Ethical Aspects of Pediatric Genetic Care

Testing and Treatment

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KEYWORDS

• Ethics • Autonomy • Future interests of the child • Best interests
• Surrogate decision making

KEY POINTS

- Genetic testing in children requires the identification of an appropriate surrogate decision maker, and considerations about the value of relevant information for the biological relatives of the child.
- Predictive genetic tests, particularly those with typically adult onset, should be evaluated carefully in the consideration of the future autonomy interests of the child. Professional guidelines are available.
- Caring for children with genetic diseases raises ethical issues beyond simply genetic testing; additional clinical care issues may include treatment decisions, goals of care, and end-of-life care, as well as just access to available care options.

INTRODUCTION

Genetic and genomic testing has expanded dramatically since 2010. Pediatricians, both in general pediatric practice and in various pediatric specialties, will encounter diagnostic and predictive genetic screening and testing and the subsequent cascade testing that follows a new diagnosis, gene-based treatments (such as gene therapy, somatic gene editing, and molecular gene silencing treatments), and will support parents learning about and adapting to new diagnoses and difficult prognoses for their current (and potentially future) children. In this article, we review some of the ethical issues specific to pediatric medical care, with a focus on those that arise in the context of providing genetic care to children and their families.

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Ethical issues (or ELSI, which stands for ethical, legal, and social issues) are frequently discussed when talking about genetics and genomics. This likely derives from several things. First, the history of eugenics. Second, genetics is inherently a family affair - not only do genetic conditions also indicate potential risk to other family members, but genetic testing can inadvertently discover information that identifies family members or information about the family structure. It also raises the question of whether it is ethically permissible to perform pediatric genetic testing primarily for family benefit. Genetic information can be diagnostic or predictive and probabilistic, depending on the timing and type of testing that is performed. The uncertainty and future predictability of this sort of information is not entirely novel to genetics, but in pediatrics it raises issues around the future autonomy of a child in deciding whether they do or do not want to know it. Genetic information, and our potential to change it, also raises discussion about what it means to be human and how our genes relate to our identity. And finally, genetic and genomic testing and treatments often blur the lines between clinically accepted treatments and research offerings. The rich history of ELSI research in the United States is nicely reviewed by Dolan et al (2022).[1]

Most pediatricians and pediatric health care providers will have taken a course in medical ethics during their training, and as a result will be familiar with a "Principles based approach" to ethics.[2] *Autonomy* references the importance of respecting individual persons, and is often enacted through informed consent. *Beneficence* references the importance of "doing good" and providing benefit to patients through our medical care or research, and *nonmaleficence* is the Hippocratic principle of "do no harm" and minimizing risks. Finally, the principle of *justice* argues for equity in access, and often reflects issues such as access issues, cost and insurance coverage, and accessibility across different populations (eg, ancestral backgrounds, LGBTQ+, sex). These principles are applicable in both a clinical setting and research setting, and in fact these principles underlie much of research ethics in the United States as they informed the Belmont Report.[3] Many other ethics approaches exist, including virtue ethics, which focuses on the importance of the conduct of the person, and gives guidance toward what virtuous or "right" actions might be. For example, veracity (truthtelling), or fidelity (trustworthiness) or transparency (which also comes up in conflict of interest issues) might be described as virtuous actions. To use veracity as an example, this ethical principle may arise when providing difficult prognostic information to parents (for example, breaking the news about a fatal diagnosis), when telling children the truth about their health or about inherited genetic risks, and when clinicians are asked to withhold information (or even lie) from children or adolescents.

Having now discussed many of the foundational ELSI issues around genetic testing in children, we will present some case examples to elaborate on additional ethical issues that may arise. When considering one's own practice and evaluating the ethical issues that may be in tension, there are many approaches that one might consider to standardize the process. Key across all the approaches are to (1) identify the potential ethical issues, (2) identify the range of options, (3) determine the relevant patient/family values, and (4) determine the course of action in consultation with the family. In ethics, there is not a "formula" for how to resolve ethical conflicts - no single principle or ethical framework trumps all others. Context is important, and the ethical frameworks that exist primarily provide clinicians with ways to think through the conflict, identifying which issues are important and why. Many times, ethics frameworks will reach the same conclusion based on the factors that are considered. The goal of this article is not to turn readers into clinical ethics consultants, but rather to sensitize pediatric

care providers to the relevant ELSI issues that arise when providing genetic care, and to help them identify potential issues, the relevant professional guidelines that exist, and when cases may benefit from referrals and/or ethics consultation.

COMMON ETHICAL ISSUES IN PEDIATRIC GENETICS

Pediatric medical care raises the issue of surrogate decision making, which becomes even more complex when we add the importance of preserving the future autonomy of the child ("an open future"), the role of identity (particularly around treatment decisions or discussions around treatments that could be considered enhancement), and the potential for future identifiability and privacy issues. While we will not discuss them in detail, ethical issues that cross all areas of genetic testing and care include transparency about the uncertainty and changeability in variant interpretation, as well as about the potential use of AI and machine learning in variant interpretation, social justice, and equity issues that arise due to the fact that currently the majority of genetic data comes from persons of primarily white European ancestry, and issues related to the cost and accessibility of genetic testing and treatments.

Applying Autonomy to Genetic Testing Decisions: Informed Consent

As with any other medical procedure, the process of informed consent is critical to ensuring respect for persons and their autonomy. In general, informed consent means that a person is free to make a decision without coercion and that they can comprehend the risks and benefits of their medical options, and voice a choice. When evaluating the potential risks and benefits with genetic testing in general, it is important for health care providers to remember that unlike many medical procedures where the primary risks are physical risks, in genetic testing these risks are usually minimal (usually a blood draw or buccal swab), while the social and psychological risks may be more impactful. For example, some genetic tests pose a chance that unexpected family relationships could be discovered, as could an unexpected diagnosis (either incidentally or as part of a secondary findings analysis). Others may pose psychological risks such as anxiety or depression (for example a predictive test for a condition that has no medical treatments to change its course). And still others may pose risks to privacy or for discrimination, or that covered services may change with a diagnosis (for example in a school setting, or therapies). When considering benefits, clinical utility (medical actionability through screening or treatment) is also not the only potential benefit. Many individuals and families find personal utility in genetic testing[4]; for example, finding a genetic cause for current symptoms can relieve parental guilt that they somehow caused the condition through actions in pregnancy or early childhood, a predictive diagnosis can allow for research moving into the future, as well as potential lifestyle changes that may improve morbidity and long term mortality risks (for example, avoiding starting to smoke as a teen). Even when genetic test results are positive, the reduction in anxiety that arises from uncertainty can be helpful, and may allow adolescents and young adults to plan their future lives (eg, schooling, career, and family planning) in a more informed manner.[5–7] A recent systematic review suggests that at least for genomic sequencing, parents struggle to understand and recall relevant components of informed consent,[8] particularly around privacy and potential discrimination, future use of data beyond the clinical purposes, and secondary findings. This suggests that providers should simplify relevant principles, utilize appropriate health literacy-based communication strategies, and refer to skilled genetics providers when possible.[9]

The Special Case of Medical Decision Making for Children: Developing Autonomy and Interests for "an Open Future"

When discussing medical decision making in *pediatric* genetic care, we must also start by thinking about decision making capacity and the promotion of the autonomy of the child. In most countries, children do not have legal competence until age 18 or the age of the majority, though this varies slightly by country. Some countries and states also have specific regulations that allow children to make some medical decisions prior to reaching that age of majority (for example, emancipated minors; see the UN Convention of the Rights of the Child, 1989[10]). However, there is general appreciation that children develop decision making capacity over time, and as such, most children older than age 7 are asked to assent or dissent to medical procedures (including genetic testing), and as they become adolescents and young adults they should be increasingly actively included in the decision making process. Each health care provider should be familiar with the laws and regulations in their location of practice.[11,12] In most locations, the parent or guardian is considered the legal decision maker for children, and because children do not typically have enough lived experience for them to make surrogate decisions based on previously expressed values and wishes, most decision making follows the "best interest standard." The best interest standard assumes that parents and guardians generally know the child best, and will make decisions that will benefit the child and family. There is typically a lot of latitude granted to parents as long as the medical choices are not seen as being harmful or neglectful of the child.[11,12]

Beyond the traditional issues that surround pediatric decision making, genetics raises a new set of issues that relate to the autonomy of the child under care. While some genetic testing occurs symptomatically, and provides a diagnosis that explains a constellation of symptoms currently experienced by a child (eg, a karyotype or array CGH to explain intellectual disability, or an exome or genome sequence performed on a child suspected of having a genetic condition), even these diagnostic tests can lead to unexpected findings - whether about a family relationship or about an unexpected diagnosis. Beyond these diagnostic tests, a large percentage of genetic testing is predictive. For example, an exome test might identify a genetic variant that causes illness in late childhood, but it may also identify a variant associated only with adult-onset symptoms. These conditions may also have variable penetrance, variable expressivity and variable ages of onset, and may or may not have medical actionability. And finally, stored genetic material (and even stored genetic data) can pose potential privacy risks down the line.

A topic that has arisen often in the discussion about pediatric predictive genetic testing is often referred to as the right (or interest) that children have in an open future. This principle was first expounded in 1980,[13] with applications to genetic testing soon in the 1990s (eg, work by Dena Davis). Broadly, this concept suggests that while parents can generally raise their children based on their own values, there may be some key life choices that may have irreversible impact, and the child has a "right" (or, as per Garrett and colleagues, 2019, an interest) in keeping their options open, thus saving the option for them to exercise their future autonomy. A child's right to an open future is a right in trust, that is "to be *saved* for the child until he is an adult, but which can be violated "in advance," so to speak, before the child is even in a position to exercise [it]. His right while he is still a child is to have these future options kept open until he is a fully formed self-determining adult capable of deciding among them."[14] Testing children for adult-onset conditions, particularly for those which no treatment exists (eg, Huntington disease), would deprive the child of the possibility of deciding whether

to undertake a test later on in his or her life while not offering any medical benefit. Many have argued however that knowing in advance about such conditions may indeed be important for the child and the family alike in terms of advanced planning. Garrett and colleagues (2019) argue that this is best understood not as a right but as an *interest*, which provides flexibility to balance future interests against other benefits and harms, as compared to a *right*, which would generate a duty on the parents (and potentially health care professionals) to strictly avoid pediatric predictive genetic testing.

Because of the many types of genetic testing that exist and the complexity of these issues, genetics societies across the world have created guidance about genetic testing in children, frequently centering around preserving the future interests of children to decide whether or not they wish to learn their genetic information,[15] and around the premise of reducing potential harms. We have summarized many of these guidelines in **Table 1**, though this is not an all-inclusive list of guidelines.

Reviewers of this table will note that all the professional societies support diagnostic testing, with some suggesting that clinicians order the most "narrow" test so as to minimize the chances of unexpected findings. This includes diagnostic genetic tests including for children who are being considered for adoption, even if they do not have medical treatments available. It is worth noting these recommendations preceded some organizations recommending exome or genome sequencing as a first-line diagnostic test, and that generally these tests are considered acceptable on the basis that the potential benefits (treatments, prognostic knowledge) outweigh potential harms in the face of symptoms. As one moves across the table, tests which provide less immediate clinical or personal utility are less supported. For example, testing for conditions that occur in childhood, even if not yet presenting symptomatically, are considered acceptable by most professional organizations. However, as conditions have later onset (eg, in adulthood, including carrier testing) they become less supported, with most organizations suggesting either complete deferral of these tests or, in specific situations where an adolescent and family are in agreement about their desire for testing, ensuring that a rigorous consent process is undergone. Importantly, most of the recommendations to defer predictive testing into adulthood are based on normative concerns for harm[16]; several also add reminders that even if testing is deferred, there can be significant benefit to communicating about genetic risk and future testing options to children (eg,[17]). There is limited empiric data about the actual harms when testing is performed[18,19]; most of the information about predictive testing centers around carrier testing,[7,20–22] familial adenometous polyposis (FAP) testing[23,24] and BRCA testing.[25] There is also a growing body of literature to suggest that young adults desire information sooner than it is given to them by their parents, and that an open communication approach about genetic risk status in the family is beneficial ([26,27]). As a result of this empiric data, over time many of the genetic society guidelines have become more flexible about the potential consideration of predictive genetic testing for adolescents, reflecting what had been happening in practice over time (for example,[28,29]). It is important to consider the developmental stages of childhood and adolescence when contemplating genetic testing of children[30]; several authors have also proposed conceptual frameworks for sharing genetic risk information, genetic counseling, and consideration of genetic testing in children.[31–33]

The Issues of Unsolicited Findings

The expansion of genetic testing toward genomic testing has raised the issue of unsolicited findings in the past 10+ years. These findings are sometimes referred to as incidental findings (by which we will refer to findings that are unexpected and not searched for) and secondary findings (by which we will refer to findings that are

Table 1
Summary of international guidelines on genetic testing in children (as of 2022)

Type of genetic Test//Professional group	Predictive, Childhood, Treatable	Predictive, Childhood, not Treatable	Predictive, Adult	Incidental or Secondary Findings (Adult)	Carrier Screen	Adoption (Symptomatic and predictive Testing)	Direct to Consumer
AAP/ACMG 2013 (USA)	Yes	Yes	Defer (flexibility)	Refer to Miller et al., 2021. Offer regardless of age.	No, unless pregnant	Consistent with general recommendations for any child	Strongly discourage
ASHG 2015 (USA)	Yes	Not overtly discussed	Defer (flexibility)	Optional, with strong consent process.	Neutral	Consistent with general recommendations for any child	Discourage
Canadian Pediatric Society	Yes		Defer	Refer to Boycott et al. 2015.	Discuss	Consistent with general recommendations for any child	Strongly discourage
ESHG 2009 (EU)	Yes	Optional	Defer unless early actions possible	See deWert et al. 2021 - recommend avoid opportunistic screening	Discourage	Not overtly discussed	Not overtly discussed
BSMG 2022 (UK)	Yes. Special notes re: cardiac testing	Yes	Defer (flexibility)	No consensus. Refer to deWert et al. 2021	Defer (flexibility)	Consistent with general recommendations for any child	Not overtly discussed
HGSA 2020 (Australia)	Yes	Discuss	Defer (flexiblity)	Not overtly discussed	Not overtly discussed	Not overtly discussed	Not overtly discussed

searched for but unrelated to the primary testing indication, such as genes included on the ACMG v3.0 secondary findings lists[34]; some literature also refers to this as "opportunistic screening"[35]) The return of incidental and secondary findings to children has been well debated in the literature, and the normative concerns primarily surround the feasibility to obtain informed consent (particularly when parents are focused on issues that surround the primary testing indication), and issues that mirror predictive testing in children and include privacy, discrimination, future autonomy, and emotional harms, particularly if a condition is not medically actionable for years. Some researchers also raise the potential family benefits that may accrue if a secondary finding is identified in a child, such that at risk parents could be identified and with the potential to decrease their morbidity or mortality.[36,37]

Shortly after genomic sequencing became available, studies assessed the hypothetical interest in receiving secondary findings.[38–41] More recently, adolescents and children enrolled in genomic research have also been studied with regards to their hypothetical and actual interest in return of results.[42–44] Importantly, some studies[45,46] have found that parents do not necessarily differentiate between primary and secondary results, but rather consider all to be potentially relevant health information. While parents were often interested in receiving predictive secondary findings, they may wait until adolescence to disclose the results to the child and there is emerging data that they found familial benefit to knowing about a hereditary risk.[45]

Expanding Towards Genomic Newborn Screening

Newborn screening (NBS) was initially based on principles developed by Wilson and Junger[47] and elaborated upon by Dobrow.[48] These principles generally suggest that NBS can be offered for asymptomatic infants if we have sufficient information about a health condition (including its natural history), an acceptable and effective test and treatment is available, and that the implementation of a screening program is feasible and cost-effective. The public health format of newborn screening means that is offered universally, and that it also involves a more limited consent model (in some cases, an "opt-out" approach, where a parent must actively decline newborn screening, rather than consenting to have their child undergo it). This near universality of NBS combined with the loss of parental autonomy require that the included conditions are well justified with regards to their seriousness, urgency, and treatability.[49]

In the early 2000s, newborn screening began to expand from the traditionally included conditions such as phenylketonuria (PKU) to a much wider list of conditions, including some (eg, Krabbe, Pompe and X-linked adrenoleukodystrophy, X-ALD) that were controversial for their later childhood onset, significant phenotypic variability and limited treatment options.[49] The potential inclusion of these conditions raised public health ethics concerns that focused on the potential increase in harm and decrease in beneficial outcomes, raised ethical questions about how conditions are chosen for inclusion on NBS panels. For example, how is benefit for a public health screening tool assessed when you move beyond clinical utility into personal utility and family benefits? Also, who should determine which conditions are included?[49,50] Over time in both in the United States and Europe this NBS expansion has happened inconsistently and despite the existence of a Recommended Uniform Screening Panel in the US, primarily since policy decisions about newborn screening being made on a state-by-state or country-by-country basis respectively.[51–53] This consequent variability in screening approaches raises the important ethical issue of equity and access. Finally, one last ethical issue haunts newborn screening: in recent years there have been privacy concerns about the re-use of dried blood spots without parental

permission.[54] Since these blood spots contain DNA, and are inherently identifiable, there are worries about privacy violations, potential discrimination, and familial implications.

In recent years, genomic screening of neonates is becoming increasingly realistic (https://www.genome.gov/Funded-Programs-Projects/Newborn-Sequencing-in-Genomic-Medicine-and-Public-Health-NSIGHT, accessed 8 Nov 2022). Some of these genomic approaches use a focused approach (eg, a targeted gene panel), while others use an exome or genomic sequencing approach that could analyze and report on any potential genes. Neonatal genomic approaches raise similar issues to those already discussed in pediatric screening: how to obtain appropriate consent, the selection of the conditions returned, particularly if they are later childhood or adult onset, the balance of benefits and harms, and the equity issues that will arise. There is an emerging body of knowledge available about the use of newborn genomic testing in sick neonates (eg, rapid sequencing in a NICU), as well as the potential to use genomic sequencing in healthy appearing neonates to predict a range of future illnesses.[55,56] Most professional organizations and ethics advisory panels (eg the NSIGHT EAB) have found that broadly offering genomic screening to healthy neonates is premature as the potential for harm outweighs the current potential for benefit[57–60] While there may be beneficence in the case of a new treatable diagnosis that would not otherwise be identified in standard NBS, the potential benefits (and often the interpretations and prospective meaning of the information) remain unclear. As was evidenced by the expanded NBS examples of Krabbe and Pompe disease, harm may occur through unnecessary interventions and long term monitoring, parental anxiety, and impact on the parent-child relationship.[61] And importantly the issues of how to achieve consent and cost implications on the public health system remain unanswered.

GENETICS AND THE FAMILY

Genetic testing impacts both the patient and the family. Typically in medicine, the "care unit" is considered to be the patient. But of course any clinician will recognize that medical decision-making impacts family members in a number of ways. With genetic testing, a new genetic diagnosis has implications on other family members who are at risk.

Case example 1: a genetic test is performed on a symptomatic child for cystic fibrosis, an autosomal recessive condition. The child has two identifiable pathogenic mutations; one of which is carried by the mother, but the other is not carried by the purported father, suggesting he is not the biological father of the child. What are the duties of the medical provider to disclose the relevant information, particularly that the couple is not at 25% risk in future pregnancies, and the "father" is not a carrier of CF.

Case example 2: A child is diagnosed with a genetic condition that is carried by a parent. The parent does not wish to disclose the genetic risk information to relatives who may also carry the mutation (eg, the child's aunts and uncles, who are also of reproductive age), putting their future children at potential risk. What are the duties of the medical provider to encourage sharing this genetic information? Are there any "duties to warn" these at-risk relatives?

Key ethical principles including privacy, veracity, beneficence, and nonmaleficence are important in evaluating these cases; the ethic of care and its focus on relationships is particularly relevant in cases that involve the family as a unit. In both cases, privacy and veracity are directly in conflict when a family member does not wish to divulge relevant genetic information. This potential lack of truthfulness impacts family

members' ability to exercise their autonomy. However, these cases highlight several challenges when ethical principles may conflict. For example, in Case 1, potential approaches include (1) fully disclosing the information to both members of the couple, (2) privately disclosing to the mother with encouragement to disclose relevant details and assessing the situation, or (3) disclosing simply that they are not at elevated risk for having a future affected child. Full disclosure to the parents that misattributed parentage was present prioritizes veracity, but may pose a risk of harm to the family relationships, which could potentially lead to harm of the mother and/or child. However, a prospective parent may make reproductive decisions differently if informed accurately about their reproductive risks (or lack thereof). Options such as 3, which accurately discloses the couples risks but do not clarify that the putative father is not a carrier, withholds important information that his biologic offspring are not at risk to be affected (and that his siblings are not at increased risk above the population rate). Withholding this information may lead to unnecessary anxiety and future testing in some individuals. Professional societies provide different advice on how best to handle the conflicting obligations of privacy and veracity in the case of misattributed paternity. Here one might start by asking: Will the child's care change on the basis of disclosure? What are the potential harms on each person with each option of disclosure, and how likely are they to occur?[62] From there, one could weigh the impact on privacy, autonomy, and the ratio of beneficence and nonmaleficence.

Case 2 raises issues about disclosure to family members who are more distant and not part of the immediate family that is being tested. These family members will frequently not be patients of the care provider. How does the clinician handle the conflict of protecting the privacy of their patient, who has explicitly said they do not wish to share the information? Here again, one might ask: What is the condition under discussion, and what are the potential harms with and without disclosure? For example, is the condition highly penetrant and the relatives are at a high risk? Could they change the morbidity and mortality associated with the condition through screening or early identification? Are they likely to undergo routine testing or screening for this condition for other reasons (for example is it included on routine carrier screening panels)?

In the case of a family disclosure, the clear moral duty of the medical provider is to ensure that the relevant family member is provided with accurate information and encouraged to share the it with the at-risk family members, with some recent legal findings (ABC vs St Georges Health Care) suggesting there may be stronger legal duties to inform in some jurisdictions.[62–67] As in many ethically complex situations, often a combination of encouragement by the medical provider and time will resolve the situation and lead to the disclosure of important genetic information. Beyond this, the law in different countries varies regarding what the legal duties for informing relatives are even when a patient declines to do so themselves[68–71] These examples emphasize one final key point – given the chance that unexpected family relationships can be identified, and that pathogenic genetic testing results should be shared with at risk family members so they can consider cascade testing, these outcomes should be raised as part of the informed consent discussions *prior* to genetic testing so that the patient or their parent is aware of the possibilities in advance.

TREATMENTS FOR GENETIC DISEASE

While genetic disease has always had symptomatic treatment approaches, there are increasingly new approaches that may lead to significant changes in morbidity and mortality for those with genetic conditions. Koogler and colleagues (2003) thoughtfully reviews the historical examples of treatment being withheld or withdrawn from

children with genetic conditions (for example, a child with Down syndrome being denied heart surgery) and the underlying ethical issues that these situations raise.[72] Despite changes, parents still report challenges in obtaining health care for their children with genetic disease (eg,[73,74]).

Increasingly, new treatments are being developed for genetic conditions - these include treatments that provide lacking enzymes or decrease substrate buildup (for example, a bone marrow transplant or stem cell transplant for an inborn error of metabolism), gene-focused treatments that silence or "turn on" genes by addressing genetic mechanisms such as splicing (eg, treatments for Duchenne muscular dystrophy or spinal muscular atrophy), or somatic gene therapies or gene editing approaches (eg, for sickle cell disease or specific forms of congenital blindness). Given the rare frequency of most genetic diseases, there can be a blur between research and clinical treatments, sometimes meaning that the only potential option for treatment is a clinical trial. They may also have quite invasive and potentially risky forms of administration. For example, Nusinersen is injected via lumbar puncture, requires frequent doses and has a cost into the millions of US dollars; it is just one example of the potential harms that are associated with the treatment of rare disease.[75] Once safety testing is complete and regulatory approvals are obtained, treatments may become expensive or limited to specific high-level hospitals, both of which limit potential access to the treatments. In recent years, there has been a shift from discussions about these potential harms (including potential death, stemming from the death of Jesse Gelsinger in early gene therapy trials), to excessive hope that the therapy will be a disease cure.[76] From the perspective of justice, is it ethically appropriate to offer treatments that are realistically only available to a small segment of the population that may need them? In countries that provide nationally funded health care systems, what are the ethical issues in choosing to pay for these rare but extremely expensive treatments when it takes away health care dollars from other sick persons? How do we balance these public health funding issues?[77]

Recent technical advances in gene and cell therapy hold great promise to tackle numerous conditions, including hereditary ones. A number of clinical trials are underway regarding innovative regenerative medicine treatments with the potential to address a variety of pediatric conditions that have a genetic component. Such trials usually have very strict inclusion criteria and are open to very few patients. Family and caretakers may rightly see trial enrollment as a concrete chance of accessing a potentially beneficial treatment. It is thus important that enrollment decisions are fully transparent and inspired by ethically robust criteria and decisional mechanisms. As a result of the extremely limited opportunities to enroll in innovative clinical trials, many families may be tempted to obtain yet unproven treatments, often offered abroad, in countries with insufficient safeguards and regulatory standards.[78,79]

Finally, while many people focus on the issues of safety and cost for somatic gene-based therapies, they also raise important issues around identity and issues such as support and stigma that center around the social model of disability.[80] In contrast to the medical model of disability, which assumes that a genetic condition impairs quality of life and should be corrected when possible, the social model of disability suggests that the impairments that occur due to chronic illness are socially based. Extending the expressionist argument beyond prenatal testing,[81] one might imagine that decreasing the number of people impacted by a genetic condition might decrease social support, and also lead to stigma when an individual or family chose not to undergo a specific treatment. There are also a growing number of studies that suggest that people with genetic illness and their families have differing, and sometimes quite

nuanced, views toward gene editing and gene therapies as treatments for their condition.[82–86]

END-OF-LIFE ISSUES FOR A CHILD WITH A GENETIC CONDITION

Genetic conditions have a higher mortality rate, and are in fact responsible for a substantial percentage of neonatal intensive care unit (NICU) stays and neonatal and early childhood deaths.[87] As such, pediatricians caring for children with genetic disease will be faced with having hard conversations with parents about their child's prognosis, and to help them set goals of care toward the end of life that match their family values. Some studies suggest that rapid genomic sequencing in a NICU setting can help clarify a diagnosis and help guide these care decisions.[88–92]

End-of-life decision making is complex and emotionally challenging for patients of any age. In childhood, while the parents (or guardians) are the legal decision makers, children's autonomy should be respected to the degree that is appropriate for their age. Ethical principles such as veracity and autonomy are important here and could be respected by sharing age appropriate information with children about their health status and treatments, and including older children and adolescents in decision-making to the extent that it is appropriate.[93,94]

Ethical conflicts may arise with regards to disagreements between the parents, between parents and the child, or between the family and the medical team with regards to end-of-life care, particularly when it comes to withholding or withdrawing treatments. Major goals might include avoiding suffering (beneficience and nonmalefecience) and facilitating informed decisions (veracity about the prognosis and uncertainties, autonomy to make decisions based on personal values, and consideration of future quality of life issues).[95] Palliative care specialists and ethics consultants can often assist in navigating these complex discussions about goals of care and medical decision making at the end of life.

SUMMARY

There are many ethical issues that arise in caring for children and their families facing genetic disease. In considering genetic testing, one must consider the type of screening or testing being offered, the age of the child, and the larger context as it relates to the child's current and future interests. Professional guidelines can provide a health care provider with a starting place for discussion with the family, including the consideration of the interests in preserving the child's future autonomy for predictive genetic testing decisions. Any provider who is ordering genetic testing should identify the proper surrogate decision maker and involve the child in testing discussions and obtain assent as is developmentally appropriate. Beyond genetic testing, caring for families with genetic disease can raise issues of family disclosure, privacy, treatment decisions and end-of-life care.

CLINICS CARE POINTS

- Many professional organizations around the world have published guidelines regarding the use of genetic testing in childhood.
- Informed consent for genetic testing and considering of the developing autonomy of children is important, especially for predictive genetic tests and those that return secondary or incidental findings.

- Genetic testing results can raise complicated family issues, such as misattributed parentage and issues regarding sharing genetic test results to at risk family members. These should be mentioned as part of the informed consent process.
- Health care providers can consider ethical consultations when they feel unprepared to address ethical issues that arise in providing genetic care to children.

DISCLOSURE

Nothing to disclose.

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