UNIT 21 QUANTITATIVE TRAITS AND GENETICS OF TWINS

Structure **Page No.**

21.1 INTRODUCTION

In previous units you have studied phenotypic variation hat is easily classified into distinct traits, such as, irregular or regular variation of coleus leaves; presence or absence of horns in cattle; coat colour in rabbits; blood group in humans. These phenotypes are examples of **discontinuous variation** where discrete phenotypic categories exist.

However, not all inherited traits are expressed in this discontinuous fashion. For example, height, skin and eye colour in humans, colour and food yield in various plants, size in many plants and animals, as well as degree of coat spotting in some animals are examples of **continuous phenotypic variation.** It is now known that traits exhibiting continuous variation are often controlled by two or more genes and are termed **polygenic.** In cases where several genes make additive contributions to the phenotype, the trait is said to exhibit quantitative or **continuous variation.**

In this Unit you will study about the phenotypic traits which are controlled by genes at two or more loci. You will also know how statistical tools are used by geneticists to study traits that exhibit continuous variation. Further, you will learn about the effect of nongenetic factors on gene expression; these include environmental influences. In addilion, you will be introduced to the concept of **heritability,** which is used to estimate the degree of genetic and environmental influence on the expression of traits controlled by genes at many loci. You will also study about twins. This study is necessary to determine the relative role of heredity and environment in the differences existing between individuals. Before reading this unit you must read Block I and II of MTE-03. It will also be helpful in comprehending various statistical concepts used in this Unit.

Objectives

After studying this unit you will be able to:

- distinguish between continuous and discontinuous variations,
- distinguish between the role of genotype and environment in controlling the phenotype of a quantitative traits,
- estimate the possible number of genes involved in the expression of a given phenotype,
- identify the relative role of heredity and environment by the twin studies.

21. 2 CONTINUOUS VARIATION

Most of the genetic traits can be identified by their distinct phenotype. That means mutants can be easily distinguished from wild type because of a clear cut phenotypic difference. All individuals fall into a few phenotypic classes with respect to such traits. Such traits are called discontinuous traits, some examples are ABO blood groups of humans, coat colour of cattle, prototrophs and auxotrophs in bacteria. For discontinuous traits, the relationship between phenotype and genotype is clear and simple except under co-dominance and epistasis. Therefore, it is possible to infer about the genotype when the phenotype is known.

Certain characteristics such as birth weight, adult height, I.Q., and skin pigmentation in humans exhibit a wide range of possible phenotypes. Similarly in cattle a trait like milk production shows a continuous range in phenotype with no clear separation between one phenotype and the next. These traits can be measured numerically in single individuals and can fall anywhere on a continuous scale of measurement and the number of possible phenotypes is virtually unlimited.

After rediscovery of Mendel's laws in 1900, many controversies arose, one of them was whether all traits follow the classical Mendel's laws or there are differences in the inheritance patterns. During the latter part of 19th century, Francis Galton and his associate Karl Pearson studied a number of continuous traits in humans such as height, weight and I.Q., by developing various statistical techniques, they could show that these characters do not have a simple mode of transmission, i.e., the inheritance pattern is not controlled by a single gene. Continuous variation is determined by multiple genes, each of which is segregated independently in a classical Mendelian manner. These traits are also influenced by the environment.

21. 2.1 Origin of Continuous Variation

Continuous variation exists as a number of phenotypes among individual.. of a group. This is due to the influence of many loci and alleles influencing the trait. For example, there are three genotypes for a gene at a single locus with two alleles. If a trait is controlled by two loci each with two alleles, the number of genotypes becomes 3^2, i.e. 9 (AABB, AABb, AAbb, AaBB, AaBb, Aabb, aaBB, aaBb and aabb). Therefore, the general formula calculating the number of genotypes is 3^n, where 'n' is the number of loci with two alleles. The number of genotypes also increases as the number of alleles at each locus increases (Fig 21.1).

Therefore, these traits are called polygenic traits as they are controlled by many gene loci. If each genotype of a polygenic trait encodes a separate phenotype, then many phenotypes with slight differences will be the result. For polygenic or multifactorial traits, no single relationship exists between genotype and phenotype. Therefore, the simple modes of inheritance predicted by Mendel do not provide information about genes involved in continuous traits. The genetic basis of these traits can be understood by special analytical procedures/methods, and cannot be studied by the usual pedigree analysis.

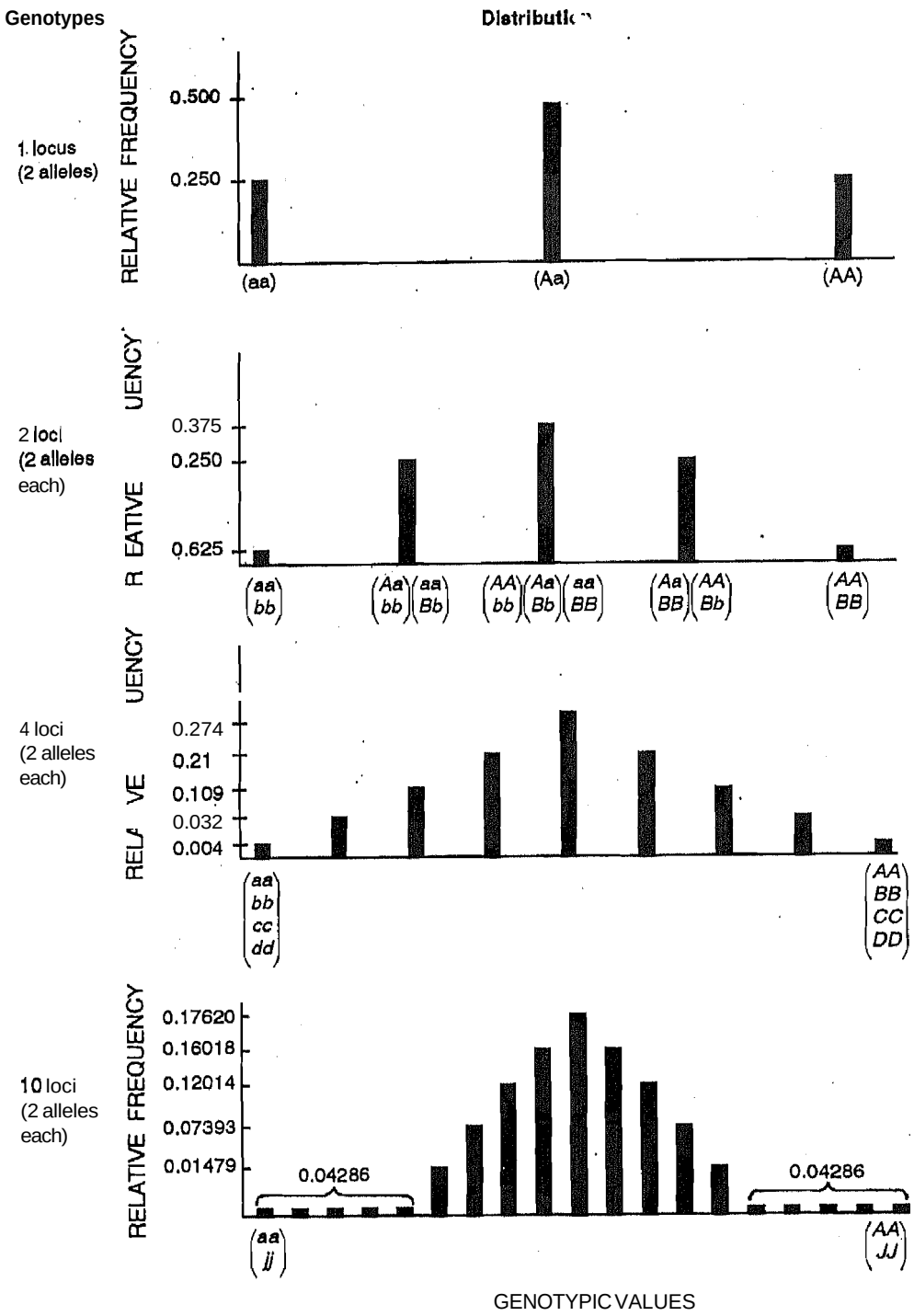

Fig 21.11 Distribution of Frequencies in Genotype.

When dominance is present at any of the loci, different genotypes may express the same phenotype. This could be the reason for lesser number of phenotypes observed than expected. The second important effect is that of the environment, When environmental factors influence the genotypes, each genotype can produce different phenotypes depending on the extent of interaction with the environment.

Phenotype = Genotype + Environment (P = *G* + E). One common example is yield in crop plants. This depends on the gene pool, as well as the rainfall, fertilisers, plant density and soil quality. Many applications of genetics are based on an understanding of continuous traits. In agricultdre, yield from plants, in animal husbandry, milk production, egg-laying and fleece weight, and in humans, height, weight, IQ, serum cholesterol and lifespan are such quantitative traits.

SAQ 1

Let us assume i) that a trait is controlled by the loci on different chromosomes, A/a, B/b, C/c, ii) that A locus has average phenotypic effect of the three genotypes as AA = 4, Aa = 3, aa = 1, and that iii) similar effects exist for B + C loci. Now, calculate the distribution of phenotypes when two triple heterozygotes (AaBbCc) are crossed.

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21.3 QUANTITATIVE INHERITANCE

Many traits are not controlled by only alleles of two or more genes, but are also influenced by the effects of environment. Consequently, by the study of quantitative traits you will be able to comprehend the following:

1) The contribution of genetic and environmental factors to the phenotypic variation.

2) The number of genes involved and the contribution from each of them.

3) The extent of interaction between different alleles and the role of additive and epistatic interactions.

4) The effect of natural selection on phenotypic expression.

With the help of an example the inheritance of a quantitative trait is explained below.

21.3.1 Inheritance of Ear Length (Cob Size in Corn)

Corn has been the subject of genetic and cytological studies for many years. Ear length of corn is one of the characters that was studied by Emersson and East in 1913 to demonstrate a pattern of quantitative inheritance. A cross was made between two pure lines, i.e., Black Mexican sweet corn (which had short ears of mean length 6.63 cm) and Tom Thumb popcorn (which had long ears of mean length 16.80 cm). The F_1 plants had mean ear length of 12.12 cm which was approximately intermediate between ear length of the two parental lines. Assuming that the parental lines were homozygous, the F_1 plants are then heterozygous for all the genes and should theoretically have cobs of the same ear length. But the observations indicated a variability in the ear length from plant to plant. Therefore, the range of ear length phenotypes seen in F_1 plants must be due to factors other than genetic factors. These are environmental factors since it is impossible to grow all the plants in exactly identical conditions (Fig 21.2).

In F_2 the mean ear length was 12.89 cm. F_2 mean was about the same as the F_1 mean. But the F_2 population has a much larger variation around the mean than the F_1 population. Is this variation is the result of the effects of environmental factors? Certainly, if the environment was responsible for variation in the parental and the F_1 generations, we have every reason to believe that it would have a similar effect

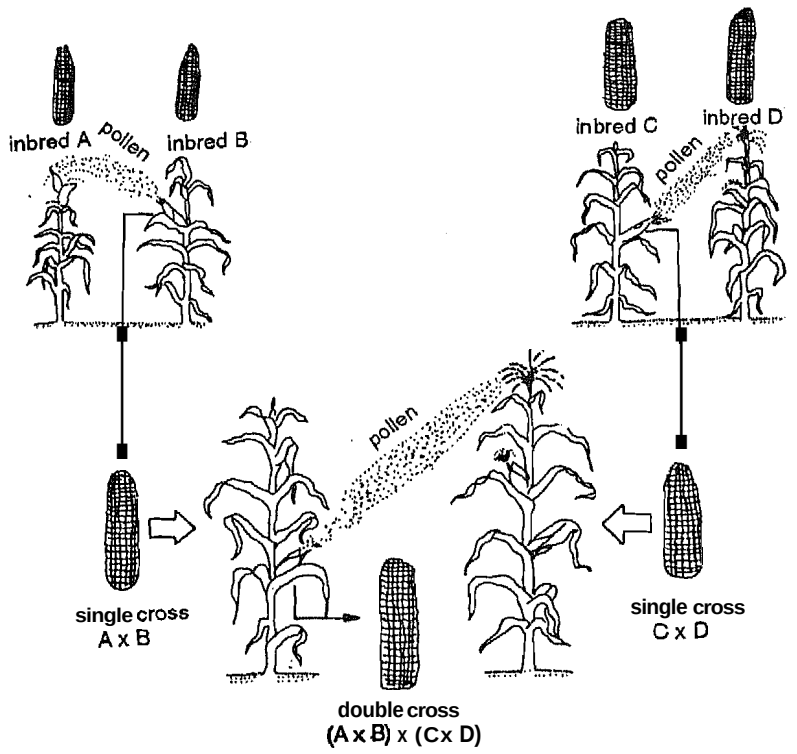


Fig 21.2: Quantitative inheritance in maize.

on the F_2 generation. However, there is no reason to believe that environment would have a greater genetic variation in the F_2 generation.

For a moment if we keep the environmental influence aside, from our data we can make the following four observations:

1) The mean value of the quantitative trait in the F_1 is approximately intermediate between the mean of the two true-breeding parental lines.

2) The mean value for the trait in the F_2 generation is approximately equal to the mean for the F_1 population.

3) The F_2 shows more variability around the mean than the F_1 does.

4) The extreme values for the quantitative trait in the F_2 extend further into the distribution of the two parental values than do the extreme values of the F_1.

21.3.2 Polygenic Hypothesis for Quantitative Trait

The simplest explanation that could be given for the data described above is that quantitative traits are controlled by many genes. This hypothesis is called **polygene** or **multiple gene hypothesis.** This hypothesis can be dated back to 1909 when Nilson-Ehle crossed two true breeding wheat plants, one with red kernels and the other with white kernels. The F_1 had grains of intermediate colour between red and white. When F_1 plants were interbred, F_2 progeny showed a ratio of 15 red (all shades) : 1 white kernel (Fig 21.3).

The polygene or multiple gene hypothesis for quantitative inheritance is regarded as one of the landmarks of genetic thought.

If we assume that there are two pairs of independently segregating alleles that control the red colour pigmentation i.e., 'R' and 'C' both would result in red colour and 'r' and 'c' result in white colour. From this variety of wheat, genetically pure

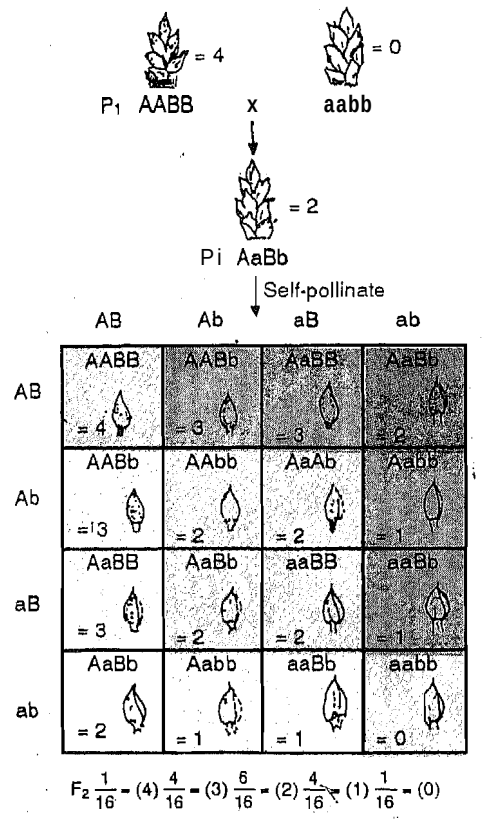


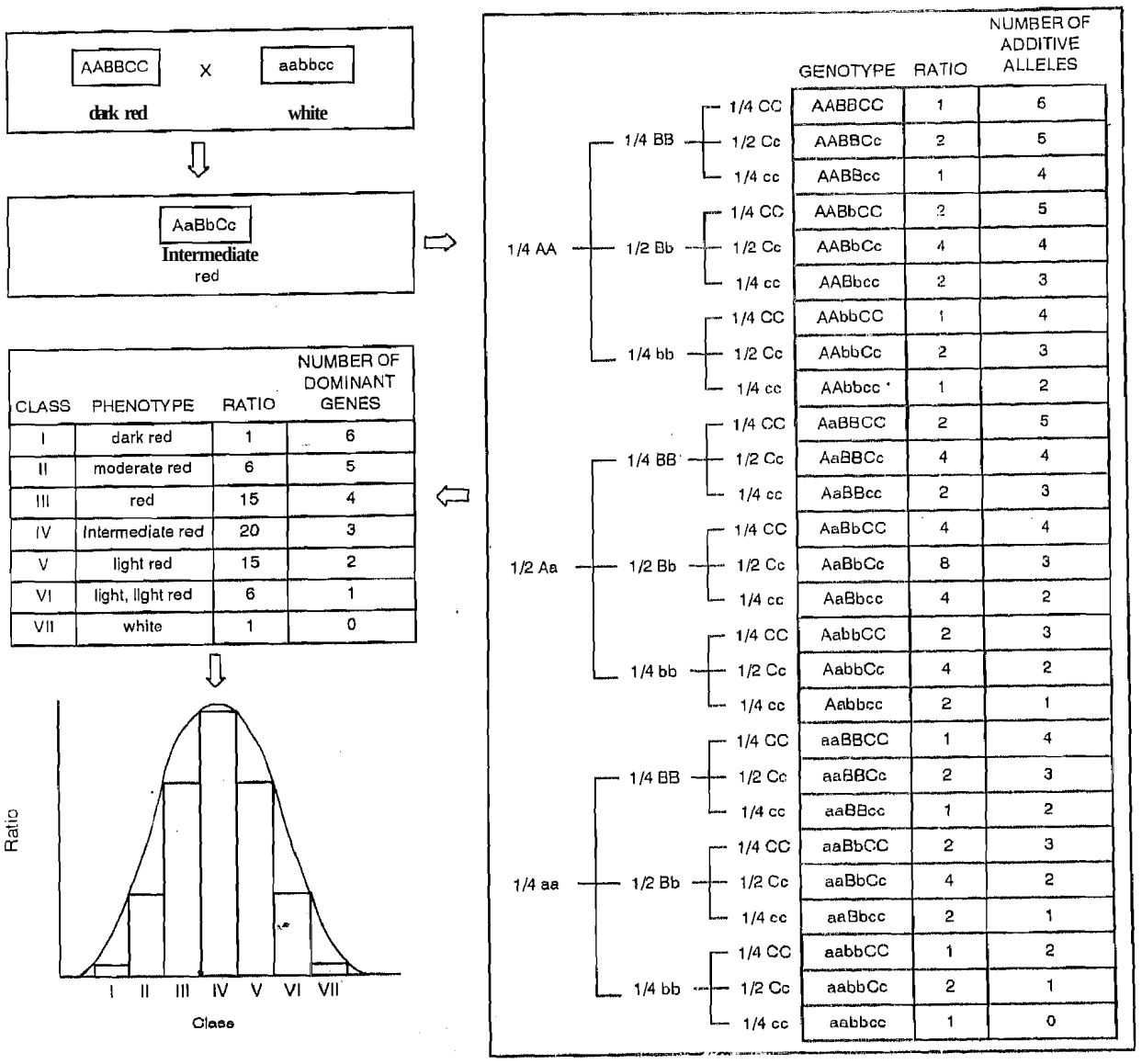
Fig 21.3: Quantitaive Inheritance. Diagrammatic representation of Nilsson-Ehle's crosses between a red variety (MBB) of wheat and a white variety (aabb). The 16 possible gamete combinations of the F_2 generation areshown as a normal distribution based on number of plus genes present in genotype. (The curve area of F_2 generation have been enlarged to accomodate all the genotype)

strains were developed by inbreeding and used as parents. IT R and **C** are dominant over **r** and **c** we get a phenotypic ratio 1:4:6:4:1. The most plausible explanation is that each of the two genes controlled the production of the colour pigment. Therefore, the intensity of red colour is a function of the number of dominant R and C alleles. The alleles (like R and C) which contribute to the phenotype are called contribution of alleles while those (like **r** and c) which do not contribute to the phenotype are called the non-contributing allcles. In the present context the inheritance of red kernel colour in wheat is an example of polygene series of as many as 4 contributing alleles. Depending upon the number of contributory alleles involved different phenotypic ratios are obtained. In the case of 3:1 ratio one gene with two alleles is involvcd, while in 15:1 there are 2 genes with 2 alleles and in the **63:1** case, a polygenic series with 6 contributory alleles from **3** genes are involvcd.

Identification of the number of genes in a quantitative trait has not been accomplished as yet in most cases. You can see from the theoretical model (presented) in Fig 21.4 that the number of genotypes increases with the increase in number of loci each having two alleles.

In its basic form, multiple gene hypothesis proposes a number of attributes of quantitative inheritance. It can be explained on the basis of action and segregation of alleles at a number of loci that have identical additive effects on the phenotype without complele dominance. It can be summed up that quantitative traits are influenced by many gcnes, each of which contributes a small and additive effect on the the phenotype.

By now you will realise that in support of polygenic hypothesis a number of assumptions have been made. Amongst the genes involved in the expression of the trait:



CLASS	PHENOTYPE	RATIO	NUMBER OF DOMINANT GENES
I	dark red	1	6
II	moderate red	6	5
III	red	15	4
IV	Intermediate red	20	3
V	light red	15	2
VI	light, light red	6	1
VII	white	1	0

Fig. 21.1: Polygenic inheritance where three genes are contributing to grain colour in wheat.

1) No allelic pairs exhibit dominance.

2) Only a series of contributory and non-contributory alleles are involved.

3) Each contributory allele has an equal effect.

4) The effect of each contributory allele is additive.

5) There is no genetic interaction between alleles of different loci.

6) There is no linkage between the loci involved.

However, in practice it is difficult to meet all these assumptions.

21.3.3 Some Examples of Quantitative Traits in Humans

i) **Stature in Man** : Height is a good example of a quantitative trait in humans. A number of loci with two alleles control the trail. Let us assume that there arc 4 gene

Sometimes diseases like pituitary deficiency can lead to dwarfism. Individuals affected with such diseases tend to be short despite their carrying many genes for tallness.

loci with two alleles each (A/a, B/b, C/c and D/d). Then the stature of individuals will depend on the number of contributing alleles. For example, according to this hypothesis a very tall person would be AABBCCDD, a very short aabbccdd and person with medium height Aa Bb Cc Dd.

On an average the height of children falls between the range of the parents. For example, if the father is 170 crns and the mother 152 crns then the offspring height is usually between 170-152 cms.

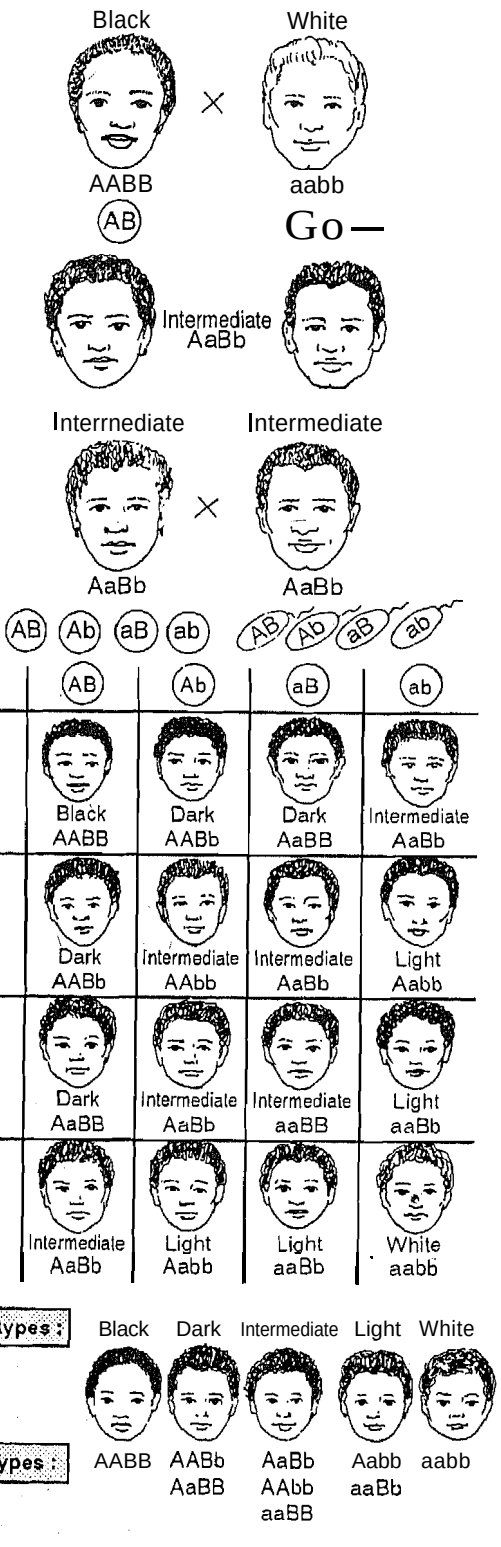
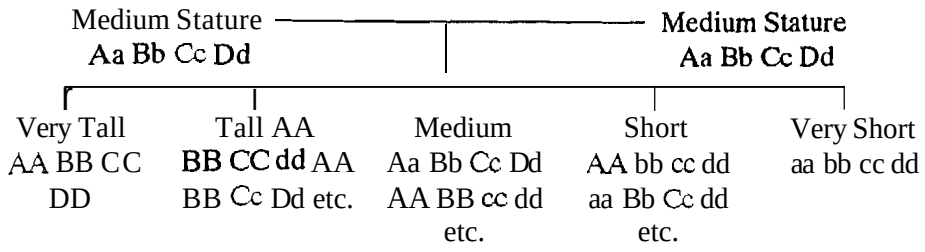


Fig. 21.5: **Skin colour inheritance - the skin colour** is **attributed** by **two chief genes. They both contribute** equally to melanin production, The black **colour** square **represents such melanin producing** gene. In white **colour individual** all four **alleles** produce minimum **amount** of melanin. But when **one of** the parent is black and **other** is **white** the children have intermediate brown skin colour. In **such heterozygote** children two alleles produce large **amount** of melanin. Since skin colour is additive effect such children **are** borwn.

Now it would be demonstrated to you how medium sized parents can have a very tall or a very short child.



Apart from this, non- genetic factors, like diet, also play a major role in the development of human stature.

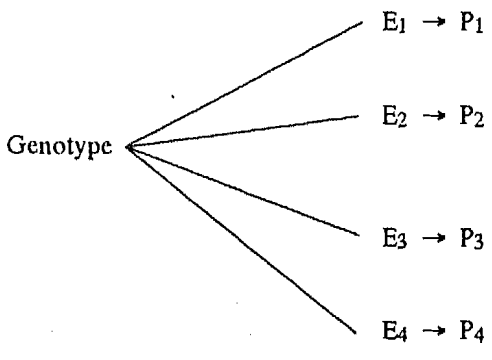
ii) **Skin Colour :** Skin colour is also dependent on a number of genes. We can see many gradations in human skin colour ranging from extremely fair to very dark. Colour of the skin is dependent on a pigment called **melanin.** The difference in skin colour of Negroes and Caucasians is very clear and about 4 to 7 genes are considered to be involved in controlling it.

The offspring of marriages between Negroes and caucasians have an intermediate skin colour, and are referred to as Mulattos (Fig 21.5). The progeny of mulattos may range from very fair to very dark. This variation may be explained on the same basis as that for height.

In this case in the presence of noncontributory alleles the individuals inherit white colour and the dark individuals possess alleles which contribute lo colour formation.

21.4 EFFECT OF ENVIRONMENT ON QUANTITATIVE TRAITS

By now you know that the phenotypic variation observed has genotypic as well as environmental contributions. Johannsen (1909) studied the responses of a genolype to different environmental circumstances and results can be modelled as follows:



'E' denotes envlronmcnt, 'P' denotes phenotype.

It indicates that the same genotype interacts with different environmental factors that influence the phenotypic expression of the traits. Environmental factors can be physical (nonbiological in origin) biological (other organisms and products of other genes within the organism) or both.

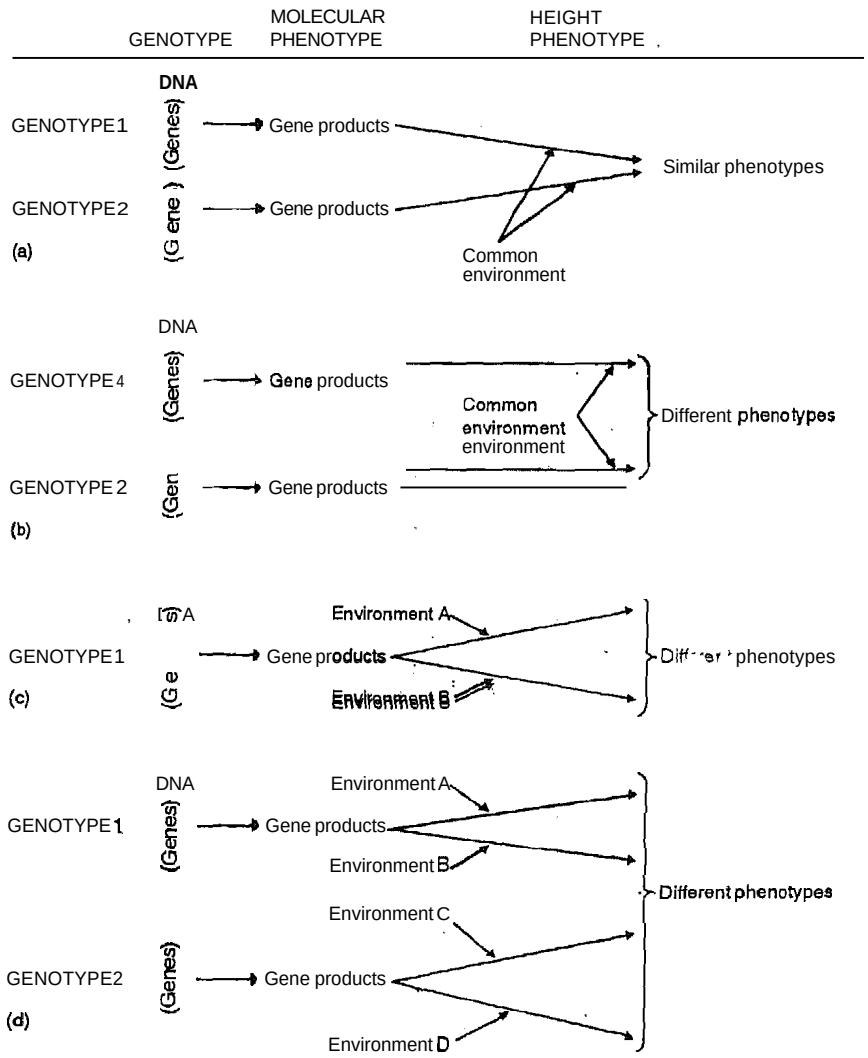


Fig 21.6: *Quantitative phenotypes* are affected by interplay *between* genotype and environment.

Three different types of interplay occur between genotype and environment to affect the phenotype. These are depicted in Fig 21.6. The interaction between genes and environment make the study of quantitative phenotypic variation rather complex.

21.5 HERITABILITY

The concept of heritability is used to examine the relative contributions of genes and environment to variation in a specific trait. As we have seen continuous traits are frequently influenced by multiple genes and by environmental factors. One of the most important question arises in quantitative genetics is; how much of the variation in phenotype is due to genetical differences and how much is due to environmental variation. For example, multifactorial traits such as weight of cattle, number of eggs laid by chickens, and fleece produced by sheep are important for breeding programs and agricultural management. Many ecologically important traits such as variation in body size, fecundity and developmental rate are also multifactorial and the genetic contribution to this variation is important for understanding how natural populations evolve. Thus we can define **heritability as the proportion of variability, attributable to genetic factors out of the total phenotypic variability existing in a population.**

21.5.1 Components of Phenotypic Variance

In this section we will learn how to identify and measure the relative contribution of the genetic effects to the total phenotypic variation of a trait.

The phenotypic variance is a measure of the variability of a trait. It is calculated as the total variance observed in a population with respect to the trait in question and is designated as V_P. Differences among individuals arise from several factors, and therefore, we can partition the phenotypic variance into several components attributable to different sources. Contribution of genetic differences among individuals to the phenotypic variation is called genetic variance and denoted by V_G.

The individuals experiencing different environment may contribute to the differences in their phenotypes. The environmental variance is symbolised by V_E and by definition, it includes nongenetic source of variation; temperature, nutrition and parental care are example of obvious environmental factors that may cause difference among individuals.

A third component of phenotypic variance is an interaction between genetic and environmental factors and is represented as V_{GE}. For example, in cold temperature, a plant with AA genotype may grow 40 cm tall, and that with Aa may grow 35 cm tall. But in warm temperature plants with the same genotypes may grow to 45 cm and 60 cm respectively (Fig 21.7).

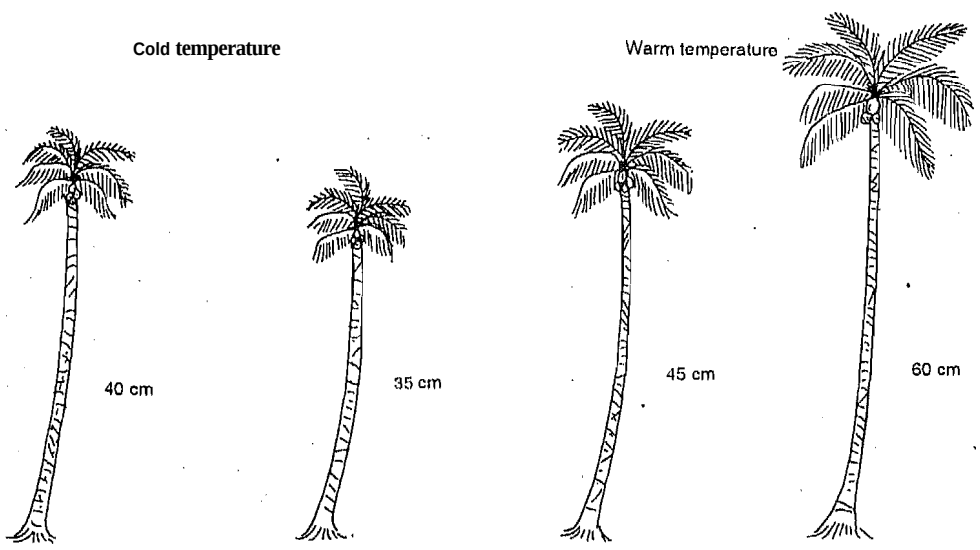


Fig 21.7: Hypothetical example of genetic and environmental interaction.

In this hypothetical example of genetic and environmental interaction, the plant with a genotype of Aa which grows slower at cold temperature outgrows AA at higher temperature. This suggests that genotypes express differentially in different environmental conditions. Plants with both types of genotypes grow taller at higher temperatures, but the effect varies with the type of genotype. Therefore, these differences contribute to the phenotypic variance but the effects of genetic and environmental factors cannot be added together. So an additional component of variance that accounts for interaction between genetic and environment effects (V_{GE}) must be considered.

Hence we come to the conclusion that the total phenotypic variance is composed of a number of factors: 1) Genetic composition of a population, 2) Specific environmental conditions, 3) The manner in which genes interact with the environment.

Variance also includes random factors that occur during development, which are sometimes referred to as developmental noise

The genetic variance (V_G) can be further subdivided into components arising from different types of interaction between genes. Let us assume 'a' allele contributes 2 cm to plant height, while 'A' allele contributes 4 cm. Thus **aa** genotype would contribute 4 cm in height, while Aa contributes 6 cm and AA contributes 8 cm in height. Then to determine genetic coiitribution of these alleles to the phenotype the effects of alleles at this locus would be added to the effects of alleles at other loci which are known to influence the phenotype. Such genes are said to have additive effects. The variation that arises due to additive effects is called additive genetic variance, and symbolised as V_A.

Some genes exhibit **dominance** and this becomes a source of genetic variance. This is called dominance variance (V_D). Dominance of one allele masks the effect of the other allele at the same locus.

We must also consider the interactions of alleles at different loci. Epistasis (allele at one locus alters the expression of alleles at another locus) is another source of variance arising out of interaction of genes is designated as V_I genetic variation. So the genetic variance can be partitioned as:

$$V_G = V_A + V_D + V_I$$

Total phenotypic can finally be partitioned as:

$$V_p = V_A + V_D + V_I + V_E + V_{GE}$$

Table 21.1: Components of Variance

Variance Component	Symbol	Value whose variance is measured
Pheriotypic	V_P	Phenotypic value
Genotypic	V_G	Genotypic value
Additive	V_A	Breeding value
Dominance	V_D	Dominance value
Interaction	V_I	Dominance deviation
Environmental	V_E	Environmental deviation

The components of variance are listed in Table 21.1. This partitioning of phenotypicvariance is very important to understand the relative contribution of different factors towards the variation in phenotype.

21.5.2 Broad Sense and Narrow Sense Heritability

Geneticists frequently partition the phenotypic variance of a trait to determine the extent to which variation among individualsresults from genetic differences. Thus, they are interested in how much of the phenotypic variance V_P can be attributed to genetic variance V_G. This quantity, the proportion of the phenotypic variance that consists of genetic variance is called the broad-sense heritability and is expressed as follows:

$$\text{Broad-sense heritability} = H^2 = \frac{V_G}{V_P} = \frac{V_G}{V_G + V_E}$$

Heritability of a trait can thus range from 0 to 1. If H^2 is '0' it means that differences found between individuals are not due to genes. And a heritability of '1' indicates that phenotypic variation is completely or 100 per cent genetic in origin. Heritability depends on magnitude of all the components of variance, a change in any of which will affect it. Therefore, it is a value for a population under specific conditions.

The proportion of phenotypic variance due to additive gene effects is of more interest because additive genes are those that allow the prediction of the phenotype of an offspring from the phenotype of the parents. Let us consider a cross involving a trait that results from effects of alleles at a single locus; one parent has a genotype of $A^1 A^1$ and is 10 cm tall, while the other parent $A^1 A^2$ is 20 cm tall. All the offsprings (F_1) from this cross will be $A^1 A^2$. If these alleles are additive and contribute equally to height, the offsprings should be 15 cm tall, exactly intermediate between the parents. Such an additive genetic variance helps in predicting the resemblance between offspring and parents. Therefore, quantitative geneticists frequently determine the proportion of phenotypic variance that results from additive genetic variance; this proportion is termed as narrow sense heritability and is represented as :

$$h^2 = V_A/V_P$$

21.53 Estimation of Heritability

Heritability is an important property which expresses the total variance that is attributable to the average effects of genes and which determines the degree of resemblance between relatives. Estimation of heritability involves related and unrelated individuals or individuals with different degrees of relatedness (Table 21.2).

The estimate of heritability gives the relative importance of genetic versus environmental factors. If genes are more involved in determining phenotypic variance, then closely related individuals should be more similar in phenotype, as they have more common genes. Alternatively, if environmental factors are responsible for determining differences in the trait, then related individuals should be no more similar than unrelated individuals,

Table 21.2: Degree of Regression and Correlation

Relatives	Covariance	Regression (b) or correlation (t)
Offsprings and one parent	½ V_A	$b = ½ h^2$
offspring amd mid-parent	½ V_A	$b = b^2$
Half sibs	¼ V_A	$t = ¼ h^2$
Full sibs	½ V_A + ¼ V_D + V_{Ec}	$t > ½ h^2$

Only the plienotypic values of individuals can be directly measured; however, it is the breeding value that determines their influence on the next generation. The degree of correspondence between phenotypic values and breeding values enables us to predict if it is possible to change the characteristics of the population. Heritability is the measure of such a degree of correspondence.

Quantitative genetics relies extensively on similarity among relatives to assess the importance of genetic factor. Therefore, narrow sense heritability, could be estimated from the degree of resemblance between relatives (correlation).

21.5.4 Variance versus Correlation

Genetic data about families is frequently collected as pairs of numbers like parent-offspring, sib-sib and twins. For example, height of three pairs of mother-daughter, is given in Table 21.3. To know if tall daughters are born to tall mothers, a correlation coefficient (r) between variables is calculated as follows:

$(x_1\ y_1), (x_2\ y_2), \ldots, (x_n\ y_n)$ are N pairs of measurements obtained. The x and y values correspond to the mother and daughter (parent-offspring) measurements, which are used to calculate covariance (C)

$$(C) = [1/(N-1)][(x_1-x)(y_1-y)+(x_2-x)(y_2-y)\ldots+(x_N-x)(y_N-y)]$$

The correlation coefficient (r) between x and y is then calculated from this covariance.

$r = C/(S_x S_y)$ in which S_x and S_y are the standard deviations of the variables. The correlation coefficient can range from -1.0 to $+1.0$. When $r = +1.0$ it indicates a perfect association. Thus, r is the usual measure of the precision of a relationship between two variables. Taking the values from Table 21.3.

Table 21.3 : Adult Height of three Mother-daughter Pairs

Pair	Height of Mother (inch)	Weight of daughter (inch)
(x_1, y_1)	65.0	61.5
(x_2, y_2)	64.0	65.5
(x_3, y_3)	69.0	69.0

Mothers : mean (X) = 66.0, variance (S_x^2) = 7.0 Standard deviation (S_x) = 2.65

Daughters : mean (y) = 65.3, variance (S_y^2) = 14.1 Standard Deviation (S_y) = 3.75

$$C = [1/2](65-66)(61.5-65.3) + (64-66)(65.5-65.3) + (69.66)(69-65.3)]$$
$$= 7.25$$
$$r = 7.25/(2.65 \times 3.75) = 0.73$$

The r value of 0.73 which suggests that tall mothers do tend to have lall'daughters.

SAQ 2

Correlations coefficient measured for three traits between mothers and daughters were as follows:

Trait	Corelation coefficient (r)
Blood Pressure	0.21
Height	0.49
Serum cholesterol	0.28

What can you comment about the heritability of these traits?

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21.5.5 Uses of heritability estimates

Plant and animal breeders use information on heritability estimates in planning breeding programmes, for improving traits with economic value. Heritability estimates in humans provide useful information in predicting diseases caused by continuously varying phenotypes such as blood pressure. The identification of a gentic component in the causation of a disease can help in determining preclinical phenotypes. Individuals with risk for developing a disease can be identified and advised suitably.

21.6 TWIN STUDIES

One experiment of nature useful in the study of complex traits is the occurrence of multiple births — twins, triplets and so on. Because of greater prevalence twin briths provide good opportunities for observations. The utility of twin briths arises from the existence of two kind of twins: monozygotic (MZ or identical) or dizygotic (DZ or fraternal). MZ twins arise from a single zygote that forms two separate embryos very early in development. Since only one zygote is involved, the twins are genetically identical. DZ twins arise from two zygotes that are produced by fertilisation of two separate ova. Thus they have the same genetic relationship as ordinary sibs. They may be either belong to same sex (two boys or two girls) or opposite sexes (a boy and a girl). MZ twins are always of the same sex.

To determine the relative role of heredity and environment in the differences existing between individuals the phenotypic variation can be assessed in individuals with the same genotype. It is relatively easy to test the effect of nature and nurture in experimental animals or plants. Different strains can be produced, each of which is isogenic and thus environmental differences can be studied. In humans such isogenic strains are not available. Nevertheless, twins, seem to be ideal subjects to separate genotypic and environmental components of the observed phenotypic variance.

21.6.1 Frequency of Twinning

Frequency of twinning varies from one population to another. It is highest in Belgium with 1 in 55 births, result in twins. In the United States about 1 in 85 births is of twins, while among Japanese 1 in 145 births is of twins. Since the sample size in most twin studies is not very large the data should be interpreted with caution.

An empirical rule of thumb, known as Hellins's Law (see table 21.4) can be used to estimate the expected frequency of the higher multiple births. According to this law the frequency of twin births was $1/b$, the frequency of triplets $1/b^2$ of quadruplets $1/b^3$, and so on. Actual data from 21 countries for 10 years consisted of 120,061,398 pregnancies. It showed 1,408,912 twins or 1/85.2, 15[illegible]8 triplet or $1/(87.3)^2$ which is very close to the expected. By this rule, quintuplets would be very rare, expected in less than 1 in 50,000,000 pregnancies. However, it may be noted that widespread use of birth-control pills and fertility drugs may well have significant effects on these frequencies.

Table 21.4: Dr Hellin Rule:

Frequency of Birth	One birth in
Twins	89
Triplets	$(89)^2$
Quadruplet.	$(89)^3$
Quintuplets	$(89)^4$

The frequency of monozygotic and dizygotic twins has also been found to vary in different populations. These frequencies can be estimated because of the fact that all unlike-sexed twins must be dizygotic. If we assume the probability of a boy to be a and of a girl b, and that the formation and development of the two zygotes are independent events, then the proportions of boy-boy, boy-girl/girl-boy, and girl-girl pairs can be estimated from the bionomical expansion of $(a + b)^2$, or a^2 (boy-boy), 2ab (boy-girl/girl-boy) and b^2 (girl-girl). Since a = b = ½, p (boy – boy) = ¼, p (boy – girl/girl – boy) = ½ and p (girl – girl = ¼.

Thus, the total for all dizygotic twins should be twice the observed number of boy-girl/girl-boy pairs. The number of monozygotic pairs is then determined by subtracting the estimates for the number of dizygotic twin pairs from the total number of all twin pairs.

This method of estimating the frequencies of monozygotic twins is known as Weinberg's differential method. When the method is applied, it revealed that in the USA about 1/3 of the sets of twins born are monozygotic but in Japan, nearly 2/3 of the twin pairs are monozygotic.

21.6.2 Diagnosis of Zygosity

In twin studies the question of whether dach set of twins is monozygotic or dizygotic has been of great importance. If the sexes are similar they are identical but it is not necessary because fraternal twins can also be female-female or male-male pairs. Therefore, it is evident to find some method to determine the zygosity of monozygotic or dizygotic twins. Usually it is known that dizygotic twins that looked very much alike were misclassified as monozygotic twins. The reverse also occurred, however, because monozygotic twins formed by a relatively late separation of the cells of the original zygote can exhibit mirror imaging in some characteristics, that is, one may be right-handed and other left handed

A more objective diagnosis of zygosity has been based on the type of placentation. But this, too, is fraught with possibilities of error. The developing zygote is enveloped by two membranes, the inner delicate one is amnion and outer tougher chorion attached to the maternal tissue of the placenta. The most common arrangements of these membranes and the placentas in twins are indicated in Table 21.6 and Fig. 21.8 A.

Unequivocal diagnosis of zygosity is possible only when there is a monochorionic placenta (Fig. 21.8 B), a condition that prevails in about 70 per cent of monozygotic twins but not in dizygotic twins. Dizygotic twins, on the other hand, are always dichorionic, because dizygotic twins always implant separately into the uterine epithelium and always develop their own membranes. They need not, however, present separate placenta of the type (Fig. 21.8 A). In some 50 per cent of dizygotic twins the two placentas are sufficiently close that they become secondarily fused (Fig. 21.8 C). Such dizygotic twins of like sex are not infrequently misdiagnosed as monozygotic.

Most dependable method of diagnosing zygosity is by the skin graft test. A skin graft will always be accepted by monozygous twins because of their identical tissue antigens. Though the skin graft is often rejected by a dizygous twins this outcome is not certain. In addition, the method posses many practical problems.

However, the overall probability that dizygotic twins will be alike in all of the traits studied is almost always much smaller than the corresponding probability for monozygotic twins. In other words, the similarity approach is simply a method of arriving at degrees of probabilities as to the zygosity of a given pairs of twins.

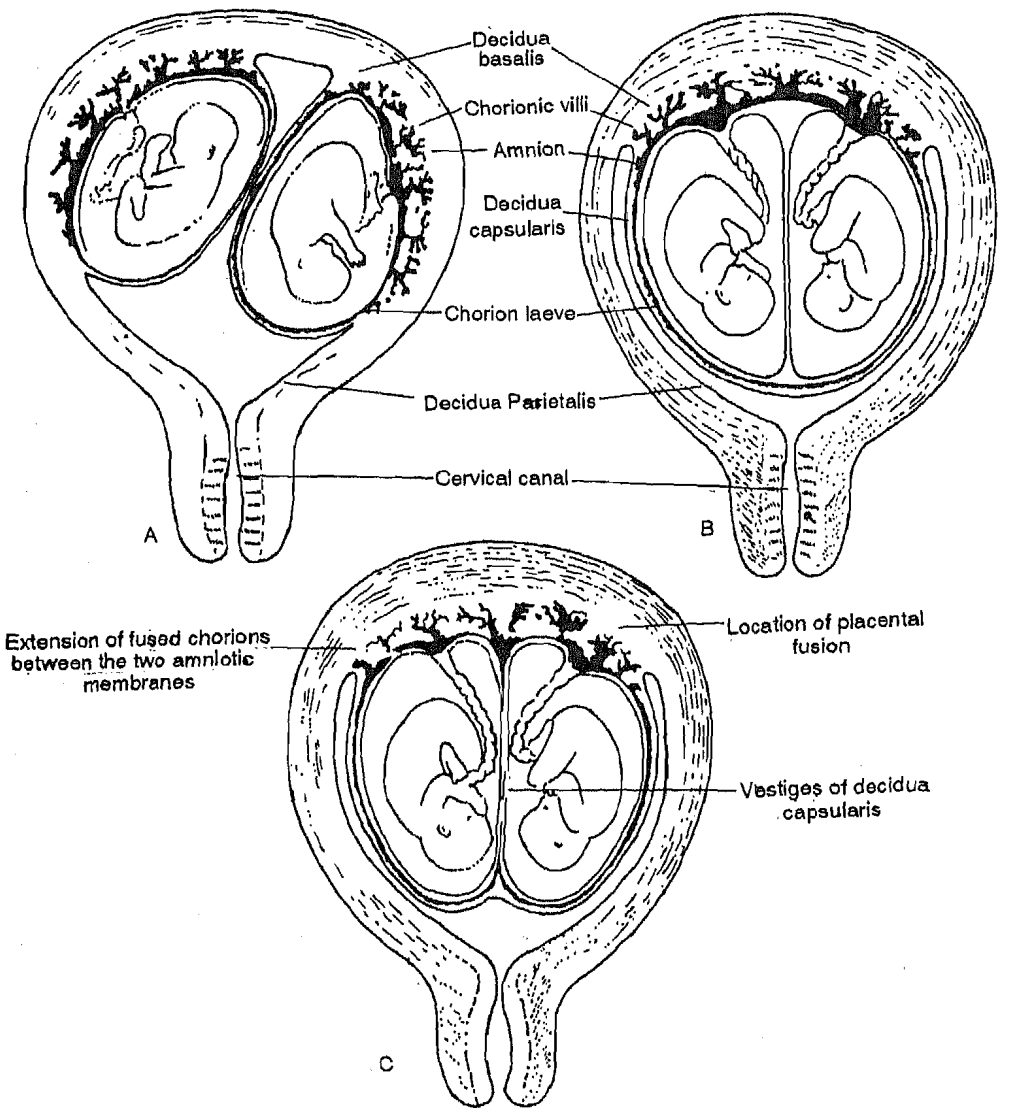

Fig. 21.8: Diagram showing the three most frequent relations of the fetus membranes of twins. A. Twins with entirely separate placenta. B. Twins with a single chorion and separate amnions. C. Twins implanted very close to each other with resultant secondary fusions of their membranes.

21.63 Use of Twin Studies

Francis Galton emphasised the importance of studying twins to obtain information on nature-nurture problem. Since monozygotic twins provide individuals of identical genotypes, the observed or measured phenotypic variance enables the estimation of the environmental components. Many studies have been conducted on human traits. They are of two main types.

i) Differences between identical and fraternal twins (Table 21.5).

Table 21.5 : Composition of the components of variance between and within pairs of **twins**

	Within Pairs	Between Pairs
Different	1/2 V_A + 3/4 VD	1/2 V_A + 3/4 V_D
Fraternals	1/2 V_A + 3/4 V_D + V_{EW}	1/2 V_A + 1/4 V_D + V_{EC}
Identicals	V_{EW}	V_A + VD + V_{EC}

ii) Comparison between identical twins reared together and reared apart. A simple way of scoring differences between twins is to evaluate traits which are either present or absent. Thus twins may be either concordant (i.e. both individuals of a pair possess the trait or are free of the trait in question) or discordant (i.e. only one member of the pair possess the trait)

Concordance is the percentage of cases in which both members of a twin pair have a particular trait. For example, 100 pairs of monozygotic twins were studied for a particular disorder, in 70 pairs only one member was affected while in 30 pairs both members were affected with the disorder. In this case the condordance would be 30/(30 + 70). Concordance varies with the degree of genetic determination of the trait. A 100 per cent concordance indicates that the trait is under complete genetic influence. An example of such a trait is blood group. Blood pressure and pulse rate, two physiological traits studied in twins, are represented in the Figure 21.9. Concordance in continuously varying traits like blood'pressure, is defined as similarity within a specified range. Thus in the study of blood pressure, concordance meant agreement of the twins within a pressure difference of less than 5 mm mercury. Concordance of 63%indicates that there is an environmental influence inspite of the geneticsimilarity. Thirty six per cent concordance in non-identical twins also leads to the interpretation that heredity has a role in determining the differences in blood pressure.

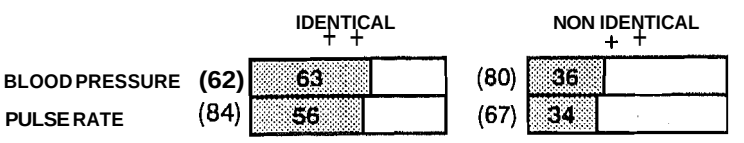

Fig. 21.9: Concordance and discordance in turns for blood pressure and pulse rate. The total width of bar is equal to 100%. And diagonally lined section denotes per cent of concordance. While white section represents discordance total number of twin pair investigated are given in parenthesis.

Congenital deformities and other pathological conditions affecting twins were also studied. These are represented in Figure 21.10. Members of identical pair of twins have been found to be extremely alike in most characters like facial expression even when they were reared apart.

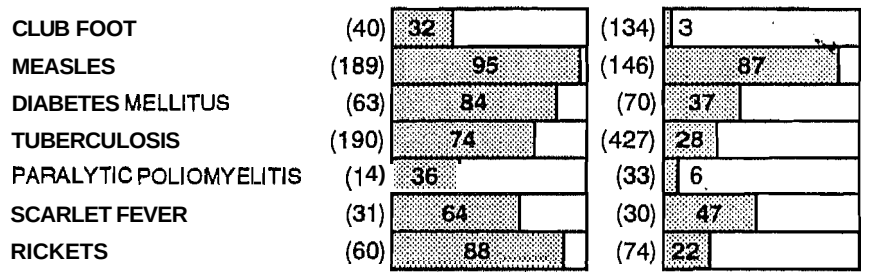

Fig. 21.10: Concordance and discordance in twins affected by various pathological conditions. Percentage of concordance based on affected pairs only.

In addition, numerous anatomical traits (e.g. height, weight, head lenght or width physiological conditions and pathological agent (e.g. clubfoot, diabetes and rickets) have been studied in twins. Non-identical twins and sibs have been found to be alike in distribution and degree of expression of traits. The similarity in these studies reflects the genetic correspondence between fraternal twins and sibs (Fig. 21.11 and Table 21.6).

Table 21.6: Average differences between.the two members of identical twins nonidentical twins, pair of sibs neared together; and identical twins, reared apart

Difference in	Identical	Nonidentical	Sibs	Indentical reared apart
Height	1.7	4.4	4.5	1.8
Weight	4.1	10.0	10.4	9.9
Head length	2.9	6.2		*2.20*
Head width	2.8	4.2		2.89

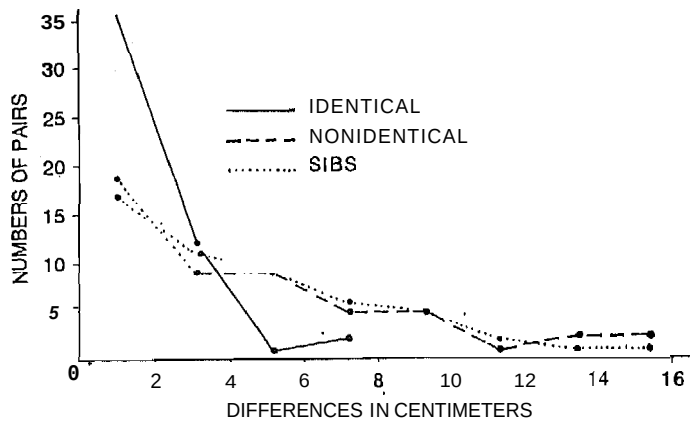

Fig. 21.11: Curves of distributions of differences in standing height of 50 identical twins, 52 nonidentical twins, 52 pairs of sibs.

21.6.4 Genetic Inference from Twin Studies

There have been many attempts to develop quantitative indices of heritability from twin studies. Heritability estimates based on twin studies for certain traits are represented in Table **21.7.**

Table 21.7 : Resemblance between Twins

Character	Correlation coefficients		Differences	Hertability
	Identicals	Fraternals		
MAN				
Height	.93	.64	.29	**0.81**
Weight	.92	.63	.29	**0.78**
Intelligence	**.88**	.63	.25	**0.68**
Birth weight	**.67**	**.58**	.09	**0.21**
CATTLE				
Milk-yield, 1st lactation	.91	**.65**	.26	**0.74**
Butterfat-yield, 1st lactation	.90	.51	.39	**0.80**
Fat % in milk, 1st lactation	**.95**	**.86**	.09	**0.64**
Weight at 96 weeks	.83	**.78**	.05	**0.23**
Body length at 96 weeks	**.75**	**.62**	.13	**0.34**

Unfortunately for most characters the degree of genetic determination is very high indicating several important sources of error in twin studies. They are:

i) Genotype-environment interaction which will increase the variance in fraternal but not identical twins.

ii) Sharing of embryonic membrane making it mandatory for a similar intra-uterine environment.

iii) Similarity in the treatment of twins by parents, and teachers resulting in a decreased envircnmental variance in identical twins (Fig. 21.12). These errors can be overcome partly by comparison of traits between monozygotic and dizygotic twins. In Table 21.7 you can see the list of some traits estimated in identical and fraternal twins. If a trait has genetic component then the identical twins will be more alike with respect to the trait in question than will fraternal twins.

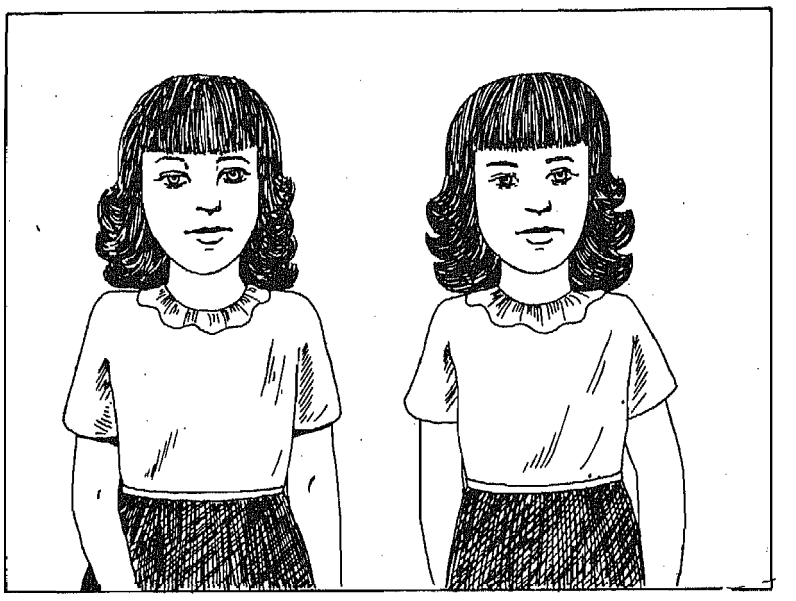

Fig. 21.12: Monozygotic Twins.

One of the earliest concepts was simply to divide the frequency of monozygotic concordance by the frequency of dizygotic concordance. Such a statement of relative frequencies can be misleading. Under it the point on the scale indicating "no heritability" is not zero but one, that is, when dizygotics are just as likely to be concordant as monozygotics. Further confusion comes from the fact that the bottom of the scale is 100 per cent. One of best improvements is Holzinger's formula under it.

$$\text{Heritability} = \frac{\text{Percent Monozygotic concordance} - \text{Percent Dizygotic concordance}}{100 - \text{Percent Dizygotic Concordance}}$$

Or, in short, it is

$$H = \frac{C_{MZ} - C_{DZ}}{100 - C_{DZ}}$$

The theoretical maximum would occur if monozygotics were 100 per cent concordant and dizygotics never, so that

$$\text{Heritability} = \frac{100 - 0}{100 - 0} = 1$$

Similarly the minimum would come when concordances in both types were equal and both were 30 per cent concordant, for instance

$$\text{Heritability} = \frac{30 - 30}{100 - 30} = 0$$

Thus, heritability could be scaled from zero to one.

Unfortunately, Holzinger's formula wbuld not be applicable to the majority of quantitative traits that, as has been noted above, need some such method as twin studies to elucidate their heritability component. When variation is continuous,

difference in the genetic component does not take the form of all-or-none distinctions such as concordant or discordant. One cannot state, for instance, that concordance for intelligence means that both twins have identical IQ scores, any other result being labelled discordant. Clearly, a case in which twins have scores of 104 and 115 is less discordant than a case in which they have scores of 100 and 125.

So Holzinger himself modified his formula given above to use the correlation coefficient (r) as the measure of relative concordance and discordance; thus

$$H = \frac{r_{MZ} - r_{DZ}}{1 - r_{DZ}}$$

A further slight modification of this formula was the basic method of the classic study comparing monozygotic twins reared together (MZt) and similar twins reared apart (MZa) by Newman, Freeman and Holizinger:

$$H = \frac{r_{MZt} - r_{MZa}}{1 - r_{MZa}}$$

Another frequently used form is:

$$\text{Heritability} = \frac{\text{Variance of dizygotics} - \text{Variance of Monozygotics}}{\text{Variance of dizygotics}}$$

If the monozygotics were always to present identical phenotypes, their variance could be zero, and the heritability one; in that case heredity is all. If, on the other hand the two types of twins vary to the same extent, the heritability is zero; in that case all of the observed variability must be environmentally determlhed.

21.6.5 Problems of Twin Studies

In addition to questions concerning the reliability of zygosity diagnoses, twin studies have been subject to a number of other criticisms. One is that even if twin study has demonstrated that a trait is 100 per cent inherited it would not show how it is inherited. Is it due to a single locus? Is there dominance? If it appears associated with another trait, is this due to linkage, and if so, to what degree?

Also attempts to study specific traits in this way have encountered many obstacles of a technical nature. Many scientists disagree, for example, on the propriety of using the typical IQ tests as measures of inherited intelligence, especially across class and cultural boundaries. However, we can conclude that by studying twins we can obtain some evidence for the involvement or noninvolvement of genes in various traits. But we must be careful in interpreting the results of such a study since the variation in penetrance can complicate the results.

21.7 SUMMARY

In this Unit you have studied the quantitative traits and genetics of twins. More specifically we talked about the following:

- The traits which are determined by many genes are known as continuous traits or multifactorial traits and the study is known as quantitative genetics.
- The continuous traits like height, skin colour, and eye colour in human beings are expressed on a continuous scale.
- The trait exhibiting continuous variation, which are often controlled by two or more genes are termed as polygenic and where several genes, make additive contribution to the phenotype the trait is known as quantitative or continuous variation.

- To study the such traits statistical tools are used by geneticist.
- The effect of nongenetic factors on gene expression that include environmental effect and heritability is also considered **i.e.** $V_p = V_g + V_e$. The ratio of genotypic variance to the total phenotypic variance is called heritability. The heritability can be measured in several ways.

The study of twins have played an important role in understanding genetics of traits and there have been several genetical inferences from twin studies. But there are also several problems in twin studies.

28.8 TERMINAL QUESTIONS

1) Kernal colour in wheat is determined by the action of two pairs of polygenes that produce colours varying from dark red to white. If AABB (dark red) and aabb (white) are crossed. What fraction of the F_2 generation can be expected to be like either parent?

2) Height in a certain plant species is controlled by two pairs of independently assorting alleles, with each participating allele A or B adding 5 cm to a base height of 5 cm. A cross is made between parents with genotype AABB and aabb. Disregarding environmental influences.

a) What is the height of each parent?

b) What is the expected height of the members of F_1 generation?

c) What is the expected phenotypic ratios in the F_2 generation?

3) Put (√) mark on the correct answers.

In a polygenic interaction:

a) each contributing gene in a series produces an equal effect.

b) there is no dominance

c) there is no epistasis among genes of different loci.

d) there is no linkage.

e) all of the above

4) The cross between two plants of equal heights results in a progeny with five different phenotypes. How many pairs of polygenes were involved.

a) 2

b) 3

c) 4

d) 5

5) a) A _____ is a phenotype produced by the environment which simulates the effects of a known mutation.

b) Intelligence is somewhat influenced by the environment, therfore, its heritability is _____

6) i) _____ is the measure of the degree to which a phenotype is genetically determined and environmentally influenced.

ii) The study of human inheritance is not always possible because individual mating produces _____ number of offsprings.

iii) The _____ curve is widely used to describe continuous variables.

7) Two homozygous varities of *Nicotiana longiflora* were crossed to produce F_1 hybrids. The average variance of corolla length for all three populations was **8.76.** The variance of the F_2 was 40.96. Estimate the heritability of flower length in the F_2 population.

8) One thousand pairs of twins attend a twin convention in Minneapolis. Eight hundred pairs of these twins are of like sexes (Male/male and female/female). The remaining two hundred pairs are of unlike sexes (Male/female). What percentage of these twins is monozygotic and what percentage is dizygotic?

21.9 ANSWERS

Self Assessment Questions

1) Average phenotypic effects of A locus are given as AA = 4, Aa = 3 and aa = 1. Similarly average phenotypic effects of B or C loci are BB or CC = 4, Bb or Cc = 3 and bb or cc = 1. Using the branching method, phenotypes of a cross between two triple lieterozygotes will be as follows:

				Genotype		Phenotype
			1CC =	1AABBCC	=	1 (12)
	1	BB	2CC =	2AABBCc	=	2 (11)
			1cc =	1AABBcc	=	1 (9)
			1CC =	2AABBCC	=	2 (11)
1	AA	2	Bb 2Cc =	4AABbCc	=	4 (10)
			1cc =	2AABbcc	=	2 (8)
			1CC =	1AAbbCC	=	1 (9)
	1	'bb	2Cc =	2AAbbCc	=	2 (8)
			1cc =	1AAbbcc	=	1 (6)
			1CC =	2AaBBCC	=	2 (11)
	1	BB	2Cc =	4AaBBCc	=	4 (10)
			1cc =	2AaBBcc	=	2 (8)
			1CC =	4AaBbCC	=	4 (10)
2	Aa	2	Bb 2Cc =	8AaBbCc	=	8 (9)
			1cc =	4AaBbcc	=	4 (7)
			1CC =	2AabbCC	=	2 (8)
	1	bb	2Cc =	4AabbCc	=	4 (7)
			1cc =	2Aabbcc	=	2 (5)
			1CC =	1aaBBCC	=	1 (9)
	1	BB	2Cc =	2aaBBCc	=	2 (8)
			1cc =	1aaBBcc	=	1 (6)
			1CC =	2aaBbCC	=	2 (8)
1	aa	2	Bb 2Cc =	4aaBbCc	=	4 (7)
			1cc =	2aaBbcc	=	2 (5)
			1CC =	1aabbCC	=	1 (6)
	1	bb	2Cc =	2aabbCc	=	2 (5)
			1cc =	laabbcc	=	1 (3)

The results can be summarised as follows:

Category	Phenotypic value	No. of Individual
1	12	1
2	11	6
3	10	12
4	9	11
5	8	12
6	7	12
7	6	3
8	5	6
9	4	0
10	3	1
		64

2 A relatively higher correlation between mothers and daughters indicates a higher tendency for the daughters to resemble their mothers as compared to a lower correlation. A higher correlation of 0.49 for height as compared to that for blood pressure (0.21) and serum cholestrol(0.28) is indicative of the fact that there will be greater resemblance between the daughters and mothers for height than that for blood pressure and cholestrol. Similarly, daughters will have a somewhat higher tendency to resemble their mothers for serum cholestrol than that for blood pressure.

Terminal Questions

1) This problem is based on the principle of polygenic inheritance. Polygenic inheritance differs from the classical mendelian pattern in that the whole range of variation is covered in a graded series. In polygenic inheritance certain assumption are made.

1 Each contributing gene in the series produces an equal effect.

2) Effects of each contributing allele are cumulative.

3) There is no dominance.

4) There is no epistasis among genes of different loci.

5) No linkage is involved.

6) Environmental effects are either absent or may be ignored.

a) If we symbolize the gene for red with capital letter A and B, and the alleles resulting in lack of pigment production by a and b the cross can be diagrammed like this:

P : AABB x aabb

darkred white

Gametes AB x ab

F_1 Aa Bb
intermediate red
F_2

	AB	Ab	aB	ab
AB	ABBB	AABb	AaBB	AaBb
Ab	AABb	AAbb	AaBb	Aabb
aB	AaBB	AaBb	aaBB	aaBb
ab	AaBb	Aabb	aaBb	aabb

Assuming each capital allele increases the depth of colour equally, we can classify the F_2 generation in this way:

Number of Genes for Red	Genotype	Phenotype	Fraction of F_2
4	AABB	dark red	1/16
3	AABb, AaBB	medium red	4/16
2	AAbb, aaBB, AaBb	intermediate red	6/16
1	aaBb, Aabb	light red	4/16
0	aabb	white	1/16

We can see that 2/16 of the F_2 generation resembles either parent from P generation, 1/16 of white and $\frac{1}{16}$ of dark red.

2) Base height = 5 cm

Since each allele contributes an additional 5 cm, we use the following formula:

Total height = (each effective allele x 5 cm + base height)

a) Height of AABB = (4 × 5 cm + 5 cm)

Height of AA BB = 25 cm

Height of aabb = 0 + 5 cm

Height of aabb = 5 cm

b) P : AABB x aabb

Gametes AA x ab

F_1 AaBb

Height of AaBb = (2 x 5) + 5

= 15

	AB	Ab	aB	ab
AB	ABBB	AABb	AaBB	AaBb
Ab	AABb	AAbb	AaBb	Aabb
aB	AaBB	AaBb	aaBB	aaBb
ab	AaBb	Aabb	aaBb	aabb

The genotypes and phenotypes of the F_2 can be arranged in tabular form.

Genotype	Number of genes for Height	Fraction of F_2	Height
AABB	4	1/16	25
AABb, AaBB	3	4/16	20
AAbb, aaBB. AaBb	2	6/16	15
aaBb, Aabb	1	4/16	10
aabb	0	1/16	5

3) e)

4) a)

5) a) phenocopy
   b) high

6) i) Heritability.
   ii) small
   iii) bell shaped

7) Since the two parental varieties and the Flare all genetically uniform, their average phenotypic variance of the F_2 (Vt) is partly genetic and partly environmental. The difference $(V_E - V_e)$ is the genetic variance (V_g)

$$h^2 = \frac{V_g}{V_t} = \frac{Vt - Ve}{Vt} = \frac{40.96 - 8.76}{40.96}$$

$$= 0.79$$

8) To solve this problem, we must simply think logically—which may or may not be easy. First, remember that males and females are born with equal probability (1:1 ratio). So dizygotic twins stand a 50% chance of being of unlike sexes. Monozygotic twins, on the other hand, must be of the same sex. We know that 200 pairs of twins are of unlike sexes--these twins must be dizygotic. That is half of the dizygotic twins. The other half must be of like sex. Remember that there is a 50% chance of being of unlike sex so there must be a corresponding 50% chance of being of like sex. This gives us 200 extra pairs of dizygotic twins. Therefore, a total of 400 pairs of twins are dizygotic. This leaves 600 remaining pairs of twins as monozygotic. Dividing 400 dizygotes and 600 monozygotes by 1000 twins and then multiplying by 100% we have the answers. The twins at the minneaplis convention are 60% monozygotic and 40% dizygotic.