geneteg feddygol
GWASANAETH i GYMRU

medical genetics
SERVICE FOR WALES

CARDIFF AND VALE UNIVERSITY HEALTH BOARD

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Access to medical technologies in Wales

Evidence from All Wales Medical Genetic Laboratory – MT 17

Laboratory Genetics
Institute of Medical Genetics

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Access to Medical Technologies in Wales
All Wales Medical Genetic Laboratory

1. The All Wales Medical Genetics Laboratory (AWMGL) provides diagnostic genetic services for the population of Wales. Once a specialist service providing only rare tests for inherited disease, the laboratory now provides many services for paediatricians, neurologists, oncologists, haematologists, and obstetricians, as well as Clinical Geneticists. The growing discipline receives over 15,000 requests each year for complex genetic analyses. As genetic and genomic services become mainstream the demand for genetic testing increases (see below). Over 70 staff are currently employed by the accredited AWMGL.

2. Genetic and genomic services are rapidly evolving as our understanding of the human genome, molecular technologies and their application to healthcare also improve. New genes are constantly discovered bringing with them the opportunity for diagnostic services for rare genetic diseases; these have the benefit of improved treatment / management for the patient, and risk analysis for their family members. We are entering the age of stratified (or personalized) medicine; detection of simple genetic changes in a patient's blood or tumour sample determines the likelihood that the patient will respond to drug A or B, and if they will have an adverse response.

3. Through the pioneering work of our research colleagues in the UK Sanger centre and around the world, vast steps in genetic technologies have been made. Whereas it took 10 years (and $1bn) to sequence the human genome in the 1990-2000's, we now have the technology to do the same in 48 hours on a bench-top in an NHS laboratory. This technology is available and applicable for healthcare.

4. Examples of new genetic technologies and their applications include **array comparative genomic hybridization** (array CGH). This technology has been available for well over a decade; it has many applications in R&D. In healthcare, it can be applied to detect copy number changes in chromosomes. These include deletions and duplications that cause well-known conditions

such as Down's syndrome, and many rare syndromes only seen in single families. The technology has a sensitivity of ~20% in patients referred with developmental delay, this compares with traditional chromosome analysis with a sensitivity of 2-3%. For those 20% patients and their families with a positive diagnosis, endless appointments and investigations are avoided, treatment and management options become available, and testing is offered to family members. The healthcare provider also benefits through the savings in unnecessary appointments and often costly investigations for the patient.

5. Array CGH analysis has been available throughout the UK and Europe for 4-5 years for this patient group, and in the US for significantly longer. The service has still not been commissioned in Wales, resulting in considerable distress amongst patient groups. Healthcare professionals have now acted to implement the technology and service, although at the expense of other genetic services, and in 2013 lagging considerably after the rest of the UK.

6. **Next generation sequencing (NGS)** has revolutionized our ability to sequence DNA. We can now sequence whole genomes (total chromosomal DNA) in a couple of days, for around £1000. Diagnostic healthcare genetic sequencing was confined to the analysis of single genes, and was slow (4-6 weeks) and expensive. During the last 2-3 years, NGS technology has begun to be adopted as a healthcare diagnostic platform. It can be used for the analysis (a) multiple genes / gene panels for diseases where many genes are known to contribute, (b) exome or genome analysis, where the gene(s) associated with a disorder are unknown. In both cases NGS analysis will enable genetic diagnoses that would not have previously been possible. The identification of a genetic defect and a genetic diagnosis avoids unnecessary appointments, treatment and management options become available, and testing is offered to family members.

7. Diagnostic NGS platforms are available, a number have been purchased in Wales (by the Wales Gene Park and NHS service). However, the delivery of diagnostic services requires the development and validation of specific (gene-panel or genome) assays. The technology is new and not "kit-based", requiring local optimization. The technology produces vast quantities of "big" data; this requires analysis by trained bioinformaticians, and appropriate capacity for data handling and secure storage. Until these support functions are addressed, Welsh patients will not benefit from the major benefits of this new genetic technology.

8. **Stratified Medicine (or Personalised Medicine)** describes the use of biomarkers, in this case genetic markers, to predict a patient's response to a drug and their likelihood of an adverse effect. This is a rapidly growing area of medicine; at the current time many genetic biomarkers have been proven to have clinical utility. Key examples are in oncology where simple and rapid genetic testing can identify those patients who are most likely to respond to novel biological agents, instead of standard chemotherapy. These patients have a far better prognosis, and overall survival. They can be treated at home and have fewer adverse events. Within the whole patient pathway the additional cost of genetic testing is far off-set by the significant savings in drugs and patient treatment.

9. There is currently no identified commissioning route for the adoption of stratified medicine services in Wales. The AWMGL has the capability to deliver these services, there is considerable demand from clinicians and patients.

10. It is essential that available genetic medical technologies are rapidly assessed, developed and integrated into clinical care in Wales. At the current time Welsh patients and clinicians are not able to access those technologies which would make a significant difference to diagnosis, treatment, and health economy. Services are not available equitably for Welsh patients.

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