BLEEDING DISORDERS in WOMEN

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BLEEDING DISORDERS in WOMEN

- Physiopathology: which bleeding disorders can be seen in women?
- Clinics: consequences of bleeding disorders in women
- Therapeutic approaches

Physiopathology: which bleeding disoders can be seen among women?

- Congenital
  - Primary haemostasis disorders
    - Congenital platelet defects
      - Glanzmann disease, Bernard-Soulie disease, other
      - Congenital thrombocytopenia: amegacaryocyitic, absent radii…
    - Willebrand disease

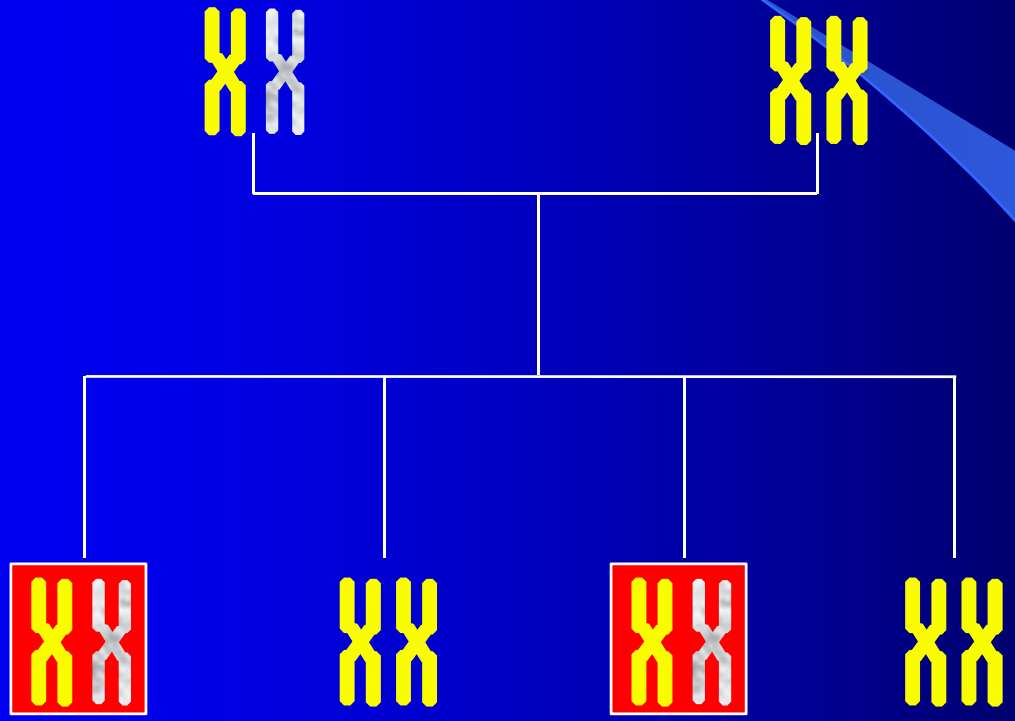
Physiopathology: which bleeding disoders can be seen among women?

- Congenital
  - Primary haemostasis disorders
  - Coagulation defects
    - Homozygous or compound heterozygous for rare coagulation disorders: F VII, FX, FV, F II, F XI, afibrinogenemia
    - Hemophilia (rare): homozygous, Turner + hemophilia
    - Hemophilia carriers: lyonisation

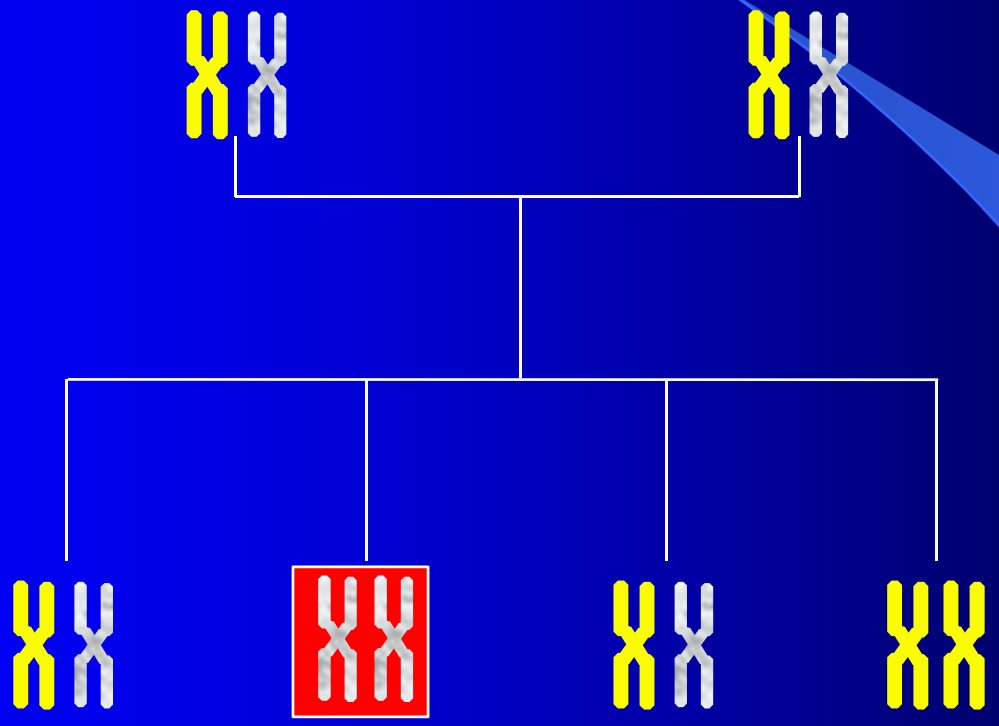
HEMOPHILIA: Lyonisation

- **Lyonisation** refers to random inactivation of an X-chromosome in the cells of females.
- Due to lyonisation, adult females may have **low anti-hemophiliac factor level** and suffer from bleeding disorders
- Hemophiliac daughters are more common than they once were, as improved treatments for the disease have allowed more hemophiliac males to survive to adulthood and become parents.

WILLEBRAND DISEASE: AUTOSOMIC DOMINANT

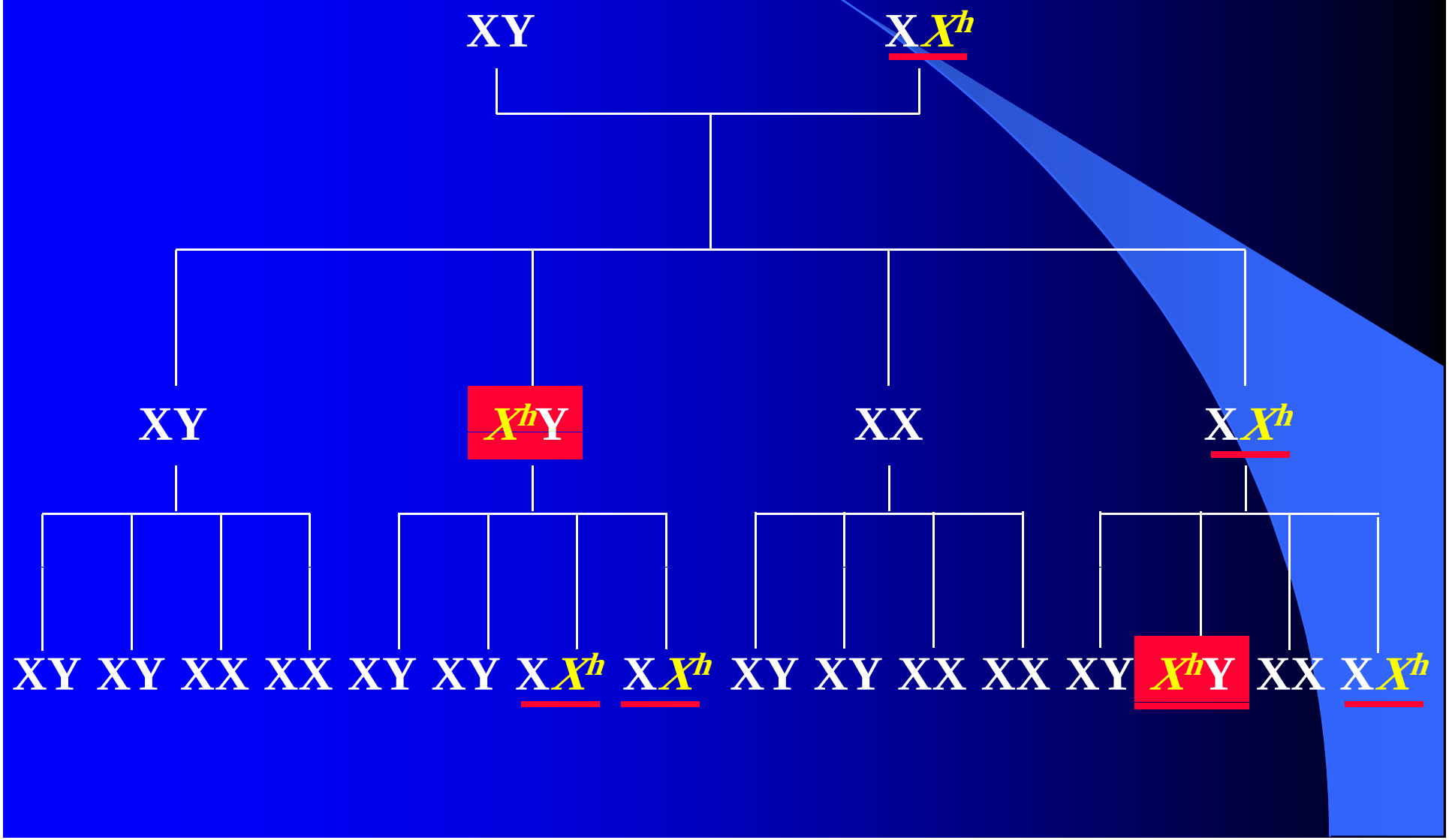


RARE COAGULATION DISORDERS: AUTOSOMIC RECESSIVE



HEMOPHILIA:

X-LINKED RECESSIVE



Physiopathology: which bleeding disoders can be seen among women?

- Congenital
  - Primary haemostasis disorders
  - Coagulation defects
- Acquired
  - All acquired haemostasis disorders can be seen:
    - ITP, acquired hemophilia or willebrand, diseases of liver or kidneys, DIC, drug-induced disorders
  - They may rise the same problems

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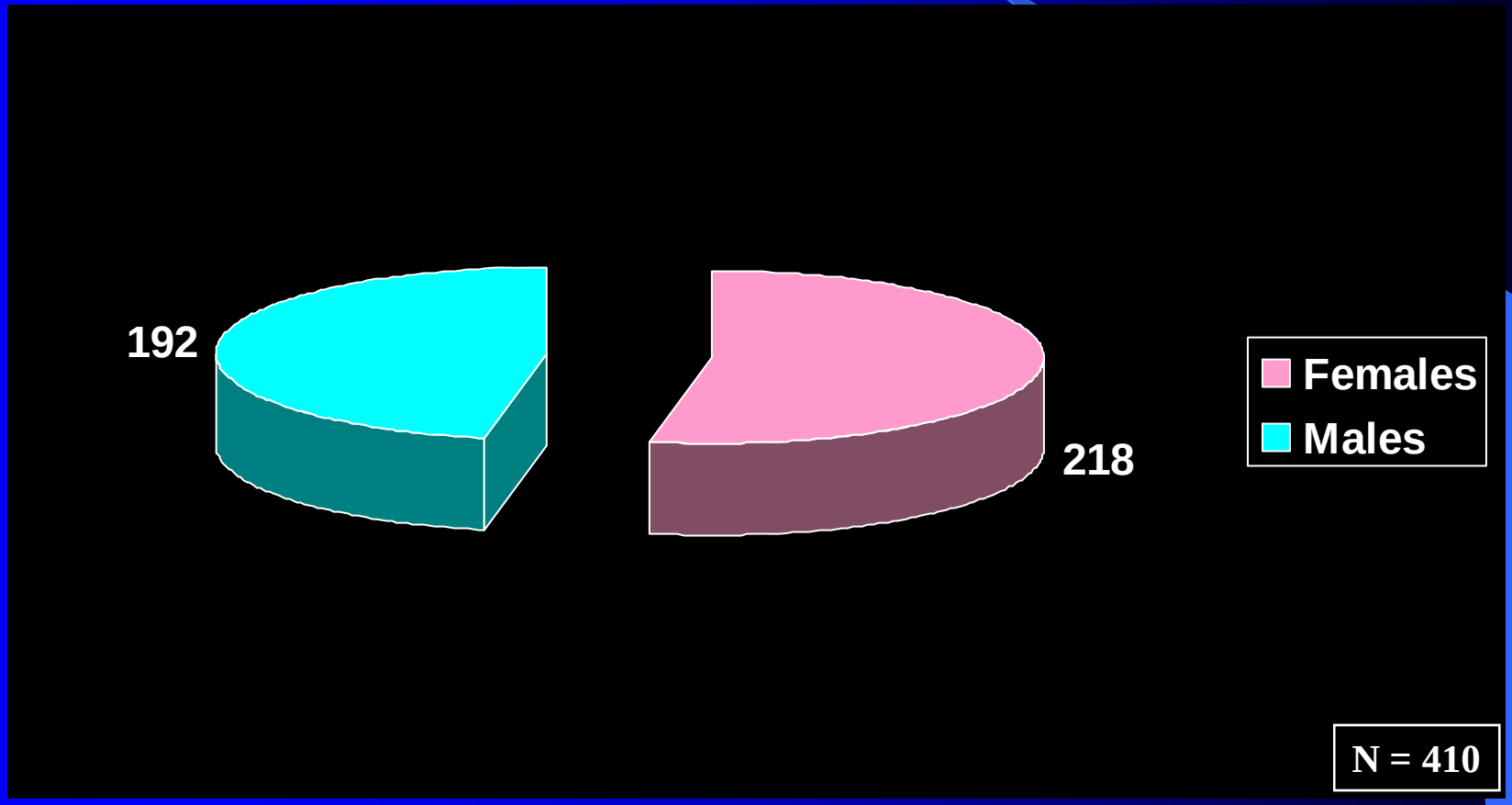
Clinics: consequences of bleeding disorders in women

- Problems seen equally among men and women
- Specific problems
  - Menorragia, pregnancy

EXAMPLE of FACTOR VII DEFICIENCY



From International Registry on F VII

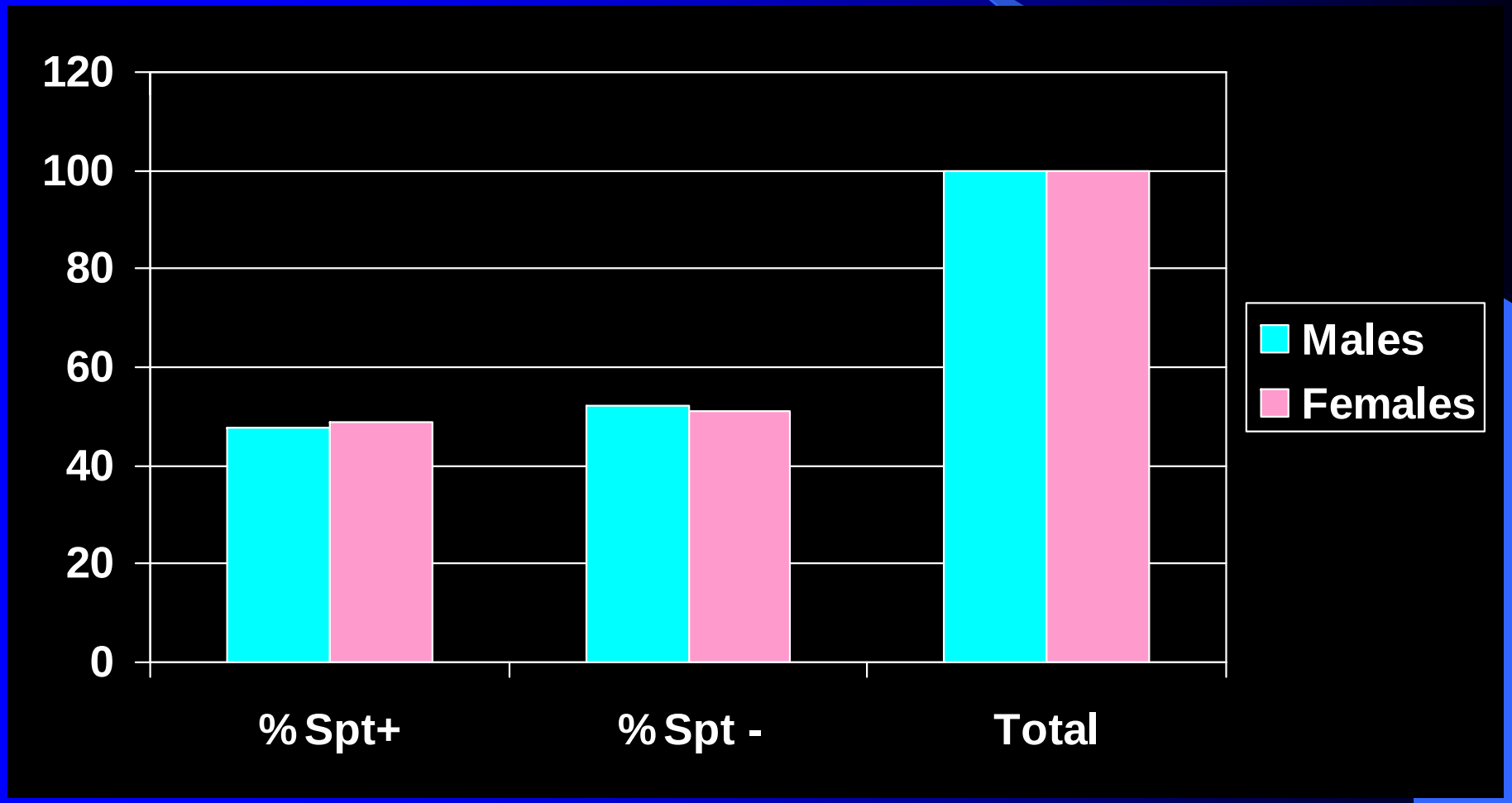
Symptoms in factor VII deficiency males vs females

F VII DEFICIENCY: Clinical picture

Clinical picture	N	%
Asymptomatic	23	10.8
Symptomatic	189	89.2
Epistaxis	84	39.6
Easy Bruising	62	29.2
Menorrhagia	45	21.2
Gum Bleeding	39	18.4
Hemarthrosis	21	9.9
Muscle Hematomas	20	9.4
GI Bleeding	14	6.6
Chronic Arthropathy	14	6.6
Hematuria	11	5.2
Chronic Synovitis	7	3.3
Thrombotic Episodes	7	3.3
CNS Bleeding	6	2.8

From International Registry on F VII

Symptoms in factor VII deficiency males vs females after excluding menorrhagia



BLEEDING DISORDERS in WOMEN: The problem of Menorrhagia

- Frequently the main – the alone – symptom
- Raises frequently difficulties concerning
  - Diagnosis
    - When can we considere that menarche are excessive?
    - Consultation of haematology are not appropriate to speak about menorrhagia
  - Severity
  - Treatment

BLEEDING DISORDERS in WOMEN: The problem of Menorrhagia

- **Diagnosis and severity**
  - Different scores have been proposed
  - Difficult to apply in current practice
- **Evaluation of the consequences could be considered**
  - Subjective consequences: scale as used for pain
  - Biological aspect: ferritinemia, MCV, MCH, anemia
  - Therapeutic aspect: antecedents of transfusion, iron treatment, minor or major surgery (hysterectomy)

BLEEDING DISORDERS in WOMEN: PREGNANCY

- **Pregnancy raises other problems**
  - At least 2 questions from the patient (and the doctors)
    - Is pregnancy possible despite haemorrhagic diathesis?
    - Risk for the baby to have the same pathology
  - The answers depend on the type of pathology
  - Some congenital hemorrhagic disease are associated with recurrent abortion
    - Afibrinogenemia, F XIII deficiencies
  - Risks for the newborn in case of severe deficiencies: F VII, F X, F XIII : cord bleeding, cephalhematoma or intracerebral bleeding

FACTOR XI DEFICIENCY
The problem of pregnancy

- Salomon et al. *Blood Coag Fibrinol 2005*
  - 85 vaginal delivery adn 8 cesarians without substitutive treatment
  - 69.4% : no bleeding
  - 30.6%: hemorrhage (no correlationwith genotype or F XI plasma level)
  - Thus the authors do not recommend systematic treatment : on-demand if bleeding occur

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BLEEDING DISORDERS in WOMEN: Therapeutic aspects

- **Emergency:**
  - Diagnosis unknown: infusion of platelets and FFP bring all the components necessary to hemostasis
  - Diagnosis is known: infusion of the missing factor
    - Thrombocytopenia, thrombopathy: platelets transfusion
    - Willebrand disease: F W concentrate or desmopressin
    - Afibrinogenemia: fibrinogen concentrate or FFP
    - F II or VII or X: PCC or FFP
    - F IX or F VIII: specific concentrate
    - F V: FFP
    - F XI: Hemoleven™ of FFP

BLEEDING DISORDERS in WOMEN: Therapeutic aspects

- **Treatment of consequences**
  - Iron therapy, transfusion
- **Specific treatments**
  - Willebrand disease
    - Desmopressin (IV or inhalation)
    - Estrogens increase vWF plasma levels
    - Willebrand factor concentrates
  - Carriers of hemophilia with bleedings: desmopressin
  - Factor XI deficiency: tranexamic acid
  - Factor XIII deficiency: Fibrogammin

BLEEDING DISORDERS in WOMEN: Therapeutic aspects

- **Non specific treatment**
  - Tranexamic acid can be used in nearly all hemorragic diathesis
  - Desmopressin
- **Symptomatic treatments**
  - Menorragia
    - Hormone therapy leading to stop menstruation
  - Pregnancy
    - Rest, prophylaxis

BLEEDING DISORDERS in WOMEN: CONCLUSIONS

- While women are not exposed to hemophilia (with some exceptions), bleeding disorders are frequent in women
- They raise some specific problems, mainly menorrhagia and pregnancy
  - Menorrhagia are frequently very difficult to manage
  - For pregnancy, consider the risks of recurrent abortions or hemorrhagic complication for the newborn