

Ageing

CE Ruse et al. *Age and Ageing*. November (2001) Vol. 30 #6 p 450.

Increased longevity presents increased opportunity for the manifestation of long tail diseases. However, the contribution of genetics to the diseases of later life should be taken into account. Associations between early life exposure and later life manifestation of disease could be misleading.

It is generally accepted that the process of natural selection is most dynamic and efficient when concerned with the ages relevant to reproductive fitness. Living beyond a reproductive age, may expose survivors to unimportant risks for selection but which are threats to health in later years.

Late onset disease includes chronic obstructive pulmonary disease (COPD). But does this have a genetic basis?

One test of genetic contribution is the lambda (λ) test. λ is defined as the prevalence in first degree relatives/prevalence in general population. E.g. $\lambda = 3.5$ (95% CI = 1.3 to 9.4) for Parkinson's. This is indicative a potential role for genetics but is not convincing on its own. Compare this with $\lambda = 500$ for cystic fibrosis, highly convincing.

It is common practice for researchers to analyse genetics of extreme groups to find evidence of a proposed genetic link. Early signs are, that there are genetic risk factors for COPD. (Am. J. Resp. Crit. Care Med. 2001 Vol. 164#8 p 1419). Extreme groups usually include those who get the disease much earlier in life than usual. However, there may be other reasons for early presentation.

False positive and false negative association can be anticipated as a result of:

- exposure history
- selection survival e.g. if the risk factor COPD was also a risk factor for early death from CVD.
- co-morbidity and its treatment may affect presentation and ascertainment biases

One way to avoid direct errors is to establish the age profile of the proposed risk factor.

Risk increases with age both because of ageing and because of continued environmental exposure. If a high proportion of the population eventually gets the disease in question, age profiling is essential to the identification of genetic factors.

Comment

Increased longevity will provide researchers with increased opportunities to detect associations between exposure and ill health. Such associations may be subject to unusual biases. Studies including elderly cases should allow for these potential biases and should make use of age profiling.