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IS NEWBORN SCREENING FOR CYSTIC FIBROSIS A BASIC HUMAN RIGHT?

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Summary

Because it is clearly in the best interests of children with cystic fibrosis to be diagnosed early at <2 months, which can only be achieved routinely by newborn screening, it can be argued that this should be a human right. However, if more harm than good is likely, or if regional "readiness" does not exist, newborn screening should be deferred.

Keywords

Cystic fibrosis; newborn screening; rights; ethics

As part of the "Unanswered Questions in Cystic Fibrosis" plenary session at the 30th ECFS conference, the question was posed: "Is newborn screening for CF a basic human right?" When considered in the context of modern European and North American health care, this is a most challenging topic and truly is an "unanswered question." Instructions from the conference organizers made it clear that "basic human right" means entitlement-- something an infant with cystic fibrosis (CF) is entitled to have assured by regional health care delivery systems.

The larger question, of course, relates to health care in general. Is healthcare a basic human right? This has been debated intensely since 1999 when the "Tavistock Group" (1) asserted that "health care is a human right" and the first of five major ethical principles that should govern health care systems. Arguments against the assertion have raised issues such as the difficulties inherent in defining health care and the implication that if health care is a basic human right then providing it becomes a "duty" (2). While this debate will continue, it is advantageous to focus on a limited component of the modern health care system, namely newborn screening (NBS) and specifically for CF.

Depending on your perspective and your geographical situation, I believe the answer to the "basic human right" question on NBS for CF is both "yes" and "no." Interestingly, when the audience of the ECFS plenary session was asked this question and to raise their hands as to an affirmative or negative answer, the majority voted "yes." On the other hand, when the question was posed again in a more focused, regionalized version about the country of Japan where the incidence of CF is apparently ~1:350,000, very few answered "yes." Obviously, therefore,

*Presented at the 30th ECFS conference in Belek, Turkey on 16 June 2007

geographical circumstances, as well as other factors to be reviewed herein, might influence the answer to this question. Furthermore, this "show of hands" exercise made it clear that NBS is at the most a relative human right, but the important question remains: "Is early diagnosis of CF a human right?"

A New Era in the Care of Children with Cystic Fibrosis

One of the factors influencing the answer to this question is the context and capability of health care in the 21st century for young children with CF. Clearly, we have reached a new era (2) as summarized in Table 1. The most significant overarching change is a paradigm shift in therapeutic strategy from primarily *intervention in individuals with illness* (3 I's) to *prevention in presymptomatic populations* (3P's). This is not to imply that intervention for illness does not occur in CF during the new era because it does on a regular basis, but the predominant philosophy is prevention or even preemption. Thus, efforts are underway in regions with NBS to prevent early deaths [as many as 5% of CF patients (4,5)], salt depletion, malnutrition with growth failure, "cross infection" leading to acquisition of virulent respiratory pathogens, chronic *Pseudomonas aeruginosa* (PA) infections and early development of mucoid PA. And, eventually, with therapeutic strategies to correct the chloride channel defect, even prevention of lung disease would become a goal.

With these preventive opportunities already in hand, the consequences of delayed diagnoses are quite disconcerting. Suffering of patients, parents, and siblings occurs unnecessarily with diagnostic delays, and this often leads to parental anxiety, frustration, and anger as they experience a diagnostic "odyssey" (6). Added to the short-term risks of delayed diagnoses such as severe malnutrition and chronic pulmonary infections, we now know that long term implications may include failure to approach genetic growth potential (7), impaired development of cognitive function (8), and increased risk of early lung disease (9).

The Rationale for Newborn Screening

Table 2 lists the gastrointestinal/nutritional and pulmonary advantages of early diagnosis through newborn screening and provides compelling rationale. In essence, except for patients with the meconium ileus, infants with CF are generally healthy at the time of birth. Their nutritional status is normal, and the 90% with class I, II or III mutations who will develop pancreatic insufficiency (PI) can be anticipated and provided with therapies to preempt malnutrition. Thus, they are quite likely to grow in the normal range (7,10).

The pulmonary rationale for newborn screening is straightforward. Fortunately, the CF lung is normal at birth (11), although this may not continue beyond 2 months of age (12,13). To my knowledge, there has never been a CF patient diagnosed promptly through newborn screening that showed PA in the respiratory tract; in contrast, approximately one-third of patients diagnosed after signs or symptoms already are colonized with PA and many with mucoid PA (14).

In addition to the clinical rationale, there are other considerations that may be compelling. Some of these are also listed in Table 2 and have implications for how CF NBS is performed, i.e., what test is used. Clearly, to provide reproductive counseling, which many parents regard as a significant benefit, the IRT/DNA strategy must be employed rather than IRT/IRT.

More Rationale: Ethical Principles Applied to CF Newborn Screening

The question "to screen or not to screen" (15) ultimately becomes an ethical argument when regions are well-prepared to initiate NBS for CF, as discussed subsequently. The five ethical principles generally applied to medical care and research are listed in Table 3. The first two

principles, respect for persons and protecting privacy, are both important but have limited applicability to public health programs such as newborn screening. Nevertheless, when screening programs are implemented, respecting the autonomy of people and their privacy must be given priority. The third principle, beneficence, is a dominating consideration in the rationale for implementing CF newborn screening. Beneficence requires clinicians taking care of individual people and populations to achieve more good than harm in their practices by consistently doing what is the best interests of those served. Obviously, it is in no one's best interest to be undiagnosed with a 5% mortality risk (4,5) or a much higher probability of severe malnutrition (7).

Clearly, as an extension of beneficence, the principle of non-malfeasance also applies because "not causing harm" relates to having the infrastructure to implement and operate an efficient, effective program. Obviously, early diagnosis through NBS will not necessarily be beneficial without early detection *and* treatment. A variety of observations (18,19) indicate that *early* means by 2 months of age at the latest and ideally before then. Thus, NBS-CF follow-up systems have a duty to implement and manage efficiently and effectively.

Finally, the principle of justice is paramount in arguments to implement NBS for CF. Indeed, screening is the only method of diagnosis that may be considered equitable and egalitarian because every infant has the same excellent opportunity for early diagnosis. Otherwise, the probability of early diagnosis depends upon geographic, financial, and demographic factors. For instance, those in rural areas are less likely to be well served than those in urban communities, whereas access to health care in some countries such it is the USA depends largely on health insurance and financial wherewithal. Furthermore, no matter what the financial and geographic factors, girls with CF experience significantly longer delays in diagnosis than boys (16), especially when they present with respiratory disease (17); this tragic situation which defies explanation thus far may be an important factor in the reduced longevity of females with CF.

The "Yes" and "No" Answers to the Human Rights Question

Because it is clearly the best interests and eminently fair for every child with cystic fibrosis who has two CFTR mutations that are classes I,II, or III to be diagnosed early, and since early diagnosis [defined as <2 months of age (18,19)] to prevent unnecessarily suffering can only be achieved routinely through newborn screening, it may be argued that this is a human right if the following four conditions apply:1) if you are born in a region with a significant incidence of CF (e.g., at least 1:10,000), and 2) if a satisfactory newborn screening program for CF exists or can be created, and 3) if follow-up of screen-positive families is organized properly, and 4) if excellent CF leadership and sustained funding are available. Research on newborn screening for CF has demonstrated not only benefits but how programs should be organized and managed (20). It is fortunate that more research has been done on CF newborn screening than for any other genetic disease during the past two decades, as literature searches reveal. In fact, comprehensive studies have enlightened all aspects of diagnosis and treatment, although the delivery of care and patient adherence have not been perfected anywhere.

On the other hand, the "no" response to the human rights question applies if more harm than good is likely, or if regional "readiness" does not exist (6), or if resources/services cannot be sustained. As the CDC concluded (6), "the net balance of benefits and risks is contingent on how newborn screening for CF is implemented." More information on benefits and risks of NBS is provided in a recent article by Balfour-Lynn (21), which concludes that "the task now is to ensure it is carried out smoothly and effectively."

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References

1. Smith R, Hiatt H, Berwick D. Shared ethical principles for everybody in health care: A working draft from the Tavistock Group. Brit Med J 1999;318:248–251. [PubMed: 9915738]
2. Barlow P. Health care is not a human right. Brit Med J 1999;319:321. [PubMed: 10426762]
3. Farrell PM. the Wisconsin Cystic Fibrosis Neonatal Screening Study Group. Improving the health of patients with cystic fibrosis through newborn screening. Adv Pediatr 2000;47:79–115. [PubMed: 10959441]
4. Doull IJ, Ryley HC, Weller P, Goodchild MC. Cystic fibrosis-related deaths in infancy and the effect of newborn screening. Pediatr Pulmonol 2001;31:363–6. [PubMed: 11340682]
5. Grosse SD, Rosenfeld M, Devine OJ, Lai HJ, Farrell PM. Potential impact of newborn screening for cystic fibrosis on child survival: a systematic review and analysis. J Pediatr 2006;149:362–6. [PubMed: 16939748]
6. Grosse SD, Boyle CA, Botkin JR, et al. Newborn screening for cystic fibrosis: evaluation of benefits and risks and recommendations for state newborn screening programs. MMWR 2004;53:1–36.
7. Farrell PM, Kosorok MR, Rock MJ, et al. Early diagnosis of cystic fibrosis through neonatal screening prevents severe malnutrition and improves long-term growth. Pediatr 2001;107:1–12.
8. Koscik RL, Farrell PM, Kosorok MR, et al. Cognitive function of children with cystic fibrosis: deleterious effect of early malnutrition. Pediatr 2004;113:1549–1558.
9. Rosenfeld M. Overview of published evidence on outcomes with early diagnosis from large US observational studies. J Pediatr 2005;147:S11–S14. [PubMed: 16202774]
10. Siret D, Bretaudeau G, Branger B, et al. Comparing the clinical evolution of cystic fibrosis screened neonatally to that of cystic fibrosis diagnosed from clinical symptoms: a 10-year retrospective study in a French region (Brittany). Pediatr Pulmonol 2003;35:342–9. [PubMed: 12687590]
11. Bedrossian CWM, Greenberg Sc, Singer DB, Hansen J, Rosenberg H. The lung in CF: a quantitative study including prevalence of pathologic findings among different age groups. Hum Pathol 1976;7:195–204. [PubMed: 1262016]
12. Abman SH, Ogle J, Horbeck R, Butler-Simon N, Hammond K, Accurso F. Early bacteriological, immunologic and clinical courses of young infants with cystic fibrosis identified by neonatal screening. J Pediatr 1991;119:211–217. [PubMed: 1907318]
13. Farrell PM, Li Zhanhai, Kosorok MR, et al. Longitudinal evaluation of bronchopulmonary disease in children with cystic fibrosis. Pediatr Pulmonol 2003;36:1–11. [PubMed: 12772216]
14. FitzSimmons SC. The changing epidemiology of cystic fibrosis. J Pediatr 1993;122:1–9. [PubMed: 8419592]
15. Farrell PM. Early diagnosis of cystic fibrosis: to screen or not to screen – an important question. Pediatr 1984;73:115–117.
16. Lai HC, Kosorok MR, Laxova A, Makholm LM, Farrell PM. Delayed diagnosis in females with cystic fibrosis in the United States. Am J Epidemiol 2002;156:165–173. [PubMed: 12117708]
17. Farrell PM, Joffe S, Foley L, Canny GJ, Mayne P, Rosenberg M. Diagnosis of cystic fibrosis in the Republic of Ireland: epidemiology and costs. Irish Med J 2007;100:557–560.
18. Sims EJ, Clark A, McCormick J, et al. Cystic fibrosis diagnosed after 2 months of age leads to worse outcomes and requires more therapy. Pediatr 2007;119:19–28.
19. Farrell PM. The meaning of “early” diagnosis in a new era of cystic fibrosis care. Pediatr 2007;119:156–7.
20. Comeau AM, Accurso FJ, White TB, et al. Guidelines of implementation of cystic fibrosis newborn screening programs: cystic fibrosis foundation workshop report. Pediatr 2007;119:e495–518.

21. Balfour-Lynn IM. Newborn screening for cystic fibrosis: evidence for benefit. Arch Dis Child 2008;93:7–10. [PubMed: 18156475]

22. Lee DS, Rosenberg MA, Peterson A, Farrell PM. Analysis of the costs of diagnosing cystic fibrosis with a newborn screening program. J Pediatr 2003;142:617–623. [PubMed: 12838188]

Table 1

The 21st Century is a New Era for Children with CF

- An established trend of early diagnosis through NBS
- A paradigm shift in therapeutic strategy from *intervention in individuals with illnesses* (3 I's) to *prevention in presymptomatic populations* (3P's)
- No longer dominated by intervention in individuals with illnesses
- But prevention in presymptomatic patients
  - – Prevention of early deaths
  - – Prevention of salt depletion
  - – Prevention of malnutrition and growth failure
  - – Prevention of "cross-infection"
  - – Prevention of chronic PA and early mPA
  - – Prevention of hospitalizations
  - – Prevention (eventually) of lung disease

* The concept of transforming from the "3 I's" to the "3 P's" was developed by the author for lectures to medical students and practicing physicians while he was serving as Dean of an institution transformed to the University of Wisconsin School of Medicine and Public Health

Table 2

The Rationale for Early Diagnosis Through Newborn Screening

A. The GI/Nutrition Rationale for NBS

1. CF patients are generally well nourished at birth
2. PI will develop in ~90% of patients by ~1 year
3. Severe malnutrition will develop in ~50% untreated
4. PI can be anticipated and malnutrition prevented
5. Long term benefits of normal nutrition are significant

B. The Pulmonary Rationale for NBS

1. The CF lung is normal at birth, but not for long.
2. Lung disease often develops as early as 2 months.
3. Pseudomonas aeruginosa (PA) colonization may occur in ~1/3 of undiagnosed patients.
4. PA conversion to mucoid PA is of great long term risk for children with CF.

C. Other Rationale

1. Psychological harm associated with the “diagnostic odyssey” (6) may be prevented.
2. Parents are provided with informed reproductive options for future pregnancies.
3. Economic benefits may be realized for both diagnosis (22) and treatment (18).
4. Clinical research is facilitated (21), especially study of upstream preventive strategies.

Table 3

Ethical Principles Providing More Guidance for CF Newborn Screening

1	Respect for persons while assuring autonomy and allowing people to choose for themselves.
2	Protect privacy in organizing and delivering information and care.
3	Beneficence with a favorable benefit-risk relationship (best interests principle)*
4	Non-malfeasance through efficient, effective program implementation/management.
5	Justice for all persons with equitably delivered care.

* Best interests for people and populations