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An old problem in a new age: Revisiting the clinical dilemma of misattributed paternity☆

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A B S T R A C T

Clinical genetics has wrestled with the problem of misattributed paternity for decades. While there are no clear directives on policy, surveys suggest that genetics professionals are inclined to avoid disclosure when possible. Changes associated with the increased use of genomic testing will alter the context and may limit the benefits of non-disclosure. Multi-site testing will preclude the uncertainty often associated with single-gene testing. Increased use of genetic testing in clinical and non-clinical settings will create new opportunities for the subsequent unmasking of misattributed relationships, as will the presence of test results in the electronic medical record. Family health history information will become more valuable as it is used more often and to better effect in risk assessment, diagnosis, treatment and reproductive decision-making. These changes associated with genomic testing increase the risks and decrease the benefits associated with the nondisclosure of misattributed paternity. For ethical and practical reasons, genetics professionals, and those who advise them, should consider a greater emphasis on the value of carefully planned disclosure.

1. Introduction

There is nothing new about the problem of misattributed paternity; it is biblically old. The unmasking of it via genetic testing produces a clinical dilemma that pits the value of truthfulness and our duty to inform against our profound disinclination to disrupt relationships within a family. While this conflict remains, its context is changing rapidly due to developments on at least three fronts. First, multi-site and genomic tests identify misattributed relationships with greater certainty than the single-gene tests that predate them. Second, a steady increase in the use of genetic testing in and out of clinical settings makes it more likely that misattributed relationships will be uncovered, and more likely that they will be uncovered subsequently if not revealed at the time of testing. Third, improvements in our ability to use family health history information in risk assessment, diagnosis, treatment and reproductive decision-making raise the stakes on nondisclosure. All of these changes force us to take a new look at an old problem as we transition into the post-genomic era.

2. The status quo: a de facto policy of non-disclosure

The discovery of misattributed biological relationships as a result of clinical genetic testing can take several forms. For example, single-nucleotide polymorphism (SNP) arrays can reveal parental consanguinity, which may be unknown to members of a family (Helm et al., 2014). Revelations about misattributed maternity may also increase in frequency as more couples opt to conceive using donor eggs or embryos (CDC, 2012). However, the discovery of misattributed paternity—in which the presumed biological father of a patient is discovered not to be the father—is still the most common scenario, with rates of occurrence estimated to be between 0.8 to 30% (Bellis et al., 2005). This paper discusses misattributed paternity specifically; similar arguments would apply to alternative scenarios such as unanticipated consanguinity or misattributed maternity, as has been documented in a case involving an IVF error.

There is no formal consensus on how to handle the discovery of misattributed paternity. The few guidelines that exist are contradictory. In 1983, the President's Commission for the Study of Ethical Problems in Biomedical and Behavioral Research recommended that misattributed paternity be disclosed to both partners; eleven years later, an Institute of Medicine (IOM) committee suggested that: "on balance… information on misattributed paternity be communicated to the mother, but not be volunteered to the woman's partner." (Commission et al., 1983). A recent opinion paper from the American Society of Human Genetics (ASHG) on the ethical, legal and psychosocial implications of genetic testing in children and adolescents gave a nod to truthfulness but came down on the side of nondisclosure to either parent: "While honoring their broad responsibility to be truthful with patients and their families, we recommend that health-care providers avoid

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disclosure of misattributed parentage unless there is a clear medical benefit that outweighs the potential harms." (Botkin et al., 2015).

From available surveys, it would appear that most genetic professionals agree with the IOM. In a survey of genetic counselors in 1989, over 95% said they would not disclose misattributed paternity to the father (Pencarinha et al., 1992). A survey of medical geneticists the following year by Wertz et al. found an equally resounding 96% would not tell the father when recessive disease testing indicated misattributed paternity, most of them adding that they would opt to tell the mother in private (Wertz and Fletcher, 1991; Wright et al., 2002). Case reports suggest that decisions are made on a case-by-case basis, taking into account pertinent specific details like the state of existing relationships within the family and potential medical ramifications of nondisclosure (Soderdahl et al., 2004). However, these studies provide strong evidence that absent compelling reason to do otherwise, clinicians in practice default to not telling the father as the safer alternative.

Evidence is less conclusive regarding patient preferences and expectations. The handful of studies that exist suggest that patients are more likely than doctors to say that a man should be informed about paternity. In a 1993 survey of American patients, 75% said that a doctor should disclose if a man inquires about paternity. Lyn Turney, in a 2005 article in Qualitative Health Research, reported that Australians showed a "higher-than-average" level of comfort with disclosure of misattributed paternity to the presumptive biological father (Turney, 2005).

Modern technology has revitalized interest in this age-old question. In a recent article for the Hastings Center Report, Amulya Mandava and colleagues note that the growing number of genomic research studies necessitates an ethics framework to determine if researchers ever have a duty to disclose the incidental discovery of misattributed parentage to study participants (Mandava et al., 2015). Using a framework they propose, the authors conclude that there is typically no such duty, because a researcher's role-specific commitment to avoid the hypothetical harms of disclosure is stronger than any duties they have to realize its potential benefits. In other words, providing a research participant with accurate information about a diagnosis or reproductive risk may or may not be valuable, but it is not a researcher obligation.

In the medical realm, where a clinician's duties of beneficence and honesty to patients are considerably stronger, recent reflection on the disclosure of misattributed relationships has amounted to a doubling down on the status quo. In a 2014 article in Pediatrics, Marissa Palmor and Autumn Fiester acknowledge the limitations of informed consent in the pediatric setting, when parents' attention "is not fully on the ramifications of non-parentage but on the health of their child", and contend that it is unlikely to provide a thoughtful and trustworthy measure of parents' interest in paternity testing. Instead, the authors propose, all informed consent forms for genetic testing of minors should contain boilerplate language indicating an ironclad policy of nondisclosure: "we advocate the incorporation of a new clause into the informed consent forms for pediatric genetic testing that clearly states that any incidental information about parentage will not be revealed, regardless of the result (Palmor and Fiester, 2014)"

3. New contextual considerations in favor of disclosure

Palmor and Fiester's argument in favor of nondisclosure as a policy is based on the assumption that the potential harms of disclosure outweigh the potential benefits. They argue that increasing use of genetic testing will lead to more cases of misattributed paternity, and overwhelm our current case-by-case model. "The incidental discovery of nonparentage either burdens individual providers with the agonizing and near-impossible task of weighing the pros and cons of disclosure in the particular case or prompts the providers to call a consult with the institution's ethics service so that the ethics committee can engage in an assessment of those risks and benefits. Case-by-case decision-making…is not a satisfactory solution to this ever-increasing clinical occurrence because it undermines consistency, transparency and uniformity across the institution or practice."

Although this blanket stance may seem like an attractive option in that it simplifies a complex situation, new circumstances enabled by modern technology warrant a careful reconsideration. Consider the classic scenario Turney presented to her focus groups and survey participants: a mother, a father and a child with recessive disease, where tests results showed one deleterious allele in the child that matched the mother and a second deleterious allele in the child that did not match the father. Among the challenges that have been associated with such cases is the vanishingly rare but real possibility of a new mutation. It is not a good thing to tell people they are mistaken about the paternity of their child; it is an even worse thing to make that suggestion and be wrong. Presumably, the possibility of a new mutation, however rare, gave clinicians another reason not to reveal misattributed paternity.

Modern tests that interrogate multiple sites throughout the genome, or the genome as a whole, offer no such room for temporizing. Many new tests, including cell-free fetal DNA (cffDNA) testing and parental follow-up testing to determine the clinical significance of a variant of uncertain significance identified in a child regularly require maternal and paternal DNA for comparative purposes and can reveal much more information about the degree of genetic relationship between two individuals. Clinical use of whole exome sequencing (WES) is also enhanced by the use of maternal and paternal DNA. In a UCLA report on their initial experience with WES, diagnostic yield was 22% without parental DNA, and 31% for trios (mother, father and child) (Levenson, 2015). Indications long known to produce findings of misattributed paternity, such as recessive disease carrier testing and haplotype testing for organ donation, are all increasing in frequency. We are entering an era of both greater certainty in and greater opportunity for the discovery of misattributed paternity as the number and type of tests available and the use of those tests continue to rise year over year.

At the same time, a universal policy of nondisclosure presumes that disclosure is reliably in the hands of the clinician. It is not. By federal law, patients (or their parents and guardians) have a right to all test results. It is not safe to assume that patients or family members will not be able to deduce the possibility or even the certainty of misattributed biological relationships on their own. If it does not happen at the time of testing, it may happen down the road. Strategies for nondisclosure often rely heavily on limited genetic literacy. In Wertz's 1990 study, 20% of geneticists said that they would "fudge the issue," and 13% said that they would tell the couple that they were "both genetically responsible." Lies, evasions and artful, tactful lack of communication may or may not succeed in keeping the secret at the time of testing. New information, new suspicions, more time to think, access to the internet, and possibly even a much hoped-for increase in genetic literacy could all undermine the effectiveness of that approach over time.

The idea of universal nondisclosure assumes a passivity on the part of patients that is backward-looking, and not appropriate to an age where many people are actively engaged in their healthcare decision-making and have access to all the resources of the internet. If an individual realizes what the test indicates despite nondisclosure, the downside to nondisclosure is not only a potential loss of trust, but also a loss of any discussion, counseling or support the clinician might have been able to offer.

Genetic testing is no longer confined to the clinical realm. As Dena Davis points out in her 2014 article, "The Changing Face of Misidentified Paternity," the use of direct-to-consumer paternity tests has risen steeply worldwide, as cost has decreased and availability widened (Davis, 2007). Recreational testing can reveal misattributed paternity incidentally as well as by design. In the U.S. alone, millions of people have used genetic testing from companies such as Ancestry.com and 23andMe that provide information on genealogy and ethnicity. 'Relative-finder' services that indicate degree of kinship can expose family secrets, as can SNP data that a variety of companies make available to their clientele.