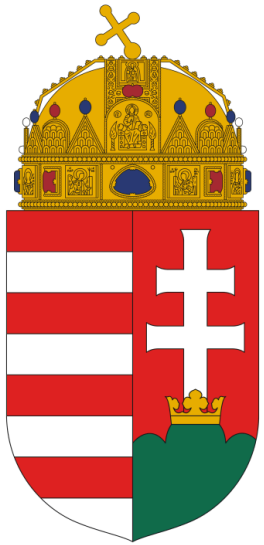
Hemophilia care in Hungary



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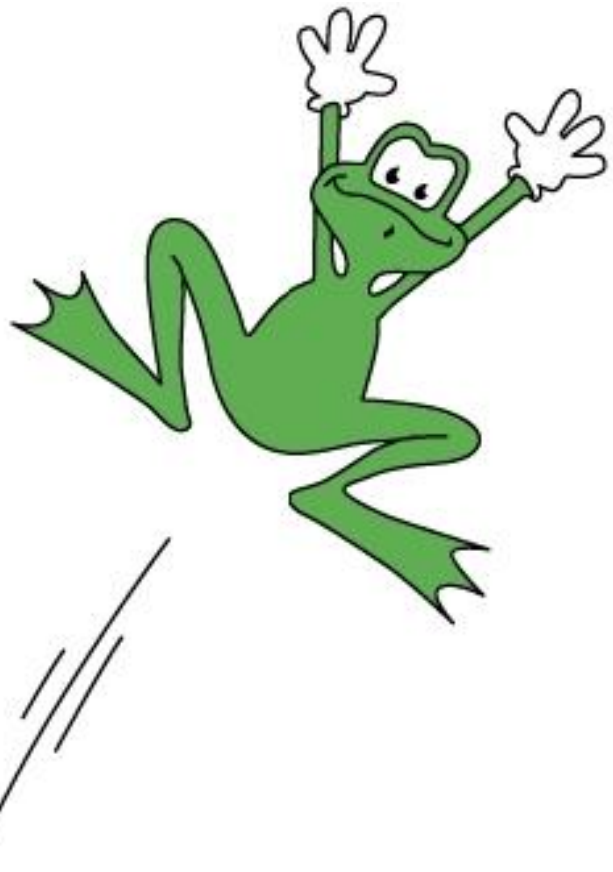
Transfusiology Department

Development of factor supply for hemophilia is a successful story in Hungary.



2010:

FVIII use per capita: 7,2 IU (18-fold increase)

Before 1990:

FVIII use per capita: 0,4 IU

It was a long way with many difficulties.

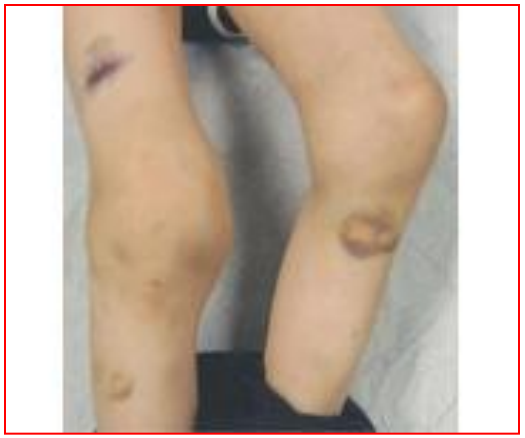
The cooperation of doctors, patients and national healthcare agencies was necessary to the success.

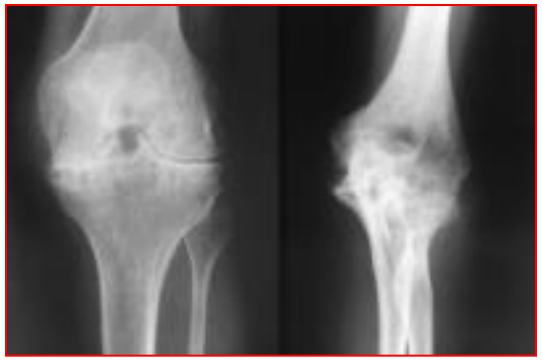
Characteristics of hemophilia care in Hungary before 1990

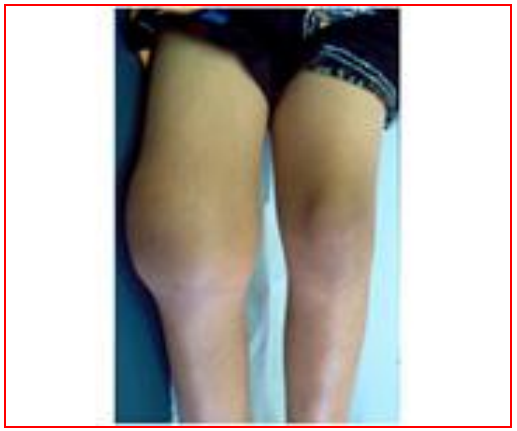
- **No systemic organisation of hemophilia care**
  - **Patients were treated in local blood transfusion centres or internal medical clinics**
- **No commercial factor concentrates**
  - **Predominant source of FVIII/IX was domestic (whole blood, cryoprecipitate, FFP, PCC) – non-virus inactivated products**
- **No guidelines**
- **No registry**
- **No home care**
- **No prophylaxis**
- **No ITI**
- **No patients' organization**

Consequencies:

- **No the same level of treatment in different hemophilia treatment centers**
- **High rate of viral infections among patients with hemophilia (HCV: 90%),**
  but low rate of HIV infection (32 patients, 19 still alive)
- **Patients were „undertreated”**
  (severe pain, joint deformities, arthropathy, disabilities, death in childhood or early adult life, no possibilities of surgery, ITI)







Changes of hemophilia care in Hungary after 1990

- **Political, economical changes**
- **Organized hemophilia care: regional network of hemophilia treatment centers in 1992.**
- **Safe factor concentrate supply**
- **Establishment of a nationwide register**
- **Hungarian Haemophilia Society was founded in 1990.**
- **Education of medical staff dealing with people with hemophilia**
- **Introduction of home treatment (Jan. 1999)**
- **Guidelines (same treatment to all patients throughout the country)**
- **Possibilities:**

  orthopedic management, major operations, ITI, prophylaxis, treatment of infectious complications (HCV, HIV), HCV-compensation, molecular genetic program

Regional network of hemophilia treatment centres

1992 – 2008:

- **National Hemophilia Centre (Budapest)**
- **Regional Hemophilia Centres:**
  - **Budapest: adult**
    children
  - **Szombathely**
  - **Pécs**
  - **Miskolc**
  - **Debrecen**
  - **Szeged**

From Jan. 2009:

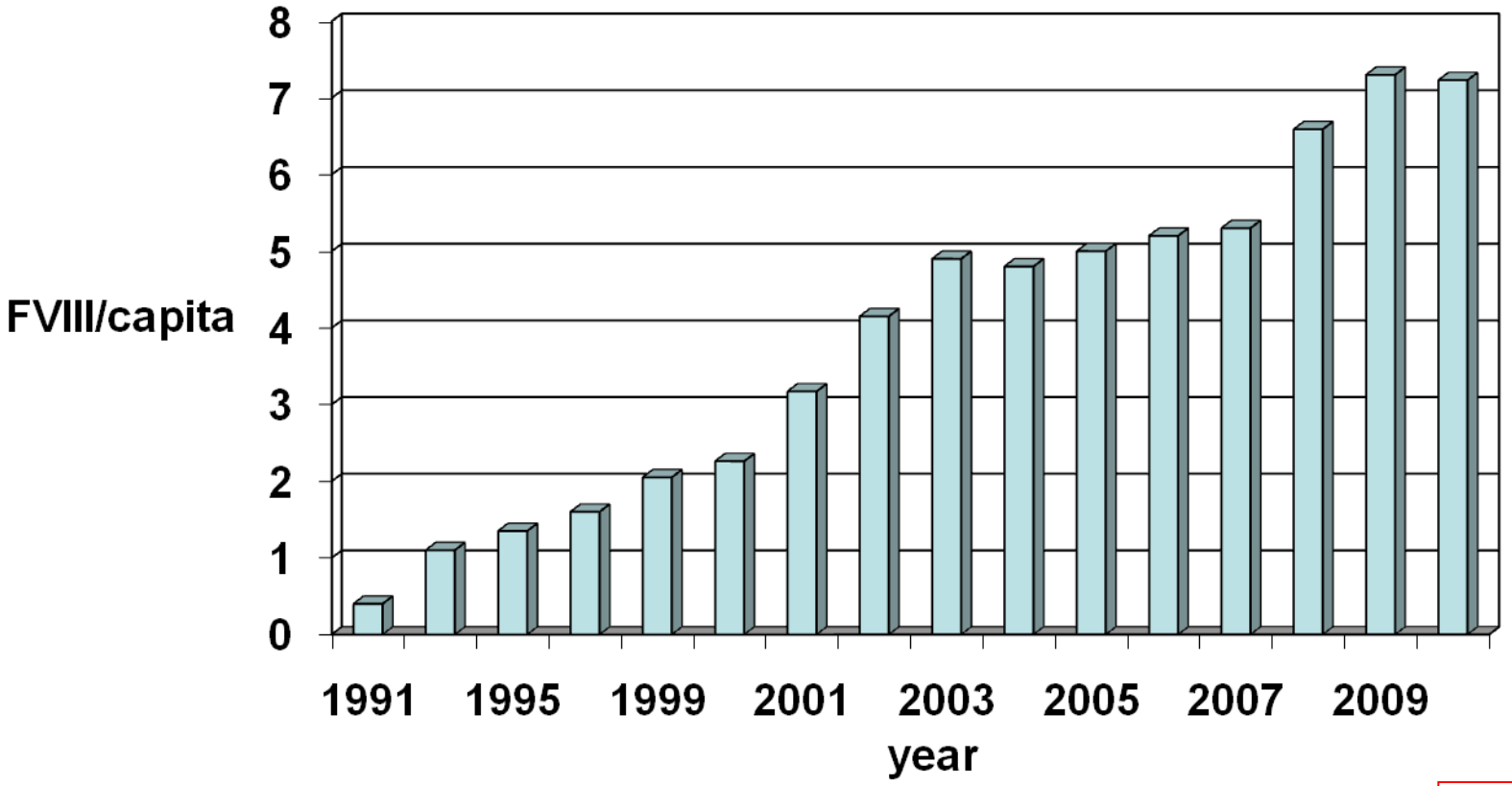
- **19 treatment centres (instead of previous 43)**

Factor supply

- **Since 1992 safe plasma-derived factor concentrates have been applied for the treatment of patients with hemophilia. The cryoprecipitates were withdrawn in 1993.**
- **The Hungarian Haemophilia Society had an important role in the introduction of safe factor concentrates.**
- **The Hungarian Health Ministry is responsible for factor supply.**
- **Factor concentrates are bought in annual centralized open tenders (participants: hemophilia experts, representatives of factor companies, National Health Insurance Fund Administration /OEP/, Hungarian Haemophilia Society).**
- **Patients have to pay neither for the factor concentrates nor the treatment.**
- **Factor FVIII supply has been increased from to close zero level in 1990 to 7, 2 IU per capita in 2010.**

FVIII supply per capita in Hungary

(Recombinant: 2002: 0%, 2003: 2%, 2007: 23 %, 2008: 24 %, 2009: 26,6 %, 2010: 30 % (21,7 M IU)



FVIII IU: 0,4 1,35 2,05 3,17 4,9 5,0 5,3 7,3 7,23

1,1 1,6 2,26 4,15 4,8 5,2 6,59

Proportion of factor concentrates in the total pharma (drug) budget

In 2009: ~ 2,6%

2010: 3,3 %

(10/300 milliard Ft)

- **20% of FVIII concentrates are produced from plasma given by the Hungarian unpaid donors (80-90000 l plasma/year).**
- **Hungary has an own factor-manufacturing capacity: the Humafactor-8 is made under licence of Beriate P.**

- **The ratio of supply of recombinant products is increasing year by year.**

Home treatment

- **Before 1999 there were only sporadic experiments with home care**

  (the law didn't allow the administration of iv. injections, only by medical staff).

- **After Jan. 1999: home care became a possibility for every severe patients with hemophilia.**
- **It was legalized by the regulation of the Ministry of Health in Dec. 1998.**

Home treatment led to a better quality of life.

Many children had been learned the technic of self-injection in summer camps for hemophiliacs organizing by Hungarian Haemophilia Society.

Prophylaxis

- **Currently, the general treatment of hemophilia in Hungary is on-demand.**
- **Prophylactic treatment, mainly for hemophilic children, was introduced in 2001.**
- **One of the main goals of the Hungarian Haemophilia Society is to provide prophylactic treatment for all severe hemophiliacs.**
- **Prophylaxis today (data of National Registry, 2008):**
  - **All age group: 29,4 %**
  - **< 15 years: 51 %**
  - **< 10 years: 68 %**
  - **< 5 years: 80 %**

New protocol of prophylaxis to PUP children

(according to the results of the CANAL study and Auerswald G, Kurnik K, 2009)

- **Avoid first FVIII treatments into a bleed**
- **Start FVIII replacement therapy as early as possible in absence of danger factors (bleedings, surgery, inflammation)**
- **Start with low dose FVIII prophylaxis (25 IU/kg) once weekly as soon as venous access allows without Port-A-Cat**
- **Treat bleeds early and with higher than prophylaxis doses to avoid the need for peak treatment.**
- **Do not vaccinate at a FVIII treatment day**
- **Vaccinate s.c. (instead of i.m.)**

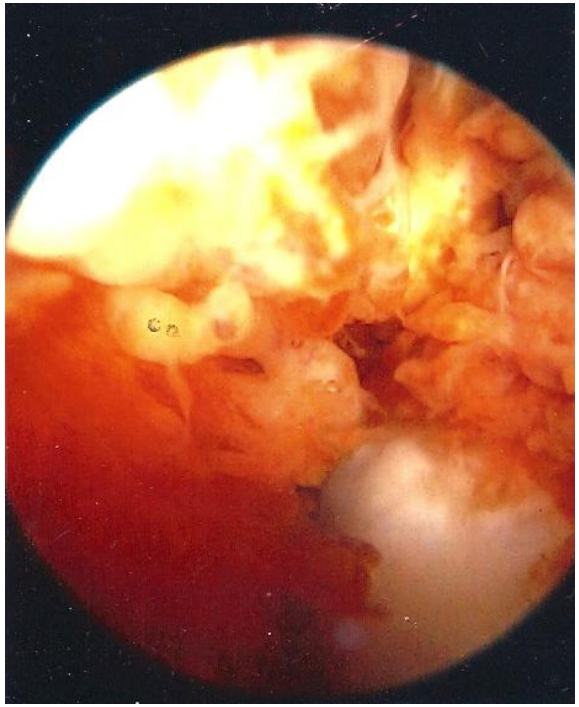
Inhibitor, ITI

- **Hemophilic patients with inhibitor in Hungary (data of National Registry, 2008):**
  - **Severe hemophilia A: 31**
  - **Mild hemophilia A: 5**
  - **Hemophilia B: 1**
- **Method of ITI (L. Nemes, National Hemophilia Centre, Budapest):**
  - **1x 150 IU/kg/day FVIII/vWF**
  - **Treatment of acute bleeding:**
    - **< 5 BU inhibitor titer: high dose FVIII/FIX**
    - **> 5 BU: FEIBA, rFVIIa**

Orthopedic surgery in hemophilia

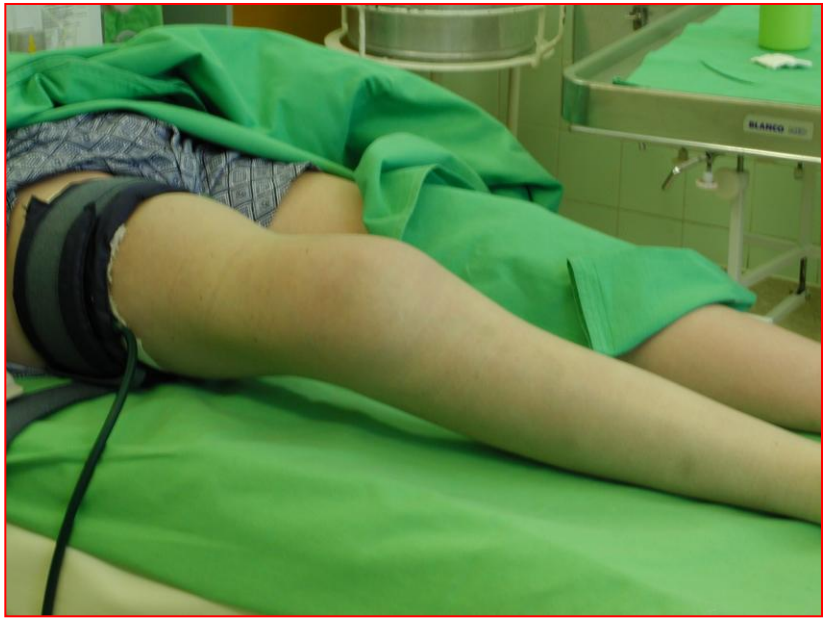
- **Synovectomy (open, closed = arthroscopic)**
- **Elective joint replacement, arthroplasty currently are possible in Hungary.**

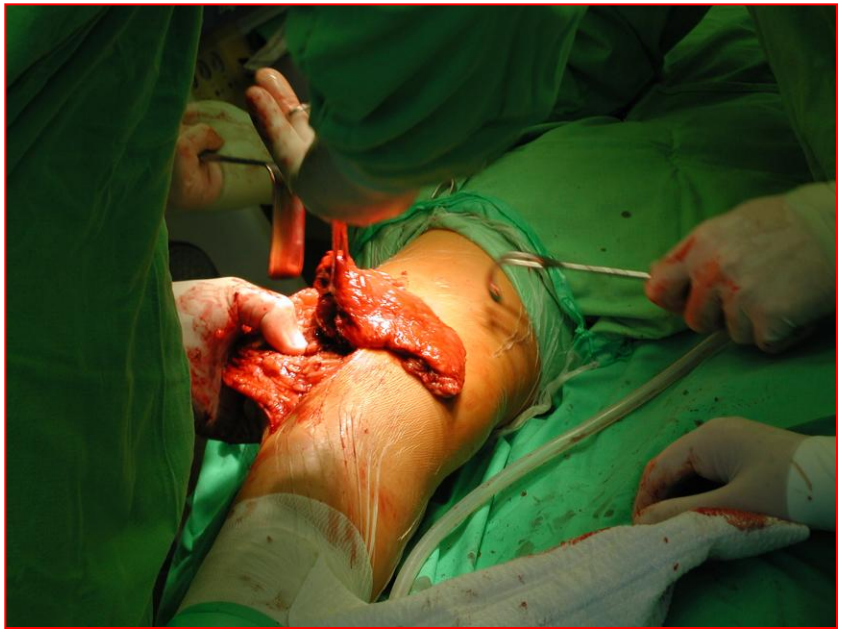
Closed (arthroscopic) synovectomy using endoscopic shaver

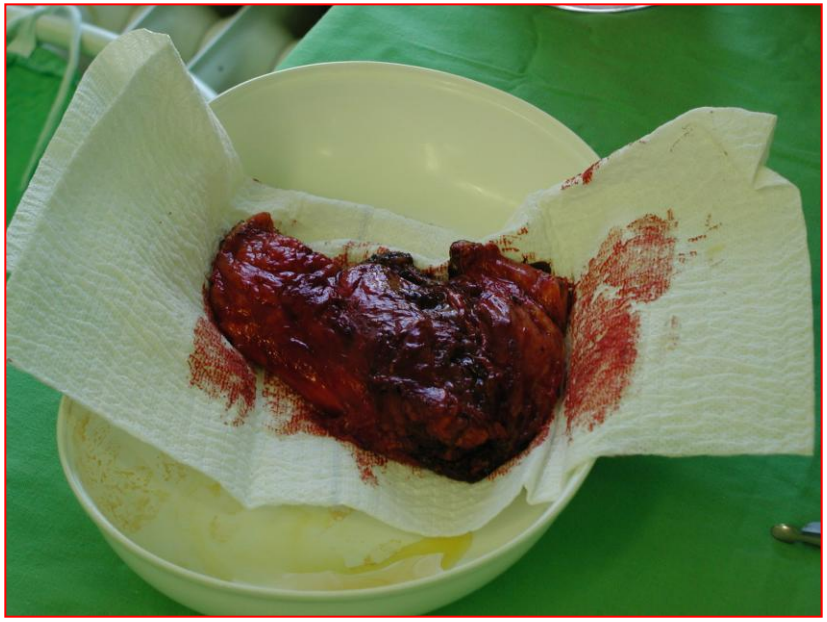


Open synovectomy

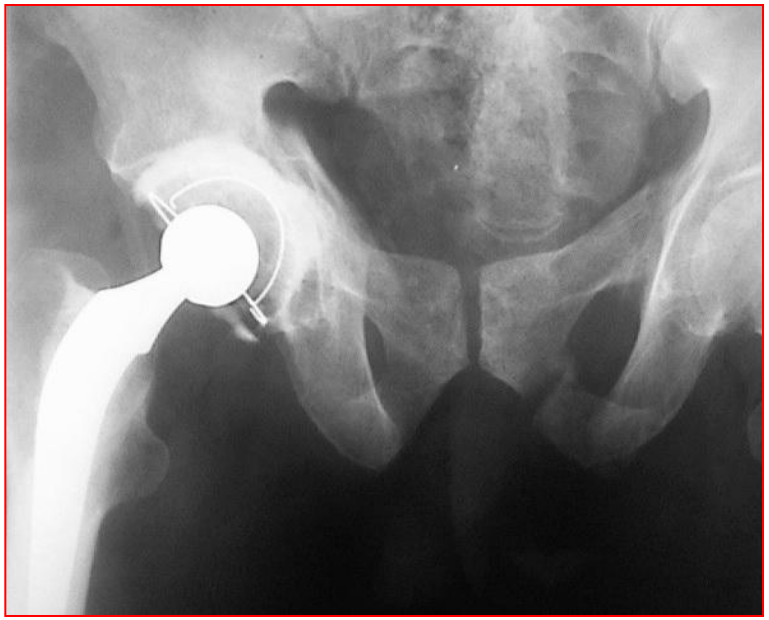
(M. Kardos, Children Hemophilia Treatment Center, Mohács)

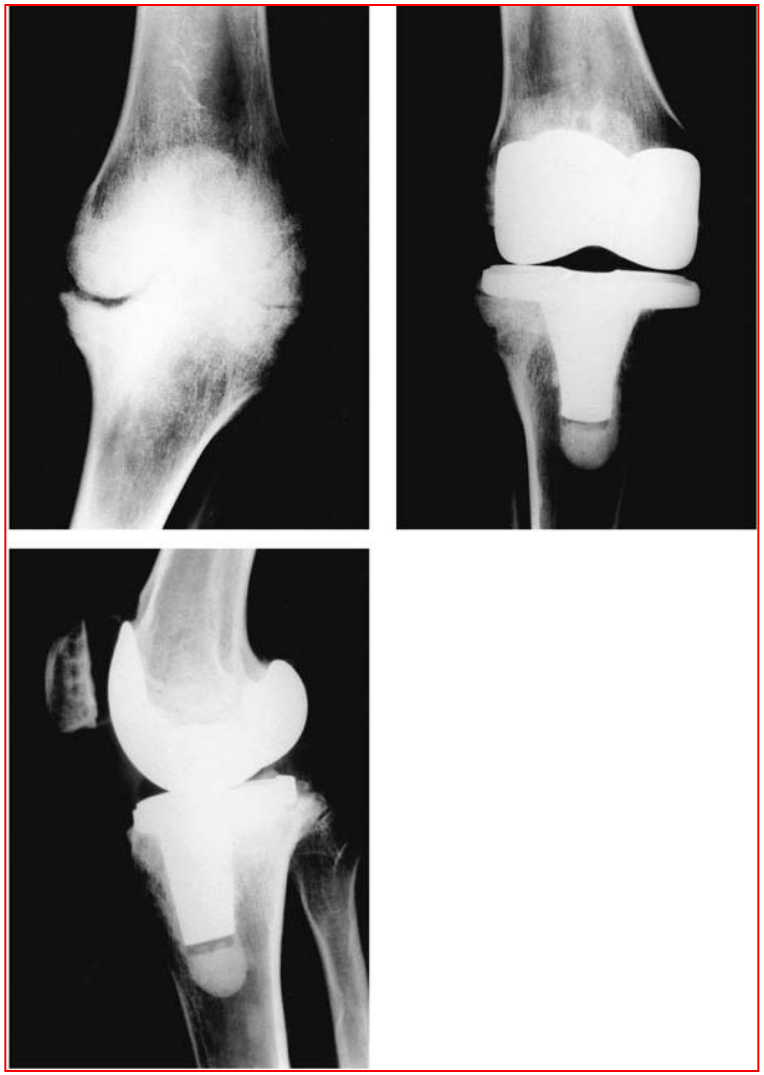






Total hip, knee replacements





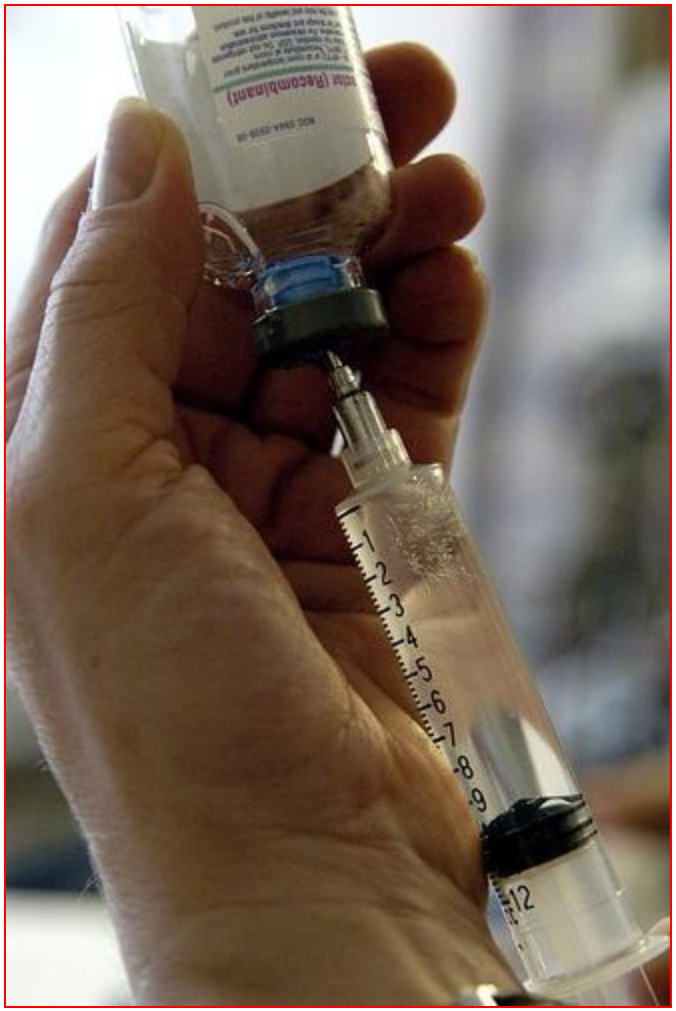
Major orthopaedic procedures performed at the NHC in the past 5 years

- Closed arthroscopic synovectomy of the knee: 23
- Closed arthroscopic synovectomy of the ankle: 2
- Other open synovectomies (shoulder,elbow) 5
- Total hip replacement: 5
- Total knee replacement: 12
- TKR revision operation: 1
- Other corrective orthopedic operations: 8

L. Nemes, 2008

Global factor supply -

Where is Hungary?



- **There is a big difference in hemophilia care between the developed world and developing world.**

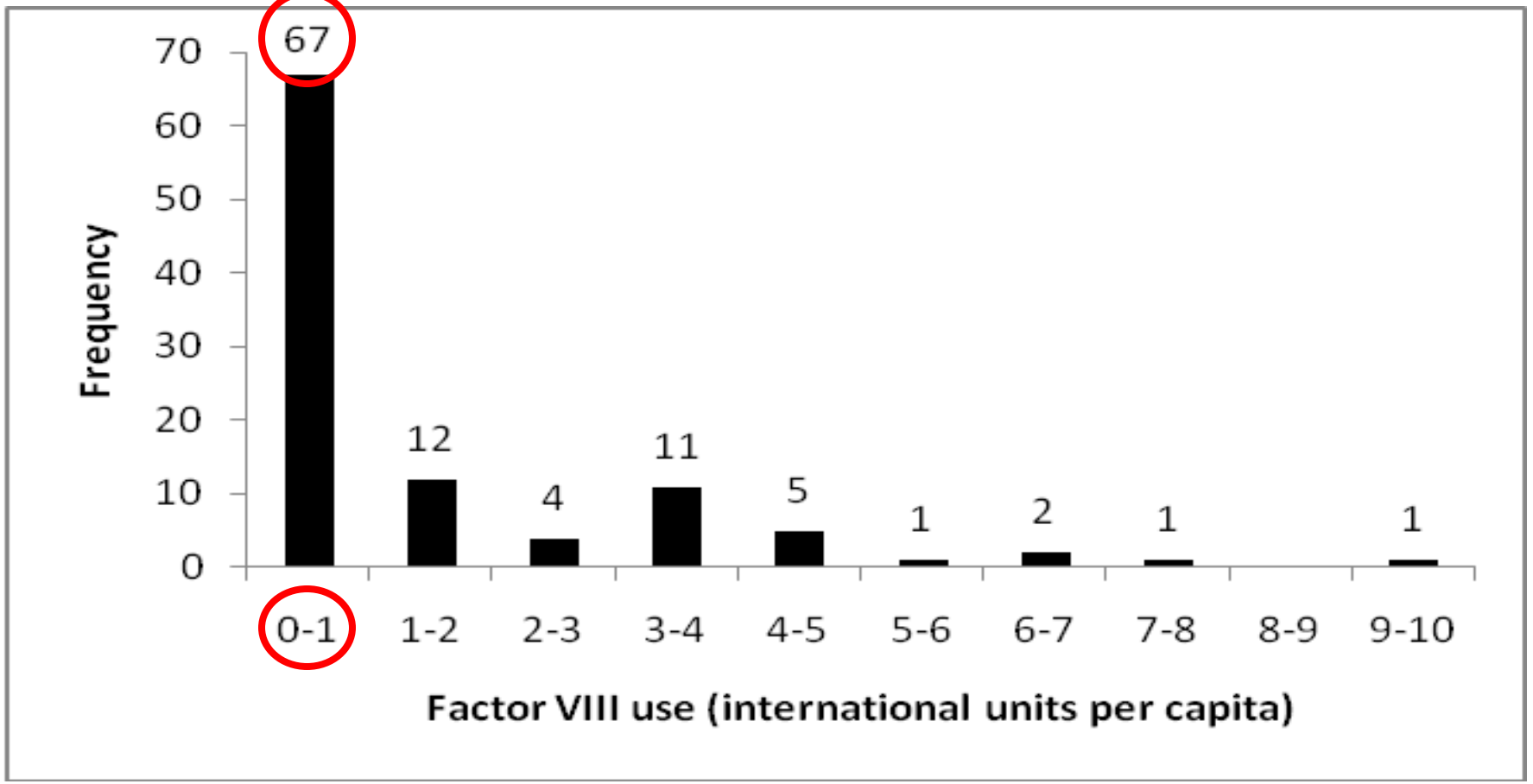
  Today ~ 70% of the estimated patients with hemophilia in the world are still not diagnosed and ~ 75 % receive inadequate or no treatment (primarily in the developing world).

- **The use of FVIII concentrate increases as economic capacity increases.**

- **1IU per capita is approximately the 20000 IUs per patient with hemophilia per year (PWHA). It is the minimum clinical target for hemophilia care (WFH).**

64 % of countries reported FVIII IU per capita of 1,0 or less. (Data of 104 countries from MRB and WFH, 1996-2006.)

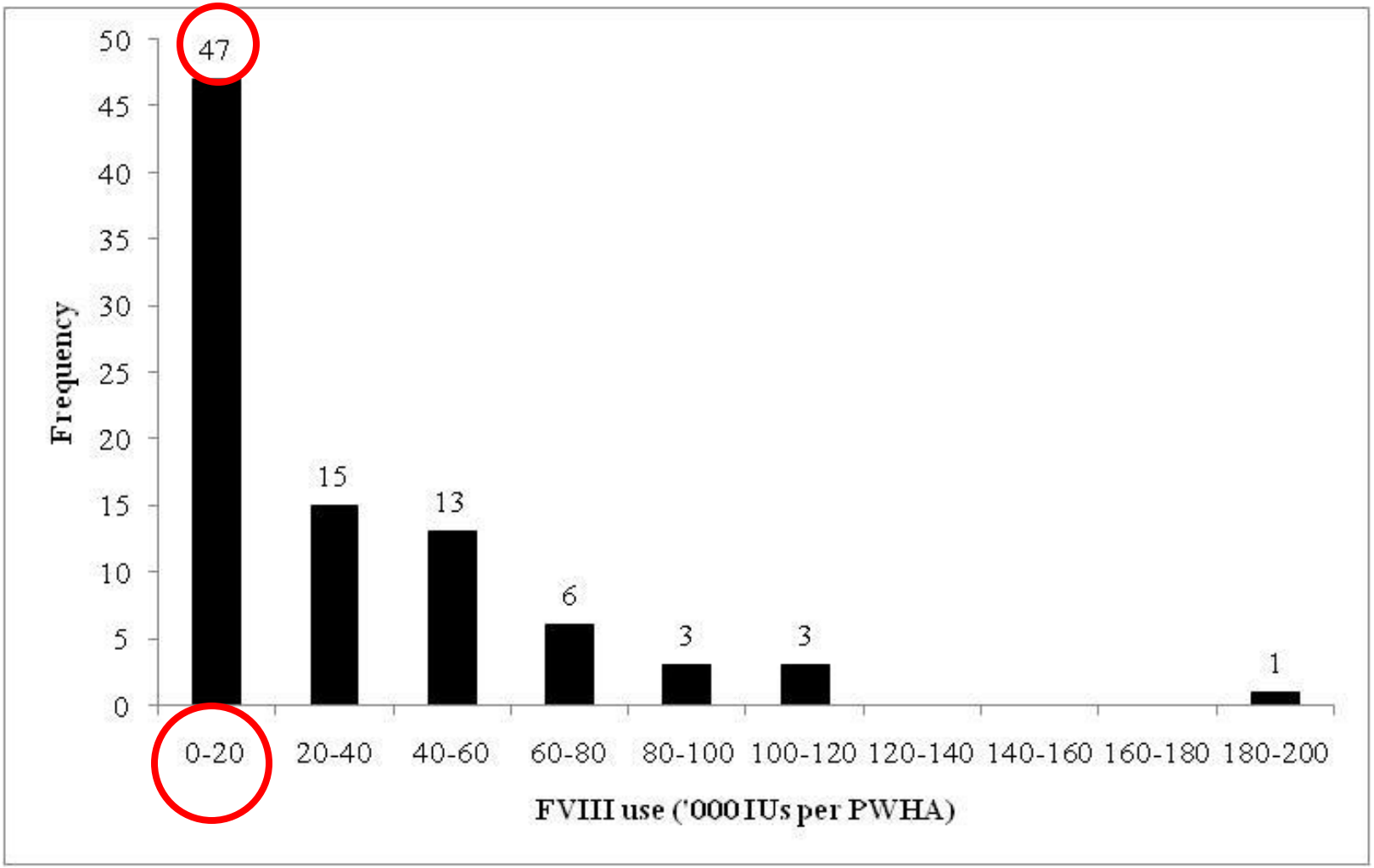
Stonebraker JS et al: Haemophilia, 16, 33-46, 2010.



MRB: Marketing Research Bureau, WFH: World Federation of Hemophilia

More than half of the countries (47 out of 88) are consuming less than 20000 IUs per PWHA.

(Stonebraker JS et al: Haemophilia, 16, 33-46, 2010).



Countries with similar economies use very different amounts of FVIII per capita.

- **Causes:**
  - **No consensus on therapy**
    (treatment strategies /prophylaxis, surgery, ITI/ vary from country to country)
  - **Reported prevalence of Hemophilia A varies**
    (different diagnostic possibilities)
    - **The prevalence/100000 males for high income countries: 12,8 ± 6,0, for the rest of the world: 6,6 ± 4,8**
    - **Iceland (small, isolated population): high prevalence (38,6 ± 0,8)**
    - **Ukraine: 0,7 ± 0,4, Nigeria: 0,05**
    - **Hungary: 17,5 ± 2,3**
    - **Romania: 11,8 ± 0,5**

(1998-2006)

World Bank's economic classification

(according to the 2006 gross national income /GNI/ per capita in US dollars)

Economic classification:	GNI ($) per capita:
1. High income (a member of OECD):	11116
2. High income non-OECD:	11116
3. Upper middle income:	3596 – 11115
4. Lower middle income:	906 – 3595
5. Low income:	905

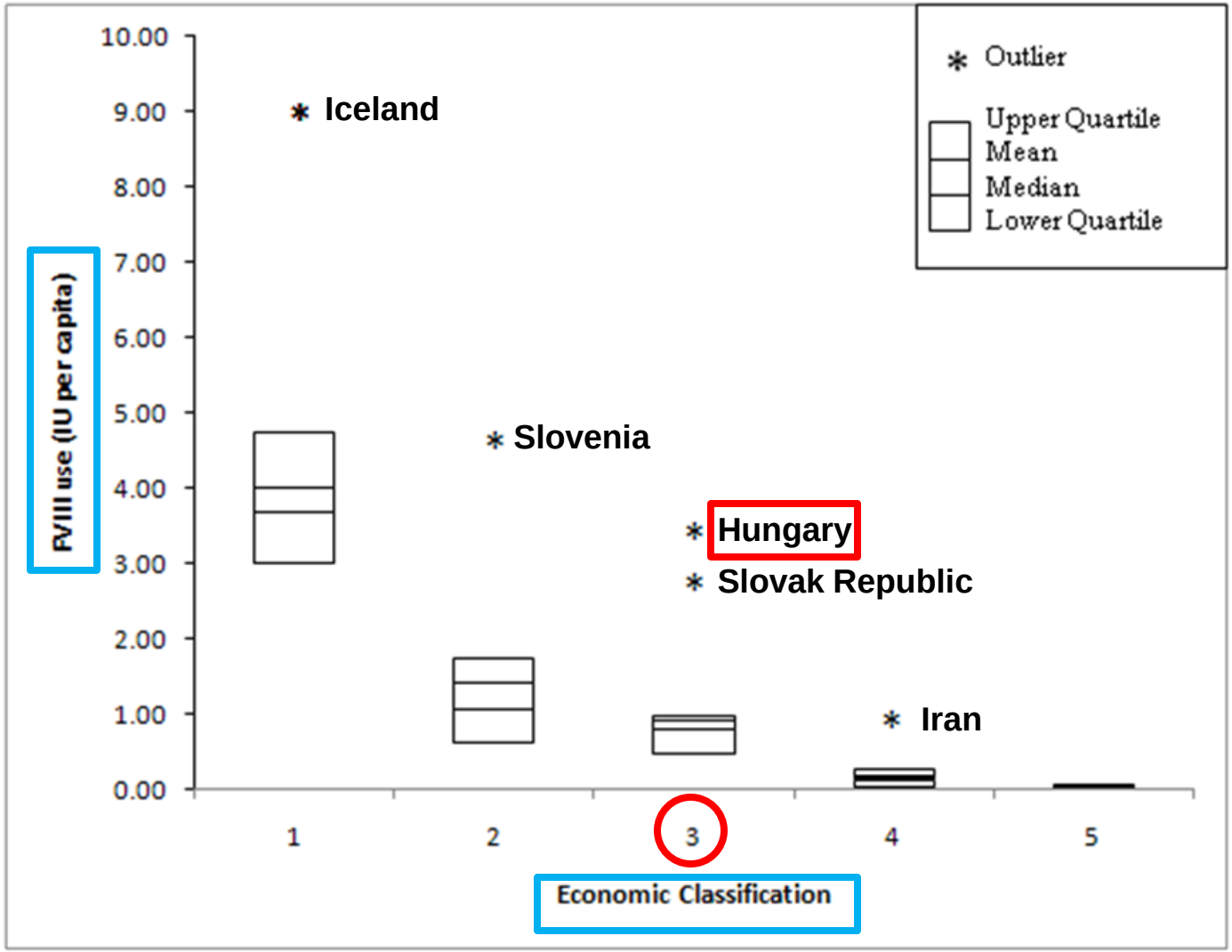
OECD: Organisation for Economic Cooperation and Development

FVIII use per capita by economic classification

(104 countries, 1996-2006)

Economic classification:	Mean FVIII (IU) use per capita:
1. High income (a member of OECD)	3,83 (1,28 Korea – 9,02 Iceland)
2. High income non-OECD:	1,40 (0,23 Trinidad & Tobago – 4, 65 Slovenia)
3. Upper middle income:	0,97 (0,21 Romania – 3,39 Hungary, in 2010: 7,2)
4. Lower middle income:	0,21 (0,006 Armenia – 0,96 Iran)
5. Low income:	0,03 (0,0004 Nigeria – 0,128 Eritrea)

Some countries had unusually high FVIII use (IUs per capita) when compared to the countries within their economic classification. (Stonebraker JS et al: Haemophilia, 16, 33-46, 2010).



FVIII use per PWHA by economic classification

(88 countries, 1998-2006)

Economic classification:	Mean FVIII (IU) use per PWHA:
1. High income (a member of OECD):	64111 (24713 Czech Republic – 114333 Germany)
2. High income non-OECD:	47105 (14940 Singapore – 191736 Saudi Arabia)
3. Upper middle income:	22943 (3913 Romania – 43907 Turkey) Hungary: 43392
4. Lower middle income:	9659 (133 Armenia – 35088 Guatemala)
5. Low income:	3986 (48 Uzbekistan – 24721 Eritrea)

The FVIII consumption per capita does not necessarily reflect the overall quality of care.

Comprehensive Hemophilia Care (CHC):
to offer the complex treatment for patients with hemophilia

"Medical care for hemophilia is specialized. A person with hemophilia must receive care from healthcare workers who have expert knowledge of the bleeding disorder. The wide-ranging needs of people with hemophilia and their families are best met through Hemophilia Treatment Centres rather than by individual doctors."

(World Federation of Hemophilia: *Organizing a National Programme for Comprehensive Hemophilia Care)*

Comprehensive hemophilia care (CHC)

- **Core team:**
  - Medical doctor (adult or pediatric hematologist/internist, transfusiologist)
  - Well educated nurse
  - Physiotherapist
  - Social worker
  - Administrative assistant
  - Factor concentrate utilization management
- **Laboratory:**
  - Special hemostasis laboratory (in 24 hours)
  - Other diagnostic laboratory services (liver function, víruses)

- **Extended team members:**
  - Orthopedic surgeon
  - Hepatologist
  - Infectious disease (HIV) specialis
  - Gynecologist/obstetrician
  - Dentist
  - Genetic adviser
  - Psychiatrist/psychologist
  - Other specialists (surgeon, radiologist, transfusion medicine)

Educating the family

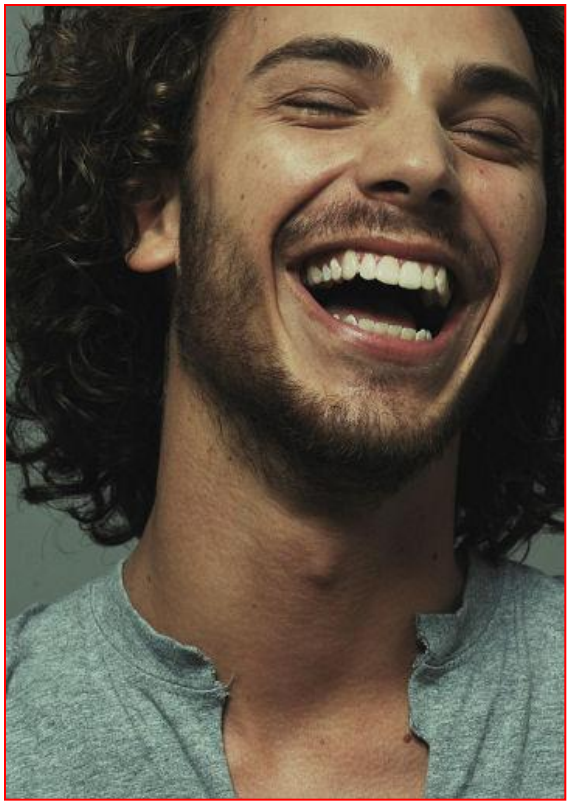
- After a child is diagnosed with hemophilia, the parents should be given an explanation of the nature of the disease and its genetic basis.
- To train them how is recognize bleeds and how to infuse the factor concentrate.
- To give a psychological support.
- To inform teachers at school about hemophilia.

Regular check-ups of all hemophiliacs at specialized hemophilia centre

- To discuss the problems of everyday life.
- Genetic counselling and family planning.
- Treatment the complications of hemophilia (chronic arthropathy, infections, others).

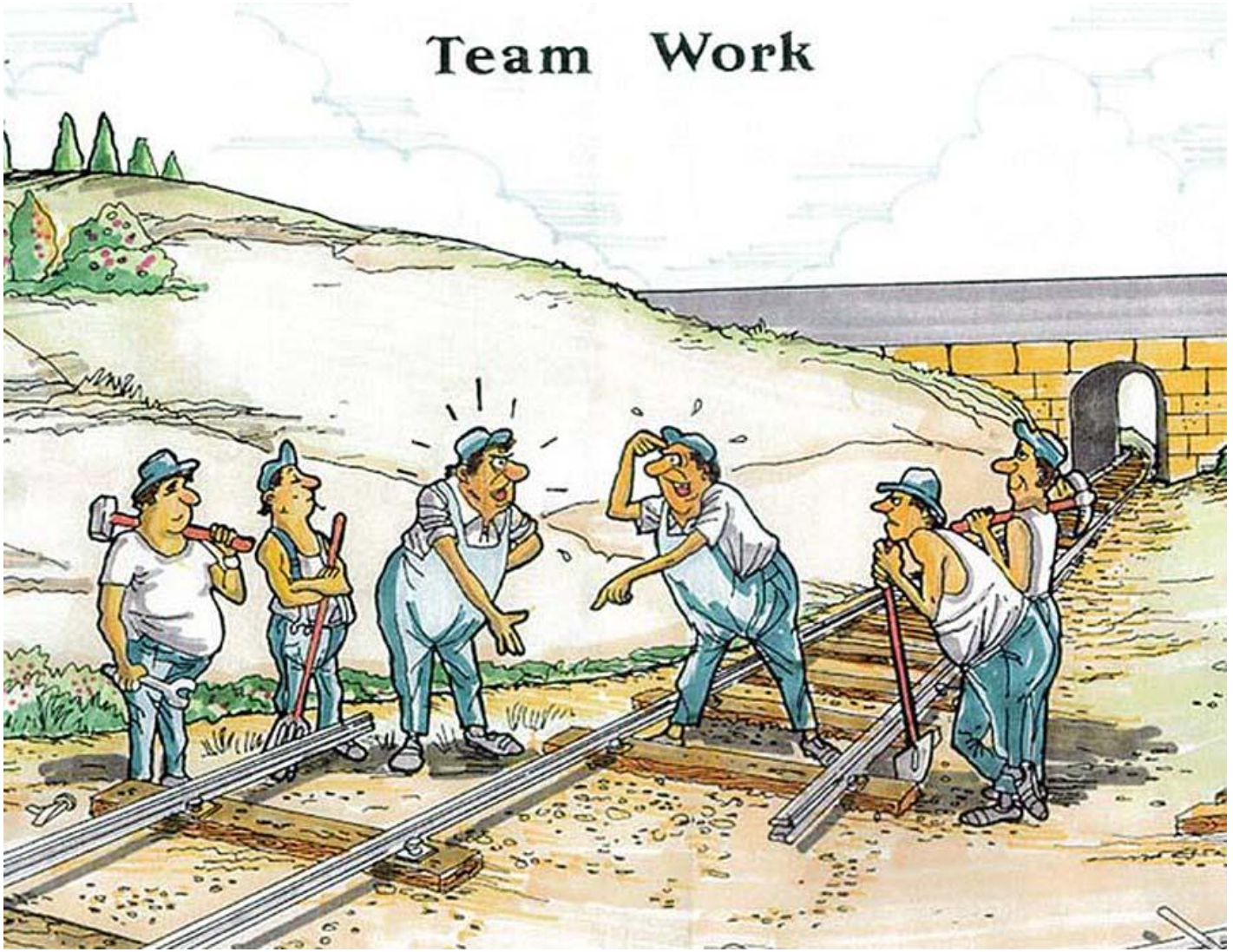
Regular dental visits – usually every 6 months – will help identify problems early.

Prevention is an essential component of oral care: it will reduce the need of treatment and the number of emergency visit.



With prevention

Without prevention



Good hemophilia care = teamwork

Future plans

Effective national healthcare policy is required in the future too:

- **To save high level of factor supply in Hungary.**
- **To increase the ratio of recombinant products.**
- **More home treatment, modification of the home care regulations.**
- **To provide prophylactic treatment for all severe hemophiliacs.**
- **More Comprehensive Care Center.**
- **Better laboratory diagnosis (more reference labs).**
- **Home factor-delivery system (?)**

Summary

The life expectancy of someone with hemophilia varies depending on whether they receive proper treatment:

- without adequate treatment, many people with hemophilia die before they reach adulthood

- the replacement therapy has improved the life-expectancy and quality of life of patients with hemophilia

- with prophylactic treatment a new generation of zero joint score adult patients is coming

- children can look forward to a normal life expectancy.


RUGBY
WILSON
7

…light and shadow…

To overcome difficulties:

cooperation of Ministry of Health, National Healthcare Agencies, Hungarian Haemophilia Society, and doctors dealing with hemophilia is necessary in the future too.