Blood Component Therapy Before Bedside Procedures

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CASE 1

- Before performing a liver biopsy, Dr A always transfuses 2 units of FFP to any patient with an INR greater than 1.3.Dr A will not do a liver biopsy if the platelet count is below 100,000/µl. He refers patients with abnormal coagulation laboratory tests to the Interventional Radiology Department ,which transfuses all of theses patients before the procedure in order to “prevent bleeding complications”.

Comment: *Although this approach may not be unusual, very little in the medical literature supports the confidence that either Dr A or The Radiology department places on coagulation times or the platelet count as predictors of bleeding after liver biopsy.*

CASE 2

- A 60 year old man in the coronary care unit recovering from an acute myocardial infarction. He has been sustained for 4 days by an intra-aortic counter pulsation balloon pump inserted into his left femoral artery .His balloon pump is about to be removed and his platelet count is 60,000/µl. Platelet concentrates are requested to be given immediately before the ballon pump is removed.

Comment: *A better strategy would be to remove the ballon and treat the patient if he demonstrates prolong oozing from the wound site. The majority of patients will not have prolonged bleeding.*

CASE 3

- A 34 year old woman with SLE is being treated in the medical intensive care unit for suspected sepsis. Her medications include steroids, hydroxychloroquine, broad-spectrum antibiotics ,and dopamine. Her platelet count is 30,000/µl, and she requires a central line placement for hemodynamic monitoring and vascular access. The MO requests that the line be placed “under platelet coverage” meaning that it should be inserted while the platelet concentrates are infusing. When this decision is questioned, the MO acknowledges that he is “nervous” about placing the line and that “ he would feel more comfortable if the patient got transfused first”.

CASE 3-Ctd

Comment: *There is no evidence that any preprocedure therapy will change the outcome of the central line placement. The concept of "platelet coverage" is probably more fantasy than reality. Transfusion of the patient to increase the comfort level of the physician is not an appropriate indication.*

- The next day , the same woman requires a diagnostic lumbar puncture to evaluate suspected meningitis. The coagulation tests are unchanged. Platelet concentrates are requested again before the procedure because the count is below 50,000/µl. When the decision to transfuse is questioned , the doctor says he would be "sued "if she had a bleeding complication.

CASE 3-Ctd

Although the literature on the issue of thrombocytopenia and the lumbar puncture is limited , a recent large retrospective study found no evidence for a "threshold "level of platelet count needed to prevent bleeding complications from a diagnostic lumbar puncture.

The physicians perception on legal risk may be completely backwards because legal action in transfusion cases is nearly always based on complications resulting from transfusions given.

Introduction

- Modern medical and surgical therapy relies on a wide variety of invasive bedside procedures.
- Patients treated in intensive care units are particularly dependent upon such procedures.
- There have been almost no prospective, randomized controlled trials investigating the preprocedure management of patients with disordered haemostasis.
- Patients who require multiple invasive procedures are frequently among the most ill in the hospital.
- They often have associated haemostatic disorders resulting from liver disease, multiple medications, uremia, sepsis and DIC.

Introduction

SO IT IS NOT SURPRISING THAT INVASIVE PROCEDURES OFTEN MUST BE PERFORMED IN INDIVIDUALS WHO HAVE ABNORMAL LABOROTARY TEST RESULTS FOR COAGULATION

Assumptions that underlie the prophylactic use of blood components.

- Three assumptions underlie the prophylactic use of blood components before invasive procedures.

1st assumption

Abnormal results of commonly used laboratory tests such as

PT (INR), APTT or the platelet count have predictive value to

Identify which patients to treat.

2nd assumption

Blood components administered before procedures effectively

correct haemostatic abnormalities.

3rd assumption

Prophylactic transfusions given before the procedure are of great benefit

than therapeutic transfusions given after the procedure.

Questioning Assumption 1

- Do common laboratory tests really predict bleeding?

PT(INR) and APTT

- Many clinicians appear to make decisions regarding transfusion before bedside procedures on the basis of results of the INR,APTT and platelet count
- Numerous studies have shown that the INR and APTT do not serve as useful screening tests for predicting blood loss at surgery.

Questioning Assumption 1

- Five aspects of the PT(INR) and aPTT make these tests poor predictors of hemorrhage.

1.1. The relationship between coagulation factors and the PT and aPTT is nonlinear

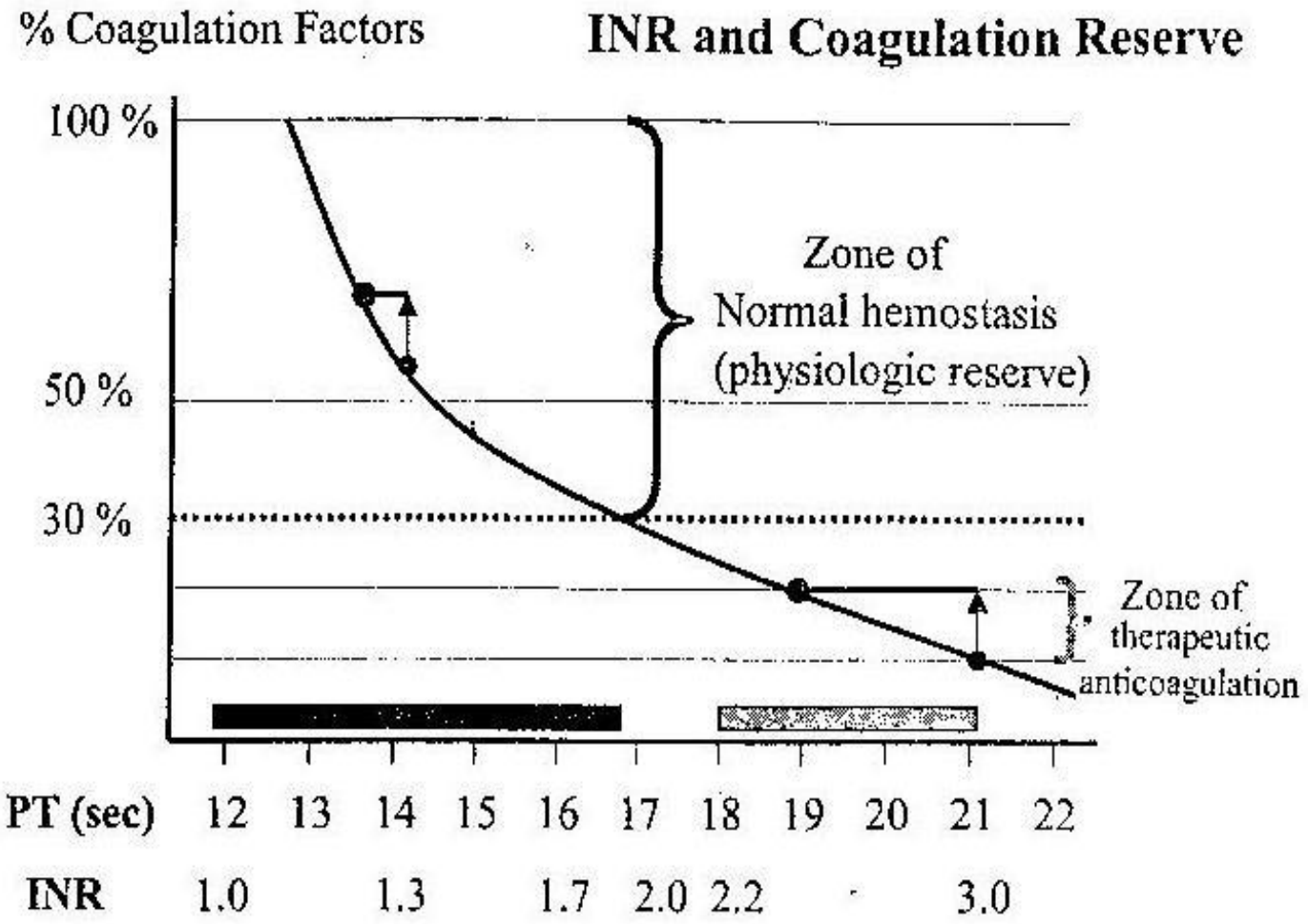
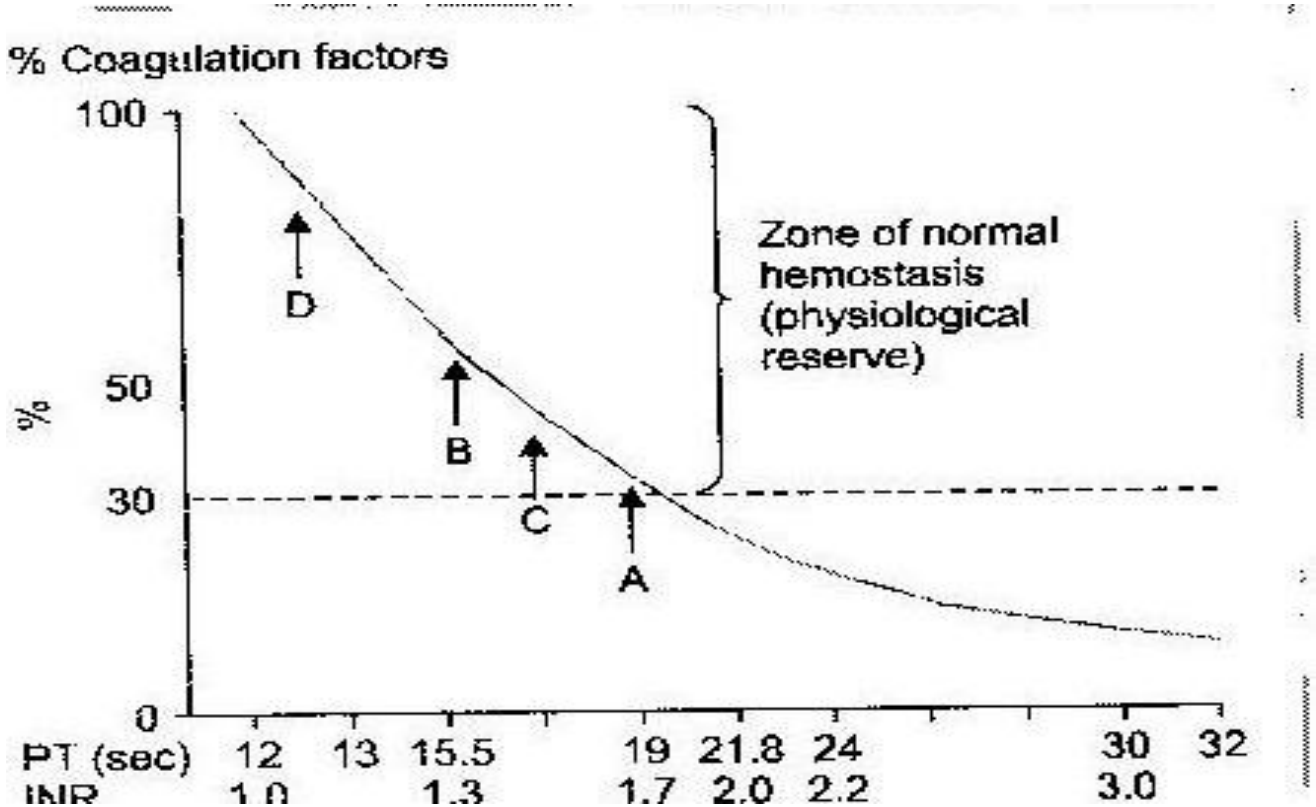


Figure 1-3. General relationship between the concentration of coagulation factors and the result of the prothrombin time (PT) test. In any laboratory, the local position of the curve will vary as a result of technical factors. Results will also vary depending on whether there are single or multiple factor defects. See text for explanation. Note that the zone of physiologic reserve is much larger than the zone of therapeutic anticoagulation.

Questioning Assumption 1

1.2. Mildly abnormal test results occur among patients with biologically normal coagulation.

- Physiologically adequate haemostasis does not require 100% levels of coagulation factors, due to physiological reserve built into human systems.
- Factor levels that are 40% to 50% of normal, and well within the physiologic reserve of adequate haemostasis, can result in prolong PT and aPTT.



In many institutes ,the threshold for transfusing plasma is an INR>1.6.When INR starts to exceed 1.6, factor levels begins to drop below 30% -Threshold for normal haemostasis.(**point A**)

A recipient with INR 1.37 would likely to have clotting factor concentrates in excess of 50% of normal**.(point B).**

Thus the recipients with INR 1.37 were unlikely to have bleed excessively even in the absence of plasma infusions.

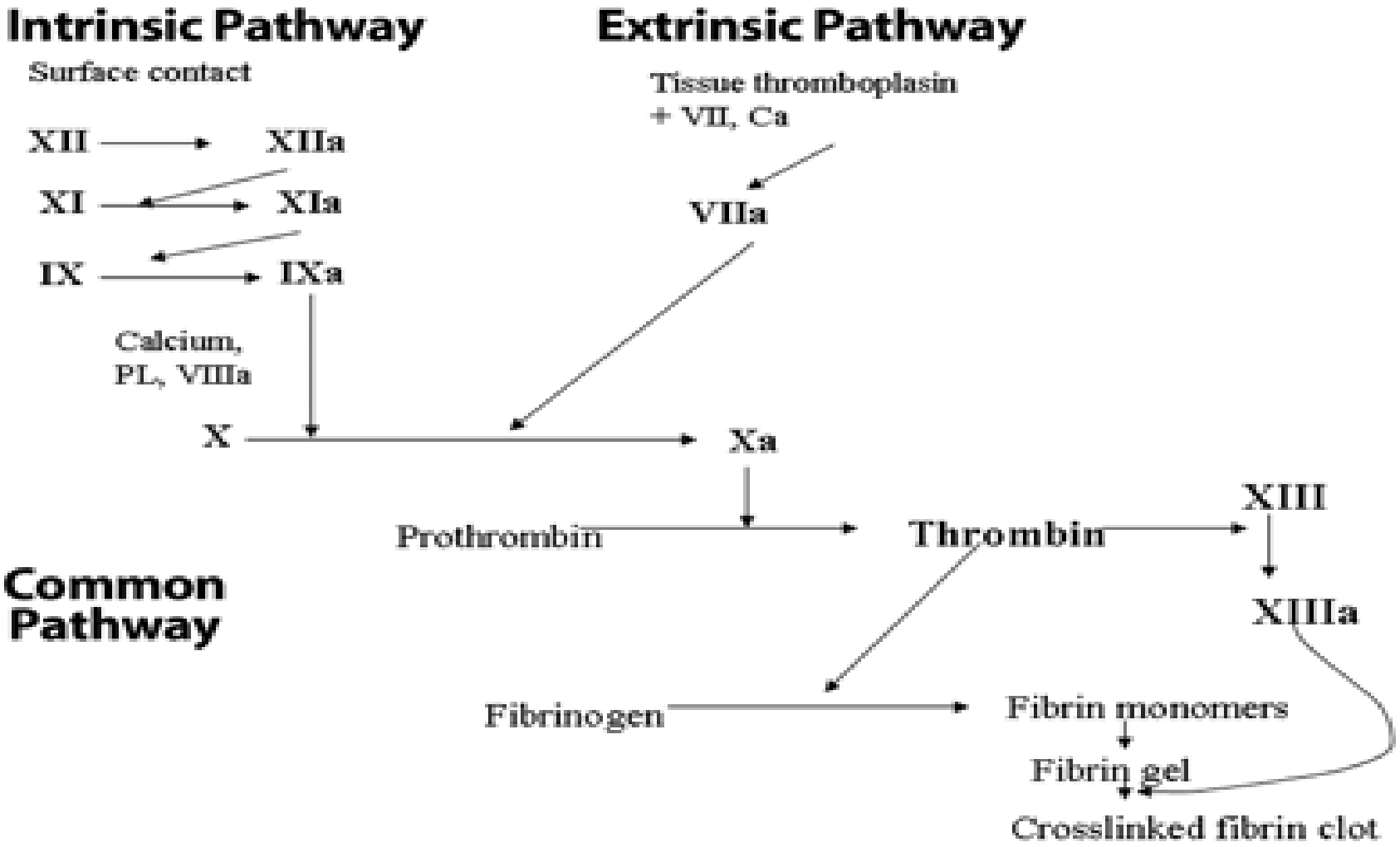
Recommended 10-15ml/Kg of plasma to correct coagulopathy would increase the concentration of clotting factors by 15%. A 15% increase in clotting factors in a recipient with an INR of 1.5 would only amount to a small decrease in their INR**.(point C**)

Questioning Assumption 1

1.3 The test overestimate deficiencies in the upper limb of the cascade and underestimate deficiencies in the lower limb.

E.g. the PT(INR) assay is dominated by the level of factor vii in the sample. Patients with levels of factor vii that are reduced but well within the range adequate for haemostasis who have high levels of other factors will have a more “abnormal” PT result than patients with high levels of factor vii and very low levels of other factors.

Coagulation pathway



Questioning Assumption 1

1.4. The test overestimate the extent of coagulation factor depletion if more than one factor is reduced.

In a series of in vitro mixing study experiments it was demonstrated that plasma samples containing 50% activity of a single factor and 100% activity of all other factors (yielding 75% activity of the single deficient factor) had a normal PT and aPTT.

When two factor deficient plasma samples were combined with normal plasma samples such that the resulting mixture contained 75% activity of two coagulation factors and 100% of the rest ,the resulting PT and aPTT were prolonged.

Questioning Assumption 1

- These results indicate that prolongation of the PT and aPTT in patients with disorders of coagulation that affect multiple factors

E.g. Haemodialution, liver disease, and therapeutic anticoagulation

represent less of a reduction in factor levels than is generally appreciated. In such cases mild-moderate prolongation of PT(INR) corresponds to factor levels well within the range of normal haemostasis .

Questioning Assumption 1

1.5. The PT and aPTT were never designed to predict bleeding but were designed to analyze one aspect of haemostasis- fibrin formation.

Clinical haemostasis depends on a complex interrelationship between the blood vessel wall ,cellular elements of the blood, platelet number and function, fibrin formation and fibrinolysis.

The PT and aPTT examine only fibrin formation in response to an artificial stimulus.

Thus , as useful as these assays have been to classify disorders of fibrin formation ,they were never designed to predict in vivo haemostasis.

Questioning Assumption 2

- Does the FFP given before a procedure correct the abnormal coagulation test results?
- The intravascular concentration of different coagulation factors after transfusion ranges from approximately 40%-100%.
- As a result , the transfusion of FFP has a variable effect on the residual concentration of clotting factor proteins.
- As an average estimate in a 70 Kg recipient, 700 ml of FFP would be expected to increase the concentration of coagulation factors by 15%.

Questioning Assumption 2

- When the pretransfusion PT is longer than 30 seconds , a 15% increase in coagulation factors will dramatically “improve the PT”.
- However, when the pretransfusion PT is less than 16 seconds, a 15% increase in coagulation factors will have a trivial impact on the measured PT.
- Physicians prescribing FFP before a bedside procedure may assume that the administered plasma will "correct” the laboratory abnormality that triggered the transfusion.
- For many patients ,specially those with mild to moderate prolongations, this will not occur.

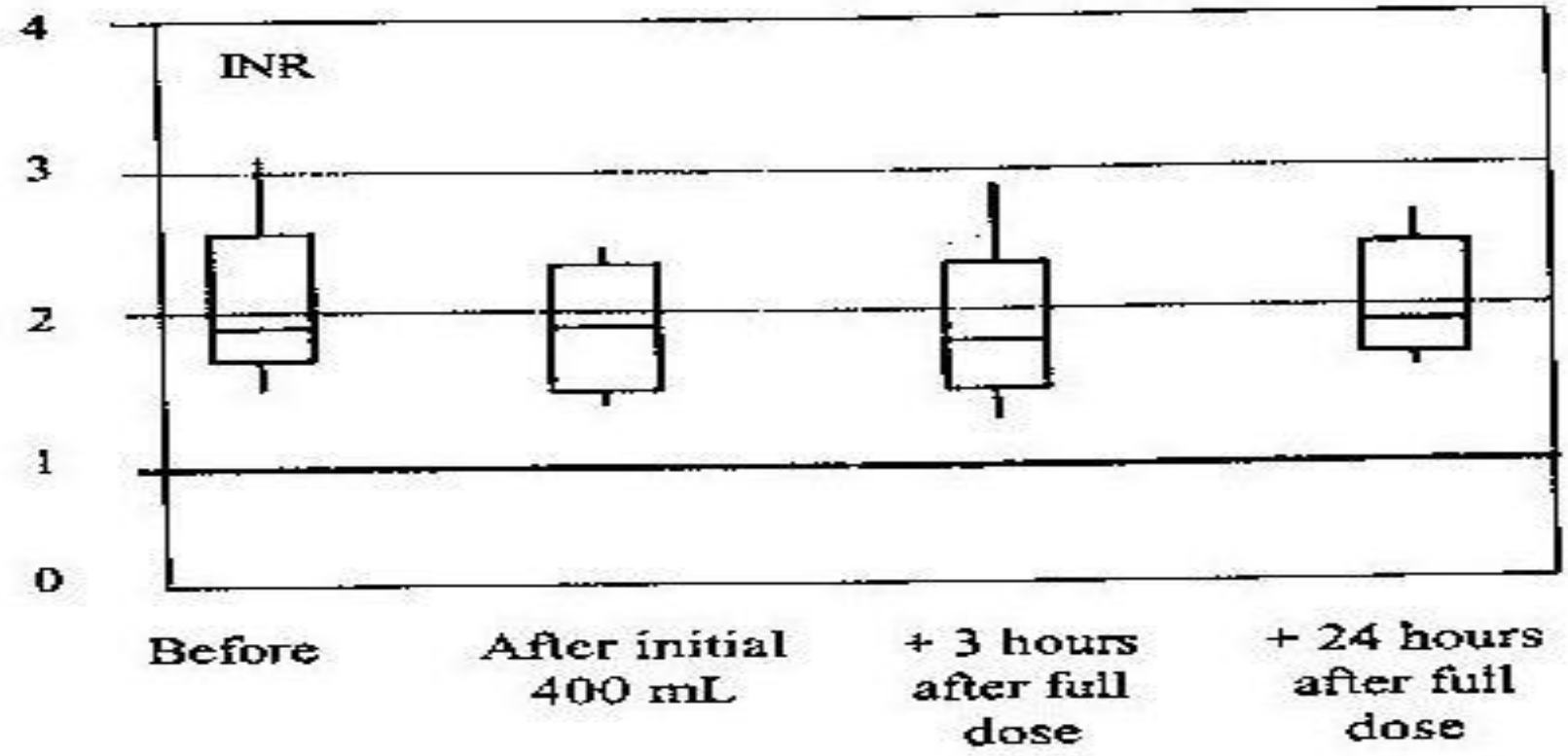
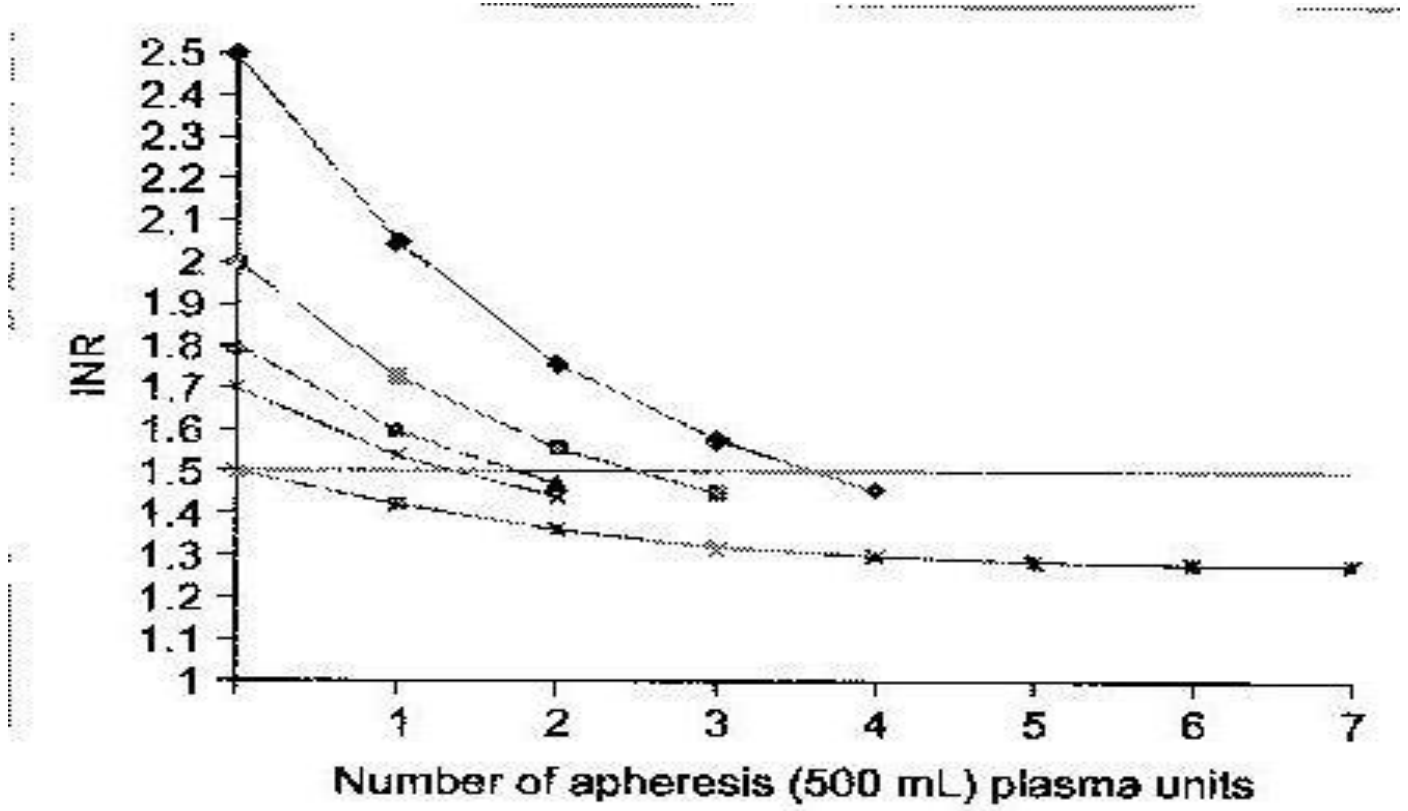
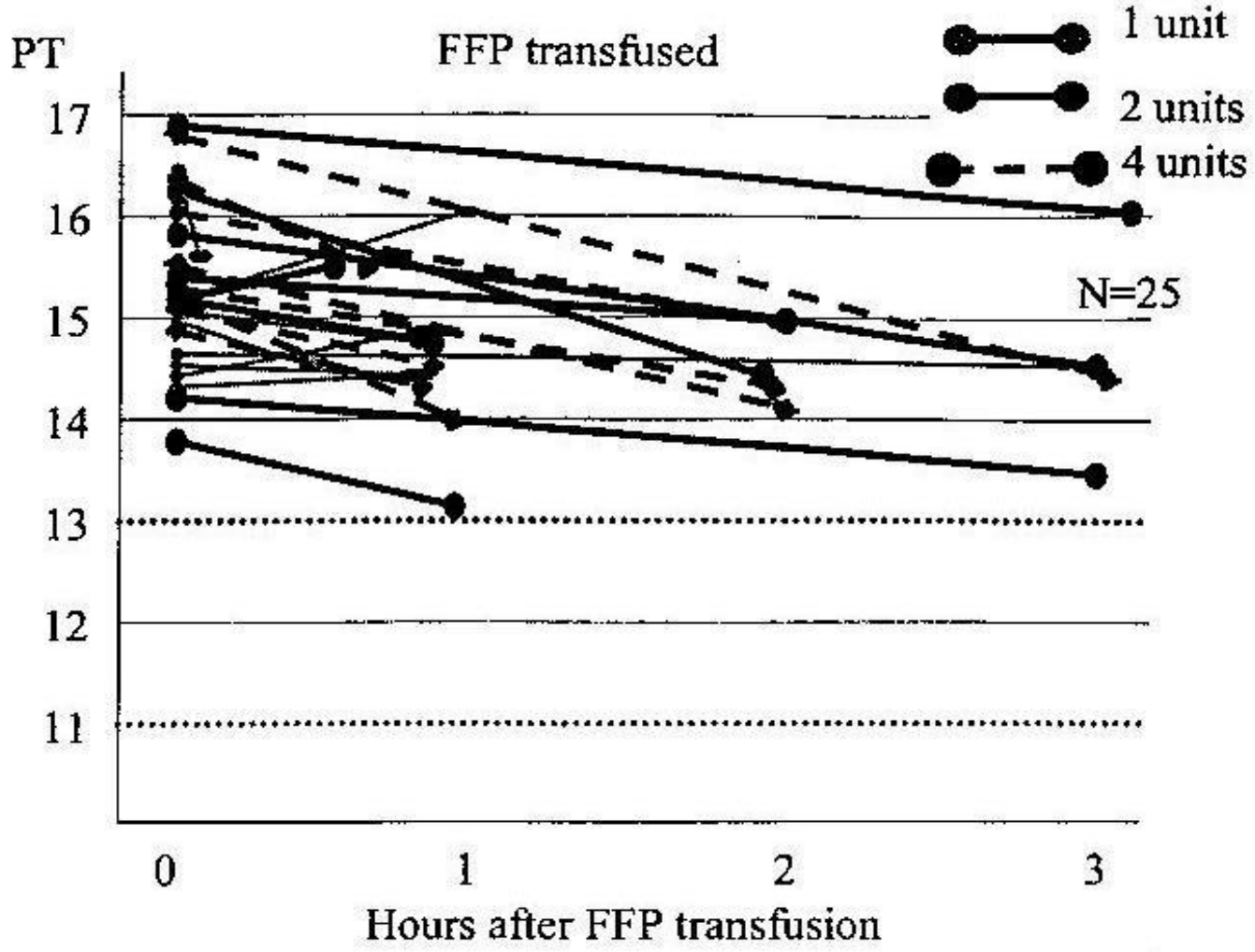


Figure 1-4. Box and whiskers plot of the effect of Fresh Frozen Plasma (FFP) transfusion on the International Normalized Ratio (INR). Patients received 12.5 mL/kg FFP. In no case did the INR correct. (Data adapted from Williamson et al.[24])



THE LARGEST REDUCTIONS IN THE INR ARE PREDICTED TO OCCUR IN RECIPIENTS WITH THE HIGHEST STARTING INRS; AS THE INR FALLS BELOW 1.5 ,CONTINUED TRANSFUSION WITH FFP WILL RESULT IN INSIGNIFICANT CHANGE IN INR, BUT THE RECIPIENT IS BEING EXPOSED TO ALL THE ADVERSE RISKS OF PLASMA THERAPY WITH NO CLINICAL BENEFIT.

Threshold response to plasma transfusion.



ure 1-5. Failure of 1-4 units to acutely correct the prothrombin time (PT) in patients with mild-to-moderate longation of the PT. (Data from Massachusetts General Hospital, Boston.)

Summary

- Clinicians commonly administer FFP to “correct “ the PT(INR) before performing an invasive diagnostic procedure.
- Without checking the effect of the FFP, the procedure is performed and the favorable outcome is *attributed to the “protective effect”* of FFP prophylaxis.
- However , had the laboratory value been checked after the FFP infusion but before the procedure, the conclusion would have been that the procedure was performed safely despite an abnormal lab test.

Questioning Assumption 3

- Will prophylactic transfusions given before an invasive procedure limit the extent of bleeding more effectively than therapeutic transfusions given after a procedure.

- From risk benefit, legal and cost benefit perspectives there are striking disadvantages to a strategy of prophylactic use of components compared with the therapeutic use of components.

Questioning Assumption 3

- A hypothetical example:
- Consider a procedure in which 1% of patients have bleeding complications.
- In hospital “A” , a prophylactic strategy of 6 units of platelets and 2 units of FFP is used for all patients who meet some “trigger value” of pre procedure lab tests.
- In hospital “B” transfusions are given therapeutically to any patients who bleeds after a procedure.
- To manage 100 such patients, hospital" A” transfuses 600 platelet units and 200 FFP units.
- In this case 99 patients receive the transfusion needlessly.

Questioning Assumption 3

- Complications resulting from any of the 792 transfusions would be difficult to defend legally.
- The single bleeding patient receives 6 platelet units and 2 FFP units- a dose not proven to be adequate to arrest bleeding.
- In contrast , hospital “B” can focus as much therapeutic blood support as needed on the bleeding patient.
- The 99 patients in hospital “B” who do not need transfusion are not subject to transfusion risk.
- In contrast to low dose prophylactic infusions, full therapeutic transfusion support of the bleeding patient is both clinically and legally defensible.

Summary

- The lowest we can correct a patient's INR using infusions of FFP is about 1.6. If any clinician orders FFP transfusions with a goal INR below this, it probably won't happen. Since transfusion of any product have risks ratio of risk vs benefit begins to fall at an INR of 1.6.Below that point the patient needs a normal temperature and good perfusion to drop their INR further.
- When deciding on the clinical approach to a particular patient, clinicians should recognize that mildly abnormal test results do not imply clinically abnormal clotting(coagulopathy) as a result of both the basic design of PT and aPTT assays and the normal physiologic reserve of hemostasis.

Summary-Ctd

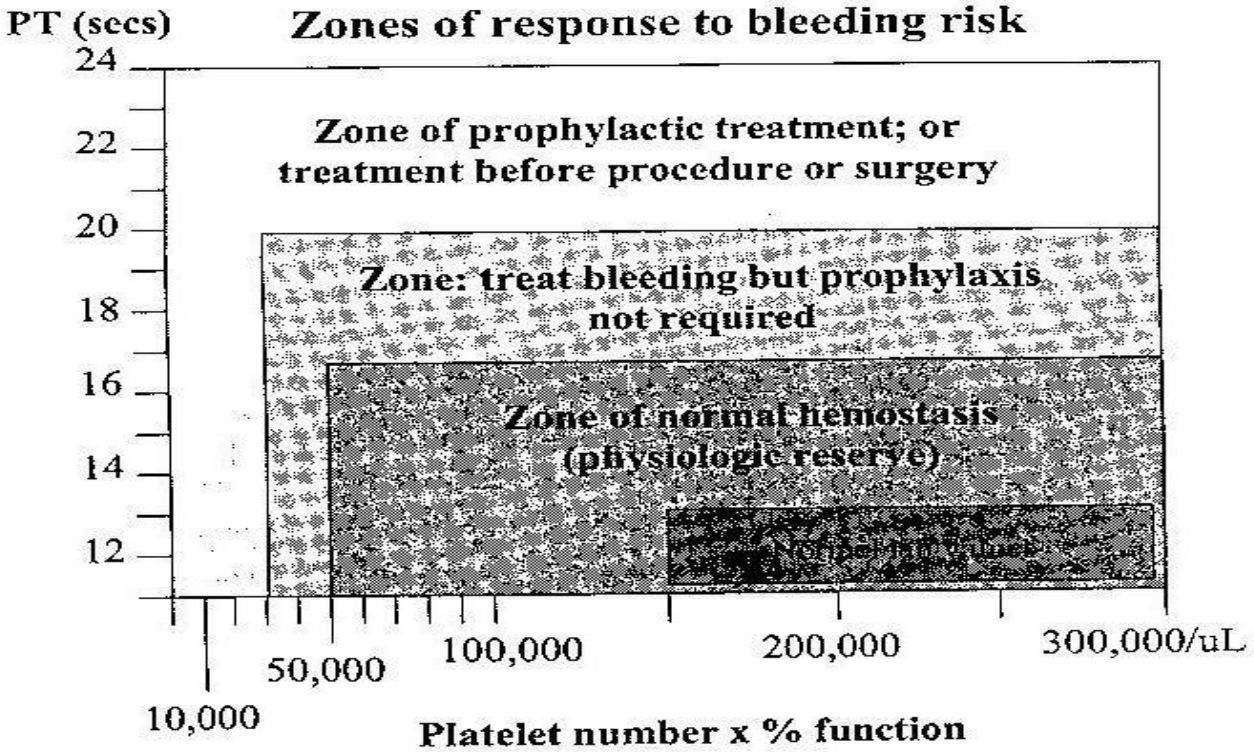


Figure 1-8. Zones of response to bleeding risk at the time of invasive procedures. The x-axis is meant to depic the product of both platelet number and functional activity. Patients with normal laboratory values are repre sented by the smallest rectangle. A large number of patients with mild-to-moderate abnormalities of prepro cedure laboratory tests are in the zone of physiologic reserve and are not likely to derive any benefit from preprocedure transfusion therapy.

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