Czech Republic

Šárka Vejvalková, M.D.

Clinical geneticist

Inst. of Biology and Medical Genetics, Prague

Czech Republic

Socioeconomic Data

Total population: 10.4 mil (2008)
Population density: 132 / km^2 (2008)
GDP per capita: 24 236 $ (2007)
% of GDP spent on health: 7.1% (2005)
Physicians 351 / 100000 (2006)

Healthcare system

Supervised and regulated by the government
Public health insurance with universal / obligatory membership
Funding: individuals, employers, state

Ownership state large hospitals
regional hospitals
private smaller hospitals
outpatient clinics, pharmacies

RD definition in CZ (European Orphan Drug Regulation) **1 / 2000**

Funding of actions, regarding rare diseases

Health care funded by public health insurance

- diagnostic services (clinics, laboratories)
- 12 regional genetics centers, private clinics
- of 51 orphan drugs registered in EU, 27 available in CZ

- treatment (clinical management) …
- rehabilitation …

… funded by public health insurance

Social care moving from institutional care to inclusion (financial support to patients, not to institutions)

Strategies for rare diseases

- Creation of a **National Working Group** for RDs under auspices of the Czech Ministry of Health **aiming to establish**:
  - **National strategy (June 2009)**
    → National plan 2009-2010
    → Information portal for RDs

- WG curretly working within the activities of the CZ EU Council Presidency (eu2009.cz) on the Czech National Strategy for Rare Diseases (2009-2010)

- Content of the CZ National Plan for Rare Diseases based on FR and BG experience.
- Takes into account recommendations from Eurordis, Orphanet and Europlan where CZ has its representatives

Strategies for rare diseases

CZ has participated in the Rapsody project (March 2007)

Main objectives:

- **To address needs and expectations** of patients, health professionals and policy makers regarding:
  - Centres of expertise for rare diseases
  - European reference networks of centres of expertise
- **To develop recommendations** for:
  - Principles and criteria for the identification of such national centres of expertise and European reference networks
  - The evaluation of their respective outcomes

RARE DISEASE PATIENT SOLIDARITY

Centres of Reference

NATIONAL WORKSHOP REPORT

CZECH REPUBLIC | 2 MARCH 2007

Prevention

Eurordis – has provided useful information in their book of the „The Voice of 12,000 patients“ on the situation in Europe and on positive / negative examples with regards to RDs

KEY FINDINGS OF THE EURORDISCARE2 SURVEY ON DELAYS IN, AND CONDITIONS SURROUNDING THE [illegible]

- **25% of patients** reported waiting between **5 and 30 years** from the time of first symptoms to a confirmatory diagnosis of their disease
- **40%** of patients were initially misdiagnosed leading to severe consequences such as inappropriate medical interventions, including surgery and psychological treatment
- **25% of patients** had to travel to a different region to obtain a diagnosis and 2% had to travel to a different country
- In **33% of cases**, the diagnosis was announced in unsatisfactory terms or conditions. In **12.5% of cases**, it was announced in unacceptable ones
- The genetic nature of the disease was not communicated to the patient or family in **25% of cases**. This is paradoxical, given the genetic origin of most rare diseases
- Genetic counselling was only provided in **50% of cases**

Neonatal screening for selected diseases

Centres of Reference

Prevention

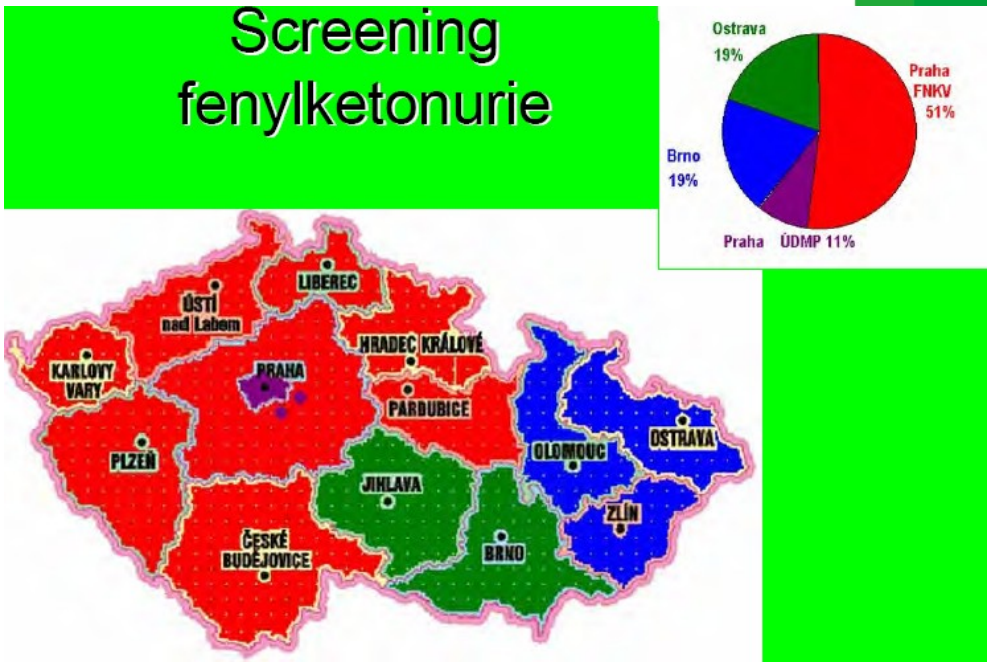
- *Neonatal screening*

- PKU screening since 1975
- Hypothyreosis since 1985
- CAH since 2006
- 2009 ongoing neonatal screening for :
    1. maple syrup disease
    2. Medium-chain fatty acid dehydrogenase deficiency
    3. Long-chain 3-OH fatty acid dehydrogenase deficiency
    4. Very long-chain fatty acid dehydrogenase deficiency
    5. carnitinpalmitoyltransferase I deficiency
    6. carnitinpalmitoyltransferase II deficiency
    7. carnitin acylcarnitin translocase deficiency
    8. glutaric aciduria type I
    9. izovaleric aciduria
    10. cystic fibrosis

- Laboratoř novorozeneckého screeningu, Klinika dětí a dorostu FNKV, Praha (Doc.MUDr.Votava, Ing. Kračmar)
- Laboratoř novoroz.screeningu OKBH Dětská nemocnice,Brno(MUDr Vinohradská)
- Laboratoř novoroz.screeningu ÚKB FNsFP Ostrava(Dr Švagera)
- Ústav dědič.metabolických poruch, Praha (MUDr.Šťastná)

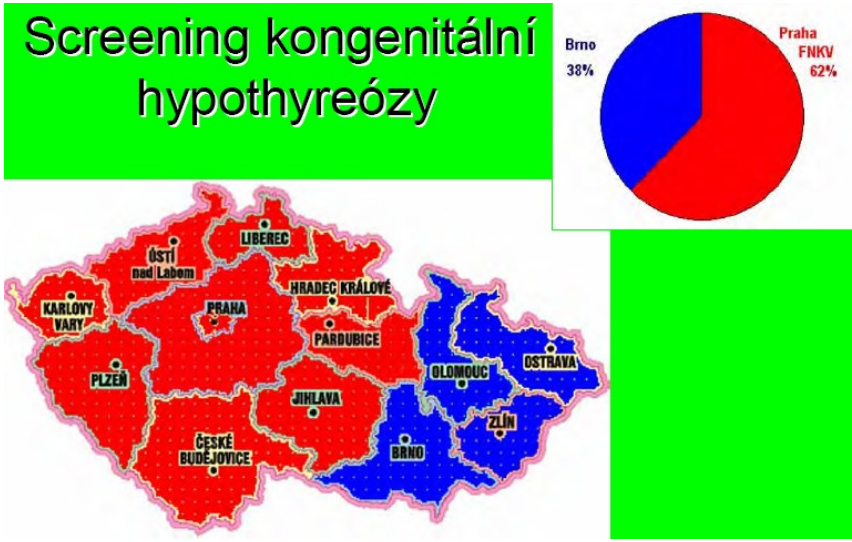
Prevention

- *Neonatal screening*
- **PKU since 1975**
- Guthrie method (1954)
- Within first 4 days of life (after exposition to milk)
- 3 regional centres + Prague



Prevention

- *Neonatal screening*
- **Hypothyreosis since 1985**
- Incidence: 1 : 4 230 live born
- Method used:
  1985-1996 RIA T4
  1996+ FIA TSH
- 2 centres



Prevention

- *Neonatal screening*

- **CAH since 2006**

- Congenital adrenal hyperplasia (CAH), autosomal recessive inherited disorder of adrenal steroidogenesis
- Results in adrenal insufficiency, which can be life threatening already in the newborn period
- Expected incidence in CZ 1 : 10 -15 000.
- Early recognition of CAH by neonatal screening may save the life of the most severely affected patients
- Based on estimation of 17-α-hydroxyprogesterone level in dried blood spot.

Prevention

- *Neonatal screening*
- **Pilot screening studies**
- Screening for **hearing impairment** in newborns using transient evoked otoacoustic emissions (1997-1999)
- Newborn Screening of **inherited metabolic disorders** by Tandem Mass Spectrometry (2005)
- Neonatal screening for **cystic fibrosis** - Pilot study (2005-2006)

Prevention

- *Pilot screening studies*

Screening for hearing impairment in newborns using transient evoked otoacoustic emissions (1997-1999)

- Outcome : TEOAE screening was performed in 4790 neonates, divided into two groups according to risk factors for hearing impairment (risk positive group n = 399, risk negative group n = 4391).
- Screen performed at th age of 2 - 4 days and preterm infants at the 40th postconceptional week of preterm babies.
- First and second repeated tests were done in 4-week intervals.
- Babies with no TEOAE response in the second repeated test were examined by auditory brainstem responses (ABR).
- Results: **Prevalence 1/384** in the risk-negative group (1/27 in risk positive newborns). **Early identification allows proper further care including cochlear implantate in prelingual deafness.**

Prevention

- *Pilot screening studies*

Neonatal screening for Cystic fibrosis - Pilot study 2005-2006

- Objective need for CF newborn screening in CZ substantiated by a significant delay of symptomatic diagnosis
- This trend most likely resulted from the process of **decentralisation of health care** which led to the deterioration of care for patients in need of specialised approaches
- Applied newborn screening model (IRT/DNA/IRT) was efficacious enough to detect CF cases with **median age at diagnosis of 37 days**

- *The **incidence** of CF (1 in 6946 live births) ascertained in this project was **lower than** that established previously by **epidemiological studies** (1 in 2700–1 in 3300). Adjustment for broadly applied ultrasound-based prenatal diagnosis (PND) in the 2nd trimester of pregnancy that was performed within the period of the project (1/2/2005–2/11/2006), however, rendered an incidence estimate of 1 in 4023. This value is closer to that observed in other CF NBS programmes and **reflects influence of prenatal diagnostics** on the incidence of CF.*

Prevention

- *Pilot screening studies*

Newborn Screening of Inherited Metabolic Disorders by Tandem Mass Spectrometry (2005)

- Objective: To confirm preparedness for newborn screening of 19 inherited metabolic disorders (IMDs) by tandem mass spectrometry (MS/MS).
- Material and Method: 40 393 samples from newborn screening, 13 315 samples from patients suspected for IMDs. Control group: 1130 samples from 118 patients with confirmed IMDs.
- Results: 97.5% sensitivity in control group
- Newborn screening detected 7 patients with IMDs
- Prospective selective screening diagnosed IMDs in 14 patients

- *Conclusion:* **Early diagnostics of treatable IMDs before clinical symptoms** together with genetic counselling and prenatal diagnostics is the most effective medical approach to IMDs. We are now **able to diagnose 19 IMDs in newborn screening by MS/MS.**

Prevention

- *Prenatal screening*

Routine non-invasive methods
2-3 steps combining USG / biochemical screening

Combined screening of I. trimester

10-12 weeks USG (GA,NT,NB)
biochemical test (HCG, PAPP A)

Biochemical screening of II. trimester

15-19 weeks biochemical test (HCG, UE3, AFP)
(Integration of I. and II. trimester scr.)
Ultrasonografic screening of CA of II. trimester (ca 20 weeks)

Invasive methods PD: amniocentesis, CVS, fetal blood samples

Type of test for CA PD: karyotyping, FISH, QFPCR,

Legal limit for PT 24 weeks by USG

Provision of information for rare diseases

- *Availability of website-based information*

- Information understood as one of the keys to efficient approach to RD

- (Planned) National Information Portal for Rare Diseases included as one of the directions of the (draft) National Strategy

- International collaboration (Orphanet, EuroGenTest, etc.)

Research on rare diseases

- *Availability of research programme for RDs*
- *Please, provide information on major sources*

- **Participation in international projects**: EuroGenTest, ECORN, EuroCareCF, ERNDIM, Orphanet, Rapsody, EuroPlan

- National funding through Research Agency of Ministry of Health (and other research agencies)

- Support to RD research included in the (draft) National Strategy

Empowerment of patients' organisations

- *Support to the activities of patient organisations*
- *Representation and consultation of patient organisations*

Patient organizations actively participating in the development of the National Strategy for RD.

Specialised social services

- *Respite Care Services*
- *Therapeutic Recreational Programmes*
- *Services aimed at the integration of patients in daily life*

Major shift in funding of social services, aiming to support patients' autonomy and integration (funding to patients, services paid by patients).

Services basically provided on commercial basis, supported by multiple sources of funding (grants, donors).

Partial tax deduction for donors.

Thank you for your attention

sarka.vejvalkova@lfmotol.cuni.cz