5.1 Genealogy and formulating genetic hypotheses

When new traits or diseases are recognized it is important to formulate genetic hypotheses as an alternative to other exogene causes. Exogene factors can be malnutrition, housing, microbiological infection or a combination of exogene and endogene (genetic) factors.

When a genetically caused disease is likely to occur, some characteristics have to be present. As for instance a family wise occurrence, and the fact that only some members of the family are affected. The typical Mendelian segregation ratios are 1:1, 1:3 and 1:7. In these context traits with intermediary inheritance is not included, as these types of inheritance are rarely seen in newly discovered diseases.

An alternative to Mendelian segregation are the so-called threshold diseases, where the sum of environmental and genetic factors triggers the disease. Threshold diseases with low frequency will exhibit family wise occurrence, which is very similar to Mendelian segregation, see section 8.3, where the inheritance of threshold traits is described.
The schematic overview of the different types of inheritance given in section 1.2 should furthermore be taken into consideration.

The simple Mendelian inheritance can occur with four different forms of inheritance. The traits can be inherited as dominant or recessive, compared to the normal type, and can exhibit autosomal or sex-linked inheritance. On the following pages the characteristics of the four simple forms of inheritance will be demonstrated. Note that the mentioned Mendelian inheritance indications can only be applied if the population frequency is low. This is always the case in newly discovered genetically caused diseases within one or a few families.

Concerning diseases with high population frequency, as for instance breast cancer in the human population, there will often be a significant amount of heterogeneity. This disease has a genetic background, which can be caused by segregation of genes in more independent loci. When large heterogeneity occurs the segregation analysis can not be carried out between families, but only within one big family. Finally there is a problem with **Phenocopies**, which is an identical disease caused by non genetic causes. Phenocopies also occur in breast cancer in humans.

The different symbols which are applied in genealogy are shown in Figure 5.1.

The proband individual is the individual that caused the initiation of the investigation. This individual or family should normally be excluded in later statistical analyses. A combination of path diagram and genealogical diagram can also be utilized along with the genealogical diagram.

Figure 5.1. Symbols used in genealogy.