

EDITORIAL

ON RARE AND "SUPER-RARE" DISEASES: AN INSIGHT FROM THE REPUBLIC OF MACEDONIA

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Abstract: Rare diseases (RD) are becoming increasingly important as possible targets of new forms of treatment, as a valuable source of a novel insight in fundamental laws of biology, and in the specific mechanisms of many diseases. Molecular methods have created a better diagnosis and oftentimes treatment. RDs pose significant problem for the patients, since their problems are often not recognized by the medical community and shunned by the health insurance. The cumulative costs of diagnosis and treatment of RDs is significant for any society, oftentimes bearably acceptable for developing countries.

Key words: rare diseases, definitions, social impact, Macedonia.

Definitions, frequency

In Europe RD is the one which affects less than one citizen in 2000 [1, 2], in the USA – one in 1250 (3), while in Japan RD is the one that affects fewer than 50,000 patients [4]. Those differences stem, at least partly, from the fact that RDs have variable prevalence in different populations. It should be stressed that many patients suffer from even rarer diseases, affecting 1 person in 100 000 or more (super RDs).

The term "orphan diseases" further adds complexity, since it is often used as a synonym for RDs [4]. Originally, orphan disease was a term used for a disease for which the pharmaceutical industry has little financial incentive to produce medications. The European Organization for Rare Diseases (EURORDIS) classifies both rare diseases and neglected diseases as orphan diseases [5].

A large fraction of RDs affect children (75%). It is a striking fact that as much as 30% die before their fifth birthday [2]. As many RDs end in early death, the true incidence and prevalence of many RDs are unclear. EURORDIS estimates that ~ 80% of RDs have genetic origins [5]. Some infections, allergies, degenerative diseases, as well malignant diseases in children are RDs, too.

It is of note that almost all children attending a subspecialty clinic in paediatrics are suffering from a rare disease. Some 700–800 metabolic diseases diagnosed in children are RDs. There are about 250 different types of immune deficiencies which all fulfil the criteria of rare disease.

In paediatric endocrinology most disease are RDs. In paediatric nephrology there are only two types of diseases are frequent: urinary tract infections and enuresis. The nephrotic syndrome, acute or chronic renal failure, tubulopathies may be caused by hundreds of underlying kidney disorders which all fit the definition of RDs.

The impact on the society, the actions taken

EU estimates that 5–8000 distinct rare diseases affect 6–8% of the population (5). The impact of RDs in the health systems is impressive: at least 3 million patients in the UK, 4 million in Germany, and between 27 and 36 million EU citizens.

RDs have significant consequences for the individuals, their families and the societies (5–8):

1. RDs impact on the families of the affected children making many parents full-time carers.
2. Patients with RDs often need a team approach and treatment.
3. RDs are a major public health problem because of their cumulative frequency.

RDs create a particular set of challenges:

1. An epidemiological challenge: there is lack of registries on the epidemiology.
2. A pharmacological challenge: there is a lack of multicentre controlled therapeutic studies.
3. An organisational challenge: there is a lack of standardised referral of patients with RDs in Europe.
4. A legal challenge: there is a lack of legal basis for cross border genetic diagnostics.

5. An ethical challenge: there are different priorities in different European countries.

Those challenges are also the goals of EU in regard of the RDs. A Committee of experts on rare diseases (EUCERD) was created in 2009. The aim of the Committee is the assist the European Commission in creating the up guidelines for implementing EU policies for RDs. The Committee recommended the institution national plans for RDs before the end of 2013 (9 June 2009). In order to raise awareness on RDs a Rare Disease Day was created [9]. The day was first held in Europe and Canada in February 2008.

Support groups

For some of the well-known RDs, such as Down syndrome, cystic fibrosis, haemophilia, there are support networks at national and international levels [10, 11].

Web resources are also important. Orphanet (a database of rare diseases and orphan drugs) quotes more than 4600 resources for more than 1500 RDs. This database contains an on-line encyclopaedia and a directory of services for patients and professionals.

Macedonia

What is the present situation with RDs in Macedonia? First, there are no official registries at the national level. Therefore the full picture and the consequences for the society are not known. Articles on metabolic, nephrologic, tumor, haematologic, genetic and dysmorphologic diseases and syndromes were found published by Macedonian professionals on Pubmed [12].

Those articles give only a very narrow insight into the frequency, diagnosis and treatment of RDs. It is obvious that this is an iceberg situation: one sees only the tip of it.

However, the sheer number of published articles indicates that a number of physicians are educated to diagnose RDs, and oftentimes find new insight in some of their particularities. Some patients are treated (Hunter's syndrome), some other children and adults not (Gaucher's disease in children and adults). The country also lacks a significant screening for multiple diseases: Macedonia screens only hypothyroidism, while some European countries screen ~ 30 diseases. Nevertheless, an education program directed towards the RDs should be created, along with a national registries and an increased assistance of the state in diagnosing and treating those diseases.

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Резиме

**ЗА РЕТКИТЕ И „СУПЕР РЕТКИТЕ“ БОЛЕСТИ:
УВИД ОД РЕПУБЛИКА МАКЕДОНИЈА**

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Ретките болести (РБ) имаат големо значење за пациентите, истражувачите, лекарите и за општеството. РБ се можни цели за нови начини на лекување. Тие се важен извор за нови увиди во базичните закони на природата и важни модели за откривање на специфични механизми во настанувањето и развитокот на многу болести (како ретки така и фреквентни). Молекуларната медицина создаде нови можности за дијагностицирање на РБ. Во некои случаи постојат и нови типови на лекување со молекуларни методи, со употреба на рекомбинантни ензими или со генска терапија. РБ се голем проблем за пациентите, бидејќи нивната болест е малку позната во општеството. Здравственото осигурување, непознавајќи ги карактеристиките на болеста и гледајќи ја високата цена за лекување, одбегнува да ги финансира трошоците. За секое општество, вкупниот издатоk за дијагностицирање и лекување на РБ е голем, бидејќи болестите се мошне ретки, но нивниот кумулативен број е голем. За земјите во развој цената за дијагностицирање и лекување на РБ често го надминува работ на економската подносливост.

Клучни зборови: ретки болести, дефиниции, влијание на општеството, Македонија.

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