PROBABILITY IN PEDIGREE ANALYSIS

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In genetics, a diagram showing the ancestral relationships and transmission of genetic traits over several generations in a family, is called a **pedigree**.

In all the crosses discussed so far, one of the two traits for each character has been dominant to each other.

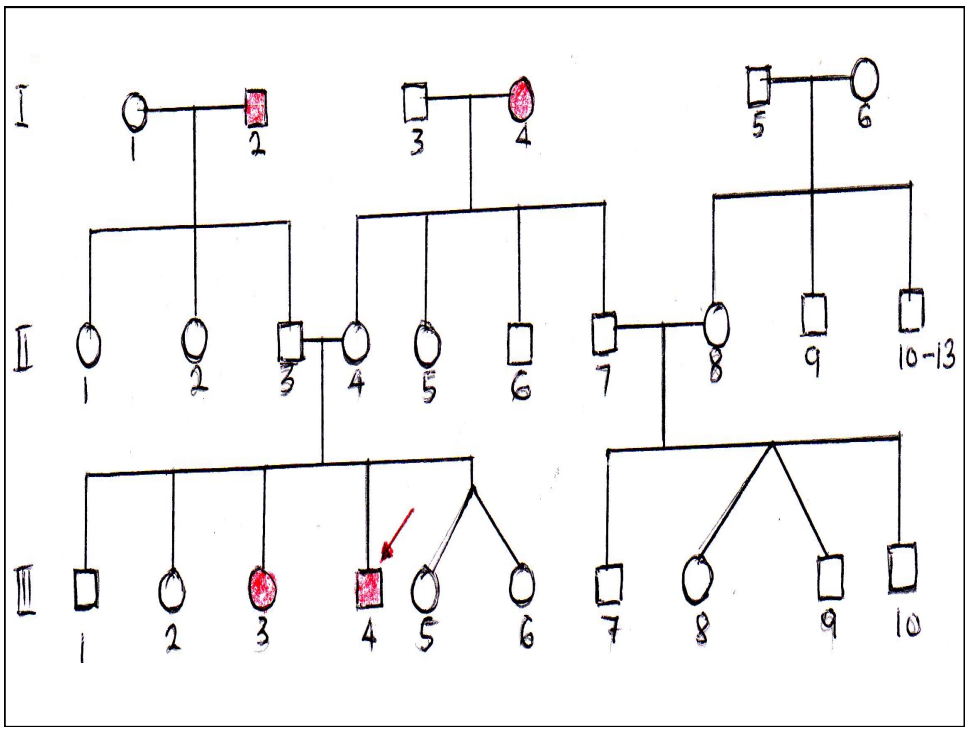
- Based on this observation, two significant questions may be asked:
  (i) Does the expression of all genes occur in this fashion?

  (ii) Is it possible to ascertain the mode of inheritance of genes in organisms where designed crosses and the production of large numbers of offsprings are impossible?

- The answer to the first question is no, because many modes of inheritance exist which modify the monohybrid and dihybrid ratios observed by Mendel.

- The answer to the second question is yes, because even in humans, the pattern of inheritance of a specific phenotype can be studied.

- The simplest way to study this pattern is to construct a family tree which indicates the phenotype of the trait in question. Such a family tree is called a pedigree.
- Pedigree analysis is used in place of breeding studies, particularly in humans, where experimental matings are not possible.
- By analyzing the pedigree, we may be able to determine the genetic basis of a particular trait or disease.

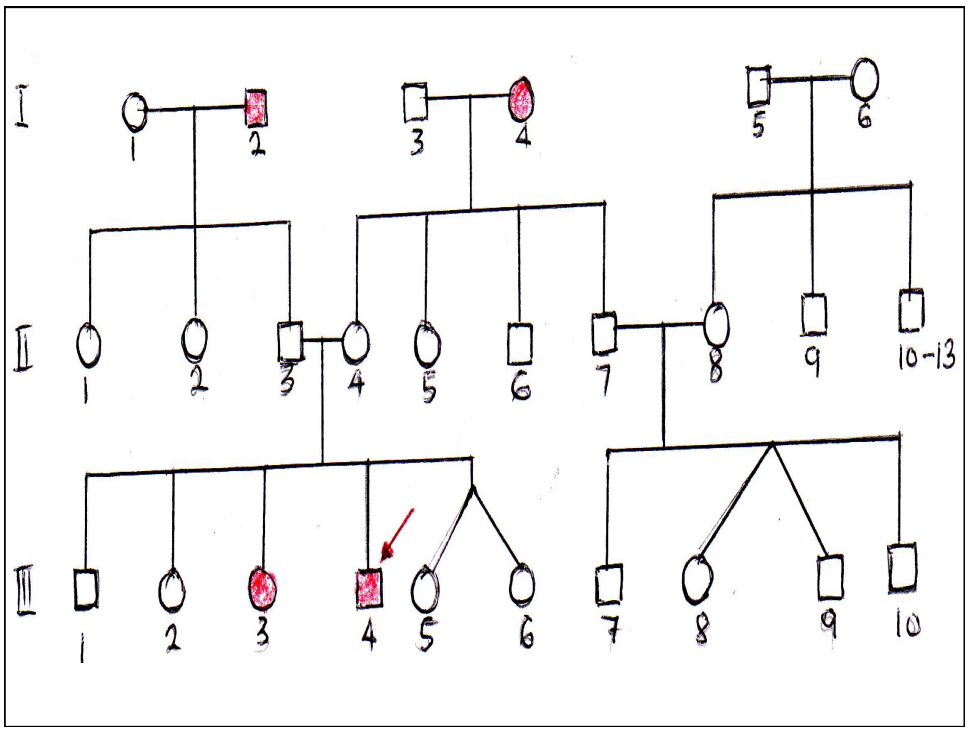


Symbols

- The conventions used in constructing a pedigree are; circles represent females, and squares males.
- If the sex is unknown, a diamond is used.
- Parents are connected by a horizontal line and a vertical line leads to their offsprings.
- Sibs are placed from left to right according to birth order and are labeled with Arabic numerals.

- Different shades or colors added to the symbols can represent various phenotypes.
- Each generation is listed on a separate row and labeled with Roman numerals.
- Twins are indicated by connected diagonal lines.

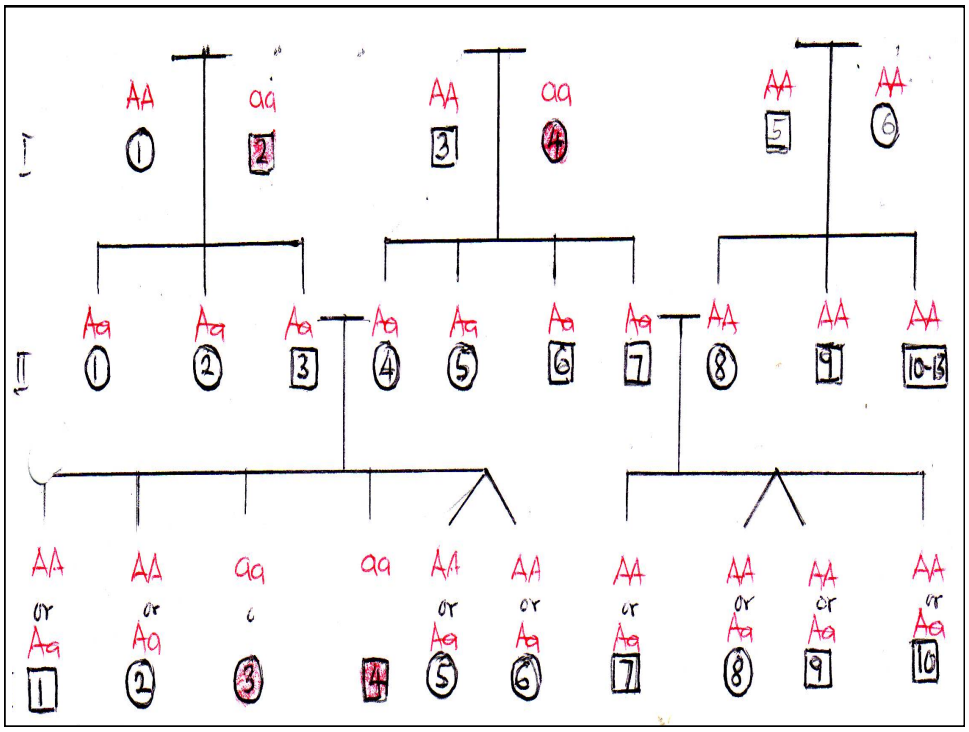
- The individual whose phenotype drew the attention of a geneticist or a physician is called the propositus (male) or proposita (female) or proband (general). In all cases, an arrow points to the proband.



- The example above traces theoretical pattern of inheritance of the human trait albinism.
- By analyzing the pedigree, it is seen that albinism is inherited as a recessive trait.

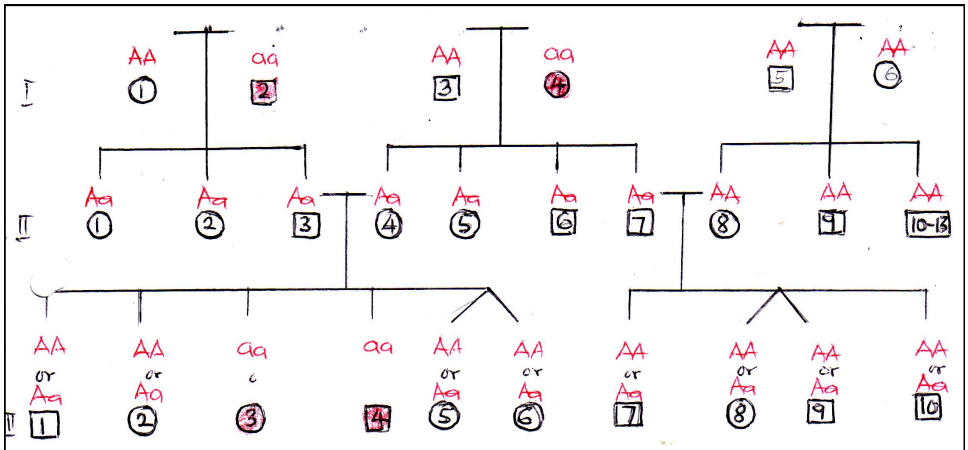
Analyzing a Pedigree

- Two of the parents of the **first generation**, I-2 and I-4 are affected.
- Because none of their offspring show the disorder, it is reasonable to conclude that the unaffected parents (I-1 and I-3) were homozygous normal individuals.
- Had they been heterozygous, one half of their offspring would be expected to exhibit albinism.



- Note: *An unaffected second generation is characteristic of a recessive trait.*
- If albinism were inherited as a dominant trait, one half of the **second generation** would be expected to exhibit the disorder in the crosses involving the I-2 and I-4 parents.

- Inspection of the offspring constituting the **third generation** provides further support for the hypothesis that albinism is a recessive trait.
- Parents II-3 and II-4 are apparently both heterozygous, therefore about one fourth of their offspring should be affected. In fact, two of the six offspring do show albinism.



- Individual II-7 is no doubt heterozygous, while II-8 is most likely homozygous normal.
- If so, we can then predict that none of their offspring (III-7, 8, 9, and 10) would be albino.

- Based on this pedigree analysis, and the conclusion that albinism is a recessive trait, the genotypes of all individuals can be predicted.
- For both the first and second generations, this can be done with certainty.
- For normal individuals in the third generation, we can only guess whether they are homozygous or heterozygous.

- In the absence of data to indicate which individuals are carriers, the geneticist may resort to probability as the best available tool for determining the likelihood of expression of a given recessive gene in a family.

- If no expression has occurred in the history of the family, an estimate indicating the frequency of the gene in the general population may be used as a basis of probability.
- If the trait has appeared in the family, more precise calculations are possible.

Problem solving

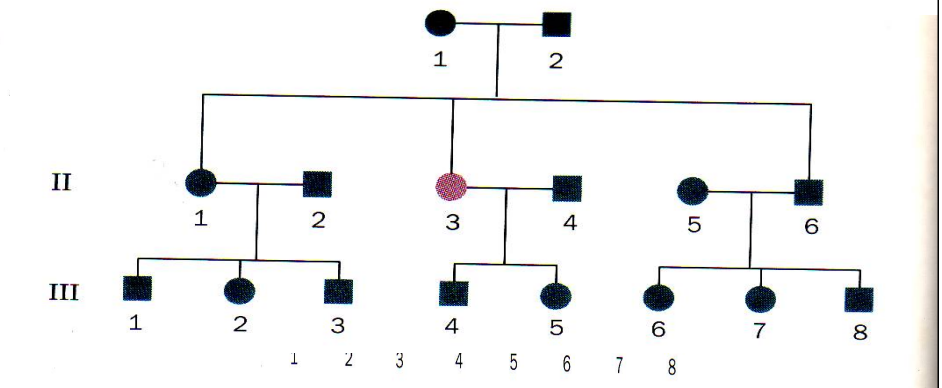


Figure 2.19 Pedigree chart to illustrate probability in pedigree analysis. In this family group, a trait (adherent ear lobes), dependent on a recessive gene, has appeared in one individual (identified by the violet circle). Three basic steps may be followed in all pedigree analysis: (1) What is the chance that one parent is a carrier of the gene in question? (2) What is the chance that the other parent is a carrier for the same gene? (3) What is the chance that a child of these two parents (genotypes) could express the trait involved? The product of the separate probabilities is the chance that a particular future child will express that trait.

3 Basic Steps in Pedigree Analysis

1. What is the chance that one parent is a carrier of the gene in question?
2. What is the chance that the other parent is a carrier for the same gene?
3. What is the chance that a child of these parent (genotypes) could express the trait involved?

The product of the separate probabilities is the chance that a particular future child will express that trait.

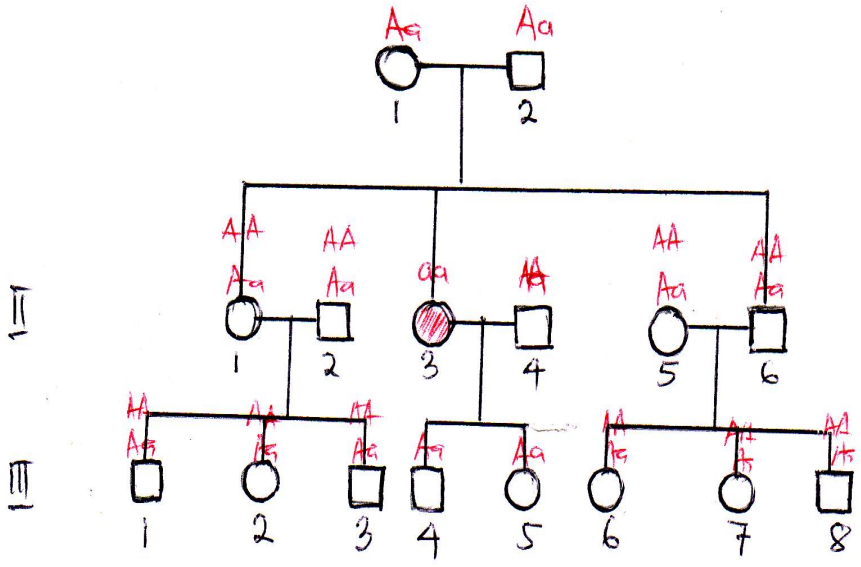
Assumption:

Unless there is evidence to the contrary, it may be assumed that, those individuals who have married into the family are homozygous for the dominant gene and do not carry the recessive gene in question

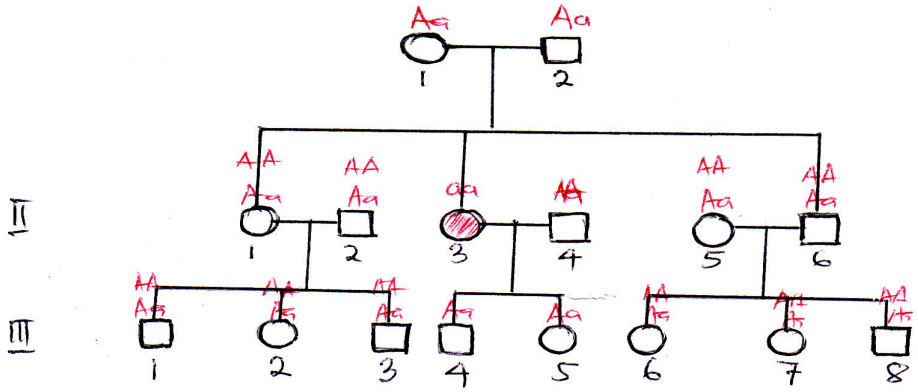
Solution:

- First, identify the genotypes of as many individual family members as possible from the information given.
- The woman (II-3) in whom the trait is expressed must be homozygous (aa) for the recessive gene.
- Each of the parents (I-1 and I-2) who did not express the trait but contributed an a gene to their daughter (II-3) must have the heterozygous genotype.

Problem solving



The sister (II-1) and brother (II-6) must be AA or Aa. *Obviously, they are not aa because they do not express the trait. There is no way to determine whether each of these individuals is AA or Aa. Therefore, the probability that each individual is a carrier (Aa) must be estimated from the available information.*

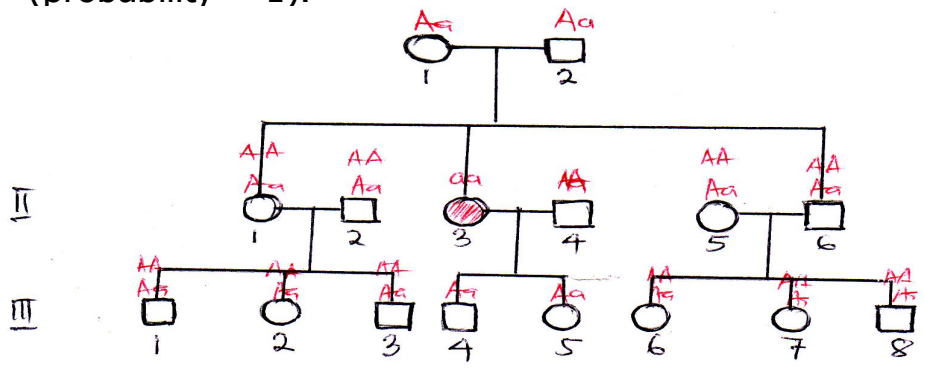


- From the parent cross (Aa X Aa), the probability for the occurrence of Aa in any child with free earlobes is ⅔ and the probability for the occurrence of AA is ⅓.
- In the absence of more definite information, II-1 and II-6 may be considered Aa with ⅔ probability.

The children of II-1 and II-6 have a ½ chance of being carriers for the gene a **if** one of their parents is a carrier. Therefore, the probability that III-1, III-2, III-3, III-6, III-7 or III-8 is a carrier is

$$\frac{2}{3} \times 1 \times \frac{1}{2} = \frac{1}{3}$$

The children of II-3 (i.e. III-4 and III-5) must be carriers (probability = 1).



- The problem may be carried a step further by calculating the likelihood for the expression of the trait (aa) in the first child resulting from a marriage between two of the cousins represented in generation III.
- The mating III-1 X III-5 will serve as an example.

- The probability of being a carrier (Aa) is ⅓ for III-3 and 1 for III-5.
- Both could be carriers and yet avoid an expression of the trait in their family. Therefore, another probability must be included, namely, that of two parents with genotypes Aa having an aa child (Aa X Aa = 1AA; 2Aa; 1aa) which is ¼ .

- Now, the probability for the expression of the trait in the child of the individuals indicated is,

(prob. III-1 is Aa) x (prob. III-5 is Aa) x (prob. child is aa) =

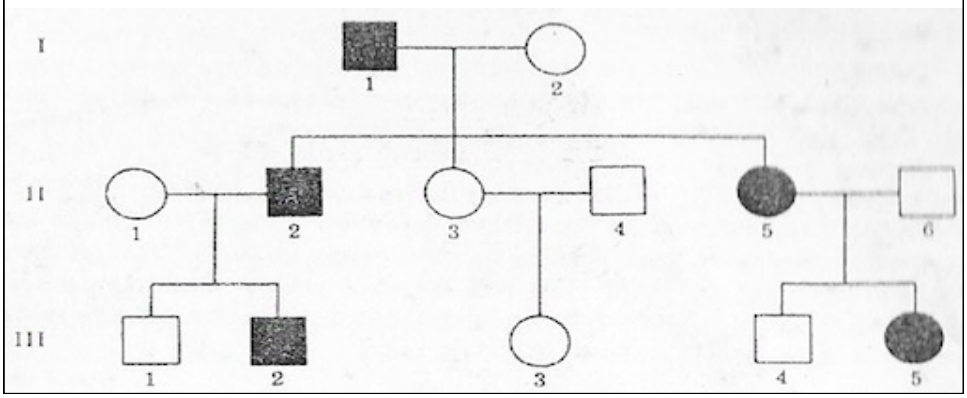
⅓ x 1 x ¼ = 1/12

Conclusion

Probability in pedigree analysis is at best, a poor substitute for certainty. It is employed in analysis only when definite information is not available.

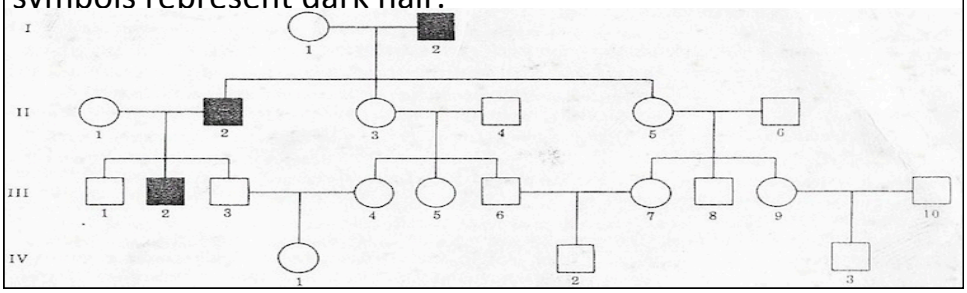
Assignment (Q#1)

The phenotypic expression of a dominant gene in Ayrshire cattle is a notch in the tips of the ears. In the pedigree below, where solid symbols represent notched individuals, determine the probability of notched progeny being produced from the matings: (a) III1 x III3, (b) III2 x III3, (c) III3 x III4, (d) III1 x III5, (e) III2 x III5.



Assignment (Q#2)

A single recessive gene *r* is largely responsible for the development of red hair in humans. Dark hair is largely due to its dominant allele *R*. In the family pedigree shown below, unless there is evidence to the contrary, assume that individuals who marry into this family do not carry the *r* allele. Calculate the probability of red hair appearing in children from the marriages: (a) III3 x III9, (b) III4 x III10, (c) IV1 x IV2, (d) IV1 x IV3. Solid symbols represent red hair; open symbols represent dark hair.



Homework

Heterozygous black guinea pigs (*Bb*) are crossed among themselves.

(a) What is the probability of the first three offspring being alternatively black-white-black or white-black-white?

(b) What is the probability among 3 offspring of producing 2 black and 1 white in any order?