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SPECIAL ARTICLE

Ethical Issues in Contemporary Clinical Genetics

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Abstract

As genetic sequencing capabilities become more powerful and costs decline, the reach of genomics is expanding beyond research laboratories to the wards, outpatient clinics, and, with the marketing of direct-to-consumer testing services, patients' homes. Increasingly, patients receiving various diagnoses—from cancer to cardiomyopathy—can reasonably expect to have conversations with their providers about indications for genetic testing. In this dynamic context, a grasp of the ethical principles and history underlying clinical genetics will provide clinicians with the tools to guide their practice and help patients navigate complex medical-psychosocial terrain. This article provides an overview of the salient ethical concerns pertaining to clinical genetics. The subject is approached with an emphasis on clinical practice, but consideration is also given to research. The review is organized around the temporal and informational sequence of issues commonly arising during the course of pretesting, testing, and posttesting phases of patient care. Drawing from medical, legal, and historical perspectives, this review covers the following topics: (1) informed consent, (2) return of results, and (3) privacy and confidentiality, and intends to equip readers with an appropriate foundation to apply ethical principles to genetic testing paradigms with an understanding of the contextual landscape against which these situations occur.

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In April 2017, the US Food and Drug Administration (FDA) announced that it would allow the genomics company 23andMe to market direct-to-consumer (DTC) genetic health risk tests for 10 medical conditions.[1] One year later, the FDA permitted the expansion of 23andMe's reach by allowing the company to market testing for selected BRCA1/BRCA2 variants, which confer risk for breast and ovarian cancer.[2] Although the FDA maintains that such tests should not be used for diagnostic or treatment purposes and that consumers should consult health care professionals with questions or concerns about results, such decisions represent a sharp departure from its 2013 warning to the company to "immediately discontinue marketing."[3] The agency's reversal—and suggestion that other DTC technologies may enjoy expeditious approval—places it at odds with the current recommendations of the American College of Medical Genetics and Genomics (ACMG) regarding the assessment of an individual's genetic risk.[4] In the setting of this discrepancy between professional society guidelines and market realities, the trend toward broader access to personal genetic information raises difficult questions for clinicians; chief among them: what are the specific ethical and legal obligations of physicians to their patients when genetic information is concerned?

The rise of DTC and genomic testing more broadly has occurred in a technological landscape undergoing tremendous flux. As genetic sequencing capabilities become more powerful and costs decline, the reach of genomics is expanding beyond research laboratories to the wards, outpatient clinics, and patients' homes. Increasingly, patients receiving various common diagnoses—ranging from cancer to cardiomyopathy or autism—can reasonably expect to have conversations with their providers about indications for genetic testing, and as such, medical practitioners will face heightened need for genetics literacy.

As the universe of biomedical knowledge and technology rapidly expands, it is imperative that clinicians and researchers be

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equipped with sound ethical reasoning skills to guide their practice. To that end, this article is intended to provide an overview of salient issues in ethics as they pertain to clinical genetics. At the nexus of these fields lie several topics, to be reviewed in this article from medical, legal, and historical perspectives: (1) informed consent, (2) return of results, and (3) privacy and confidentiality. Furnished with this background, clinicians will be able to stay current as new developments shape the field, all the while guiding their patients through complex, dynamic medical and psychosocial terrains.

INFORMED CONSENT AND PREDICTIVE TESTING

Informed Consent

Informed consent is both an ethical and legal doctrine. Its formal origins can be traced to the 1947 Nuremberg Code that was drafted in the wake of the "Doctors' Trial," which scrutinized the human experimentation conducted under the Nazi regime.[5] The code sought to establish a set of conditions defining ethical human subjects research, and included voluntary consent as 1 of its 10 critical points.[5] In the United States, after revelations of egregious misconduct in the 40-year Tuskegee Syphilis Study,[6] the National Commission for the Protection of Human Services of Biomedical and Behavioral Research was established and in 1979 published its first set of principles and guidelines to protect the rights of research subjects. Known as the Belmont Report, the document outlines 3 basic tenets in the conduct of ethical research: respect for persons, beneficence, and justice. The Belmont Report elaborates practices to safeguard these principles: informed consent, risk/benefit assessments, and the selection of subjects, respectively. *Informed consent* in research is defined as the right of subjects to decide whether to participate in research, provided they are furnished with adequate information, possess full comprehension, and enjoy voluntariness of decision.

Postwar ethical violations in the research arena brought informed consent into sharp focus, but within the clinical landscape, the concept took root more slowly and less formally. The belief that provider and patient share in a decision-making partnership—requiring physician disclosure and patient consent—began to take hold in American medical practice through developments in case law during the 1950s and 1960s.[7] Clinically, the conditions of informed consent are similar to those outlined in the Belmont Report for research purposes: the patient must be apprised of all relevant information, have the capacity to reason soundly, and have the ability to exercise decision making freely. Only when disclosure, capacity, and voluntariness are present can informed consent be obtained.[8]

A consideration of informed consent in clinical genetics practice begs the question: to what exactly are patients consenting when they agree to undergo genomic tests? Although patients may fully expect the return of primary results, they may not anticipate the trove of genetic data generated by testing and the fact that many detected variants have uncertain significance.

Although this information may be harmless, the possibility exists that the genetic testing could reveal embarrassing, stigmatizing, or deeply upsetting medical information. Furthermore, the test may reveal results with incomplete certainty, leading to misunderstanding and unnecessary concern for the recipient.

Predictive Testing of Minors

It is within this context that predictive testing of minors for genetic conditions has raised substantive ethical questions. Although minors are legally presumed to lack capacity—and thus are unable to grant consent—the legal threshold of majority is considered arbitrary by many ethicists, psychologists, and developmental specialists.[9] Nevertheless, under current law, clinicians are required to secure parental consent for medical treatment of patients younger than 18 years, with the exception of the "mature minor" common law precedents that apply to reproductive health care.

Predictive testing is defined as genetic testing of a presymptomatic individual. Members of the ethics and genetics communities broadly support predictive testing of adults for adult-onset diseases and minors for childhood-onset disorders for which medically beneficial interventions are available.[10] There exists an ethical gray zone, however, when it comes to

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