Executive Summary

"Communication: Key to Appropriate Genetic Test Referral, Result Reporting, and Interpretation"

Organizers: Mt. Sinai School of Medicine, New York, New York
Centers for Disease Control and Prevention, Atlanta, Georgia

A meeting was held May 2-3, 2003 to explore how genetic tests are ordered and results reported and what issues exist that potentially compromise patient care and increase the difficulty of medical decision-making. DNA-based cystic fibrosis testing was used as a model for this meeting. A detailed summary of this meeting is available at http://www.phppo.cdc.gov/dls/pdf/genetics/ConferenceSummary.pdf.

Background

In 2002, a study was published that showed significant variation in the way molecular genetic testing laboratories report results for cystic fibrosis and factor V Leiden testing.[1] In 2003, a follow-up study reported the results of a physician survey that indicated simple, yet comprehensive and useful genetic test result reports were sought by physicians with the implication that such reports are not often available.[2] To further explore these issues, the CDC together with Mt. Sinai School of Medicine co-hosted a meeting to explore communication issues among professionals who order, use, or otherwise are involved in the providing genetic testing services. Cystic fibrosis (CF) was used as a model for these discussions. This meeting was held at about the same time as a separate expert focus group that addressed some of the broader issues.[3]

The May 2-3 meeting was organized to bring together individuals and professional groups representing clinicians, laboratory professionals, payers, policy makers, and consumer advocates to discuss, in a workgroup setting, current practices, problems, and potential solutions in the ordering and reporting of genetic tests and results. During the course of this meeting, five workgroups were formed and each was provided a case study, together with applicable requisition and reporting forms, to debate current practices, shortcomings, and suggest recommendations for improving practices. Each workgroup included a mix of professionals from various disciplines.

Several significant issues became apparent. Foremost was the realization of the limited data available to quantify the problems associated with current practices. Central to many of the issues discussed is the realization that a commonly understood terminology useful in the ordering and reporting of genetic tests and results does not exist. This became clear from the significant variation and understanding of genetic testing practices discussed during the meeting. It was noted that although several documents are available that provide guidance for what is to be included in test requisitions and reports, these often fall short in not describing the format by which information should be collected and reported.[4,5] For example, participants emphasized significant variability in how indication for testing, ethnicity, family history, and pedigree

information is collected and how risk estimates and recommendations for follow-up are reported. Discussions suggested such practices affect the ability of clinicians to make consistent medical decisions in the best interests of their patients and insurer's abilities to evaluate the appropriateness of genetic test referrals and outcomes.

In 2000, the American College of Obstetricians and Gynecologists together with the American College of Medical Genetics published guidelines for preconception and prenatal carrier screening for CF.[3] This guideline is the first recommendation for a DNA-based carrier-screening test directed to a large segment of the US population. Participants discussed some of the problems that have arisen in implementing these guidelines, including access to the document, understanding of its content, and use in different practice settings. Amplifying this problem is the general lack of basic CF/genetic knowledge among clinicians. Resulting from this discussion was a need to evaluate the implementation of guidelines to determine if they were accomplishing the desired goals and how best to make adjustments.

The effective interaction of professionals from varied disciplines is necessary to ensure genetic tests are used appropriately. Laboratory professionals are typically experts on their test offerings and can comment on the analytic methodology used, benefits and limitations of the test for the reason referred, and provide recommendations for follow-up testing, if indicated. Clinicians are responsible for patient care and are responsible for integrating the test result into their patient management plan. The test order form and result report are often the sole means by which the laboratory and clinicians communicate. Therefore, these provide two opportunities to help ensure the correct test is ordered and results are understood. Unfortunately, we hear that in many cases it is not the clinician completing or reviewing these forms but another party who is provided limited information or is not trained in how to review and appropriately note the important aspects of the report. Nonetheless, meeting participants voiced the opinion that working with those who provide, order, prepare, and review test requisitions and reports can best ensure that genetic tests are correctly and effectively used.

Several specific issues were highlighted during the discussions. DNA-based genetic test results are often qualitative, not quantitative. For instance, a test report noting that no mutations were found does not eliminate risk to having a disease-associated mutation and therefore does not reduce the patient's risk to zero. As variable is how the significance of a mutation finding is reported. Mutations can be benign, disease-associated, modifiers requiring other mutations or environmental triggers, or of unknown significance. Our changing understanding of genetic variation also can complicate our capacity to interpret test results. For instance, the I148T mutation, recommended as part of a CF carrier-screening panel, was recently found to be much more prevalent in persons having only one CF mutation.[7] The finding of a close-by mutation that correlated much higher with CF disease has raised questions about the clinical significance of the I148T mutation. In another example, variations in the poly-T tract in exon 8 of the CFTR gene is an example of a polymorphism that modifies the clinical expression of a primary CF-associated mutation, R117H.[8] In the absence of R117H, the clinical consequences of variations in the poly-T tract are far less certain.

Another issue discussed revolved around selecting the appropriate method to best benefit the patient. This choice is ideally made based on the indication for testing, clinical information provided, and sometimes knowledge of a family disease-associated mutation. Testing platforms available for CF currently include specific mutation determination, mutation panels, exon (and limited intron) screening, and DNA sequence analysis. The sensitivity and costs for each method differs and the most appropriate choice depends on why testing is being ordered for the patient and what clinical and family history information is available. Sequence analysis is far more expensive than mutation-specific assays but can be far more informative in some cases. These discussions all hinged on two central ideas: having a common terminology and knowledge base among genetic test users and use of the requisition and reporting process as one tool to convey a common understanding of genetic tests and results.

Major recommendations and suggested actions:

Recommendation #1

Develop guidance for ordering and reporting forms that are simple, sufficiently comprehensive, understandable, and use common terminology.

Suggested Actions:

1. Develop clinical practice/laboratory partnerships to address this issue
2. Develop best practice guidance documents (including model requisitions and reports)
3. Include implementation and evaluation plans in developing guidelines.

Recommendation #2

Collect and analyze data to quantify problems associated with genetic tests that affect patient outcomes and laboratory costs.

Suggested actions:

Define outcomes desired (i.e., standards for risk assessments and their use).

Identify and minimize those factors that contribute to variable outcomes and result in higher laboratory and clinical practice costs.

Recommendation #3

Enhance the consultative role of the clinical laboratory.

Suggested Actions:

Make better use of the ordering and reporting process for users in understanding the benefits, limitations, and use of genetic tests

Include on test requisitions and reports references to resources where users of genetic tests can find help ordering the test and properly reporting and using the results.

Develop practice and continuing educational resources useful for ensuring that the correct test is selected and the results are properly interpreted and used.

References cited

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