Making the Case for Genetics:
Roles for the Public Health Laboratory

Meeting Summary

October 20, 2003, Washington DC
Hosted by the Association of Public Health Laboratories and the Centers for Disease Control and Prevention

Contents:

Purpose:

We convened a small group of public health laboratory directors, other public health professionals, academic researchers, and others to begin a dialogue to address the following two questions:

What are or should be the near-future roles for the public health laboratory in integrating genetics into practice?

Where are we in practically using what we know about genetics to aid and improve public health laboratory efforts to serve their populations?

Our intent was to look beyond the screening of newborns for heritable metabolic diseases to other promising areas in which genetics may impact public health laboratory activities. We designed a one-day meeting around the context of case scenarios that were developed to elicit discussion about where genetics may provide near-future benefits to public health laboratory services. Case scenarios covered chronic disease, infectious disease, and pharmacogenetic topics.

Major Discussion Points:

The field of genetics is rapidly evolving and public health laboratory professionals are in a position to recognize opportunities that benefit their mission. To do so requires expanding their current roles in a direction that will permit public health to proactively address genetic testing issues. Potential roles for public health toward achieving this goal are listed below.

1. Education and advocacy for genetics[1]
2. Providing access to high quality genetic testing services to vulnerable at-risk populations (This covers access, testing, and quality assurance issues)
3. Facilitating partnerships to best serve the public's health needs

4. Collecting and analyzing population-based data in a format useful for making decisions about genetic testing and the use of genetic information in health care decision making.[2]

[1]In 2001, the CDC facilitated the development of competencies for the public health workforce to provide a framework for developing educational objectives and programs (http://www.cdc.gov/genomics/training/competencies/default.html). Designing effective educational programs for the spectrum of professionals and the public toward understanding and using genetic information is an important priority.

[2]The Centers for Disease Control and Prevention sponsors several programs designed to collect and evaluate genetic information relevant to assessing the analytical and clinical validity and utility of genetic tests (http://www.cdc.gov/genomics).

Missing pieces:

Participants in the discussion suggested we lack:

1) a framework to develop criteria useful for assessing when genetic tests or other services relevant to genetic testing would be of value for implementation in the public health laboratory and,
2) a process to implement and evaluate new tests or services in the public health laboratory setting.

Beyond test offerings, services within the purview of public health laboratories may include developing quality assurance programs applicable to the larger testing community, acting as a resource to populations served (including vulnerable populations), and becoming a resource for policy makers. As these discussions continue, variations in resources and needs among the states, counties, and communities must be appreciated and carefully considered.

Other efforts have been undertaken to begin addressing these issues. A study published in 2001 (Genet Med. 3:405) provided an assessment of available tests and their potential for public health purposes. Similarly, the Health Resources and Services Administration has contracted with the American College of Medical Genetics to develop criteria to assist states in identifying tests for newborn screening programs (http://www.acmg.net/surveys/NBS-05_22_03/nbs.asp).

During the course of the discussion, a process was proposed to identify and address genetic testing and services that may ultimately prove useful for the public health laboratory to become engaged. It was suggested that we identify some contemporary examples of relevant genetic tests and services and explore how they may fit into this process (outlined below).

A Process for Adding a Genetic Test or Service to the Public Health Laboratory			
Step	**Who is involved**	**Action**	**Who is affected**
Making the case			
1. Expert input	Federal/State, Programs, Professional organizations, Private sector, academics,	Identify areas where opportunities exist. (possibly based on a criteria assessment	Federal/State Programs Professional Organizations

	legislature, Payers (a combination of these; not necessarily all)	formula)	
2. Formal Assessment	Federal/State Programs Professional Organizations	Collect, evaluate, and present data.	Population at risk, Federal/State, Programs, Professional organizations, Private sector, academics, legislature, Payers (a combination of these; not necessarily all)
Making the plans			
3a. Applied Research	Funding groups, Federal/State Programs, Professional organizations, Private sector, Academics	Conduct and perform pilot study - cost/benefit analyses.	Population at risk, Population at risk, Federal/State, Programs, Professional organizations, Private sector, academics, legislature, Payers (a combination of these; not necessarily all)
3b. Translational Research	Funding groups, Federal/State Programs, Professional organizations, Private sector, Academics	Evaluate Infrastructure - Can a new service (role) be supported and how? Determine acceptability by affected population.	Population at risk, Federal/State, Programs, Professional organizations, Private sector, academics, legislature, Payers (to include all who would have a role)
Making it Happen			
4. Implementation	Federal/State Programs, Private sector, payers, population at risk	Train the workforce. Develop infrastructure. Educate the population.	Population at risk, Programs that support interventions, legislative group, Payers (to include all who would have a role)
5. Evaluation	Population at risk, Population at risk, Federal/State, Programs, Professional organizations, Private sector, academics, legislature, Payers (a combination of these; not necessarily all)	Determine if the program is working.	Population at risk, Population at risk, Federal/State, Programs, Professional organizations, Private sector, academics, legislature, Payers (a combination of these; not necessarily all)

Notes:

1. Applied and Translational research are linked in this process.

2. Advocacy is critical for any change to be accepted and ultimately implemented. The key is to engender appropriate and sustained advocacy throughout the process keeping in mind that any change must ultimately benefit the populations being served.

3. Education and professional/public awareness are important. Appropriate efforts should coincide with each stage.

4. Quality assurance issues and measures should be considered and integrated into each stage of the process. Special attention should be given to the quality assurance practices that will be important if the effort is integrated into public health laboratory practice.

Case scenarios:

Three general areas were covered by the case scenarios presented: chronic disease, infectious disease, and pharmacogenetics. Arguably, other areas, such as environmental exposures, would have been equally useful to address, but time limitations restricted inclusion. No doubt these other areas will be brought into future discussions.

Chronic disease

Genetic tests that gauge risk for cardiac disease and diabetes type I were discussed in light of their promise as potential tests of public health importance. CARDIARisk™ is a DNA-based test developed by Myriad Genetics that is able to identify a sequence variation in the angiotensinogen gene correlated with risk for cardiovascular disease and hypertension, at least for certain ethnic groups. The sequence variation may also have implications for treatment. In evaluating this test, Myriad decided not to further pursue its introduction into the marketplace since a number of cardiologists found it to have limited value for their practice. Newborn screening for diabetes type I holds the promise of identifying those susceptible to the disease early in life so preventative efforts can be undertaken. Available screening tests have traditionally suffered from low sensitivity and specificity. With new findings, there is now optimism that a highly sensitive and specific screening test can be developed.

Infectious disease

Knowledge of the biology of infectious agents, and not the host has thus far been the most important contributory factor to infection, disease progression, vaccine efficacy, and treatment success. Nonetheless, we are learning more about host factors that do indeed contribute significantly to each of these events. We discussed HIV infection and CCR5 co-receptor genotyping along with meningitis and genotyping of the mannose-binding-lectin (MBL) as two examples where human genetic testing may have a role in identifying persons at risk for disease. CCR5 serves as a major (but not the only) host co-receptor for HIV infection for M-tropic viruses. A variant of this gene can block infection (when two copies of the variant are present) or delay disease progression (when one copy of the variant is present). *Nesseria meningitidis*, a major pathogen responsible for meningitis, occurs in approximately 1% of the population as a harmless commensal. In few individuals, active and potentially fatal disease can result. Mutation in the MBL protein accounts for disease progression in a large number of these individuals.

Pharmacogenetics

Pharmacogenetics links variations in drug metabolism and response with specific genetic variants. Each year, significant morbidity, mortality, and costs are associated with adverse drug reactions resulting from improper dosing. The cytochrome P-450 protein family serves an important role in drug metabolism. Variants in genes that code for this family of proteins correlate with the rate that certain drugs are metabolized. Using these information can minimize adverse outcomes and is anticipated to dramatically improve medical care. Variation in two genes CYP2D6 and CYP2C19 is estimated to affect the metabolism of over 50% of the drugs in use today. Evidence-based guidelines are being developed for the use of pharmacogenetics in clinical practice.

Pertinent points made during the discussion:

1. Efforts are underway to develop a newborn screening test for susceptibility to type I diabetes. The test under development will use multiple markers to attain a high level of sensitivity and specificity. There was concern voiced as to the capacity for public health laboratories to offer such sophisticated testing. These concerns were addressed through several comments. First, the technology can probably be streamlined to be effectively implemented in a public health setting. Second, if value for such testing is appreciated and resources are provided, public health laboratories have typically been very good in integrating new technologies (e.g., tandem mass spectroscopy). Third, in some states, testing services can be contracted out to the academic or commercial sector. Beyond the testing, another limitation at present is lack of guidance in how to follow up with newborns that are identified as being at risk. The ongoing pilot program is expected to address many of these issues (Genet Med 5:77).

2. Test developers and users primarily focus on the diagnostic market that provides services to patients already known or suspected of being ill. Genetics offers increased opportunities to identify healthy persons at risk for disease. In discussing the Myriad CARDIARisk test, it was apparent that this test was being developed for cardiologists who, for the most part, see ill patients. Claims made for the test, however, seem equally applicable to identifying healthy persons at risk for disease. Perhaps the test would have fared better among primary care doctors and their patients with a family history of heart disease or hypertension. **As such, there appears to be an opportunity for public health to work more closely with commercial test developers to explore the potential of their work for application in the public health and preventive medicine arenas.**

3. Minimizing adverse drug reactions can reduce morbidity, mortality, and medical costs in certain situations and have significant impact on the public's health. Pharmacogenetics provides one tool to accomplish this. The clinical community, however, has been slow to respond (see Science 302:588-590) and implement practice standards. **As a first step for public health to explore the potential for pharmacogenetics, an expert workgroup should be formed to identify and address those issues determined to be pertinent.**

4. Currently, genetic issues relevant to chronic disease are deserving of increased attention at the public health programmatic level. **There should be laboratory representation to ensure inclusion of testing issues in the discussion.**

5. For infectious disease testing, the biology of the infectious agent is the primary factor in gauging the public health response. Our knowledge of host factors lends little to available interventions today. In time, we will be able to use knowledge of host factors to identify persons and populations more likely to become infected, manifest serious disease, and benefit (or be harmed by) treatments and vaccines.

6. Public health efforts are largely funded by state legislatures and other funding bodies that are constantly challenged with competing priorities. Ideally (many would say minimally), in requesting additional funding, arguments must be compelling, show clear and obvious benefit, and significant cost savings. **Using a process outlined in the table above may provide both the data, advocacy, and knowledge needed to push for funding for services that are clearly beneficial to a population.**

7. It will be useful to have representation from the payer community (Medicaid/Medicare, third-party) at future meetings.

Not discussed: We did not address environmental issues at the meeting. One example that comes to mind is identifying those at risk for Beryllium disease. At one time, and perhaps still, some companies in the beryllium industry offered job applicants testing for HLA-DPB1. This allele is reported to place persons from various racial/ethnic groups at higher risk for disease, although the predictive value of the genetic test is reported to be relatively low (http://www.cdc.gov/genomics/hugenet/reviews/print/Beryllium.pdf). Since such tests can impact health outcomes, employment, insurance and health care coverage for certain populations, the question arises as to the public health role.

Recommendations for next steps:

This meeting served as a reasonable primer in considering the issues discussed. We can move our discussions forward at a follow up meeting. Below are some discussion points for a future meeting.

1. **Share information about what has worked for public health laboratories in integrating genetics into their activities.** Several state public health laboratories have been successful in integrating genetics into their various activities. It will be useful to hear from these states and see what has worked and where challenges exist. **Such presentations can be used to facilitate a discussion to identify activities that are broadly applicable and to define roles for APHL, CDC, and others in developing and supporting efforts.**

2. **Refine and evaluate the implementation process proposed in this report.** We want to explore the potential usefulness of the process at a follow up meeting and develop an "inventory" of tests and other services that may be useful in evaluating the process.

The previous section of this report contains several recommendations for specific follow up items pertaining to the topical areas discussed (e.g., enhancing links between public health and the commercial sector; exploring the intersection of public health and pharmacogenetics). These may form the basis for some of the discussion and provide examples to assist in evaluating the proposed process.

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