

Inheritance of multifactorial traits and diseases in man

To understand the inheritance of multifactorial traits and diseases, it is necessary to refer to the Threshold/Liability Model. (https://www.wikilectures.eu/w/Genetic_Liability,_Threshold_Model.)

Short summary of the model :

- This model explains how multifactorial disorders like diabetes and autism display discontinuous variations in individuals, either being affected or not, with no intermediate state.
- Unlike of other multifactorial traits like height or intelligence which display continuous variation, which is logical because of the large amount of genetic and environmental factors that affect them.

Liability

- Describes the genetic and environmental factors that contribute to the development of a multifactorial disorder.
- Represented as a standard distribution curve.

Threshold model

- When an individual has a certain liability they will be affected by the disorder, and the level of the liability is referred to as the threshold level.
- For instance, individuals with affected first degree relatives will have a higher chance to exceed the threshold level and being affected.

Multifactorial inheritance

- Using the model, we can provide a simple explanation for observed patterns of familial risks in various conditions, for example cleft lip/palate :
- The occurrence of cleft lip/palate is greater among relatives of the most severely affected patients, because they are the most extreme deviants along the liability curve.
- The cleft lip/palate proportion of affected first degree relatives is 6% if proband has bilateral cleft lip and palate, but only 2% if proband has unilateral cleft lip.
- Risk is greater among close relatives and decreases rapidly in more distant relatives.
- If there is more than one affected close relative, the risk for other relatives increases accordingly.
- Risk of recurrence for first degree relatives - approximately the square root of general population incidence.

Reference :

Emery's elements of medical genetics - 14th edition.

Thieme - genetics color atlas.