workshop a1: friday, march 10

Overcoming Obstacles to Clinician/Researcher Interaction

Orphan Genetic Disease – making testing a reality. S. Das, P.L. Mills, J. Hedrick, W.B. Dobyns, and D.H. Ledbetter. University of Chicago, Chicago, IL.

Rare or 'orphan' diseases, defined as those affecting fewer than 200,000 people in the United States, when taken as a group, affect approximately 20 million Americans. Over 6,000 rare orphan diseases have been documented, with the genetic basis for many now well understood. Genetic testing for orphan diseases has not been considered practical because of the rarity of the conditions, the frequency of private mutations and because the genes involved are often too large for efficient analysis. As a result, genetic testing for orphan diseases is largely not available, mainly being restricted to research laboratories working on the involved gene or disease. Our goal is to develop testing for orphan diseases in an organized fashion, with necessary quality control measures, and in a manner that is widely available. We have initiated testing for lissencephaly by mutation analysis of the *LIS1* and *DCX* genes, in our DNA diagnostic laboratory, where we have analyzed close to 50 patients. Clinical testing for this disorder has arisen from the research interest of members in our group and our experience of transferring mutation analysis from the research setting to the clinical setting will be applicable to other orphan diseases. Our experience has demonstrated to us the value of a close collaboration between a research and clinical laboratory in the establishment of genetic testing for orphan diseases. As specific mutations in patients with orphan disease are identified in research laboratories, they can be confirmed in a DNA diagnostic laboratory by DNA sequencing. Such targeted mutation analysis can be performed at a cost of $300 to $400 and allows for prenatal testing and testing for other family members, in compliance with general regulations under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). The decision of when a clinical laboratory moves onto whole gene sequencing for testing purposes will depend on factors such as gene size, cost, demand, associated research interest and expertise.

The Consumer's View of Research. Peggy Mann Rinehart. University of Minnesota, Minneapolis.

There is a growing interest in soliciting rare condition tissue samples from clinicians and families. Clinicians generally encourage this, and families want to be part of the research because participation in such studies can help

- Families both directly and indirectly and
- Contribute to medical knowledge and general welfare.

In addition, even though these studies are not intended to provide clinical services, these studies often provide information that may help in diagnosis, care or counseling. However, professionals involved in patient care often encounter difficulties with researchers and their laboratories. Likewise, families are often unaware of how different the role of research can be from provider.

While many researchers are helpful and appropriate, almost every clinician and many families have negative experiences that can affect patient care and relationships between families and clinicians. These researchers and their laboratories have a cavalier attitude towards the families who contribute tissue samples and their clinicians who recruit them. Often they: neglect to communicate when there is a culture or other failure lose samples, recruit the same families from different sources – clinicians, web sites and support groups – without realizing they are testing the same family.

Our goal is to discuss and suggest guidelines for research laboratories using clinical specimens. Such guidelines should protect everybody's interests with a minimum of effort and should reflect good practice and basic decency.

One Clinician's View of Clinician/Researcher Interaction. Mark S. Lubinsky, MD, Medical College of Wisconsin, Milwaukee.

Research studies may help with diagnosis, care or counseling. However, many labs deal with contributors of clinical materials in ways that subvert professional relationships and care. Difficulties with sample handling, both short and long term, poor communication, disrespect for clinicians, and disregard of clinical needs are common, and interfere with clinical genetic services.

The Great Lakes Regional Genetics Group Subcommittee on Delivery of Clinical Genetics Services has developed guidelines for research labs using clinical specimens. Any part can be modified, but it should be clear what a lab will or will not do. We also hope that a mechanism can be developed so problems with a specific lab can be made known. Guidelines include: *1. Receipt of material is acknowledged. 2. The submitting center is told of problems preventing analysis. 3. Clinicians are notified if material is transferred, and secondary investigators should follow agreed upon guidelines. If a researcher moves, status of project and specimens is clear. 4. Notification if a project is inactivated, and the status of the material. 5. If studies are "on hold" materials should be available for others if needed. 6. If material is to be discarded, return should be offered. 7. There is a regular (e.g. yearly) update on the status of an active investigation. 8. A report is available if new needs arise, e.g., a possibly at risk pregnancy. 9. Final results (positive or negative) are promptly reported, with a chance to directly discuss them with the lab. 10. Written results are provided. 11. The counselor or nurse clinically involved should be able to discuss the status of a study, or results and their implications, with the lab. 12. Material is included. 14. A genetic counselor, nurse, or other appropriate contact should be part of any research project involving genetic studies. 15. Clinicians are told of publications or major presentations involving material that they helped provide, and contributions acknowledged.*