Chapter 1

The Role of Human Genomics in Acute Public Health Investigations: Current Practice and Future Strategies

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Incorporating Human Genomics into Acute Public Health Investigations

Public health investigations are fundamental to the Centers for Disease Control and Prevention's (CDC's) mission to improve the health of the people of the United States. CDC has gained both national and global recognition for its rapid and effective investigations of acute adverse health events, which include **epidemiologic aids (Epi-Aids)**. CDC currently responds to approximately 80 to 100 Epi-Aid requests annually, and individual states together conduct 600 to 800 additional acute public health investigations (APHIs) annually. Although these studies generally focus on infectious diseases, they also investigate chronic diseases, environmental hazards, injuries, and occupational health.

Eidemiologic aid (Epi-Aid)
An epidemiologic field investigation of an urgent public health problem.

By collecting human genomic data, APHIs can potentially help in identifying additional risk factors for disease susceptibility, severity, and transmission. The results of such investigations could be used to:

- Characterize environmental exposures more accurately.
- Assess variation in disease outcomes.
- Assess the effectiveness and side effects of therapeutics and vaccines.
- Refine certain public health interventions, including vaccination, exposure reduction, chemoprophylaxis, behavioral modification, and education.

Examples of Investigations

Some examples of APHIs in which CDC collected human genomic data are as follows:

- An APHI in 1998 investigated leptospirosis among athletes at an Ironhorse Triathlon (1). Of the 887 triathletes included in the investigation, 98 were clinically ill with the disease. Analysis of *TNF-alpha* **polymorphism**

Polymorphism
Variants of a gene that are found in >1% of the population.

HLA (human leukocyte antigen) genes
Genes for cell surface proteins that vary among individual people and are important in immunity.

Vaccine adverse events (VAEs)
Symptoms or diseases that occur shortly after immunization and may be related to the administration of a vaccine.

and ***HLA* (human leukocyte antigen)** Class II genotypes (*DR*, *DQ*, *DP*) showed that triathletes who were *HLA DQ6* positive were more likely than those who were *DQ6* negative to have laboratory-confirmed leptospirosis. In addition, *DQ6*-positive triathletes who swallowed lake water had the greatest risk of developing the disease, an example of gene-environment interaction.

- Efforts are underway at CDC to study human genomic factors and **vaccine adverse events (VAEs)**. The emergence of myopericarditis following smallpox vaccination has highlighted the potential importance of human genomics in studying VAEs. The Clinical Immunization Safety Assessment (CISA) centers, a network of clinical academic centers in partnership with CDC, have a new initiative to evaluate VAEs, including human genomic factors (2). Human genomics may help in identifying risk for VAEs and in guiding the development of safer vaccines. *For more information on this topic, see Chapter 3, Genomics and Vaccine Safety: Research for Future Practice.*

- Approximately 35% of people exposed to tuberculosis (TB) develop latent infection, but only 2% develop active disease. CDC's Division of Tuberculosis Elimination (DTBE) (3), in collaboration with state partners, is studying human genomic factors in TB disease susceptibility, transmission, and outcome in the context of case contact investigations.

APHI Workshop Held in May 2004

During 2004, CDC, in collaboration with the Council of State and Territorial Epidemiologists (CSTE), formed a multidisciplinary APHI working group to outline key research priorities for incorporating genomics into APHIs and to develop the needed tools as outlined in the article that accompanied CDC's Genomics and Population Health: United States 2003 Report (4). The APHI working group held a meeting on May 12–13, 2004, inviting external consultants from the National Institutes of Health, state and local health departments, and academic medicine. The meeting participants had diverse expertise in the epidemiology of infectious and chronic diseases, occupational health, gene-environment interaction, laboratory genomic science, public health law, vaccine adverse events, bioinformatics, and population-based human genome epidemiology.

The goal of the meeting was to assist CDC and CSTE in developing a strategic plan for research priorities aimed at incorporating human genomics into APHIs at both the state and federal levels.

Conclusions from APHI Workshop

The external consultants who participated in the May 2004 APHI workshop generally agreed on the following:

- APHIs can provide unique opportunities to use genomic tools to analyze why clusters of individuals in communities become ill and to assess the impact of prevention and control strategies.
- Methodology (e.g., analytic, statistical); capacity (e.g., laboratory, specimen banking, bioinformatics); and ethical, legal, and social issues must be addressed.
- Research is needed to assess the value of genomics in improving the accuracy and effectiveness of investigations and the translation of results into public health interventions.
- Investigations that include genomics should be prioritized based on public health value, feasibility, resources, practicality, and community understanding.
- In high-priority investigations, consideration should be given to storing samples for future studies.
- Efforts should include the development of federal and state/local government, private, academic, and community partnerships.

Current Public Health Research Priorities

Since the conclusion of the APHI workshop in May 2004, CDC has been moving forward to incorporate human genomics into APHIs by creating a foundation for the following research priorities:

- Assessing and developing public health genomics infrastructure and capacity (including laboratory practice, analytic, informatics, banking, ethical/legal/social issues) and identifying gaps and needs.
- Synthesizing a relevant science base on human genomics and diseases/exposures.
- Identifying, developing, and applying appropriate analytical methods in epidemiology, statistics, laboratory practice, and bioinformatics.

- Developing standard language for informed consent for DNA sample collection, storage, and testing.

- Developing standard guidelines for the following procedures:
  – Specimen collection, processing, and transport.
  – Specimen banking.
  – Standardization of tools for data collection and management.

- Addressing education and training needs for constituents at all levels (i.e., CDC, states, communities, policy makers, media, and community partners).

- Creating partnerships with states to address the feasibility of APHIs, education, funding, and capacity.

- Developing mechanisms for sharing resources (e.g., templates, tools, laboratory support).

- Prioritizing investigations and conducting pilot studies in collaboration with state partners.

References

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