www.raredis.org April 2013 (Issue 15, Year IV)

# RARE DISEASES ORPHAN DRUGS

Official Newsletter of the Bulgarian Association for Promotion of Education and Science (BAPES)

## FOCUS ON:

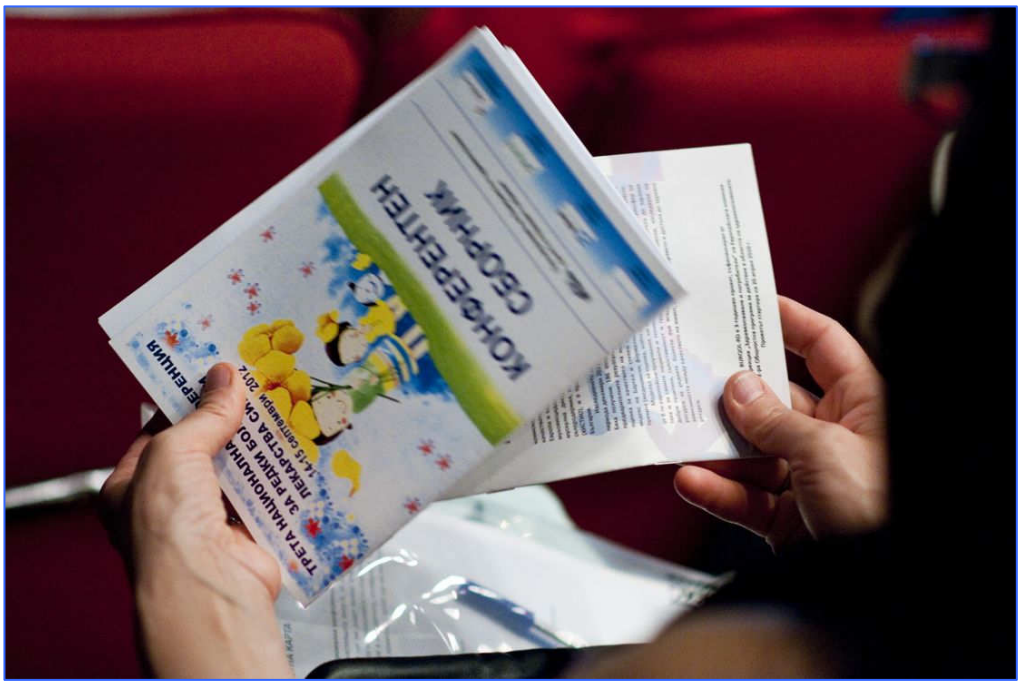
## A NEW BEGINNING FOR RARE DISEASES IN BULGARIA

Dear friends,

Last month has brought us some very interesting news. Long time expected official centres of expertise for rare diseases in Bulgaria are close to the finish line. These centres are expected to be regulated simultaneously with the transposition of the provisions of the European Directive on cross-border healthcare. This should be done in a separate ordinance of the Ministry of Health. So, the first major result of last year's National Conference for Rare Diseases is a fact. Let us remind you that these centres and their criteria for designation were the central theme of the event. Medical professionals and patients participated actively in the discussion about what exactly these criteria should be in order to allow these structures to meet the expectations of the various rare diseases stakeholders, as well as to be as efficient as possible under the Bulgarian health system's framework. Today, the then-collected potential began to realise itself and we all hope that these promises will be a fact very soon.

The Fourth National Conference for Rare Diseases and Orphan Drugs is now in front of us. This year again we would like to kndly invite all patients and patient organisations, medical professionals and students, representatives of health authorities and media, all rare diseases stakeholders working for the common progress in the field of rare diseases. Dear friends, we hope you will participate in this year`s event and contribute to further develop the idea that we are working on together for so many years – a better environment in which changes in rare diseases field do happen. The European Cross-Border Healthcare Directive is a good opprtunity to start solving these problems. Everything is in our hands now – our ability to work together and to achieve consensus is crucial for making all of our dreams come true.

Speaking of a new beginning, we must mention the official announcement of the preparation of a second national plan for rare diseases in Bulgaria. Yes, the current programme has not matched high expectations, but we have to be realistic and to be able to learn from our own mistakes. We hope you will support us and let's us put together a "new" start during the Fourth National Conference for Rare Diseases on 13-14 September 2013 in Plovdiv!



# 4th NATIONAL CONFERENCE FOR RARE DISEASES AND ORPHAN DRUGS

**13-14 September 2013**
**Congress Centre, Novotel-Plovdiv**

- The biggest rare diseases event in Bulgaria for 2013
- Speaker panel of leading rare diseases experts
- Multidisciplinary programem
- Poster session
- Printed conference proceedings book

**For further information and early registration, please visit**

## www.conf2013.raredis.org

# RARE DISEASES IN RUSSIA –

# TOWARDS MORE MUTUAL COMPREHENSION AND SOLIDARITY

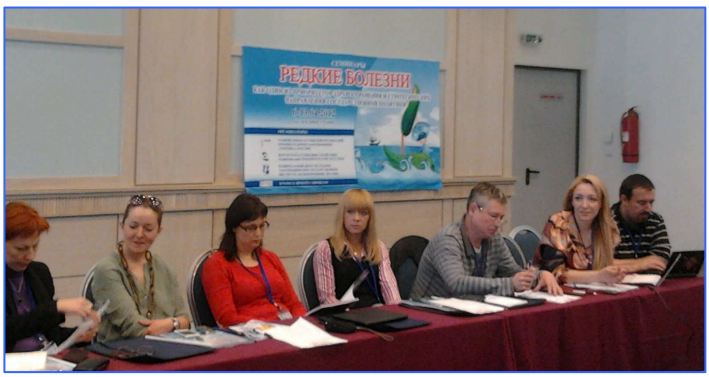
Two years ago, in September 2011, ICRDOD, together with the Russian National Association of Patient Organisations “Genetics” and the Italian National Centre for Rare Diseases initiated the Rare Diseases Summer School for health authorities and legislators. The idea had its logical explanation. For years the three organisations have been working together at international level for the overall progress on rare diseases in Europe. Additionally, common experience shows that any change starts with small stakeholder action group (patients and/or physicians) to slowly develop and after that to become an overarching measure or activity, of which all sides will benefit (e.g., national programme, specialised service, etc.). The successful outcome requires first and foremost political will and attention to the problem of rare diseases.

In Eastern Europe until very recently rare diseases were perceived as a dark, unknown topic by the general public and the politicians in particular. The limited healthcare resources in combination with the growing health services demand and increased expectations of the society have made the politicians be very cautious with health policies. They must respond to numerous claims with few resources. In this context, it is difficult for rare diseases to compete for attention. But at the heart of the matter it is neither the “prioritisation” of a disease over another, nor the scarces finances. The question comes down to a simple lack of awareness on rare diseases. Having been once “inside” these issues, no one could remain indifferent and uncompassionate. This is how the idea of a school on rare diseases for health policy makers and legislators was born. This was supposed to be a counterpart to the understanding that rare diseases are uninteresting topic for the society, as well as to be an effort to raise public awareness of people, whom progress in this area actually depends on.


During the last few years, rare diseases issues in Russia are getting more and more answers. The enormous progress of the local patient organisations is to be considered in first place. These associations have come a long way, putting a lot of efforts in order to make these claims heard. The newly found opportunities for international cooperation in this area are another important factor. Russia has already held the Fifth Eastern European Conference for Rare Diseases in 2010, various EUROPLAN events, and at the end of 2013, St. Petersburg would host the annual ICORD conference, the largest platform worldwide for physicians, patients and industry for global partnership on rare diseases. It should also mention the so-called “7 Nosologies” Programme, as part of which Russia is implementing a national registry for seven groups of rare diseases. This is an especially significant achievement, given the fact that there are no other state funded rare disease specific registries in Eastern Europe. In this sense, Russia could already offer its very own input and expertise in the field of rare diseases public health.

During last year's second edition of the Summer School for Rare Diseases, held in April 2012, the participants, including representatives of federal and regional authorities, academic institutions, hospitals, patient organisations and industry had the opprtunity to get indroduced to the rare diseases' topic and all its aspects – from the definition of a rare disease to finding out specific problems and ways to solve them. At the end of the training cycle, the participants could give their own assessment on what the level of progress is, as well as what kind of priorities for actions and measures in this area could be defined. The results are interesting, as it represents the views of all rare diseases stakeholders in Russia, and consensus and collaboration within this group are key to moving on these issues.

In terms of rare diseases awareness and specialised education the participants couldn't reach agreement. However, positive changes in this area were noted. The factor of first "contact" with rare diseases is also important to consider. Healthcare professionals demonstrated high confidence in their rare diseases competence, while all other categories of participants were relatively "new" with rare diseases and their first experience dated back from 2-3 years ago. Similar results were obtained about the provision of healthcare and social services to rare diseases patients, as well as the development of rare diseases research in Russia.




An interesting relation and almost unanimity are detected about the access to orphan drugs and rare diseases registries. Access to orphan drug therapy is unambiguously evaluated by all groups as unsatisfactory. The reasons for this are complex and very similar across Eastern Europe. These innovative medications are required to provide reliable evidence of clinical effectiveness and superiority, safety and so on. These are quite reasonable demands, but here it comes to medications for a few and sometimes very isolated cases. Therefore, the opinion that there is a need to strengthen the activities associated with rare diseases registries is more than reasonable. This is a proven way to gather such information.

The role of the patient organisations was another consensus issue. All participants highly appreciated the work and the contributions of the Russian patients with rare diseases regarding awareness and advocacy for the development of specific strategies in this area. Especially for Russia, these organisations serve as a bridge for exchange of experience and ideas with others. This is certainly extremely beneficial to all stakeholders.


All participants were asked to identify specific priority areas for solving rare diseases problems in Russia. Having in mind the strong correlation between all rare diseases-related issues, all attendants reasonably stressed that parallel work is needed on all fronts. Progress in one area can not be achieved at the expense of another, as the "weakest" link would affect the whole chain. Participants declared support for comprehensive measures to improve access to treatment and rehabilitation of patients with rare diseases.

When asked whether they considered that a national plan for rare diseases will help to achieve these priorities, the majority agreed. Patients were consistently referred as leading partners in preparing and implementing such policies. Close collaboration with federal officials and medical community is also underlined. All stakeholders believe that steady progress can be ensured only if all sides work together and respect each others' specifics. So, actually participants see the whole Russian society as a locomoteur for rare disases' advance. When discussing how they see ensuring the sustainable development of these measures, the majority of respondents were in favor of special legislation at federal level. For a large country like Russia it is important to have uniform regulations between the regions in order to seek stability and harmonisation of the measures for rare diseases. Public consensus and political will to address these issues were further indicated, as they were the main reason for holding the event.

All participants praised the benefits of initiatives like the Rare Diseases Summer School. This positive opinion, as well as the subsequent results shows that awareness is indeed the most important consideration when looking for and offering solutions for rare diseases. Rare diseases do not suffer from lack of attention. The lack of understanding of their nature is the real obstacle. Any initiative that raises awareness among certain social groups, that improves education and training, or that allows for the exchange of experience and ideas, is certainly a step forward for rare diseases. The more people learn about them, the more solidarity and comprehension are built that will eventually lead to successful solutions in this area.

# CENTRES OF EXPERTISE FOR RARE DISEASES, NATIONAL EXPERT COUNCIL FOR RARE DISEASES, AND A NEW NATIONAL PLAN FOR RARE DISEASES

***A new beginning after the Second Balkan Conference for Rare Diseases***


Important news for everyone connected with the problem of rare diseases in the country were announced during the Second Balkan Conference on Rare Diseases, held on 20-21 April, Sofia. This year's event entitled "Better communication – better treatment" was organised by the National Alliance of People with Rare Diseases and was attended by participants from Bulgaria, Greece, Romania, Turkey, Croatia, Montenegro, Slovenia, Serbia, Bosnia and Herzegovina, Macedonia and Albania. The European organisation of patients with rare diseases EURORDIS also delegated a representative and leading clinicians from Bulgaria took part as well, presenting recent developments in the diagnosis, treatment and prevention of rare diseases.

The initiative went under the auspices of the Ministry of Health (MoH), whose representative reported what stage the transposition of the European Directive on patients' rights in cross-border healthcare has reached. It was announced that the planned amendments to the Health Law are in the final stage and is expected rare diseases centres of expertise to be regulated soon. The criteria for designation, adopted by the EU Committee of Experts on Rare Diseases (EUCERD) in 2011 and actively discussed during the Third National Conference for Rare Diseases in 2012, will be used as basis for this new regulation.

These centres in Bulgaria are supposed to be integrated into the existing and future European reference networks for rare diseases which are meant to improve and standardise the access of patients with rare diseases in Europe to timely and quality health care. This is something that is not always possible especially in smaller countries of Eastern Europe.

Collaboration and interaction between these centres must increase the visibility of these structures for patients and general practitioners, as well as to reinforce the organisation of professional training and research in the highly specialised hospitals, which treat and follow up these people. In this regard, hard work is also underway in our country on the inclusion of rare diseases in different medical specialties' standards that are currently being updated.

MoH also announced that the newly formed National Expert Council on Rare Diseases (NECRD), established in February this year and replacing the National Advisory Council on Rare Diseases is to start working very soon. NESRB has a new member composition and includes a significant number of clinicians and a patient representative. The main task of the new body will be the preparation of a new national plan for rare diseases. This news is undoubtedly a positive sign for the attention and commitment of the health authorities in Bulgaria to the problems of people with rare diseases. But at the same time we could not forget the current programme, which despite good ideas on paper could not meet the expectations of doctors and patients, and many questions remained unsolved. Now it is very important to analyse why the good measures were not be implemented and what led to the imbalance between objectives and actions. Patient organisations used this opportunity to note the persistence of serious problems with the access to drug therapy and the lack of a national registry of people with rare diseases. These and many other questions are to be done and would require a significant amount of work. There would be a meeting of NECRB that has to outline the objectives and priorities of the future national programme and the framework of its funding. Whether the second national plan for rare diseases will have a different fate than the previous one would greatly depend on these steps.

First of all, it is necessary to draw a detailed analysis and assessment of progress to date in order to restructure future tasks to accomplish, as well as to achieve consensus among doctors and patients about the upcoming goals and objectives. Last but not least – sufficient funding and transparency control of the execution of the programme are a must too. We will continue to monitor this topic and provide you with more views on this issue in our next issues.

*Photos © National Alliance of People with Rare Diseases, 2013*

# GUILLAIN-BARRÉ SYNDROME

## DEFINITION AND PREVALENCE

Guillain-Barre syndrome (GBS) is an acute inflammatory demyelinating polyneuropathy characterised most commonly by symmetric limb weakness and loss of tendon reflexes. GBS represents a spectrum of rare post-infectious neuropathies that usually occur in otherwise healthy patients. GBS is clinically heterogeneous and encompasses acute inflammatory demyelinating polyneuropathy (AIDP), which is the most common form of GBS, Miller Fisher syndrome (MFS), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), acute panautonomic neuropathy and Bickerstaff's brainstem encephalitis (BBE). Annual incidence is about 0.6–4 per 100 000 people. Men are one and a half times more likely to be affected than women. The incidence increases with age.

## ETIOLOGY

Although rare familial cases have been reported, GBS is considered to be a complex multifactorial disorder with both genetic and environmental factors rather than a disorder following simple mendelian inheritance. In GBS the immune system starts to destroy the myelin sheath that surrounds the axons of many peripheral nerves, or even the axons themselves. The myelin sheath surrounding the axons speeds up the transmission of nerve signals and allows the transmission of signals over long distances. As a result of myelin or axon loss, impulse transmission along nerve pathways is disrupted, giving rise to weakness, sensory loss, and unusual sensory symptoms such as tingling and burning. In the majority of cases GBS occurs after infectious respiratory or gastrointestinal disease. Most often this happens after past infection with Campylobacter jejuni bacteria causing acute enteritis. There have been reported cases of GBS after vaccinations and surgeries.

## DIAGNOSIS

GBS disgnosis is based on rapid development of muscle paralysis, areflexia, absence of fever and a likely inciting event. Cerebrospinal fluid analysis (through a lumbar spinal puncture) and electrodiagnostic tests of nerves and muscles are the common diagnostic tests for GBS.

## CLINICAL PICTURE

Clinical picture of GBS includes muscle weakness, sensory loss, bulbar weakness, oropharyngeal dysphagia, dysfunction of the autonomic nervous system, respiratory failure, as well as neurological findings. The first symptoms of the disorder include varying weakness or tingling in the legs. In many cases, abnormal weakness and abnormal sensations spread to the upper limbs. In most cases, spontaneous pain in the spinal cord and the muscle of the body or limbs occurs at different stages of the disease. The intensity of symptoms increases, while muscles cannot be used due to weakness and the patient is almost totally paralyzed. In these cases the condition is life threatening and is treated as an emergency. The patient is often put on a respirator for assisted breathing. Despite severe course of the disease, most patients recover from even the most severe cases of UDB, although it remains available in some degree of weakness. The first signs of the disease are usually several days or weeks after the patient has had symptoms of respiratory or gastrointestinal infection.

GBS can be a debilitating condition due to its sudden and unpredictable development. The most pronounced weakness develops in the period up to two weeks from the beginning, and by the third week 90% of patients are in the worst condition. The recovery period can be from several weeks to several years. Studies show that residual symptoms are observed in approximately 30% of the patients after three years, and in 3% of them can be observed sensory or motor disorders such as relapse years after the disease.

**TREATMENT**

There is no known cure for GBS, but therapies can lessen the severity of the illness and accelerate the recovery in most patients. There are also a number of ways to treat the complications of the disease. Currently, plasmapheresis and high-dose immunoglobulin therapy are used. Plasmapheresis seems to reduce the severity and duration of GBS episode. In high-dose immunoglobulin therapy, physicians give intravenous injections of the proteins that in small quantities, the immune system uses naturally to attack invading organism. Investigators have found that giving high doses of these immunoglobulins, derived from a pool of thousands of normal donors, to Guillain-Barré patients can lessen the immune attack on the nervous system. The most critical part of the treatment for this syndrome consists of keeping the patient's body functioning during recovery of the nervous system. This can sometimes require placing the patient on a respirator, a heart monitor, or other machines that assist body function. Adequate physiotherapy and rehabilitation are also important.

Prognosis varies depending on the form of GBS, ranging from full recovery to inability to walk and fatal outcome.

**REHABILITATION AND FOLLOW-UP CARE**

Accurate rehabilitation and follow-up care are extremly important, especially after the acute phase of GBS. Treatment with the help of a multidisciplinary team focuses on improving activities of daily living. Although most people eventually recover, duration of the disease is unpredictable and may require months of care and rehabilitation. During this period, patients need to learn again how how to use the affected muscles.

There is evidence supporting physiotherapy in helping patients with GBS regain strength, endurance, and gait qualities, as well as helping them prevent contractures, bedsores, and cardiopulmonary difficulties. Physiotherapists assist to correct functional movement, avoiding harmful compensations that might have a negative effect in the long run. If the patient was intubated or received a tracheostomy, speech and language therapy may be needed as well.

Use of assistive devices (braces, walkers, wheelchairs, etc.) is very often also recommended to support mobility during recovery or in case of long-term damage.

**Bibliography**


1. Van Doorn PA, Ruts L, Jacobs BC. Clinical features, pathogenesis, and treatment of Guillain-Barré syndrome. Lancet Neurol 7 (10): 939–50.
2. Pithadia AB, Kakadia N. Guillain-Barré syndrome. Pharmacol Rep 62(2): 220–32.
3. Brooks H, Christian AS, May AE. Pregnancy, anaesthesia and Guillain-Barré syndrome.Anaesthesia 55 (9): 894–8
4. Ang CW, Jacobs BC, Laman JD. Guillain-Barré syndrome: a true case of molecular mimicry. Trends in Immunoology 25 (2): 61–66.
5. Kuwabara S et al. Does Campylobacter jejuni infection elicit "demyelinating" Guillain-Barré syndrome?. Neurology (Lippincott Williams & Wilkins) 63 (3): 529–33.
6. Sivadon-Tardy V et al. Guillain-Barré syndrome and influenza virus infection. Clinical Infectious Diseases (The University of Chicago Press) 48 (1): 48–56.
7. Lehmann HCP et al. Guillain-Barré syndrome following influenza vaccination. Lancet Infect Dis 10 (9): 643–51.
8. Hughes RA, Wijdicks EF, Barohn R et al. Practice parameter: immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology.. Neurology 61 (6): 736–40.
9. Davidson I, Wilson C, Walton T et al. Physiotherapy and guillain-barre syndrome: Results of a national survey. Physiotherapy, 95(3), 157-163.

## UPCOMING RARE DISEASES CONFERENCES, WORKSHOPS AND INITIATIVES

- **12-14 June – 12th European Symposium on Congenital Anomalies, Zagreb**
- **17-21 July – 8th International Prader-Willi Syndrome Conference, Cambridge**
- **13-14 September – 4th National Conference for Rare Diseases and Orphan Drugs, Plovdiv**
- **19-23 October – Thalassemia International Federation World Congress, Abu Dhabi**
- **1-3 November – 8th ICORD International Conference for Rare Diseases, Saint Petersburg**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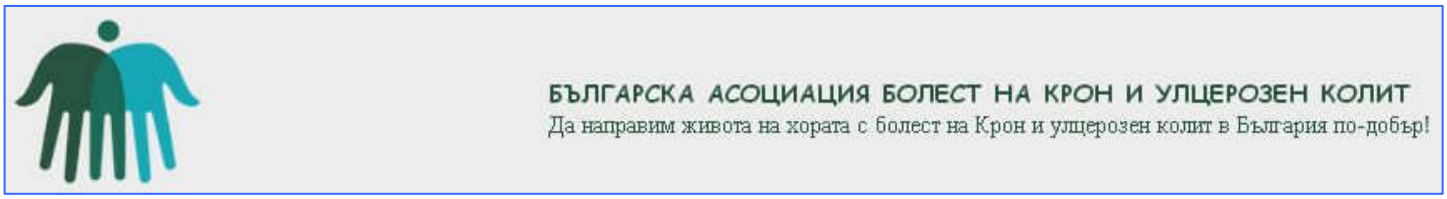


## BULGARIAN PATIENT ASSOCIATION FOR CROHN DISEASE AND ULCERATIVE COLITIS

The Bulgarian Patient Association for Crohn Disease and Ulcerative Colitis (BABKUK) is one of the youngest patient organisations of people with rare diseases in Bulgaria. Founded by seven enthusiasts led by their desire to fight chronic-inflammatory bowel diseases and improve the quality of life of people suffering from these diseases in Bulgaria, the organisation is now recognised by physicians and patients as responsible and active partner on rare diseases issues. Since the beginning of 2013 BABKUK has launched its own website where you can find useful information about the disease, as well as many practical tips on everyday topics.

*For further information, please visit BABKUK official website – http://www.babkuk.org/index.html.*

**Editorial Box**

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