STAGE 2

AFTER STAGE 1

TRANEXAMIC ACID	PROTHROMBIN COMPLEX CONCENTRATES	FIBRINOGEN CONCENTRATES
100 mg/kg EV (additional dose)	25 UI / kg EV (additional dose)	40 mg / kg EV (additional dose)

CONSIDER ON EVERY STAGE: SURGICAL HEMOSTASIS AND/OR CELL SAVER

STAGE 3

AFTER STAGES 1 AND 2

RECOMBINANT ACTIVATED FACTOR VII	FACTOR VIII/FVW CONCENTRATE	FACTOR XIII CONCENTRATE
40-90 mcg/kg EV	25-50 UI/kg EV	20-35 UI/kg EV

NOTES

1 ABREVIATIONS AND SYMBOLS: ISS: Injury Severity Score (Trauma); INR: International Normalized Ratio; APTT: Activated Partial Thromboplastin Time; ACT: Activated Clotting Time

2 DOSAGE, DILUTION, ADMINISTRATION and MEDICINE COUNTERINDICATIONS (RELATIVE), refer to the Pharmaceutical Guide for Hemostatics below.

PHARMACEUTICAL GUIDE FOR HOMESTATICS
DOSAGE, DILUTION AND ADMINISTRATION

EPSILON-AMINOCAPROIC ACID: 4-5 g, EV, in 1h (diluted in 250 mL of SF 0,9%), followed by continous infusion of 1 g/h (diluted in 50 mL) for 8h or until bleeding has ceased. Maximum dose: 36 g/day. If severe bleeding, can be administered without dilution. Pediatrics: 100 to 200 mg / kg of weight , DESMOPRESSIN (DDAVP): 0,3 mcg/kg, EV, repeating 1-2 times at 6-12h intervals. Dilute in 50mL SF 0,9% and EV infusion: in 15-30 minutes. Pediatrics: dosage as of an adult (0,3 mcg/kg). daily, dividided by three to four times.

TRANEXAMIC ACID: 50-150 mg/kg EV. Can be administered without dilution (up to 10 vials); in this case, slowly administrated (1 mL/min). In case of dilution (SF 0,9% or SG 5% 25 to 250 mL) to be administrated in 30 minutes. On average, prepare 1-6 g EV every 6/6 hours. Pediatrics: 10 mg/kg, 2 to 3 times/day, maximum dose of 3000 mg/day.

PROTHROMBIN COMPLEX CONCENTRATE (PCC): 25-50 UI/kg via EV. Administrate via EV, infusion speed of 1 mL/min for the first 10 minutes. Do not exceed 8 mL/min. Pediatrics: dosage has not been determined in controlled clinical tests.

FACTOR VIII/FVW CONCENTRATE: 25-50 UI/kg via EV every 8-24 hours. The required dose is determined by this formula: Required units = corporal mass (kg) x desired increase of coagulation factor VIII (% or IU/dL) x 0,5. The amount to be administrated and aplication frequency should be effectiveness oriented, in individual cases. After 24-48 hours of treatment, consider reducing dosage and/or increase administration intervals to avoid non-controlled increase of FVIII:C. Administrate via slow EV (infusion should not exceed 4 mL/ minute). Pediatrics: there is no pharmacokinetic data available for children.

FACTOR XIII CONCENTRATE: 20-40 UI/kg via EV. Injection speed should not exceed 4 mL/minute. Pediatrics: Clinical studies do not diferentiate from adult patients safety profile.

FIBRINOGEN CONCENTRATE: 25-70 mg/kg via EV. When fibrinogen level is known, dosage can be determined by the following formula: Dose (mg/kg) = [level of target fibrinogen (mg/dL) – level of measured fibrinogen (mg/dL)] divided by 1,7; when fibrinogen level is unknown, the dose of 70 mg/kg can be used. Administrate via slow EV (maximum speed of 5 mL/minute). Pediatrics: 1 to 2 g EV.

CRYOPRECIPITATE: 1,0-1,5 bolsas EV every 10 kg of corporal mass to reach the level of hemostatic fibrinogen of 100 mg/dL (recalculate every 3-4 days).

DESMOPRESSIN (DDAVP): 0,3 mcg/kg, EV, repeating 1-2 times at 6-12h intervals. Dilute in 50mL SF 0,9% and EV infusion: in 15-30 minutes. Pediatrics: dosage as of an adult (0,3 mcg/kg).

ELTROMBOPAG OLAMINE: 50-100mg/day oral intake for 14 days. If after 2 weeks of treatment platelets < 50.000/mm3, increase daily dose in 25 mg to maximum of 100 mg/day. Pediatrics (above 6 years old): 50 mg once a day.

RECOMBINANT ACTIVATED FACTOR VIIA (RFVIIA): 90 mcg (4,5 KUI)/kg, EV, every 2-3h until hemostasis, for 1 or 2 days. After that, intervals can be raised to 4, 6, 8 or 12h, during 2 to 3 weeks or more. Administration: direct EV injection, slow 2 to 5 minutes. The dilution vial comes with the product (water for injection). Pediatrics: 70 to 90 mcg/kg EV, slow (2 to 5 minutes), every 2 to 3 hours, until hemostasis.

HUMAN IMMUNOGLOBULIN: 0,8 1,0 g/kg on first day, can be repeated on third day or 0,4 g/kg, daily, for 2 to 5 days. Initiate with 0,3 ml/kg/hour speed, if tolerance is good, gradually increase 0,5 ml/kg/hour every 30 minutes, until maximum infusion rate of 4,8 ml/kg/h. If dilution is needed, use SG 5%. To obtain immunoglobulin solution at 5%, dilute with volume equivalent to glycose solution. Pediatrics: 400-1000 mg/kg/dose once/day for 2-5 days.

PROTAMIN: dose of 1 mL of protamin neutralizes 1000 IU of heparin. It is recommended not to administrate more than 1 mL of protamin, if heparin concentrate is not determined. As a general rule, one dose of protamin that neutralizes 50% of the last heparin dose can be used. Administrate via Slow EV (1 to 3 minutes). Maximum of 50 mg in 10 minutes. Pediatrics: there is no pharmacokinetic data available for children. Refer to adult dosage.

ROMIPLOSTIM: 4-10 mcg/kg via SC, weekly, adjusting dosage based on platelets count. If platelets < 50.000/ mm3, increase weekly dosage to 1 mcg/kg. Administrate via SC. A syringe with 0,01 mL gradation should be used due to the small volume. No dilution (reconstitution of 0,72 mL of AD) and concentration: 500 mcg/mL. Pediatrics: dosage has not been determined in controlled clinical tests.

VITAMIN K (PHYTONADIONE): Dilute 10 - 20 mg (1-2 vials) in 20 mL of SF 0,9% with slow EV (injection speed: 1 mg/min). Repeat every 6 hours until maximum dose of 50 mg/day. Injectable phytonadione (solution) 10 mg/1 mL. Pediatrics: dose 2-10 mg via EV.

PHARMACEUTICAL GUIDE FOR HOMESTATICS
COUNTERINDICATION AND USE FOR KIDNEY AND HEPATIC FAILURE

IMPORTANT: In case of life-threatening bleeding, always consider the benefits of using the resources below higher than the risk.

MEDICINE	COUNTERINDICATIONS (RELATIVE)	KIDNEY AND/OR HEPATIC FAILURE
EPSILON AMINOCAPROIC ACID	▸ Active intravascular coagulation; ▸ Acute occlusive vasculopathy; ▸ Hipersensitivity to the active ingredient.	**Kidney failure:** reduce around 20% of dosage. **Hepatic failure:** there is no need to adjust dosage.
TRANEXAMIC ACID	▸ Active intravascular coagulation; ▸ Acute occlusive vasculopathy (acute thromboembolic events); ▸ Hipersensitivity to the active ingredient.	**Kidney failure:** adjust dosage if moderate or severe failure **Hepatic failure:** there is no need to adjust dosage.
PROTHROMBIN COMPLEX CONCENTRATES (PCC)	▸ Acute occlusive vasculopathy; ▸ Hipersensitivity to the active ingredient. In case of disseminated intravascular coagulation, use only by the end of consumptive effects. Known history of heparin induced thrombocytopenia.	There is no need to adjust dosage.
FACTOR VIII CONCENTRATE/FvW	▸ Hipersensitivity to the active ingredient.	There is no need to adjust dosage.
FACTOR XIII CONCENTRATE	▸ Hipersensitivity to the active ingredient.	There is no need to adjust dosage.
FIBRINOGEN CONCENTRATE	▸ Acute occlusive vasculopathy; ▸ Hipersensitivity to the active ingredient.	There is no need to adjust dosage.

MEDICINE	COUNTERINDICATIONS (RELATIVE)	KIDNEY AND/OR HEPATIC FAILURE
DESMOPRESSIN (DDAVP)	▸ Unstable angina pectoris; ▸ Decompensated heart failure; ▸ Von Willebrand disease type II; ▸ Hipersensitivity to the active ingredient.	There is no need to adjust dosage.
ELTROMBOPAG OLAMINE	▸ Hipersensitivity to the active ingredient.	Monitor use on patients with moderate to severe kidney failure and/or heptic failure. Initial suggested dose of 25 mg per day. Wait 2-3 weeks before increase dosage.
RECOMBINANT ACTIVATED FACTOR VIIA (rFVIIa)	▸ Hipersensitivity to the active ingredient.	There is no need to adjust dosage.
HUMAN IMMUNOGLOBULIN	▸ Hipersensitivity to the active ingredient.	No information on dosage adjustment found When Clcr < 10. Use with caution.
PROTAMINE	▸ Hipersensitivity to the active ingredient.	There are no studies for dosage adjustment.
ROMIPLOSTIM	▸ Arrhythmias and heart failure; ▸ Hipersensitivity to the active ingredient.	There are no studies for dosage adjustment.
VITAMIN K (PHYTONADIONE)	▸ Hipersensitivity to the active ingredient.	There is no need to adjust dosage, but monitoring clotting parameters is needed when there is hepatic failure.

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TOPICAL HEMOSTATICS

1 ABSORBABLE AGENTS
- Oxidized regenerated cellulose
- Microfibrillar Collagen
- Gelatins

2 BIOLOGIC AGENTS
- Fibrin glue
- Topical Thrombin
- Gelatin + Thrombin

3 SYNTHETIC AGENTS
- Glutaraldehyde adhesive and Bovine Albumin
- Cyanoacrylate adhesive
- Polyethyleneglycol

IMPORTANT: Topical use of tranexamic acid (TXA) is safe and effective in reducing bleeding and allogeneic blood transfusions. Medium dose: dilute 2 g of TXA in 50 ml of saline at the bleeding site.

AUTOTRANSFUSION: CELL-SAVER

USE PROTOCOL

DEFINITION

The cell saver colects blood from surgical field during surgery and/or postoperative. **Recovered blood is washed, filtered and reinfused with the same DNA as of the patient, eliminating risks of allergic, inflammatory and immunological reactions.**

ADVANTAGES

- Allows for recovery of up to 90% of red blood cells lost during surgery;
- Cost effective and safe for the patient, reducing hospitalization rates and avoiding allogeneic blood transfusion risks, such as: infections, cerebrovascular accident, arrhythmia, cancer, kidney failure and death;Elimina a doença Enxerto X Hospedeiro;
- Eliminate graft-versus-host disease;
- Immediate availability of fresh blood (autologous);
- Decrease demand for allogeneic blood (donated);
- Recovered red blood cells have greater capacity to carry oxigen compared to those in blood bank storages.

RECOMMENDATION

- Surgical procedures in which estimated blood loss may exceed 500 ml (or > 10% of total blood volume calculated) in adult patients, or > 8 ml/kg (> 10% of total blood volume calculated) in children with > 10 kg weight;
- Anemia during preoperative and/or increased risk factors of bleeding;
- Patients with rare blood type or antibodies (sensitized patients by previous polytransfusions);
- Patients that refuse allogeneic blood for any reason;
- Pregnant women with considerable anemia before surgery, and when high risk of hemorrhage is anticipated, or if any unpredicted bleeding occurs during surgery.

NOTE: In oncological surgeries (cancer) or when blood is collected from an infected surgical field, consider using leucoreduction filters or gamma irradiation of recovered blood before infusion. In patients with hemoglobinopathies (sickle cell anemia or thalassemia) in theory there is an increased risk of hemolysis caused by hypoxia in the collection reservoir. This situation does not counterindicate the use of this technique; evaluate each case with its risks and benefits individually. Blood for autotransfusion should not be collected from a surgical field if it contains hemostasis agents, bone cement or antiseptical agents, such as iodopovidone, chlorhexidine and ethyl alcohol.

SPECIAL CONDITIONS

UNCONTROLLED BLEEDING
WITHOUT APPARENT CAUSE

✔ Interrupt blood loss as soon as possible using any necessary means (direct pressure, elevation, pressure points, compression bandaging, torniquetes, tamponing, damage control surgery, pelvic cushion, external fixture, etc.);

✔ Allow moderate hypotension (PAM of 50-65 mmHg), which means to, **allow arterial pressure at the lowest level possible to maintain tissue perfusion;**

✔ Avoid palliative measures in order not to delay definitive interventions to cease bleeding;

✔ Use less invasive methods or procedures to control bleeding;

✔ Rapid diagnostic investigation using ultrasound (US), upper gastrointestinal endoscopy (GI), diagnostic peritoneal lavage (DPL), colonoscopy, tomography or computed angiotomography, or angiography, for an IMMEDIATE SURGICAL INTERVENTION and/or arterial or venous embolization;

✔ Do not postpone surgical hemostasis, even with an anemic patient. The intervention should be fast, simple and effective.

✔ Evaluate post-surgery or trauma bleeding (incomplete surgical hemostasis due to unlinked vessel or an uncontrolled or unknown arterial lesion).

✔ Evaluate if bleeding is caused by a systemic clotting defect: thrombocytopenia, excessive fibrinolysis, dilution of coagulation factors, excessive anticoagulation, inadequate neutralization of heparin, disseminated intravascular coagulation, congenital disorders (C protein, S protein, factor V Leiden);

✔ **Perform hemostasis with EFFECTIVE DOSES of the PHARMACOLOGICAL AGENTS, according to the ALGORITHM provided in this PROTOCOL;**

✔ Always consider the use of pharmacological agents that raise clotting formation power (Prothrombin Complex Concentrate, Recombinant Activated Factor VIIa (rFVIIa), Fibrinogen Concentrate, Factor VIII/FvW Concentrate, Factor XIII Concentrate).

NOTE: CRYOPRECIPITATE contain coagulation factors XIII, VIII, von Willebrand factor and fibrinogen (I), thus can be used to replace these coagulation factors in patients with massive blood loss, when industrial concentrate is not available. It is conterindicated in case of disseminated intravascular coagulation (DIC) without bleeding.

SPECIAL CONDITIONS

MAJOR BLEEDING BY ORAL ANTICOAGULANTS (ANTÍDOTES)[14.15]

A Dabigatran reversal agents → Idarucizumab – administrate 5 g (2 vials of 2,5 g/50 mL), via EV, with two consecutive infusions during 5 to 10 minutes each or one slow bolus injection.

B Rivaroxaban or Apixaban reversal agents → Andexanet Alfa two effective dosage regimes: low dose: bolus EV of 400 mg followed by EV infusion of 4 mg/ minute for up to 120 minutes. Low dose requires 4 vials in bolus plus 5 vials for infusion. High dose: bolus EV of 800 mg followed by EV infusion of 8 mg/minute for up to 120 minutes. High dose requires 8 vials in bolus plus 10 vials for infusion. The bolus doses are directed to 30 mg/ min, followed by an infusion 2 minutes later.

ESOPHAGEAL VARICES BLEEDING (ALTERNATIVES A OR B)

A Somatostatin: dose 3 mg, slow EV (3 minutes), only dose, followed by 3,5 mcg/kg/h, EV. Once hemorrhage ceased, keep it for 48-72h. There is no need to adjust dosage in case of kidney or hepatic failure.

B Octreotide: 25-50 mcg/h, EV continuous infusion, for 5 days. Dilute in 60 mL SF0,9% each 500 mcg. There is no need to adjust dosage in case of kidney or hepatic failure.

UTERINE BLEEDING (POSTPARTUM)[16,17]

Obstetric strategy: • Bimanual compression • Reinsertion of inverted uterus • Tamponing • Intrauterine balloon tamponade • Uterine compression suture • Uterine artery embolization • Uterine artery ligature • Iliac internal artery ligature.

Medicine: 1. Oxytocin: Injectable syntocinon 5 IU/mL - vial 1 mL. Dilute each vial in 500 mL of SG 5% or SF 0,9% and infuse EV at maximum speed of 20 miliunits/min (40 drops/min). There is no need to adjust dosage in case of kidney or hepatic failure. 2. Conjugated estrogen dose 20-120 mg/day via EV in divided doses. NOTE: If bleeding is severe, associate with hemostatics described in this protocol.

MENSTRUAL BLEEDING (CEASE MENSTRUATION))

Medroxyprogesterone: dose 150 mg via IM only dose. Other option: dose 10 mg oral intake daily. Counterindicated during pregnancy. Evaluate risk if previous thrombotic event.

DISSEMINATED INTRAVASCULAR COAGULATION (DIC):

IMMEDIATE INTERVENTION

DEFINITION

Clinical condition characterized by systemic activation of blood clotting, with activation and consumption of coagulation factors, leading to thrombosis of small and medium vessels, and to organic disfunctions and bleedings.

RECOMMENDATION

Urgently reverse the causing disease or the process that unleashes the coagulopathy.

ETIOLOGY

- Infections
- Traumas
- Obstetric diseases
- Solid and hematological neoplasias
- Hepatic diseases

TESTS

- Hemogram
- PT (INR)
- APTT
- Fibrinogen
- D-dimer

TABLE WITH DIAGNOSTIC SCORE FOR DIC

(International Society on Thrombosis and Haemostasis)[16,17]:

POINTS	0	1	2	3
Platelets (x 10^3/µL)	> 100	100 - 50	< 50	
D-dímers (µg/L)	< 1000	1000 - 2000	2001 - 3000	> 3000
INR	<1,17	1,17 - 1,75	> 1,75	
Fibrinogen (g/L)	≥ 100	< 100		

if ≥ 5 points: dic

TREATMENT

- **If there is absence of active bleeding and thrombotic events predominance:** initiate complete heparinization.
- **If there is active bleeding or high risk of bleeding (platelets < 20.000, PT (INR) > 1,5 and/or Fibrinogen < 150 mg/dl):** consider use of Prothrombin Complex Concentrates; Fibrinogen Concentrate and/or Recombinant activated factor VIIa (rFVIIa).

ACUTE NORMOVOLEMIC HEMODILUTION (ANH)

DEFINITION

Blood conservation technique that involves drawing an average of 1-4 bags (450 – 1800 mL) of patient's blood right after anesthetic induction. The volume is replaced by crystalloids and/or colloids as plasma volume expander, to assure normovolemia. The drawn blood is reserved to use by the surgical team at the proper moment, during or after surgery.

RECOMMENDATION

Adult surgery with normal hemoglobin and possible bleeding with estimated loss above two blood units (900 a 1000 mL). For children, each case can be evaluated.

ADVANTAGES OF ANH

- No risks related to alergic, inflammatory and immunological reactions, as commonly happens with allogeneic blood transfusions.
- Immediate availability of fresh blood (autologous), allowing the patient to receive his own blood, with platelets and coagulation factors.
- Decrease demand for allogeneic blood (donated), by reducing blood transfusions.
- Recovered red blood cells have greater capacity to carry oxigen compared to those in blood bank storages.
- Enhance tissue perfusion by reducing blood viscosity caused by hemodilution, which facilitates oxygen release in the microcirculation and presenting less thrombotic complications.
- Low cost technique, which basically consists in drawing blood and infuse crystalloids and/or colloids to assure normovolemia.
- Effective and safe technique for adults and children.
- Decrease blood loss during surgery, since after hemodilution there is less concentration of circulating red blood cells in blood vessels.

☆ **Best blood transfusion** **your own blood**

COUNTERINDICATIONS

- Arrhythmia with hemodynamic instability.
- Severe infection (sepsis).

ANH SPECIAL CARES

Evaluate risks x benefits in the following clinical conditions:

- Heart failure (reduced ejection fraction): difficulties to increase cardiac debit (important mechanism to compensate anemia).
- Kidney failure: difficulties to eliminate fluids administrated in the hemodilution.
- Anemic, hypovolemic and hypotense before the procedure: hemodilution will reduce even more red blood cells count.
- Hypothermia: clotting might be impaired and this can get even worse with hemodilution.
- Clotting disorders: hemodilution may disrupt hemostasis.
- Other conditions: unstable angina, severe aortic stenosis, urgency surgery, severe COPD,severe pulmonary hypertension, severe carotid stenosis (>70%), hypoxemia (SO2 < 90% from ambient air), hemoglobinopathies, old age.

FANH FORMULA (GROSS FORMULA))

Used to determine the approximate value of blood to be drawn from the patient:

$$V = EBV \times (Hct\text{-}i - Hct\text{-}f) / Hct\text{-}av$$

Table of acronyms:

V= volume of blood to be drawn from the patient.

EBV= VEstimated volume of blood from patient (in liters). A general way to estimate this volume is 70 ml/Kg for men and 60 ml/Kg for women.

Hct-i = patient´s initial hematocrit.

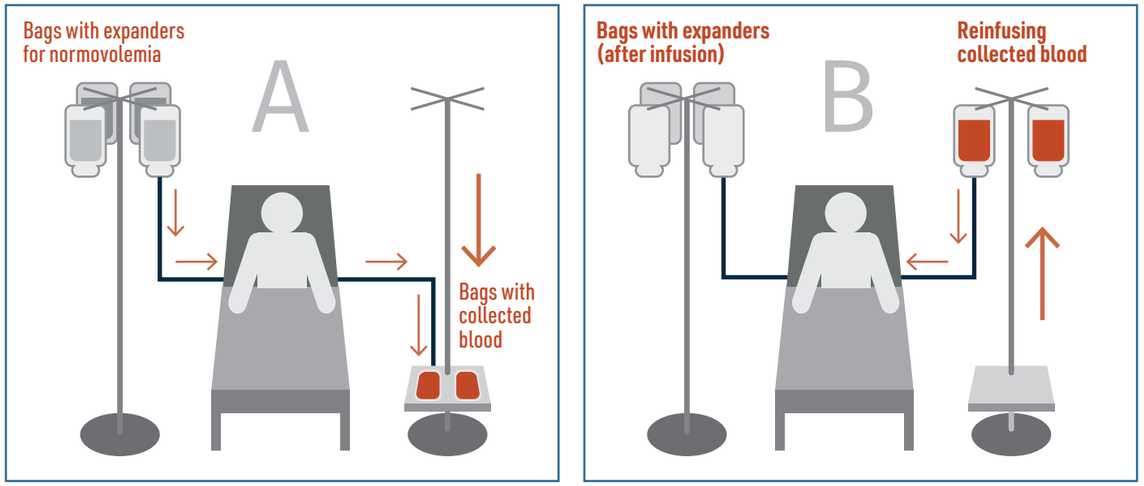
Hct-f = final desired hematocrit with hemodilution.

Hct-av = average hematocrit between initial and final (Hct-i + Hct-f /2)

Exemple:

Considering a 70kg man (EBV = 4,9 liters (70 x 70), with Hct-i of 40% and Htc-f of 30%, aplying the formula above:
V = 4,9 x (40 -30)/ 35 → V = 4,9 x (10/35) → V = 1,4 liters of blood to be drawn (equivalent to 3 blood bags).

ACUTE NORMOVOLEMIC HEMODILUTION
PLACTICAL EXPLANATION OF ANH



Representation of ANH process (illustration based on Santos and colaborators)[10]

PRACTICAL EXPLANATION Generally, the ANH is initiated after anesthetic induction and interrupted before surgical bleeding becomes significant. The patient receives 2 accesses (venous and/or arterial) so that the blood can be drawn by one access (preferably arterial) and, simultaneously, by the other access (venous) be infused with a solution of expanders fluids, which can be colloid and/or crystalloid. If a crystalloid is used as expander, generally around 3-4 mL for each mL of collected blood is infused. If a colloid is used, the proportion is of 1:1, which means, for every mL of collected blood, infuse 1 mL of colloid. The ideal is a mixed hemodilution, associating a crystalloid with a colloid, respecting each expander proportions.

For example, if 2000 mL of blood is collected, first infuse 1000 mL of colloid (1:1 proportion) and next infuse 2000 mL of crystalloid (2:1 proportion). The speed of blood collection should always be the same as the infusion of the plasmatic expander. Perform a vesical probing, to monitor urinary debt. Inside the blood collecting bags there are anticlotting and aditives to expand the stored blood lifespan. To avoid platelet aggregation and the loss of platelets function, the blood in the bag should be kept at ambient temperature (22° C), be moved gently (manually ou mechanically) and be used up to 8 hours after collected. The best moment to reinfuse the blood bags is when there is a major bleeding with significant loss of red blood cells (Hb < 7 g/ dL) and/or there is hemodynamic instability. Hb levels should be monitored at 30-60 minutes of interval during surgery. Generally, the reinfusion of the bags to the patient should be done in a reversed order of collection, which means that the first unit to be autotransfused is the one that contains the lowest level of red blood cells. But, if there is a need to facilitate hemostasis or if the patient is hypervolemic (low response to diuretics), the first bag of collected blood should be infused, since it concentrates more red blood cells, platelets and coagulation factors. A good schedule for the replacement should be done within the 8 hours to avoid wasting collected blood.

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BLEEDING MANAGEMENT WITHOUT ALLOGENEIC BLOOD TRANSFUSION

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ACUTE HEMORRAHGE AND SHOCK

10 STEPS TO SAVE LIVES

FIRST: immediately interrupt external and internal hemorrhages using any necessary means (direct pressure, elevation, pressure points, compression bandaging, torniquetes, tamponing, damage control surgery, pelvic cushion, external fixture, Trendelenburg position, etc.);

SECOND: perform moderate replacement of fluids to assure volemia. Practical rule: 1) Crystalloids replacement: for every 1 mL of blood lost, replace with 3 to 4 mL of crystalloids; 2) Colloids replacement: for every 1 mL of blood lost, replace with 1 mL of colloids, but due to clotting alterations, it is not beneficial to replace more than 1000 mL of colloids. The ideal is to make a mixed replacement of crystalloid and colloid. For example, if the patient lost 2000 mL of blood, first replace 1000 mL (1:1) of colloid and the rest replace with 2000 mL (2:1) of crystalloid.

THIRD: allow sistemic arterial pressure at the lowest level possible to maintain tissue perfusion.

FORTH: immediately call the surgery team (primary operatory focus on fast controlling the bleeding) and use the available autotransfusion equipment (cell saver).

FIFTH: always use a combination of mechanical/surgical and pharmacological measures to cease blood loss, following safe and effective dosage directions of the systemic and topical hemostatics refered on this protocol.

SIXTH: reduce local time period and on emergency room, simultaneously performing control of hemorrhage and volemic replacement.

SEVENTH: perform diagnostic investigation (ultrasound, UE, tomography and/or arteriography), that provide a fast result, for an IMMEDIATE SURGICAL INTERVENTION and/or arterial or venous embolization;

EIGHTH: optimize ventilation/oxygenization of the patient, by optimizing oxygen delivery, by means of SUPPLEMENTARY OXYGEN, increasing the FIO2. This can be done through nasal cannula, face masks or oxygen tents.

The most effective way to optimize oxygenization and avoid tissue ischemia is through mechanical ventilation. This can be non-invasive (CPAP or BIPAB with face mask) or invasive (with orotraqueal tube or tracheostomy).

NINETH: reduce demand for oxygen by the patient by rigorous control of temperature (keep normothermia of 36oC) and provide sedation/analgesia.

NOTE: Hypothermia (32-33oC) results in alterations in the clotting system and makes bleeding even worse. Warm hypothermic patients (use warm fluids) and cool feverish patients.

TENTH: initiate immediate erythropoietin therapy (use high doses of 300 - 1000 IU/kg/week via EV or SC, alternating intervals between doses) and iron EV, to reduce anemia duration.

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