Lecture 2: Nature vs Nurture

Plato

- Biological and genetic determination
- Born with it all already in us
- Biological and genetic determinism

Biological determination: the interpretation of humans and human life from a strictly biological point of view and it is closely related to genetic determinism

Aristotle

- Society and environment affect us

Social determinism: social interactions and constructs alone determine behaviour

Monogenetic conditions

- 100% penetrance during life
- all people with the genetic mutation will develop Ethel disease
- all people with the genetic fault will have the same features
- developmental disorders

single gene syndrome

- dysmorphic syndromes
- congenital anomalies
- developmental delay
- classical genetic disorders (neurofibromatosis, marfan)
- genetic forms of common conditions (cancer, neurogenetics)

Familial adenomatous polyposis coli

- develop colorectqla cancer by 40 if not treated
- Cancer occurs in multiple polyps which form from (early teens: 100 - 1000s)
- Due to mutations in the APC gene 5q
- Mean age cancer Dx = 40
- Penetrance essentially 100%
- Dominant

Peutz-Jeghers syndrome

- Intestinal polyposis (harmatomas)
- Mucoutaneous pigmentation
- Colorectal, gastric, pancreatic, breast and ovarian cancer
- STK11 gene mutations

Environmental 'teratogens'

- Birth defects caused by in utero exposure to drugs and environmental toxins
- Thalidomide was a common drug to treat morning sickness but it was found to cause limb defects in the children who's mothers used it while pregnant
- Other teratogens: infections, maternal diabetes, environmental toxins, hyperthermia, ionising radiation, reactional drug use

Causation criteria for teratogenicity

- Correlation doesn't prove causation
- Strength of association (cohort and case studies0
- Consistency between independent studies
- Temporality; timing of exposure correlates with defect
- Biological gradient; does response
- Specificity; consistent pattern of malformation
- Epidemiological sense; defect more common in population with higher exposure
- Biological sense; plausible biological explanation
- Analogy; simular compounds produce simular effects

Alcohol

- This infant has a small head, some distinctive facial features, developmental delay, short stature and a heart abnormality and was exposed to large amounts of alcohol in the first trimester.
- Alcohol use in pregnancy has been extensively studied and a characteristic set of abnormalities, foetal alcohol syndrome is now recognisable.
- Note also Alcohol-related neurodevelopmental disorder (ARND)

Environmental factors can be modified or avoided (phenylketonuria PKU)

- Mutations in both copies of phenylalanine and hydroxylase gene
- In PKU phenylalanine levels rise and cause damage to the brain severe learning disabilities
- Also decreases hair, skin and eye pigment (blonde blue eyd and pail)
- In utero this isn't a problem as it uses the mothers level of PKU
- Postnatal conditions as in utero maternal PKU level protect embryo
- The absence is of the enzyme in the child in utero has no affect but as soon as they are born they lose the protective effect of the mother PKU and phenylalanine levels build up
- Tested and diagnosed at post natal check
- Diet restriction prevents learning difficulty (diet with no phenolalanine in it)
- Positive environmental modifications of monogenetic disorders (modify the environment so you aren't affect by this genetic mutation)

Assessing the intrinsic genetic versus the extrinsic environmental components

1. Twin and adoption studies
   - Can quantify how much of a trait has a genomic component
   - Monozygotic twins (same genome and environment)
   - Dizygotic 50% simular genome and environment)
   - Same or 50% genome and different environment
   - Arpund 30% of breast cancer has a familial component
   - Currently clinical genetic testing can account for only around 14%

2. Genome wide association studies
   - Low coverage (wont have picked everything up, may have a few false positives) of whole genome
   - Exomes= encode for proteins and only account for 1-2% of your genome

Genetic: effect that is significant enough to interpret by itself (mutation, pathological, rare)
Genomic: effect that can only be interpreted correctly in the context of other simular variants (variant polymorphisms, normal, common)