evropský sociální fond v ČR
EVROPSKÁ UNIE
MINISTERSTVO ŠKOLSTVÍ, MLÁDEŽE A TĚLOVÝCHOVY
OP Vzdělávání pro konkurenceschopnost
INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

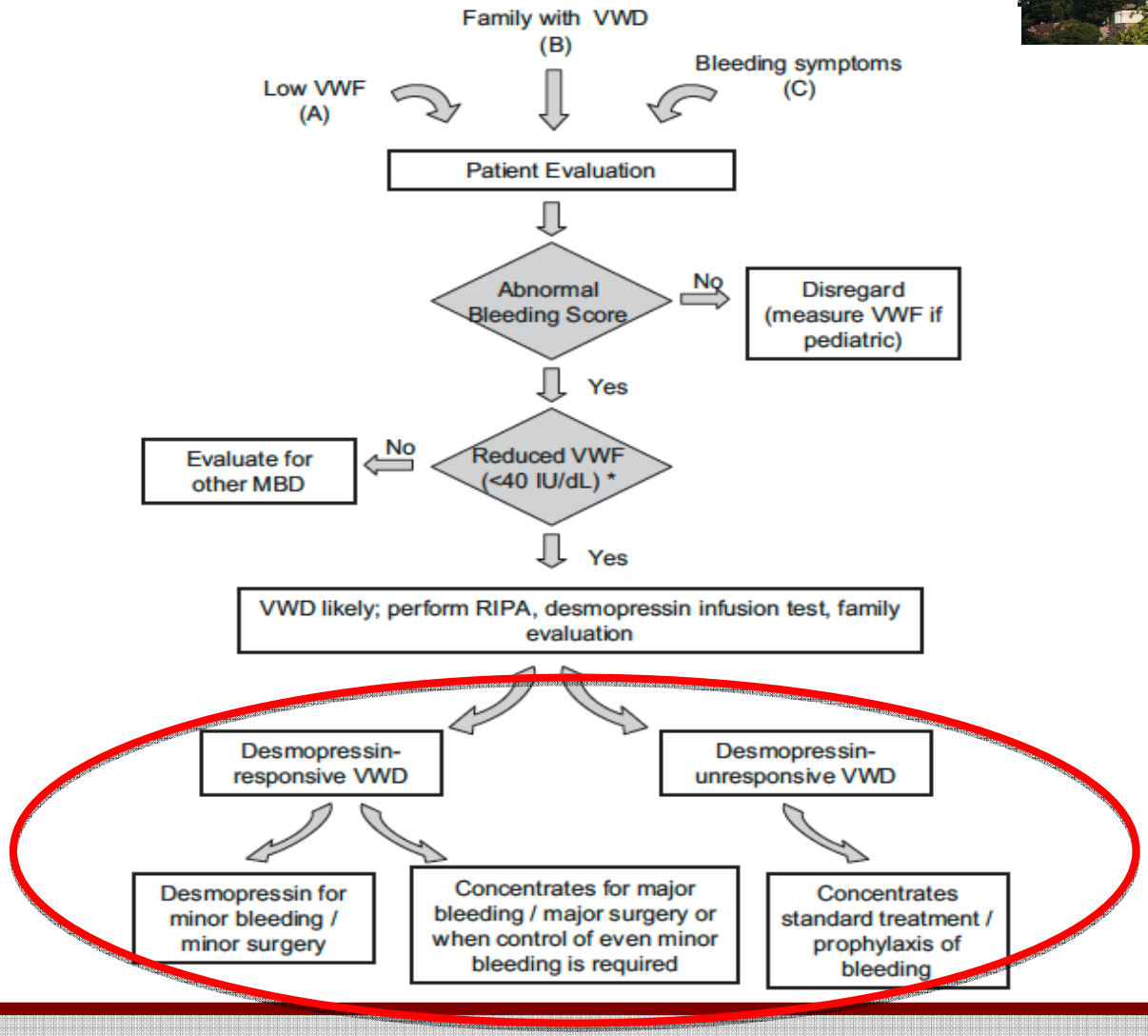
Do we need FVIII for the treatment of vWD?
Potřebujeme faktor FVIII k léčbě vWD?

Jan Blatný

Oddělení dětské hematologie
FN Brno, CZ

Diagnostic/therapeutic algorithm for vWD

(by Rogedhiero et al., Blood 2009)



Classification of vWD

Type	Description
1	Partial quantitative deficiency of VWF
2	Qualitative VWF defect
2A	Decreased VWF-dependent platelet adhesion with selective deficiency of high-molecular-weight multimers
2B	Increased affinity for platelet GPIb
2M	Decreased VWF-dependent platelet adhesion without selective deficiency of high-molecular-weight multimers
2N	Markedly decreased binding affinity for FVIII
3	Virtually complete deficiency of VWF

- Patients with good response to DDAVP
- Patients with poor response to DDAVP

VWD types are defined as described in Sadler JE, Budde U, Eikenboom JC, Favaloro EJ, Hill FG, Holmberg L, Ingerslev J, Lee CA, Lillicrap D, Mannucci PM, et al. Update on the pathophysiology and classification of von Willebrand disease: a report of the Subcommittee on von Willebrand Factor. J Thromb Haemost 2006 Oct;4(10):2103–2114.

DDAVP – Come back home!

ČESKOSLOVENSKÁ SOCIALISTICKÁ REPUBLIKA
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POPIS VYNÁLEZU K AUTORSKÉMU OSVĚDČENÍ

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Autor vynálezu

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ROZTOKY

(54) **Vasopresinová analoga a způsob jejich přípravy**

The DDAVP “Czechllenge”

- DDAVP for the treatment of vWD not available in CZ!!!!!
  - Despite the fact, that DDAVP is Czechoslovakian patent (author Ing., Dr. Zaoral, Czech Academy of Science) from 60s and has been firstly manufactured in 1967 by Spofa

- Solution suggested:
  - Urgent need for availability of this efficient and cheap medication for people with vWD in CZ

Treatment options in vWD

Federici. Advances in Haematol, 2008

- DDAVP
  - **0,3 ug/kg in 50 ml of normal saline during 30 mins**
    - Increase of vWF and FVIII 3-5x times
    - Efficient for up to 6-8 h
    - Can be repeated up to 2-3x times
    - Prior “clinical test” needed
      - Type 2B – can induce transient thrombocytopenia
      - DDAVP does NOT work in severe type 1,2 and in type 3
      - Ions in patients’ plasma to be monitored (Na, Cl)!!!
- Factor concentrates for those who cannot be treated with DDAVP
- Other treatment
  - Antifibrinolytics (tranexamic acid) etc…
    - Minimizes menstrual blood loss significantly (1 g q6-8 h)
  - OC beneficial for girls/women with excessive menorrhagia

Do we need FVIII for vWD patients?

- NOT for those, who could be treated with DDAVP
- Unfortunately, this is not the case in our country in these days.

Treatment options in vWD

Federici. Advances in Haematol, 2008

- FVIII/VFW factor concentrate
  - Different concentrates – different vWF/FVIII ratios
  - Different purification of the concentrates
    - Medium purity
    - High purity
    - Recombinants
  - **Theoretical risk o VTE?**
    - Repeated high doses during surgeries in adults
    - Daily FVIII level monitoring recommended to keep FVIII within 50-150%
  - Minimal effective level of vWF:RiCo during treatment?
    - Probably over 30%
  - *Need for balancing between efficient vWF level and "prothrombotic" level of FVIII?!?! (in some patients)*
  - **May be administered prophylactically**
    - Mainly in type 3 patients

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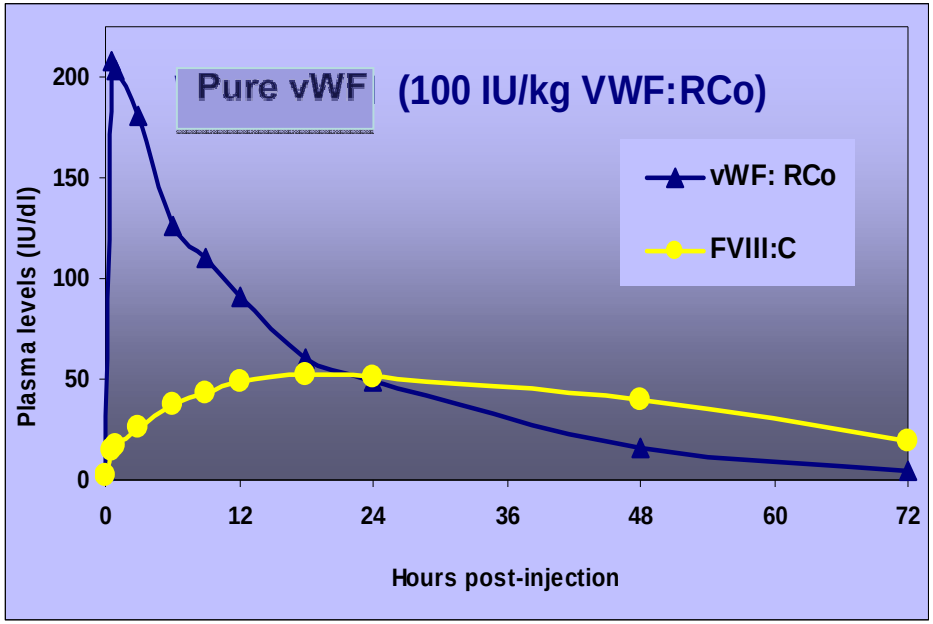
Endogenous FVIII synthesis in vWD patients

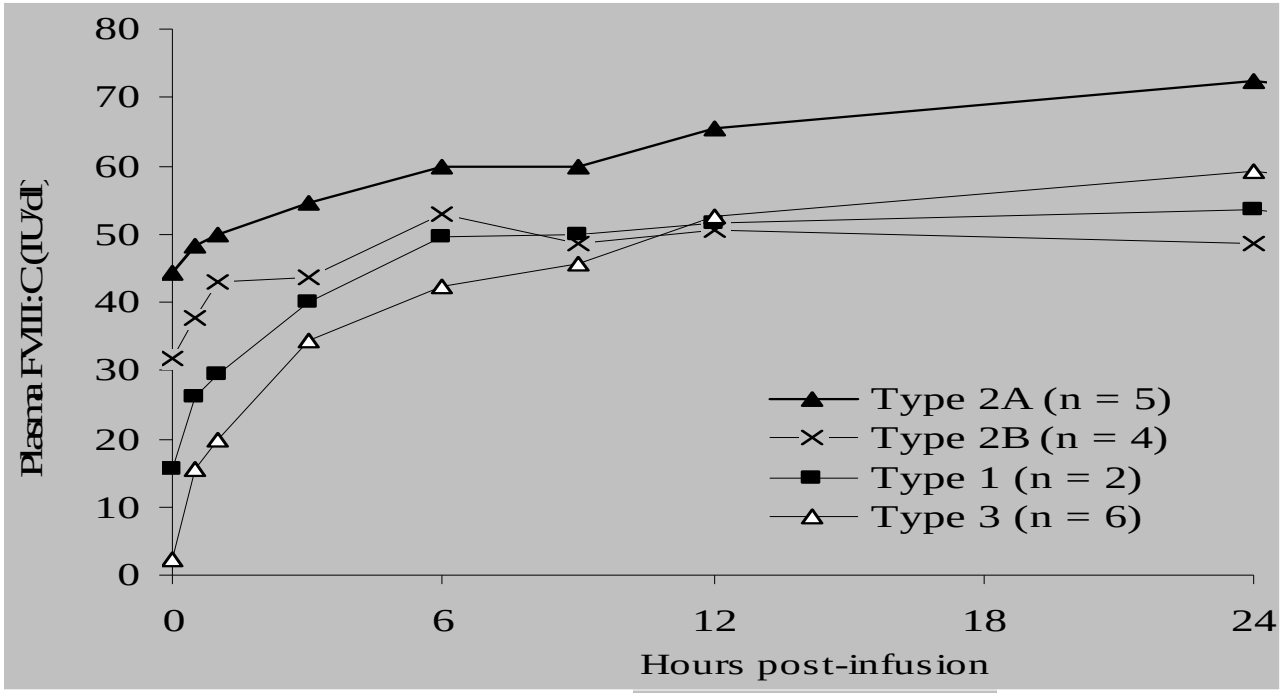
- **VWD patients :**
  - **The endogenous ability to synthesize FVIII is intact**
  - **In most situation they do not need exogenous FVIII**



➲ **Pharmacokinetics in 8 type 3 patients (mean)**

J. Goudemand *et al.*, J Thromb Haemost, 2005;3:2219-27

Description of endogenous FVIII rise



J. Goudemand *et al.*, J Thromb Haemost, 2005;3:2219-27

Do we need FVIII for vWD patients?

- NOT, unless emergency event!
- However, in general FVIII/vWF concentrates are effective enough with no harm.

- Pure vWF concentrates useful especially for
  - People/situations with increased risk of thrombosis
  - Elective procedures
  - Prophylaxis

Our experience with pure vWF (Willfact) in vWD type 3 girl on prophylaxis

- Rationale for switching her to Willfact
  - Lower and less frequent dosing
  - Better quality of life
  - More “physiological” way of treatment
  - Less to inject

- Dosing and pharmacokinetics
  - 17 IU/kg of vWF twice per week
  - Every other day (at least 3x per week) during periods
  - Response to the treatment (after 72h wash out period)
    - FVIII 17% (from 2%)
    - vWF:RiCo 21% (from 3%) - suboptimal
    - vWF Ag (LIA) 40% (from 4%)

Effect of the treatment in our patient

- No spontaneous bleedings
- Periods well controlled
- Less frequent administration
  - Will be able to administer via peripheral vein
- Good QoL

- Further steps??
  - Keep the low frequency of drug administration
  - Increase the dose (body weight dependent, clinical symptoms)
  - Keep her on convenient prophylaxis

Thank you for your attention!!