ACTA GENETICAE MEDICAE ET GEMELLOLOGIAE

Volumen XV *N. 3 - Iulii 1966*

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Theoretical Models in Twin Research *

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The study of a twin population, nonclassified by zygosity, allows to determine the relationships existing between the distribution of phenotypes and of the genotypes which determine the latter. It also allows to determine the frequency of the genotypes themselves and of their probability of manifestation in the general population from which the observed twin pairs are drawn. To this purpose, it is sufficient to draw from the twin material the information concerning within-pair combinations of the phenotypes under consideration and of sexes.

For simplicity sake, we shall consider the theoretical model of a trait with only two phenotypes determined, respectively, by the presence or absence of the observed trait. Indicating the known terms as shown in Tab. 1, and the variables considered as shown in Tab. 2, on the basis of these notations, we shall be able to write the group of relations concerning within-pair combinations of sexes, as shown in Tab. 3.

In fact, since in MZ twin pairs the fact of one twin partner belonging to a given sex automatically implies that his co-twin belongs to the same sex, while in DZ twin pairs the fact of one twin partner belonging to a given sex is independent from the sex of his co-twin, applying the principle of compound probabilities, we obtain that:

1) The frequency of same-sexed twin pairs is equal to the frequency of MZ twin pairs, times the individual frequency of the observed sex, plus the frequency of DZ twin pairs, times the squared individual frequency of the observed sex;

2) The frequency of opposite-sexed twin pairs is equal to the frequency of DZ twin pairs, times the double product of the individual frequency of the two sexes.

Similarly, considering within-pair combinations of phenotypes, the group of possible relations may be indicated as shown in Tab. 4.

In fact, since the manifestation of the trait in one twin partner does not entail

* Paper submitted to the Third International Congress of Human Genetics, Chicago (September 5-10th, 1966).

Tab. 1. Known-terms (Experimental-data)

According to trait combinations

$f_{1\text{-}1}$ = frequency of pairs with both partners exhibiting the trait;
$f_{1\text{-}2}$ = frequency of pairs with one single partner exhibiting the trait;
$f_{2\text{-}2}$ = frequency of pairs with no partner exhibiting the trait.

According to sex combinations

$f_{m\text{-}m}$ = frequency of male-male pairs;
$f_{m\text{-}f}$ = frequency of opposite-sexed pairs;
$f_{f\text{-}f}$ = frequency of female-female pairs.

Tab. 2. Variables

Symbol	Event	Frequency
MZ	monozygotic pair	$M = 1 - D$
DZ	dizygotic pair	$D = 1 - M$
G_1	genotype determining the presence of the trait	$p = 1 - q$
G_2	genotype determining the absence of the trait	$q = 1 - p$
E_1	manifestation of the trait	$\pi = 1 - \varphi$
E_2	non-manifestation of the trait	$\varphi = 1 - \pi$
O	male individual	$m = 1 - f$
O	female individual	$f = 1 - m$

Tab. 3. Relations according to sex within-pair combinations

$$f_{m\text{-}m} = Mm + Dm^2$$
$$f_{m\text{-}f} = 2Dmf$$
$$f_{f\text{-}f} = Mf + Df^2$$

Tab. 4. Relations according to phenotype within-pair combinations

$$f_{1\text{-}1} = (Mp + Dp^2)\ \pi^2$$
$$f_{1\text{-}2} = 2pqD\pi + (Mp + Dp^2)\ 2\pi\varphi$$
$$f_{2\text{-}2} = Mq + Dq^2 + (Mp + Dp^2)\ \varphi^2 + 2pqDh$$

the manifestation of the trait in his co-twin, neither in MZ nor in DZ twin pairs, it will result that:

1) The frequency of pairs with both twin partners exhibiting the trait is given by the product of the frequency of twin pairs, possessing the genotype able to express the trait, times the squared frequency of manifestation of the trait;

2) The frequency of pairs with one twin partner exhibiting the trait is given by the product of the frequency of pairs with only one twin partner possessing the genotype able to determine the trait, times the frequency of manifestation, plus the product of the frequency of pairs with both twin partners possessing the genotype able to express the trait, times the double product of the frequency of manifestation, times the frequency of non-manifestation;

3) The frequency of pairs with neither twin partner exhibiting the trait is equal to the product of the frequency of pairs with neither twin partner possessing the genotype able to express the trait, plus the frequency of pairs with only one twin partner possessing the genotype able to express the trait, times the frequency of non-manifestation, plus the product of the frequency of pairs with both twin partners possessing the genotype able to express the trait, times the squared frequency of non-manifestation.

Having so defined the relations between known terms (experimental values) and unknown ones, it may be easily observed that in the first group of relations concerning within-pair combinations of sexes, the great mass of information allows to obtain more than one solution, both for the unknown frequencies of mono- and dizygosity, and for the unknown frequencies of sexes.

Among the various solutions, we may, e. g., consider two systems of two linear equations with two unknown quantities, obtained by pooling in one single system, at first, the first and the second relations, and, then, the second and the third ones.

The following results are thus obtained (Tab. 5).

Tab. 5

A) For sex frequencies:

$$m = \frac{2\ f_{mm} - f_{mf}}{2}$$

$$f = \frac{2\ f_{ff} - f_{mf}}{2}$$

B) For zygosity frequencies:

$$M = 1 - D$$

$$D = \frac{2\ f_{mf}}{(2\ f_{mm} - f_{mf})\ (2\ f_{ff} - f_{mf})}$$

The frequencies of mono- and dizygosity in the twin population having been established, it is now possible to use such data to solve the unknown equation of the group concerning within-pair combinations of phenotypes, i.e. the frequencies of the genotypes and the frequencies of manifestation and non-manifestation.

Therefore, making use of the system formed by the first two relations, we obtain the final formulae shown in Tab. 6.

https://doi.org/10.1017/S1120962300013366 Published online by Cambridge University Press

Tab. 6

A) For genotypes frequency: $$p = \frac{M\ (2\ f_{1\text{-}1} + f_{1\text{-}2})^2}{4\ f_{1\text{-}1} - D\ (2\ f_{1\text{-}1} + f_{1\text{-}2})^2}$$

$$q = 1 - p$$

B) For manifestation frequency: $$\pi = \frac{f_{1\text{-}1}^{1/2}}{[p - (M + Dp)]^{1/2}}$$

We have thus been able to obtain from a twin material, not only the natural information of the material itself, i.e. the frequencies of mono- and dizygosity, but also the information concerning the frequency of the genotypes under consideration, and their frequency of manifestation in the general population.

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RIASSUNTO

Gli AA. dimostrano che lo studio dei gemelli permette di determinare frequenza e penetranza genica nella popolazione generale, attraverso l'analisi della distribuzione delle combinazioni fenotipiche presenti nelle coppie gemellari.

SUMMARY

The Authors show twin study to allow the determination of gene frequency and penetrance in the general population, by means of the analysis of distribution of phenotypic combinations in the twin pairs.

RÉSUMÉ

Les Auteurs démontrent que l'étude des jumeaux permet de déterminer la fréquence et la pénétrance génique dans la population générale, moyennant l'analyse de la distribution des combinaisons phénotypiques des couples gémellaires.

ZUSAMMENFASSUNG

Verf. beweisen, dass die Zwillingsforschungen es ermöglichen, die Genfrequenz und -Penetranz bei der Gesamtbevölkerung zu bestimmen, wenn man dabei die Distribution der bei Zwillingspaaren beobachteten phänotypischen Kombinationen analysiert.