

(Molecular) Epidemiology

- Distribution of disease: Descriptive

In relation to person, place and time

In terms of its consequences to the general population

- Determinants of disease: Analytical

Causative factors, host characteristics and environmental exposures that influence disease risk

It is the process by which health problems are detected, investigated and analyzed

Is the scientific basis for the practice of preventative medicine and public health

Molecular Epidemiology

- **A science that deals with the contribution of potential genetic and environmental risk factors identified at the molecular level, to the etiology, distribution and control of disease in groups of relatives (families) and populations.**

It enhances our understanding of the pathogenesis of disease & defines genetic susceptibility with molecular markers, not surrogate information

Molecular Epidemiology

- Is based on general epidemiology
- Utilizes molecular biology to define the distribution of disease and its etiologic determinants

Why study Molecular Epidemiology ?

- It provides a critical link between the Human Genome Project and medicine/public health
- Without well designed population based molecular epidemiology studies it will be impossible to interpret the risk of disease associated with the presence of newly identified susceptibility genes



It is essential for :

Development of medical diagnostics

Public Health strategies

Types of Molecular Epidemiology Studies

- ◆ Case-control
- ◆ Cohort
- ◆ Cross-sectional

In Molecular Epidemiology case-control studies are referred to as Association studies (AS)

- ◆ AS do not concern familial inheritance patterns. They are based on a comparison of unrelated affected and unaffected individuals from a population.
- ◆ An **allele A** at a gene of interest is said to be **associated** with the trait if it occurs at a significantly higher frequency among affected individuals compared with control individuals.
- ◆ Association may occur either because the disease gene and marker polymorphism are very close together or it may be that the marker alleles may influence susceptibility to disease

Case-control studies are particularly suited to ME studies

- ◆ Unlike biological markers of exposure (eg. occupational, nutritional), genetic markers are stable indicators of host susceptibility
- ◆ Case-control studies can provide an opportunity to do a ‘fishing expedition’ for the effects of several genes, along with other risk factors and to look for gene-environment interaction
- ◆ Case-control studies are suitable for many uncommon disease endpoints such as birth defects and specific cancers

Alleles, genotype and phenotype

- ◆ Most of the variation in DNA is in the non-coding regions, but some falls within genes. Different versions of the same gene at the same position on corresponding chromosomes (i.e. at the same genetic locus) are called *alleles*.
- ◆ Some alleles are identical in their action but others produce quite different effects eg. Sickle cell disease
- ◆ The set of alleles that a particular person has is known as their **genotype**. The set of observable characteristics that they have is known as their **phenotype**.

Phenotype *continued*

- ◆ The **phenotype** is the result of the interaction between the genotype and environmental factors: almost all human characteristics including susceptibility to disease, are determined by the combined effects of an individual's genetic constitution and their environment
- ◆ Sometimes the environmental effects are small, for example eye colour is largely determined by the genotype.
- ◆ Other characteristics of the phenotype, however, such as height and weight depend more strongly on environmental factors, although the genotype also plays an important role

Linkage Studies

- ◆ Related individuals are studied, either siblings or extended pedigrees.
- ◆ Linkage is present when the alleles of a marker tend to cosegregate with a disease within a family.
- ◆ The strength of evidence in favour of linkage is measured as the lod (Log Of oDDs)- this is the logarithm base 10 of the ratio of two outcomes –the likelihood assuming linkage and the likelihood assuming non-linkage

The Importance of Molecular Epidemiology studies to Public Health.....prevention/treatment ?

Use of genetic testing-to diagnose a genetic disease, to determine whether a person is a carrier of a disease-associated mutation, to predict the development of a genetic disease or to determine whether an individual has a specific genetic susceptibility to a disease.

- Diagnostic genetic testing- postnatally/antenatally
- Carrier testing
- Predictive genetic testing (presymptomatic testing)
- Testing for genetic susceptibility

Population Screening

Population Screening : Genetic screening is a term often used a synonym for genetic testing. It should be reserved for the explicit and systematic application of a genetic test across a whole population of asymptomatic people , or a subset of a population such as pregnant women or newborn infants.

Examples in the UK:

Antinatal serum screening for Down Syndrome

Antenatal carrier screening for SCA in regions with a large Afro-Caribbean population

Predictive testing for HD and hereditary cancers widespread but not on population base.

CF carriers tested on a research basis

Newborn screening for phenylketoneuria, cystic fibrosis and hypothyroidism.

- ◆ **In Ireland :**
- ◆ Newborn testing for PKU, CH galactosemia and hypothyroidism
- ◆ No population screening for carriers of recessives and for late onset genetic disorders