

# Léčba protrombinovým komplexem

*- kdy, komu a jak?*

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*no conflict of interest*

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# přehled

1. koncentráty protrombinového komplexu
  2. PCC vs PPSB
  3. typy PCC
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***koncentráty  
protrombinového  
komplexu***

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# PCC

- ✓ *Prothrombin Complex Concentrate*
- ✓ krevní derivát obsahující **vitamín K** dependentní koagulační faktory
- ✓ na trhu od 60. let
- ✓ na WHO seznamu nezbytných léků

*(World Health Organization's List of Essential Medicines)*



# PCC

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- ✓ vyráběn z **lidské plasmy**, virová inaktivace
- ✓ obsahuje faktory protrombinového komplexu F II, IX, X, ev. VII
- ✓ fakult. protein C,S, antitrombin, heparin...
- ✓ hladiny cca **25x vyšší** než ve FFP
- ✓ preparáty standardizovány (kvantifikovány) na obsah **faktoru IX (IU)**
- ✓ ostatní faktory v různé koncentraci...

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***PCC***

***VS.***

***PPSB***

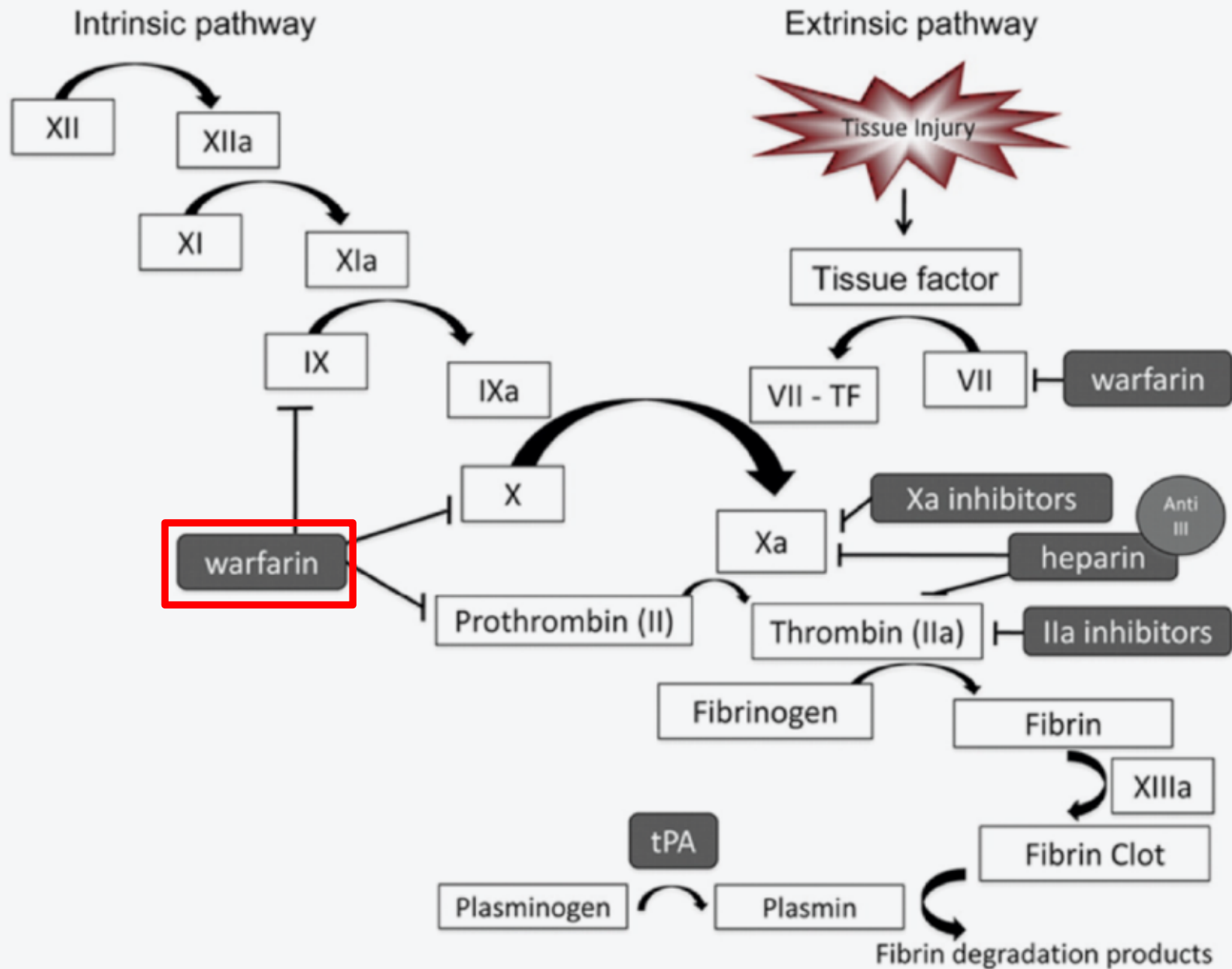
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# PCC vs. PPSB

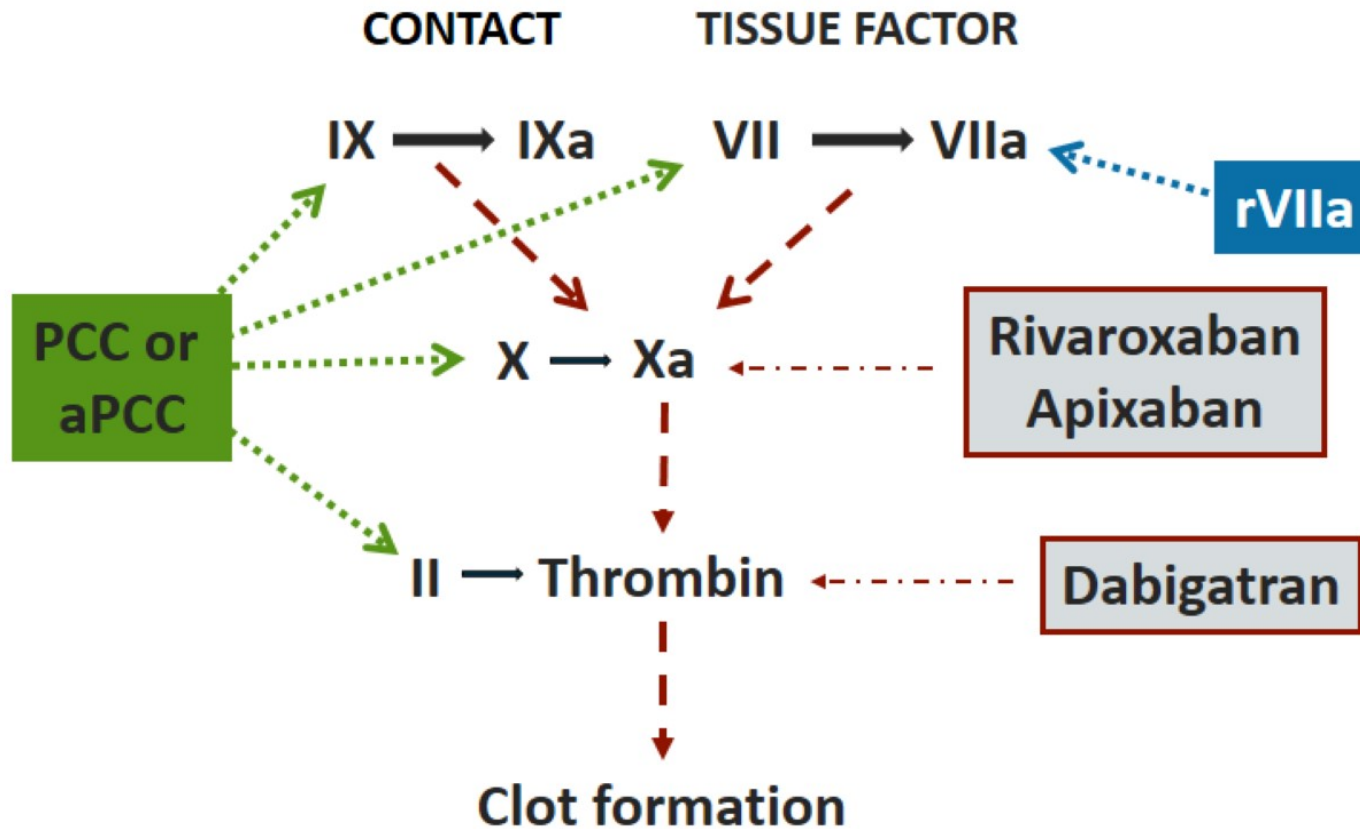
	PPSB
Faktor <b>II</b>	<b>P</b> rothrombin
Faktor <b>VII</b>	<b>P</b> rokonvertin
Faktor <b>X</b>	<b>S</b> tuart-Prowerové faktor
Faktor <b>IX</b>	antihemofilický (Christmasův) faktor <b>B</b>



# Abb.: Ansatzpunkte der Antikoagulantien in der Gerinnungskaskade



# Sites of Procoagulant Activity



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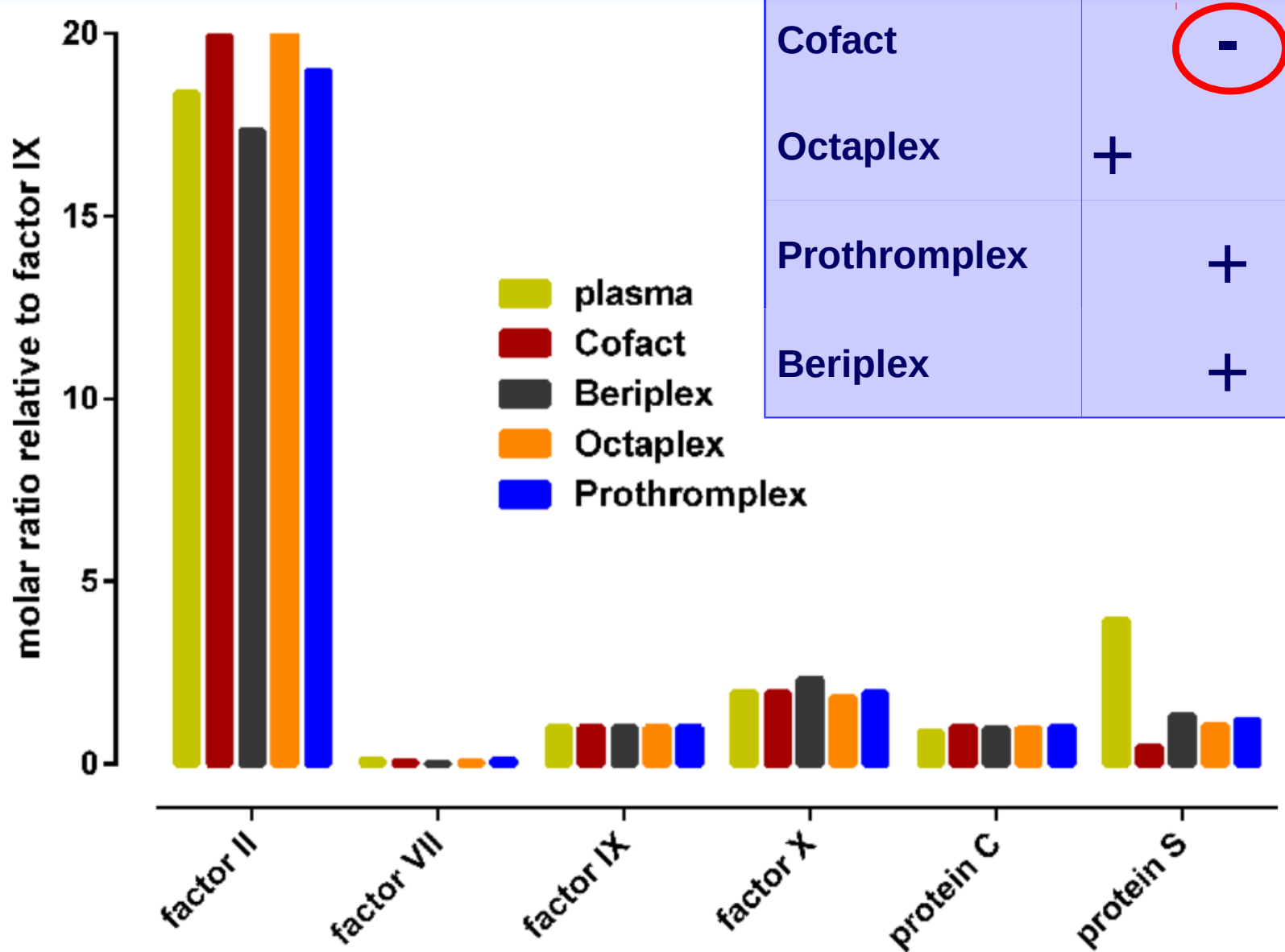
***typy***

***PCC***

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# types of PCCs

<b>type</b>	<b>abbrev.</b>	<b>brand names</b> ( <i>among others</i> )	<b>factors</b>
three-factor	(3F)PCC	Profilnine, Bebulin	II, IX, X
four-factor	(4F)PCC	Beriplex (Kcentra), Octaplex, Prothromplex, Cofact	II, VII, IX, X
activated		aPCC	Feiba



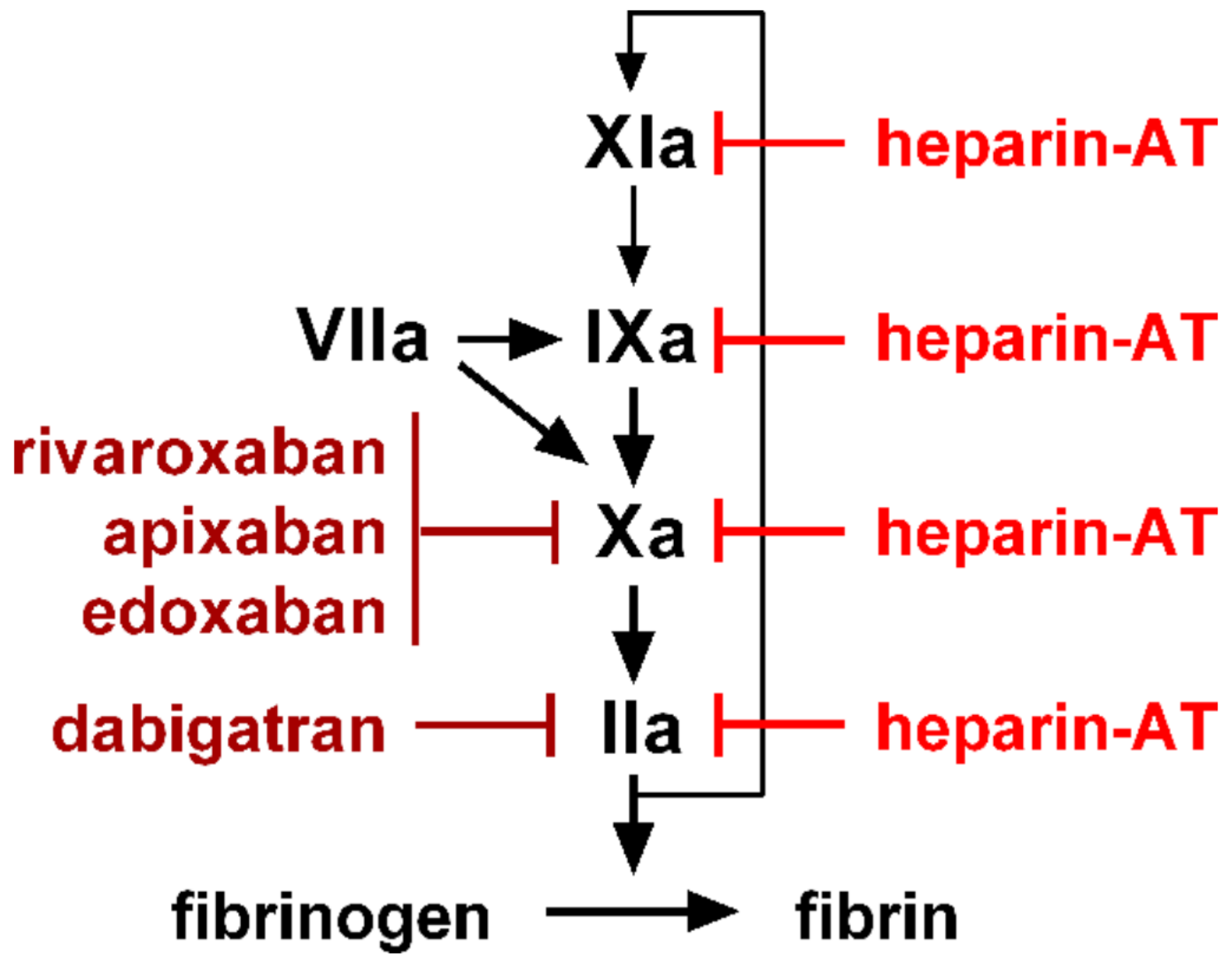
	heparin
Cofact	-
Octaplex	+
Prothromplex	+
Beriplex	+

Biochemical characteristics		PCC product			
		Cofact	Beriplex	Octaplex	Prothromplex
Specific activity	IU factor IX/mg total protein	1.7 (1.1)	4.8 (3.3)	0.9 (1.0)	1.7 (1.5)
Vitamin K-dependent coagulation proteins	mg, % of total protein	22 (23)	59 (42)	12 (14)	24 (-)
Antithrombin	IU/IU factor IX	0.01 (0.01)	0.02 (0.02)	0.004 (0.003 -0.004)	0.03 (0.03-0.06)
Heparin supplement	IU/IU factor IX	<0.01 (<0.01)	0.03 (0.02 -0.03)	0.25 (0.15 -0.88)	0.38 (0.15-0.72)
Thrombin generation	ETP, % of control plasma	217	162	71	18

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***heparin***

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# heparin - cave

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- ✓ heparinem indukovaná trombocytopenie (HIT)
- ✓ heparin působí antikoagulačně
- ✓ PCC v dávce 50 IU/kg t. hm. znamená dávku až 36 IU/kg t. hm. heparinu!
- ✓ half-life time:
  - heparin 30-60 min
  - faktor II 45-66 h
  - faktor VII 4-7 h
  - faktor IX 14-68 h
  - faktor X 24-41 h

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***indikace***

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## indikace

zrušení účinku antagonistů vit. K (warfarin, ...)

vrozený deficit koagulačních faktorů (IX, II, VII, X, ...)

získaný deficit koagulačních faktorů (hepatopatie, ...)

závažná koagulopatie, život ohrožující krvácení

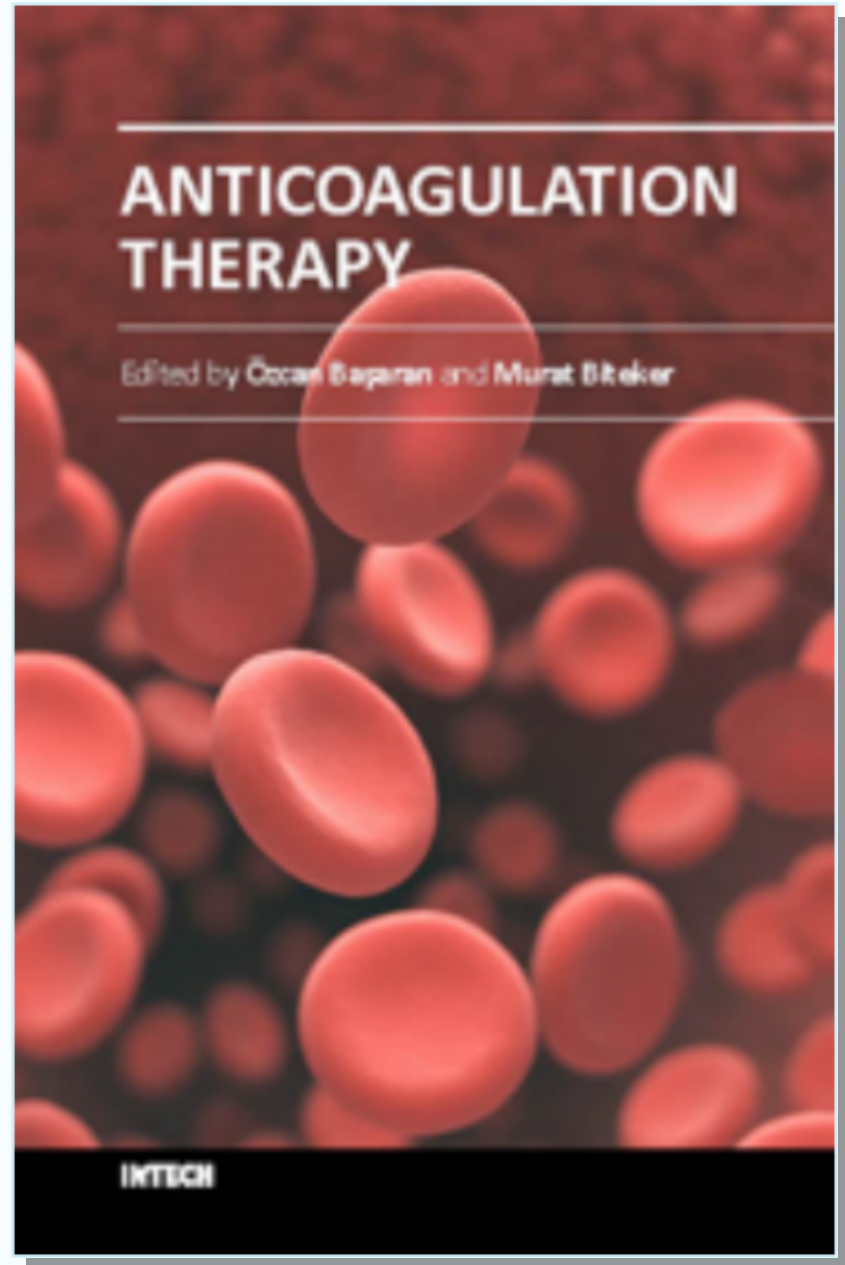
zrušení účinku *NOACs*

Concentrate	Major functional component(s)	Indications*	Off-label use/remark
4F-PCC	Coagulation factors II, VII, IX, X	<p>Treatment and perioperative prophylaxis of bleeding</p> <p>– in acquired deficiency of PCC factors, such as deficiency caused by treatment with vitamin K antagonists</p> <p>– in congenital deficiency of the vitamin K-dependent coagulation factors when purified specific coagulation factor products are not available</p>	<p>Treatment of trauma-induced coagulopathy</p> <p>Treatment of bleeds in patients with liver disease</p> <p>Reversal of anticoagulation by direct factor Xa and thrombin-inhibiting oral anticoagulants (evidence based on several bleeding models in animals and human volunteers; substantial clinical evidence is lacking)</p>

<p>3F-PCC</p>	<p>Coagulation factors II, IX, X</p>	<p>Prevention and control of bleeding in <u>hemophilia B</u> patients</p>	<p>Anticoagulant reversal agent          – for <u>vitamin K antagonists</u> (4F-PCC is superior to 3F-PCC)          – for <u>direct oral thrombin</u> and <u>factor Xa inhibitors</u> (evidence based on a few bleeding models in animals; substantial clinical evidence is lacking)</p>
<p>Activated-PCC</p>	<p>Coagulation factors II, IX, X, VII-activated form</p>	<p>Treatment and prophylaxis of bleeding in patients (hemophilia A and B as well as non-hemophiliacs) with inhibitors to factors VIII or IX</p>	<p>Anticoagulant reversal agent          – for vitamin K antagonists (evidence based on a limited number of clinical studies)          – for direct oral thrombin and factor Xa inhibitors (evidence based on bleeding models in animals; substantial clinical evidence is lacking)</p>

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Anticoagulation Therapy  
*Basaran, Biteker et al.,  
2016*



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***PCC***

***VS.***

***FFP***

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	<b>FFP</b>	<b>PCC</b>
<b>effect</b>	+	++
<b>need for blood group compatibility</b>	+	-
<b>bed side test</b>	+	-
<b>start of application</b>	slow	fast
<b>duration of application</b>	slow	fast
<b>volume</b>	large	minimal
<b>risk of TACO</b>	+	-
<b>risk of TRALI</b>	+	-



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***dávkování***

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PCC **1 IE/kg** t. hm. zvýší aktivitu faktorů cca o **1-2%**

*"despite experience, dosing is still a matter of debate "*

INR is a frequently used parameter to guide PCC dosing

a target INR of 1.3 or 1.5 is most often used

there are different dosing regimens

differences between clinical outcome are not reported

**25 IU/kg for baseline INR of 2–3**

**35 IU/kg for baseline INR of 4-6**

**50 IU/kg for baseline INR of > 6**

good to excellent hemostasis was observed in 72–100%

Česká společnost anesteziologie, resuscitace a intenzivní medicíny  
Česká společnost intenzivní medicíny  
Česká hematologická společnost  
Česká společnost pro trombózu a hemostázu  
Společnost pro transfuzní lékařství

## **DOPORUČENÝ POSTUP PRO ŽIVOT OHROŽUJÍCÍ KRVÁCENÍ**

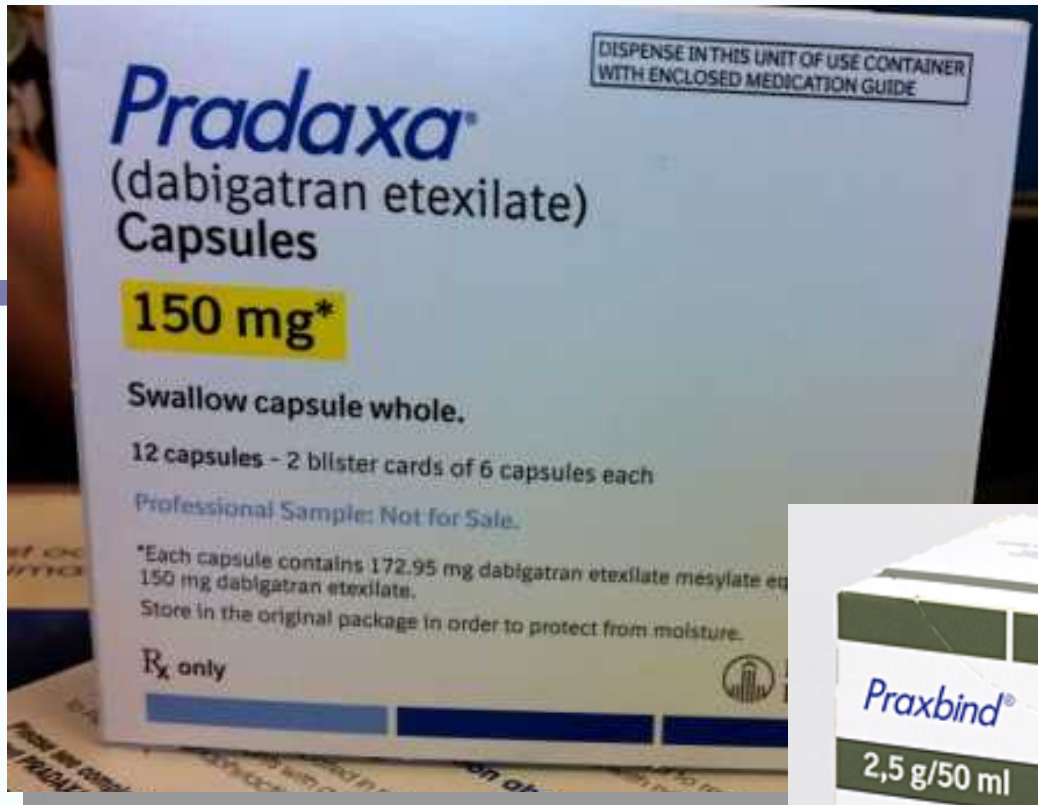
*Mezioborové konsensuální stanovisko*

### ***Koncentrát faktorů protrombinového komplexu (PCC)***

Podání PCC je doporučeno u pacientů léčených antagonisty vitamínu K nebo u pacientů s krvácením způsobeným deficitem faktorů, které preparát obsahuje.

Podání PCC je doporučeno konzultovat s hematologem.

Úvodní doporučovaná dávka je 20-25 IU/kg (*cca 1800 IU*).



B., B.S., Stephan Glund, Ph.D., Peter  
arm.D., Menno V. Huisman, M.D., Ph.D.,  
er, M.D., Jerrold H. Levy, M.D., Frank W.  
Bushu Wang, Ph.D., Chak-Wah Kam, M.D.,

## CONCLUSIONS

Idarucizumab completely reverse  
dabigatran within minutes. (Fund  
VERSE AD ClinicalTrials.gov nur



# *reversal agents*

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- **andexanet alfa**

- Fxa mimetic with high affinity binding for Xa inhibitors and LMWH
- randomized, double-blind, placebo-controlled phase 4 studies: ANNEXA™-A (with apixaban) and ANNEXA™-R (with rivaroxaban) finished

- **PER977**

- synthetic small molecule
- nonspecific binding to Xa inhibitors and thrombin inhibitors



... děkuji Vám za pozornost