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All in the Family: Disclosure of “Unwanted” Information to an Adolescent to Benefit a Relative

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Abstract

Ethical assessments of clinical decisions are typically based on the preferences and interests of the individual patient. However, some clinical interventions, such as genetic testing or organ donation, may involve multiple family members. In these cases, one family member may have the potential to benefit, while another family member is exposed to potential physical or psychological risk. In the research setting, the balancing of benefits and risks between family members may be further amplified by uncertainty about their magnitude and likelihood. In addition, when the individual facing these apparently uncompensated risks is a child, the situation becomes particularly ethically complicated, as we appreciated in a recent case. Investigators at the National Cancer Institute were faced with a decision about whether it would be appropriate to disclose apparently “unwanted” research test results (length of telomeres in leukocyte subsets) to an adolescent about risk of future disease (dyskeratosis congenita), possibly causing psychological harm and an ethical wrong. These issues were not expected at the outset of the family's study participation but rather emerged with new data about the research tests. Disclosure of the research finding was an important consideration, in order to avoid using the adolescent as a stem-cell donor for his sister. Disclosure to the adolescent could not be justified by merely weighing the immediate interests and preferences of the adolescent. However, an expanded ethical analysis that considers the adolescent's familial context offers a more complete picture of the adolescent's interests and preferences which provides justification for disclosure.

Keywords

ethics; genetic disclosure; minor children; Dyskeratosis congenita; research results

Introduction

Many contemporary clinical and medical research procedures necessarily involve the participation of more than one “patient”. For example, gamete donation, carrier testing within a family, and the transplantation of organs, tissues, or cells all require more than one individual's medical participation for the primary procedure. Often, these other involved persons are relatives. Such family-grounded procedures involve ethical considerations that

differ importantly from most other medical decisions. Typically, the primary considerations in ethical decision-making are the individual's preferences and whether the proposed procedure has a favorable risk-benefit ratio for the individual. In many of these family-grounded procedures, however, the overall distribution of risks and benefits of the procedure is unequal among the family members. Direct clinical benefits primarily accrue to one family member while other involved family members may face at least some medical risks while not receiving any clinical benefit at all. These other family members may also experience psychological harms. For example, misattributed family relationships may be revealed during genetic testing in a family, or there may be psychological distress following donation of organs or tissues to a family member. Psychological risks such as these are usually not counterbalanced by direct benefit to these individuals.

This apparently unfavorable risk-benefit ratio is generally justified in two ways. First, many argue that important *psychological* benefits accrue as a result of helping a family member [Clemens *et al*, 2006]. Second, when adults have decision-making capacity, and appreciate the psychological (and physical) risks they are taking, their autonomous choices to continue with (or refuse) participation in procedures that may not hold the potential to benefit them directly are typically respected.

But these traditional justifications are not adequate in all cases. In particular, what if the person being exposed to the psychological risk with no compensating potential for direct benefit in a family study is a child? How should parents balance the interests between their children? Furthermore, if the child is capable of considering and expressing preferences, how should parents and providers respond to such a child who expresses some dissent to the procedure that will benefit their sibling? Considering this question requires balancing respect for the emerging autonomy of the child with potential benefit to the sibling.

This paper will address the question of whether risks of psychological harm to an adolescent and overriding the adolescent's preferences, by disclosing apparently unwanted genetic information, can be ethically justified for the purpose of benefiting a relative. A recent clinical case at the National Cancer Institute (NCI) raised these issues in the context of a 13-year-old boy who was a potential stem cell match for an adult sibling with aplastic anemia due to Dyskeratosis Congenita (DC).

Case

DC is a rare genetic disease associated with the development of aplastic anemia, myelodysplastic syndrome, leukemia, and solid tumors [Alter, 2003]. Hematopoietic stem cell transplantation is a possibly life-saving treatment option for patients with severe hematologic involvement, and children under the age of 18 may sometimes be considered to serve as stem cell donors for affected siblings.

A 27-year-old woman with aplastic anemia due to clinically-diagnosed DC enrolled with her family in the NCI's Inherited Bone Marrow Failure Syndrome Study. Her father, uncle (monozygotic twin brother of the father), and a paternal cousin also had clinical evidence of DC, consistent with an autosomal dominant inheritance pattern. Twenty-three relatives, including the proband's 13-year-old brother, all participated in a natural history study in which family members' clinical and laboratory data were evaluated. When the 13-year-old joined the study, he assented to the performance of research studies, but explicitly requested not to learn the results of testing for known germline mutations associated with DC. This request had no immediate practical impact, as his sister was found to lack mutations in any of the known DC genes.

Approximately 11 months after the initial NCI visit, the proband began considering a hematopoietic stem cell transplant in consultation with the hematologist who had been providing her clinical management, from one of her four siblings, all of whom were clinically normal. Prior to the family enrolling in the NCI study, the hematologist established that three of the proband's four siblings were HLA-compatible, including the 13-year-old. For reasons of HLA-match, age, sex, and the absence of clinical signs or symptoms of DC, the hematologist told the family that the proband's 13-year old brother would be an "ideal" stem cell donor for his sister. Of the other matched siblings, one was female (less optimal than a male), and one was slightly older (age 20).

One of the many evaluations of the family members on their initial NCI visit was a measurement of telomere length in leukocyte subsets using flow-FISH, an assessment considered part of the research testing (to which the boy had assented) rather than part of the study's gene mutation testing [Alter *et al*, 2007]. At this time, this test was neither part of standard clinical practice nor available from a CLIA-certified laboratory. However, preliminary evidence that had accumulated in the NCI study since the family's initial visit suggested that abnormally short telomeres might correlate with the presence of mutations in as-yet-undiscovered DC genes and may be associated with future development of hematologic symptoms and/or cancer associated with DC [Alter *et al*, 2007]. During the course of research testing, the 13-year-old brother was found to have abnormally short telomeres. Despite the telomere test not being part of the genetic mutation testing, the research team believed that the 13-year-old's prior request specifically not to learn the results of mutation testing indicated a general preference regarding *any* medical results relating to his future likelihood of developing DC symptoms. Disclosing the results of the telomere test might accordingly violate his implied wishes.

When the research team learned that the 13 year old was considering being a donor, based on emerging reports of unsuccessful stem cell transplants from donors with unrecognized, non-penetrant genetic disease, the research team strongly believed that there was a genuine risk that the 13-year-old's stem cells might not engraft, thus failing to cure his sister's aplastic anemia [Fogarty *et al*, 2003; Orfali *et al*, 1999]. Accordingly, the team was uncertain about how to proceed. While the telomere test results did not fall into the specific category of results the boy had declined to learn, the team was concerned that disclosure would still go against the spirit of his expressed wishes. However, while the boy had expressed a wish to not know "genetic results", he also assented to have clinical examinations, including standard laboratory tests to look for overt or occult evidence for DC when he agreed to enroll in the study. In addition, further clarification of the risk of DC would be in the 13 year's interest because of potential benefit from subsequent monitoring for development of signs of DC. Furthermore, failure to disclose and to prevent transplantation from the 13-year-old to the proband could possibly endanger the health of the boy's sister due to failure of engraftment from an individual with short telomeres [Fogarty *et al*, 2003]. The NCI team was thus concerned as to whether it would be appropriate to disclose the results of the research telomere testing to the 13-year-old and his family, and contacted the NIH Clinical Center Department of Clinical Bioethics Consult Service.

Analysis

Individual-focused analysis

Typically, the *interests and preferences of an individual* primarily determine which action is appropriate. This approach specifically focuses ethical considerations on the direct effects to the individual patient, considering these effects mostly in isolation from his social and family setting. This is the standard approach for clinical decisions involving genetic testing in children. Many commentators have argued that the risks of learning distressing health

information from genetic testing can best be justified by the prospect of “*direct* benefit to the child” (*italics added*) and with the assent of the child [Nelson *et al*, 2001; American Society of Human Genetics Board of Directors, 1995]. This analysis is “decontextualized” because it focuses on the child alone and not the child in the context of the family or social setting. This decontextualized analysis would support not informing the boy of his telomere results.

First, nondisclosure can be justified by the obligation to respect the adolescent's autonomy. Informing the boy of his telomere status, given his earlier assertion that he did not wish to know the results of “genetic” tests, appears to violate at least the spirit of his wishes, if not the letter. This lack of respect for autonomous decisions is both a wrong in itself as well as a potential harm in its aftermath, as it could seriously weaken his relationship with the research team. Although one could argue that, as a 13-year-old, he is not *legally* capable of making autonomous decisions, he had expressed strong desires about what information he wished to know that ought to carry some ethical weight [Santelli *et al*, 1995].

Second, nondisclosure can be justified by the obligation to avoid the potential for causing the adolescent unnecessary psychological harm. At any age, learning from genetic testing that one has a greater risk of disease can have significant negative consequences, including psychological distress, family discord, and stigmatization [Green & Botkin, 2003]. Children may be at even greater risk, as they are more likely to lack the emotional and cognitive maturity to deal with unpleasant information [Nelson *et al*, 2001; American Society of Human Genetics Board of Directors, 1995; Ross, 1996; Codori *et al*, 1996; Codori *et al*, 2003; Packman *et al*, 1997; Michie *et al*, 2001]. Given these wrongs and harms associated with disclosure, a decision in this case to disclose the telomere test results to the boy would require some counterbalancing justification.

While disclosure can sometimes lead to improved and earlier treatment for diseases indicated by the test results (a direct clinical benefit), this is not true here. There is no known prophylactic treatment for the risk of aplastic anemia in someone with DC whose hematologic parameters are normal; close monitoring for development of any DC symptoms would take place whether or not disclosure occurs, given the family's medical history.

A further ethical consideration that might arise regards the importance of analytic validity (accuracy and reliability) of research tests and the legal issue of CLIA certification for US laboratories who wish to disclose “research findings”. In this case, the results were not from a US laboratory, but the laboratory used clinical protocols to ensure reliable results. However, concerns about inadequate analytic validity would support non-disclosure.

If nondisclosure is the ethically appropriate approach, based on this framework, there remains the issue that it would still not be clinically advisable for the boy to be the donor. He had already been informed that he would be the ideal donor in terms of age, sex, and HLA match. A recommendation to not use his stem cells would require some sort of explanation. Should the research team satisfy the obligation not to disclose by offering some sort of “creative alternative” explanation for their decision not to use him as a donor? This would protect his perceived wishes while also avoiding a potentially unsuccessful transplant. Yet, deception cannot be ethically justified, based on the same individual-focused analysis of the adolescent's interests and preferences. Deception by the research team, if revealed, would significantly weaken his relationship with the research team. Even undiscovered, this deception would leave the research team with difficulty communicating openly with the adolescent in the future [Capozzi & Rhodes, 2006]. From the perspective of the individual's interests, this is a significant argument for avoiding such intentional misinformation. For this reason, the research team rejected intentionally misleading the adolescent and his family about why the research team was concerned about him being a donor

In summary, using the standard individual focus on the individual patient's interests and preferences, there are significant ethical justifications for nondisclosure of his risk as a donor, but also for not deceiving him, which seemed necessary to avoid using him as a donor. To accommodate both concerns, it appears the best ethical alternative would be to permit the boy to be the donor, without disclosure of his suspected risk, even though it might increase the risk to his sister.

Expanded family focused analysis

The individual focus does not consider the interests of the individual in the context of their family. Ethical decisions ought to incorporate some analysis of the individual's surrounding environment in order to fully account for all the risks and benefits, both direct and indirect, faced by a particular participant [Jonsen *et al*, 2006]. This is particularly important when the patient is a child and the decision will have significant implications for his family. Many children have strong emotional and social ties with their family members, and their families tend to make up a greater percentage of their social support networks than do adults. Due to these connections, a large part of a child's psychological health relies on the psychological well-being of family members as well as the overall family unit. Accordingly, a child may experience important psychological benefits/harms as the result of a corresponding benefit/harm bestowed on a family member [Gordon *et al*, 1996].

This type of “reflected” benefit may occur contemporaneously, as when a relative is greatly benefited by the result of a treatment that has little or no direct benefit for the child patient himself. This is true of the case study presented here: to the best of the clinical research team's estimation, the patient's sister would have the greatest chance of survival if another sibling's cells were used instead of the boy's. This decision would necessitate the disclosure of his test results, but the potential benefit conferred on the sister would result in important psychological benefits to the boy himself by avoiding his loss and his family's loss of his sibling. Conversely, the sister's worsening health or death would confer an indirect but significant psychological harm on the brother.

In addition, in some cases, actions that set back an individual family member's personal interests in the short-term may be justified if they promote the health and robustness of the family. Though disclosure of the test results may deviate from the boy's presumed preferences, the family as a whole may be strengthened as a result of the sister's improved health. In the long-term, this family ideally will protect and promote the good of all its members, yielding less immediate but no less real benefits for the boy whose preferences were initially overridden. This is not to claim that the interests of family members or the overall family should automatically trump the interests of the individual patient, but rather that consequences for family members should be considered and factored into the overall risk/benefit assessment.

This argument that the psychological benefits from helping a family member justify the clinical harms to siblings from the actual donation procedure has been made by others, given the child's assent [Gordon *et al*, 1996;Fost, 1977]. This argument can be extended, when the potential harm arises from other aspects of the donation process (i.e. disclosure of potentially unwanted information) and there is no good way of attaining a child's assent to the possible harms. In this case, while the adolescent expressed a preference to not know his risk of future disease based on “genetic tests”, he was not asked this in the context of choosing between this preference and helping his sister. His decision for HLA testing indicated an additional preference to help his sister. It is difficult, in a *post hoc* fashion, to offer him the opportunity to prioritize these conflicting preferences.

While this conclusion favoring disclosure based on family considerations differs from the conclusion reached by typical ethical analysis, the conclusion that deceiving the adolescent is wrong does not change. If the parents are told of the boy's telomere tests while the boy himself is offered a different explanation, an element of secrecy is introduced to the family that may weaken familial relationships. If the deception is revealed, there is additional potential for resentment and distrust. Even given the expanded, contextualized conception of risks and benefits, lying still poses an overall potential for net harm to the patient.

Decisions and Challenges

Based on this analysis, the research team decided to inform, in stepwise fashion, his mother and then the boy (after the mother's approval) of the results of his telomere tests, and to recommend using another sibling with normal-length telomeres as the donor. Although the team acknowledged the importance of showing respect for the boy's preferences as well as the potential psychological harms that could result from learning unpleasant test results, the team concluded that the harms that could accrue to the boy because of the deception about the reasons for his unsuitability as a donor, and/or if his sister's transplant was avoidably unsuccessful because he was the donor, justified disclosure.

This was an ambiguous case, and it is possible that weighing the various ethical, emotional, and social considerations differently could have yielded alternative conclusions in a different family. For example, some teams might have considered deception to be a more viable option. It could be reasonably argued that the harms inherent in deception would be less severe than both the psychological harms associated with disclosure and the harms to family members. The research team in this case made a judgment against lying based on the expectation that an attempted lie would likely be revealed, since many of the significant harms attributed to lying occur only if the lie is discovered.

Others might object to disclosure by arguing that because the telomere test was not routinely used clinically and the particular results were not obtained from a clinically approved laboratory, the results should not be considered in making clinical decisions. Yet most clinical scenarios will involve at least some degree of uncertainty. In these situations, decision-makers must attempt to account for the predicted risks and benefits – including the fact that the magnitudes of some risks may be mostly unknown. In this case, despite lack of CLIA certification as evidence for analytic validity, the research team had significant preliminary evidence about clinical validity to suggest that harm might occur as a result of a transplant from the 13-year-old.³ Furthermore, based on similar cases, the team strongly believed that the harm to the sister had significant potential to be severe and life-threatening [Fogarty *et al*, 2003; Orfali *et al*, 1999]. All new clinical innovations will at some point be at this early-but-promising stage of development, and physicians and researchers working with families must make clinical recommendations based on their best educated guesses in the absence of conclusive data.

In this case, the mother was contacted by phone and told that there was some information from the research study that might have implications about who might be the most appropriate match. The researchers met in person with the parent and all of the siblings to explain the potential implications of the telomere test and to offer each of them their results. The 13-year old indicated that he understood that the interpretation of the research telomere test was tentative, but would provide a probable diagnosis of DC if the telomeres were short. He then requested his results, understood that his were short, and that he should not be the transplant donor. He also understood that he would need to be monitored for possible future development of DC complications (aplastic anemia, leukemia, and cancer). He never discussed his earlier decision to opt out of “genetic” testing. Another sibling was the donor

for the sister, who is fully reconstituted two years after the transplant. The teenage boy continues to have no physical or hematologic signs of DC.

Conclusions

An individual-focused ethical analysis of the direct benefits and harms may ignore important ethical considerations that ought to factor into decisions. The expanded family-focused ethical analysis, which considers the risks and benefits that might accrue to a person specifically in a wider family context, is better suited to fully capture the full range of ethically weighty considerations present. Ethical dilemmas that arise regarding family genetic testing or family related transplantation, for example, will often require decision-makers to consider the full scope of benefits and harms that could befall participants or patients. This analysis should include those reflected, indirect, or long-term harms and benefits that could occur as a result of consequences for family members or for the family unit as a whole. While the case described here involved difficult ethical balancing, it illustrates the general importance of considering a patient or participant's interests by conceiving of him as an individual embedded in an environment that may significantly impact him.

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