

REVIEW

## PHYSICIAN – PATIENT RELATIONSHIP IN RARE DISEASES: AN ETHICAL APPROACH

**Bianca HANGANU<sup>1</sup>, Irina S. MANOILESCU<sup>1,2</sup>, Elena A. BIRLESCU<sup>1,2</sup>, Veronica MOCANU<sup>1</sup>, Andreea A. HLESCU<sup>1,2</sup>✉, Beatrice G. IOAN<sup>1,2</sup>**

<sup>1</sup> „Grigore T. Popa“ University of Medicine and Pharmacy, Iasi, Romania

<sup>2</sup> Institute of Legal Medicine, Iasi, Romania

Received 28 Jan 2019, Accepted 26 Febr 2019

<https://doi.org/10.31688/ABMU.2019.54.1.23>

### ABSTRACT

Rare diseases are a special category of pathology recognized as such relatively recently, starting about 30 years ago in the USA and around the year 2000 in Europe. Rare diseases are clinically and therapeutically heterogeneous, being characterized by a number of common aspects that have a negative impact on patients' evolution and quality of life, such as: delayed diagnosis, limited scientific knowledge about some of them, lack of treatment or limited availability of treatment. At the same time, information campaigns on rare diseases are limited, and the number of associations of patients that promote their interests and rights is also reduced. The quality of physician-patient relationship is particularly important in the management of rare diseases, non-medical aspects, especially the ethical and moral aspects, being often more relevant to patients than the medical aspects. The ethical framework for the analysis of rare diseases encompasses a number of particular aspects, generated on the one hand by the need to properly approach patients suffering from rare diseases in the context of rising expectations for the medical system, and on the other hand, the pro-profit behavior of the pharma companies. This paper analyzes the particular ethical issues identified in the clinical approach on rare diseases,

### RÉSUMÉ

**La relation médecin – patients en cas de maladies rares ; une approche éthique**

Les maladies rares constituent une catégorie particulière de pathologies reconnues comme telles relativement de date récente. Elles ont débuté il y a environ 30 ans aux États-Unis et autour de l'an 2000 en Europe. Les maladies rares sont cliniquement et thérapeutiquement hétérogènes et se caractérisent par un certain nombre d'aspects communs qui ont un impact négatif sur l'évolution et la qualité de vie des patients, notamment: diagnostic tardif, connaissances scientifiques limitées sur certains d'entre eux, manque de traitement ou disponibilité limitée de traitement. Dans le même temps, les campagnes d'information sur les maladies rares sont limitées et le nombre d'associations de patients qui défendent leurs intérêts et leurs droits est également réduit. La qualité de la relation médecin-patient est particulièrement importante dans la gestion des maladies rares. Les aspects non médicaux, en particulier les aspects éthiques et moraux, sont souvent plus pertinents pour les patients que les aspects médicaux. Le cadre éthique de l'analyse des maladies rares englobe un certain nombre d'aspects particuliers, engendrés d'une part par la nécessité d'approcher

✉ Address for correspondence:

Andreea A. HLESCU

„Grigore T. Popa“ University of Medicine and Pharmacy, Iasi, Romania

Address: 16, Universitatii Str, Iasi, Romania, 700115

E-mail: [andreea.velnic@yahoo.com](mailto:andreea.velnic@yahoo.com)

with a focus on the particularities of the physician-patient relationship in this context.

**Keywords:** rare diseases, physician-patient relationship, communication, non-medical aspects, ethics.

## INTRODUCTION

Rare or “orphan” diseases are a category of pathology that includes chronic, life-threatening diseases, of various etiologies, including genetic determinism, which concerns a limited number of people either as prevalence or as total number of cases in the general population<sup>1,2</sup>. According to the Orphan Drug Act (1983) and later on to the USA Rare Diseases Act (2002), for a disease to be considered rare, it should affect less than 200,000 USA citizens<sup>1,3</sup>, meaning the prevalence rate would be around 1/1,500<sup>1</sup> or < 7.5 per 10,000 Americans<sup>3</sup>. On the Asian continent, in Japan, rare diseases are classified those that affect less than 50,000 individuals, with the corresponding prevalence of around 1/2,500<sup>1</sup>. In the European Union (EU) a disease is considered rare if its prevalence does not exceed 1/2,000<sup>1</sup>, which corresponds to not more than five per 10,000 Europeans<sup>3,4</sup>.

Rare diseases have been recognized as a special category in public health relatively recently, namely in 1983 in the USA (the year when the Orphan Drug Act – the first legislation regarding orphan drugs, was introduced in this country), in the 1990s in Japan, South Korea, Singapore, Taiwan and Australia, and in 2000 by the European Union through the adoption of the “European Regulation on Orphan Medicinal Products”<sup>4,5</sup>. To date, about 7,000 rare diseases have been identified, of which over 80% have genetic causes<sup>6</sup>. Genetic etiology adds to the severity of these diseases as currently many of the genes are still unknown and the condition to treat a disease is knowing its cause(s)<sup>6</sup>.

Efforts to improve the situation of people suffering from rare diseases are becoming more and more intense, making it necessary to determine the extent to which rare diseases are particular and require particular attitudes in public health policies<sup>2,5</sup>.

The low prevalence, the lack of information and of research, the delayed diagnosis, the lack of treatment or the high price of the treatment and the low number of experts in this field make the people

correctement les patients souffrant de maladies rares dans le contexte d’attentes grandissantes pour le système médical, et d’autre part par le comportement à but lucratif des sociétés pharmaceutiques. Cet article analyse les problèmes éthiques particuliers identifiés dans l’approche clinique sur les maladies rares, en mettant l’accent sur les particularités de la relation médecin-patient dans ce contexte.

**Mots-clés:** maladies rares, relation médecin-patient, communication, aspects non médicaux, éthique.

affected by these diseases not to benefit or to benefit to a low extent from the medical resources and medical services they need and thus to represent a vulnerable population.

Given that each of the rare diseases has a low prevalence, it is considered that they have a low impact on society. However, in assessing the impact of rare diseases, it must be taken into account that these diseases represent an important burden for the sick and the members of their families<sup>4</sup>.

## THE CHARACTERISTICS OF RARE DISEASES AND THEIR RELEVANCE TO THE PATIENT, FAMILY AND THE PHYSICIAN-PATIENT RELATIONSHIP

The group of rare diseases is very varied in etiology and symptomatology. However, rare diseases have common traits that have a negative impact on the sick and their families. Rare diseases are severe, chronic, often debilitating, degenerative, life-threatening diseases that often affect the autonomy of patients, which has a negative impact on the quality of their lives.

Rare diseases also create a psychological burden on the sick, which is aggravated by the feeling of lack of support. Persons suffering from rare diseases are at risk of being looked at differently by those who are unfamiliar with their problems, and they also risk that people around them do not understand the impact that rare diseases have on those affected<sup>7</sup>. These patients are particular for two reasons: on the one hand, because their suffering is chronic and sometimes becomes a source of stigma for those around<sup>7</sup>, and on the other hand because the rarity of the illnesses poses challenges for both the patient (e.g., they are looked at differently) and the general population<sup>7</sup>. Negligence by ignorance can also contribute to burdening society, being necessary to establish collaboration between state institutions and NGOs (or support groups) to increase public awareness<sup>8</sup>.

Most rare diseases are incurable and difficult to manage therapeutically<sup>9</sup>, and patients with rare

diseases most often require complex multidisciplinary treatment<sup>10</sup>. The development of orphan drugs is often left aside in relation to other drugs with higher demand on the market. Even if a drug for rare diseases is generated, it can be prohibitively expensive, which is why legislation has been developed to stimulate pharmaceutical companies to perform research about orphan drugs by providing incentives in the USA, the EU, Japan, and Australia<sup>11</sup>.

There are currently few information campaigns and large-scale screening programs targeting rare diseases.

Patient organizations play an important role in attracting attention to people suffering from rare diseases and catalyzing research in the field, acting as lobby groups. The role of patient associations is to be a bridge between patients and pharma companies. Associations should be involved in the design of the studies, having the role to improve dialogue and communication between pharma companies, patients and their families, contributing to a better understanding of research and a better quality informed consent<sup>12</sup>. Two large organizations from USA, founded by patients and their families- the Organization for Rare Disorders- NORD (founded in 1983) and the Genetic Alliance (GA), which are in charge of several smaller groups, offer financial support for research in the field of therapy for rare diseases in order to discover new treatments for these diseases<sup>8</sup>. In Europe, the European Organization for Rare Diseases (EURORDIS) supports millions of patients, covering over 1,000 rare diseases<sup>8</sup>. Japan is supporting patients with rare diseases through the Intractable Disease Information Center, which provides both practical information (general information about diseases, lists of experts, contact information of Japanese support groups) and free treatment that becomes possibly through collaboration with state institutions and insurance companies<sup>8</sup>.

#### **ETHICAL FRAMEWORK FOR APPROACHING THE RARE DISEASES**

Given the characteristics of rare diseases and, in particular, their rarity, it is difficult to identify the moral borders of society's obligations towards these patients. These borders are defined by several aspects, in particular: the responsibility of doctors, economic viability, national equity and fairness in the opportunities and moral obligations of society, but focused on each individual case.

Rare diseases imply particular ethical and economic considerations due to barriers to have access to diagnosis and treatment, especially in minority groups, together with geographic and cultural

marginalization and distrust in state institutions. Another issue is the existence of cohabitation in isolated communities. Likewise, the variability of symptoms and therapeutic options makes it difficult or even impossible to develop standardized protocols and guidelines<sup>10</sup>.

The high cost of treatments for rare diseases represents a major impediment to their effective therapeutic management<sup>10,13</sup>. The cost of treatment is inversely proportional to the rarity of the disease. The market for medicines for rare diseases (the number of patients using them) is low, which implies that each patient should pay an additional fee. At the same time, it is difficult to identify enough patients to run clinical trials, which increases the duration of the study, the number of research sites involved, and decreases the statistical power and the possibility the possibility to demonstrate the differences between various treatment methods. Thus, due to the high costs, the tendency of stakeholders in the medical system is to reject providing the treatment.

There are, however, supporters for providing the treatment for rare diseases. They found their approach on two arguments:

1. The so-called "Rule of the rescue", originally proposed by Jonsen in 1986, which refers to the social imperative of saving identifiable individuals facing the danger of avoidable death or disability (e.g., saving the miners captured underground, without taking into account the costs of the rescue operations). Under these circumstances, we cannot base our decisions on conventional definitions or fixed cost-effectiveness thresholds. The Australian Pharmaceutical Benefits Advisory Committee states that three conditions must be fulfilled for the application of this rule in medicine: there is no alternative treatment, the medical condition is severe, progressive and decreases life expectancy, and the number of patients suffering from this disease is very low.
2. The relatively small impact of the cost of treating these diseases for the health budget.

Therefore, the issue of rare diseases and their treatment should be approached with caution, given that classical cost-effectiveness calculations do not apply in such situations, where the principle of distributive justice is overriding. In this analysis, it should be taken into account the indirect costs and intangible costs and benefits generated by the neglect of rare diseases, such as the cost of complications, more frequent visits to the hospital, absenteeism at work etc., which increase the social burden of these diseases. All these aspects required the application of special regulations and schemes for treatments for rare diseases<sup>3,8,14,15</sup>.

A special situation in the context of rare diseases is neonatal screening designed to detect some of these. In Wilson and Jungner's opinion, neonatal screening in general should be limited to cases for which treatment exists, starting from the need to promote the best interests of the child. However, in the case of rare diseases, this condition should not be made for a number of reasons: a long interval of about 2 years, from the first clinical suspicion and until diagnosis, the good results of the early (even symptomatic) therapeutic intervention and parents' opinion that early diagnosis would have made them better parents, which would have promoted the best interests of the child<sup>16</sup>.

#### **PARTICULARITIES OF PHYSICIAN-PATIENT RELATIONSHIP IN RARE DISEASES: NON-MEDICAL ASPECTS AND IMPORTANCE OF COMMUNICATION**

In order for patients with rare diseases to cope with the long-term evolution of the disease and its particularities, in the sense of achieving a good quality of life<sup>7</sup>, it is necessary for them to receive all the information that will help them understand the disease, identify the skills and resources that enable them to survive with the disease<sup>17</sup>, information that can be obtained through effective communication between physician and patient. In order to provide the appropriate information, all medical staff must be prepared to interact with patients with rare diseases, have knowledge of these pathologic conditions, and about the manner they can be addressed<sup>7</sup>, all the more so as the reduced prevalence of rare diseases could be a risk factor to the professional interest of the specialists<sup>10</sup>. It is currently recognized that the field of rare diseases suffers from the lack of experts, which is why resources are needed in order to improve clinicians' competence in recognizing these diseases in order to establish the diagnosis and the proper therapeutic approach in a timely manner<sup>4</sup>.

A good assimilation of knowledge, which can then be passed on to patients in an acceptable and understandable manner, can be achieved through multidisciplinary teamwork, each member of the team sharing their colleagues the information they hold regarding the care of patients with rare diseases, thus resulting a better decision on how to manage these diseases<sup>10</sup>.

Physician-patient relationship strongly influences the recovery of the patient through adherence (or lack thereof) to treatment and consequently through favorable (or not) disease evolution and the patient's quality of life<sup>18,19</sup>. The many benefits of effective physician-patient communication are already recognized: disappearance of patient's feelings of insecurity<sup>18</sup>,

faster diagnosis- which will lead to pertinent therapeutic recommendations, patient's adherence to treatment<sup>19</sup> with the improvement of the healing process<sup>18</sup>, and the consecutive improvement of the quality of life, costs reduction by decreasing the number of days of hospitalization, to which we can add the psychological counseling to help the patient to increase his/her self-confidence<sup>19</sup>. Also recognized are the disadvantages of poor communication: losing the trust of the patients both in the medical system and in themselves, materialized in the lack of adherence to treatment<sup>19</sup>, the inappropriate use of medical resources, which will lead to the increase of costs<sup>18</sup>.

The traditional physician-patient relationship, in which prevailed paternalism, was replaced by the patient-centered relationship model, based on collaborative care<sup>19</sup> and mutual exchange of information<sup>18,19</sup>. This type of relationship, based on the collaboration between the physician and the patient in establishing the therapeutic scheme is especially necessary in rare diseases, where the burden of the disease is greater, especially as the specialty knowledge is reduced, and the psychological impact upon the patient after receiving the diagnosis of an incurable disease is important. Additionally, the patient may have to travel long distances to get access to specialized medical care<sup>20</sup>. The paternalist model, in which the physician dominates the relationship through his/her knowledge, cannot be applied to rare diseases precisely because of the lack of information on the diagnosis, evolution and treatment of these diseases, which may have a variety of ambiguous symptoms<sup>18</sup>.

Risks of misunderstanding rare diseases can have multiple sources. For the patient, it is about: anxiety, (created by) uncertainty, powerlessness<sup>21</sup>. People around the patient may experience fear, negative reactions, rejection- which will lead to the stigmatization of the patient<sup>22</sup>, may consider those suffering from rare diseases (e.g., epilepsy) as being violent or dangerous<sup>23</sup>. The physician risks a superficial approach of the patient or may have a tendency to place the symptoms in a psychological context (e.g., the symptoms of the Chronic Fatigue Syndrome)<sup>7,24</sup>, may be marked by ambiguity, uncertainty, unpredictability in routine, which will lead to unstable and uncontrolled situation for the patient<sup>10</sup>.

Evidence from the literature demonstrates the utility of the shared decision-making process when the physician and the patient work together to make the best decisions for the benefit of the patient<sup>19</sup>. Rare diseases represent a circumstance in which it is mostly underlined the importance of this collaboration in order to properly manage the situation by identifying together practical solutions<sup>10</sup>.

Non-medical aspects, especially the moral and political issues, play a key role in the context of rare diseases. Moral considerations regarding the correct treatment of patients with rare diseases are thus important in the context of increasing the people's expectations in the healthcare system and, at the same time, taking into account the exclusively pro-profit behavior of pharma companies currently exposed to criticism due to the negative impact on patients with rare diseases<sup>2, 5</sup>.

A study conducted in France in 2004, which consisted of 44 interviews with patients with rare diseases (29) and with parents of children with rare diseases (15)<sup>5</sup>, showed that patients do not consider as a cause of the specific difficulties they face the characteristics of the disease they suffer (such as: rarity, severity, severe prognosis). Participants consider normal and acceptable situations that are, in fact, incorrect and specific to rare diseases, provided that moral criteria are met by healthcare professionals. Participants would like to meet other people suffering from the same illness or other rare disease, which underlines the importance of support from patient associations. Delayed diagnosis is a common occurrence in rare diseases. However, the participants in the study were not affected by this aspect, considering more important the moral aspects in determining and communicating the diagnosis. Thus, they considered to be normal for physicians to recognize their own limits, to take seriously patient's concerns and to disclose their diagnosis in a proper manner. Therefore, patients and their families did not have any problem because of the delayed diagnosis, considering that the physician's behavior is more important than the period of time at which the diagnosis is established<sup>5</sup>.

In the context of the physician-patient relationship, patients with rare diseases and their families who have participated in the study, have disapproved of a number of attitudes and behaviors from the physicians' side, such as: physicians' refusal to recognize their limits and to seek help in such situations, inappropriate disclosure of diagnosis, which represents a crucial moment in the experience of the disease, or the fact that doctors have not taken seriously the concerns and hopes of patients<sup>5</sup>.

Parents of children with rare diseases who participated in the study wanted to be listened by physicians, to be properly advised and to receive explanations in a manner that shows respect for them and their children suffering from rare diseases. The study noted that physicians tend to be less respectful with the parents of children suffering from rare diseases, perhaps because they are not directly affected by the disease<sup>5</sup>.

Information is essential for patients with rare diseases and for their families. However, it is

recognized in the literature that medical knowledge relating to most of the rare diseases is insufficient<sup>4,5</sup>. It is important to underline that from all the information they have been provided, the participants in the study have retained especially those related to their daily life. Thus, the participants wanted to be informed in a way that would allow them to achieve their own goals, the non-medical advice provided by the medical staff being very important. This is explained by the fact that the patient's perspective is mainly oriented towards the abilities allowed by the illness and not to the inabilities determined by it. So, the patients prefer to receive information focused on their ability to achieve certain goals, to do certain things rather than to focus on the deficiencies (action-oriented, ability-oriented information)<sup>5</sup>.

Regarding limited or absent treatment for rare diseases, the participants did not necessarily complain about this aspect but rather emphasized the moral aspects, namely the distinction between what is morally acceptable (serious efforts to improve their medical and social care) and what is not morally acceptable (providing false information about medical progress or refusing access to known treatments for profitability reasons) within the limits of medical knowledge, regardless of disease. Most participants were satisfied with the honest and reasonable efforts directed towards the improvement of their situation, such as efforts to organize their care, reduction of time spent in the hospital, access to social care and, finally, increase in the quality of their daily lives. In case of the existence of a treatment for their illness, patients should be realistically informed about the side effects and the consequences of discontinuation of treatment<sup>5</sup>.

Associations of patients with rare diseases have a particular relevance, on the one hand, due to their role of promoting the interests of these patients, and on the other hand because of the desire of patients with rare diseases to share with others the "rarity experience", to be in contact with other people suffering from such diseases. The needs of patients with rare diseases are mainly moral, which supports the importance of patient associations<sup>5</sup>.

Multidisciplinary teams, through the variety of their training and the knowledge each member possesses, are an important advantage in approaching the patient with a rare disease. Given the complexity of rare diseases, it is necessary to address the patient in a multidisciplinary approach (involving in the team also patients and their families), the variety of training, knowledge and skills each member possesses, being a valuable asset on the road to a favorable progression and improvement of the quality of life of these patients<sup>10</sup>.

## CONCLUSIONS

Rare diseases are currently an important public health issue with implications in multiple areas: medical, social, educational, economic, governmental etc. The ethical implications of these disorders address the barriers against the access to diagnosis and treatment, with the need to apply distributive justice when it comes to cost-related issues at the expense of cost-effectiveness ratio, and the possibility of the patients of direct benefit after finishing the research on drugs for rare diseases. The particularities of rare diseases and the shortcomings given by the barriers against the diagnosis and treatment also affect the patient-physician relationship, which has particular nuances in this context. In the case of rare diseases non-medical aspects of the illness are at the forefront, and efficient communication and effective involvement of patients and their families in the decision-making and care process create the premises for a favorable evolution, especially in terms of the quality of life of the patients. Because of the complexity of rare diseases, it is necessary to approach them by a multidisciplinary team, adding to the members of this team patient associations that have a special role to play in helping patients to identify effective mechanisms of coping with the disease by offering them the possibility to share their anxieties, hardships, and feelings with other people who are like them, who understand them.

### Compliance with Ethics Requirements:

„The authors declare no conflict of interest regarding this article“

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