ETHICAL ISSUES IN NEWBORN SCREENING

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Abstract
Newborn screening represents an important preventive public health program. Over the time, there were debates about the criteria for inclusion of some diseases in newborn screening. Discussions on the expansion of newborn screening programs focus on three aspects: informed consent, costs and evidence. The authors present data on the criteria that must meet newborn screening and different ethical controversy generated by it.

Keywords: newborn screening, ethics, informed consent.

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Background

The introduction of newborn screening (NBS) is one of the most important advances in the prevention of various diseases in Paediatrics. WHO considers it “the dean” of screening programs used in the last 40 years both in developed and developing countries [1]. The purpose of NBS is to limit the morbidity and mortality ascribed to congenital diseases. NBS began in 1963 in USA when Dr. Robert Guthrie proposed a method for detecting the concentration of phenylalanine. This method (bacterial inhibition) has been adopted worldwide for the diagnosis of phenylketonuria [1]. Later, other diseases began to be detected by analyzing a blood spot: in the late ‘60s - galactosemia, maple syrup urine disease, homocystinuria; in 1970 - congenital hypothyroidism; in 1980 - sickleemia [1,2].

The availability of new technologies such as tandem-mass-spectrometry and DNA analysis have led to an increased number of diseases that can be diagnosed by NBS. Therefore, nowadays, and depending on the country, there can be detected by NBS between 29 and 54 diseases [2,3]. This also triggered, however, an increased number and complexity of NBS-related ethical issues that generate controversies. In Romania, NBS was introduced in 1976 at Mother and Child Care Institute of Bucharest and later, in 2008, in NBS Centers of Cluj Napoca and Timișoara and, in 2009, in Iași Center. Presently, there are two disorders included in NBS: phenylketonuria and congenital hypothyroidism.

Newborn screening concept

NBS tests are not used for diagnosis purposes, but rather for grouping the babies into two categories: babies who may have a specific disease and babies who may not have that disease [1].

James Wilson and Gunnar Jungner established the 10 classical criteria for the applicability of any newborn screening program, criteria that were approved by WHO:

1. the disease included should be an important health problem;
2. the early treatment should have greater benefits than in late stages;
3. the benefits should be greater than physical and psychological risks;
4. there should be a recognizable latent or early symptomatic stage;
5. there should be a suitable test that must be applied early;
6. the test should be acceptable to the population;
7. the natural history of the condition should be well understood;
8. there should be an agreed policy on whom to treat as patients;
9. the cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced;
10. case-finding should be a continuing process and not a “once and for all” project [4,5].

Recently, traditional criteria have been adapted and several new criteria have been introduced:

- the screening program should respond to a recognized need.
- the objectives of screening should be defined at the outset.
- there should be a defined target population.
- there should be scientific evidence of screening programme effectiveness.
- the program should integrate education, testing, clinical services and program management.
- there should be quality assurance, with mechanisms to minimize potential risks of screening.
- the program should ensure informed choice, confidentiality and respect for autonomy.
- the program should promote equity and access to screening for the entire target population.
- program evaluation should be planned from the outset.
- the overall benefits of screening should outweigh the harm [6,7].
- According to the ethical principle of equal rights, NBS must be universal. Emergence of private clinics can reduce the jurisdiction of the state in public health policies. Making voluntary NBS in these clinics creates a secondary screening system that is not universal, depending on the knowledge of the parents and their financial possibilities [9]. Existence of different screening panels in the same country is unacceptable [1].
- “Priciplism” is an ethical theory that was popular in the mid-70s in medical ethics and that provides a useful framework for the current dilemma of NBS. The four principles of this theory that must be respected by a NBS program are:
  a) principle of autonomy (freedom of will and action);
  b) principle of justice (equal and fair treatment for all the individuals);
  c) principle of beneficence (contribution to the welfare of persons);
  d) principle of non-maleficence (the obligation not to cause damage intentionally or negligently) [2,8,10,].

Ethical controversies

The debates on the expansion of NBS programs focus on three issues: informed consent, cost and evidence, the first being the most important. The informed consent is “a tool for the education of the parents, these having the right to know what happened with the blood collected from their child” [1]. It is a voluntary process by which the subject communicates its decision to participate or not to a particular trial after being informed about all the relevant aspects [10]. By informed consent the family of the newborn should receive information about: the purpose of the test, the validity and safety of the method, the medical implications of the test results for child and his family; benefits of the screening (detection of a serious disease treated before the appearance of the symptoms, prevention of mental retardation, identification of carriers, genetic counselling for future pregnancies); risk of screening (false-negative tests, parental anxiety in the case of false-positive tests, detection of diseases without treatment, detection of a false paternity); the necessity of other tests to confirm the diagnostic when screening is positive; the severity of the disease and the options for treatment; how the disease can be transmitted and the significance or carrier status; the way for communicating the result: negative = normal; positive = abnormal; what happens with the samples after their processing (storage of the spots for one year is essential if it is necessary to repeat the test and for the laboratory audit [10,11,12,13,14].

This data should be presented in an impartial and unbiased way and we must ensure that it was well understood. In terms of time to provide the information, most authors consider
that it is best for parents to receive the information during pregnancy or at the latest when the pregnant comes to deliver, thus having time to read, to reflect, to understand, to ask and to receive explanations [15,16,17]. Upon consent, the individual must be in the possession of all faculties and his/her judgment must not be influenced by various factors (alcohol or drugs, sleepiness, various health problems). The written informed consent is preferable to the verbal consent, but in this case problems could appear with the illiterate persons. They should be informed in an understandable way (e.g., drawing presentations) and their authorization of the test should be made by footprint, not by signature [10,17]. A persistent ethical issue is whether the NBS should be mandatory or voluntary. In 1998, WHO declared NBS mandatory if early diagnosis and treatment are in the benefit of the child [4,18]. Other ethicists accept NBS without obtaining the parental informed consent, based on the rationale that the risk is minimal and the child loses a vital benefit if the screening is not performed immediately. In addition, the obligation of the society is to promote wellness through early detection and diagnosis of the disease [2,4,18,19]. However, we must respect the parents’ right to refuse the whole screening or the information about the disease. Cultural or religious reasons can justify this decision. We believe that the parents who refuse must sign that they understand the potential risk of subsequent development of the child. According to WHO guidelines the screening for phenylketonuria and congenital hypothyroidism that has clear benefits and minimal side effects, is sufficiently important to override the parental consent. The inclusion of the informed consent in NBS programs generates potential benefits: a prompt and efficient response to positive test results, feedback from parents and the possibility to add new experimental tests [18].

After Orzalesi et al [4], several programs that incorporated the parental informed consent showed a better compliance: refusal rate was below 5‰ and the time assigned for consent was less than 5 minutes. The communication of the screening results and of its implications for the family must be confidential. Regarding the negative results of the test, they are considered good when they are communicated to the family and not when the policy of “no news received = good news” is adopted [1,4]. But for economic reasons (low budget allocated to the program) in most cases they remain undisclosed.

Cost is another ethical issue because NBS uses collective resources (public and private) to pay for tests, treatment and follow-up. Some believe that it is wrong to consider costs when children’s life is at stake. But the ethicists consider that costs should not be ignored due to the following reason: there are always other uses for financial resources that could save lives or prevent disability [12].

A common error is to consider only the costs of individual tests, having in view that NBS programs tested many newborns to identify a few cases with a certain disease. The real costs are much higher than the cost of tests and include parents’ education, tracking of cases found with positive results for a final diagnosis, treatment of children affected and the costs of research (data collection and evaluation of the introduction of a new
disease into the panel of screening) and quality improvement. Other costs upon families: the cost in time and money that must be paid by the families of children tested positive for a definitive diagnosis. The inclusion of a new disease in the existing screening panel can generate increased costs, too [12,21].

Therefore, policy makers have an ethical obligation to measure the benefits when directing the resources to NBS programmes.

The third ethical aspect is represented by the existence of scientific evidence. According to Baily M.A. and col., NBS should be introduced and should continue only with a proof of the existence of benefits. Each condition must be based on detailed information about the natural history, incidence, variability of incidence, and forms of occurrence in population, about the clinical utility of screening-test, efficiency, availability and treatment. The cost could not be evaluated without information on positive and negative effects of NBS. When evidence is limited, Newborn Screening Task Force recommends the initial introduction of the test in pilot studies [12,21].

The collection and evaluation of these data is an effort both for the state (costs) and for those who actually work (sampling and testing samples).

In Romania, the introduction of NBS was a major step forward and has many benefits:
- newborns can be tested for two rare diseases (congenital hypothyroidism and phenylketonuria);
- the possibility of early diagnosis and treatment prevented the severe consequences of the disease (mental retardation);
- genetic counselling is possible for subsequent pregnancies;
- the increased budget allowed the extension of screening in 2011 throughout the country except for Sălaj county.

Between September 2009 and December 2012, 76308 newborns were tested at Iasi Regional Center, 9 cases being diagnosed with congenital hypothyroidism and 5 cases with phenylketonuria.

But, at the same time, some ethical issues emerged:
- lack of information to the family about NBS during the pregnancy leading to a relatively large number of cases who refused the test;
- lack of a specific informed consent for screening;
- human-technical errors (incorrect sampling) that required the test to be repeated induced the anxiety to parents, as in the case of false-positive tests;
- failure of negative results for economic reasons;
- emergence of private maternities where NBS is possible even for many diseases (galactosemia, adrenogenital syndrome, maple syrup urine disease, biotinidase deficit, etc.), but depends on the financial possibilities of the family. Therefore, at this moment the screening is not universal, and there are two parallel systems of screening.

Conclusions
1. NBS is an example of ethical problems generated by the advanced technological tools available today.
2. We believe that NBS for treatable diseases should become a routine test because early diagnosis is in the best interest of the child.
3. The oldest NBS program accepted worldwide for phenylketonuria and congenital hypothyroidism saved and still saves thousands of children from severe cerebral dysfunction.

4. In Romania, the adequate informing of parents is necessary for the success and ethical acceptability of NBS programs.

References
[14]. Knoppers Bartha, Laberge C. From Newborns to DNA typing. Proceedings of Workshop on Genetic Screening, Quebec, 13th-14th October 1989.