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Blood groups in twin studies
Calculation of the probability of monozygosis

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In many cases it is desirable to know whether a twin is monozygotic or dizygotic. A good method to get information on this material is to perform bloodgroup determinations with the greatest possible number of bloodgroup antisera of different specificity. If the twin is monozygous the bloodgroups of the partners must be completely the same. It must be clear that the chance of finding a discordance between dizygotic twin partners becomes greater if one determines a greater number of different bloodgroup factors. However, also if the twin is dizygotic, in certain percentage of cases the partners may have the same bloodgroup pattern.

Therefore it may be of value to have a method to calculate the probabilities of monozygosis for twins where dizygosis cannot be excluded.

The first method to do so is to compare the chances of concordance for a monozygotic twin (= 1,00) with that of a dizygotic twin. For instance the probability of concordance for the combination father O mother O is 1,00; the children cannot have another bloodgroup but O. If the father is O and the mother AB, the chance of a non-monozygotic twin to have the same bloodgroup is 0,5: the chance that both will have group A is $0{,}5^2 = 0{,}25$ and the chance for 2 × group B is also 0,25 and thus the total probability of concordance is $2 \times 0{,}25 = 0{,}50$.

However this method does not use all the information that is given by the results of the tests. For instance in the combination father and mother both group A, twin group O. Both, father and mother are heterozygous AO; the chance of having a child of group $O = 0{,}5^2 = 0{,}25$; the chance of having a child of group $A = 0{,}75$. Thus the chance of having two non-monozygotic children with the same bloodgroup is $075^2 + 0{,}25^2 = 0{,}625$. However, in this case it is the most improbable concordant combination in the children that has been found, viz. the combination 2 × group O with a probability of $0{,}25^2 = 0{,}0625$ and this must be taken in account.

Therefore another method of calculation must be used: the probability that in a given father-mother-child combination a second child will have the same bloodgroups as are found in the first child. For instance: in the combination father A

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mother A, first child O the probability of a second child with group O is $0{,}5^2 = 0{,}25$, compared with a probability of 1,00 for the second partner of a monozygotic twin.

The first method, calculation of the chance of concordance in two children from the observed bloodgroups of father and mother is proposed in the first edition of the book of Race and Sanger; the second method, calculation of the probability of a second child with the same bloodgroups as are found in the first child in the second and the third edition.

However, also in this method, not all information available is used; for example the case of father A, mother A, 2 children A.

Genotypes of the parents may be AA or AO. AO is much more frequent than AA, so there is a great chance that both are AO.

The greater the number of children in a parents combination AO×AO the greater the probability that at least one of the children will have group O, and on the other hand if both parents are group A and in a great number of children we do not find any O, the probability that one of the parents or both are genotypically AA will be greater than when the number of children is only small. This means, that a parent-couple, both group A, and with two children also with group A, has a greater probability of being father or mother or both, AA, than A × A parents with only one A child or with a monozygotic twin pair with group A.

When calculating the probability of monozygosis of a twin we must use the full information presented by the bloodgroup investigation. This is done the following way: suppose the phenotype of the mother is X, with several possible genotypes X_1, X_2, X_3... X_m, in general X_i.

In the same way the phenotype of the father is Y, his possible genotypes are Y_1, Y_2, ... Y_n in general Y_i. The phenotype of the children (twin) is Z.

Mating types: $X_1 \times Y_1$, $X_2 \times Y_1$... $X_m \times Y_1$... $X_1 \times Y_2$... in general $X_i \times Y_i$.

Frequency of children with phenotype Z in the mating-types $X_i\, Y_i$:

$$\text{fr}\,(i,i) = {}^1/_4,\ {}^1/_2,\ {}^3/_4 \text{ or } 1$$

Frequencies of the genotypes (parents):

$$\overline{X}_1, \overline{X}_2 \ldots \overline{X}_m \text{ in general } \overline{X}_i$$
$$\overline{Y}_1, \overline{Y}_2 \ldots \overline{Y}_n \text{ in general } \overline{Y}_i$$

In families with mother X and father Y and one child Z, the ratio of the probabilities of the mating types becomes:

$$\overline{X}_1\,\overline{Y}_1\,\text{fr}\,(1,1) : \overline{X}_2\,\overline{Y}_1\,\text{fr}\,(2,1) : \ldots : \overline{X}_2\,\overline{Y}_2\,\text{fr}\,(2,2) : \text{etc.}$$

and in families with 2 Z children:

$$\overline{X}_1\,\overline{Y}_1\,\text{fr}\,(1,1)^2 : \overline{X}_2\,\overline{Y}_1\,\text{fr}\,(2,1)^2 : \quad \text{etc.}$$

The probability of 2 children with phenotype Z of parents X and Y and 2 children Z:

$$P(XY_2Z) = \frac{\overline{X}_1 \overline{Y}_1 \, fr\,(1,1)^4 + \overline{X}_1 \overline{Y}_2 \, fr\,(1,2)^4 + \ldots + \overline{X}_n \overline{Y}_m \, fr\,(m,n)^4}{\overline{X}_1 \overline{Y}_1 \, fr\,(1,1)^2 + \overline{X}_1 \overline{Y}_2 \, fr\,(1,2)^2 + \ldots + \overline{X}_n \overline{Y}_m \, fr\,(m,n)^2}$$

$$= \frac{\Sigma \, \overline{X}_i \overline{Y}_i \, fr\,(i,i)^4}{\Sigma \, \overline{X}_i \overline{Y}_i \, fr\,(i,i)^2} \qquad (1^a)$$

The probability of 1 child (or 1 monozygotic twin pair) with phenotype Z of parentes X and Y and 1 child Z:

$$P(XY_1Z) = \frac{\overline{X}_1 \overline{Y}_1 \, fr\,(1,1)^2 + \overline{X}_1 \overline{Y}_2 \, fr\,(1,2)^2 \ldots}{\overline{X}_1 \overline{Y}_1 \, fr\,(1,1) + \overline{X}_1 \overline{Y}_2 \, fr\,(1,2) \ldots} = \frac{\Sigma \, \overline{X}_i \overline{Y}_i \, fr\,(i,i)^2}{\Sigma \, \overline{X}_i \overline{Y}_i \, fr\,(i,i)} \qquad (1^b)$$

When besides the twin partners also other children (all with the phenotype Z) are known (total number of children, twins included = a):

$$\text{chance for a dizygotic twin with } Z = P(XYaZ) = \frac{\Sigma \, \overline{X}_i \overline{Y}_i \, fr\,(i,i)^{(a+2)}}{\Sigma \, \overline{X}_i \overline{Y}_i \, fr\,(i,i)^a} \qquad (2^a)$$

$$\text{chance for a monozygotic twin with } Z = P[XY\,(a-1)\,Z] = \frac{\Sigma \, \overline{X}_i \overline{Y}_i \, fr\,(i,i)^a}{\Sigma \, \overline{X}_i \overline{Y}_i \, fr\,(i,i)^{a-1}} \qquad (2^b)$$

If a number of p bloodgroup systems is used for determination of monozygosis, the probabilities are:

$$P(X^1 Y^1 a Z^1),\ P(X^2 Y^2 a Z^2) \ldots P(X^p Y^p a Z^p) \text{ and}$$
$$P[X^1 Y^1 (a-1) Z^1],\ P[X^2 Y^2 (a-1) Z^2] \ldots P[X^p Y^p (a-1) Z^p]$$

$X^1, X^2 \ldots X^p$, $Y^1, Y^2 \ldots Y^p$ and $Z^1, Z^2 \ldots Z^p$ are the phenotypes in each blood group system.

The probability of concordance in sex in a dizygotic twin = $P_{sex} = \frac{1}{2}$

General probability of monozygosis = P_m (= 0,30) and for dizygosis = P_d (= 0,70)

Probability of monozygosis of the twin $Z^1, {}^2 \ldots {}^p$ with parents $X^1, {}^2 \ldots {}^p$ and $Y^1, {}^2 \ldots {}^p$

$$P = \frac{Pm \times P[X^1 Y^1 (a-1) Z^1] \times P[X^2 Y^2 (a-1 Z^2] \times \ldots \times P[X^p Y^p (a-1) Z^p]}{Pm \times P[X^1 Y^1 (a-1) Z^1] \times \ldots \times P[X^p Y^p (a-1) Z^p] + Pd \times Ps \times P[X^1 Y^1 a Z^1] \times \text{etc.}} \qquad (3)$$

To demonstrate how to hand the formulae the probability of monozygosis in two cases will be calculated:

case 1

Mother : A_1 MNS+ P+ CcDee K— Fy(a+)
Father : O MNS+ P+ CcDee K— Fy(a+)
Twin : A_1 MNS+ P+ CcDee K— Fy(a—)

case 2

Parents and twin the same as in case 1, apart from that there are 3 other children:

1 : A_1 MNS— P+ CCDee K— Fy(a+)
2 : O MNS+ P+ ccdee K— Fy(a+)
3 : A_1 MMS+ P+ CcDee K— Fy(a+)

It will become clear that for most of the bloodgroup systems especially in case 2 simplifications can be used, because the formulae 1^a, 1^b, 2^a, 2^b are only necessary if the exact genotypes of the parents are not known. If these genotypes are known the probabilities of 2 children and of 1 child with phenotype Z are equal to resp. fr $(1,1)^2$ and fr $(1, 1)$

ABO:

Case 1 $X_1 = A_1A_1$ $X_2 = A_1A_2$ $X_3 = A_1O$
$Y_1 = OO$ $Z = A_1$
fr $(1,1) = 1{,}0$ fr $(2,1) = 0{,}5$ fr $(3,1) = 0{,}5$

gene frequencies in the population:

$p_1 = 0{,}22$ $p_2 = 0{,}05$ $q = 0{,}06$ $r = 0{,}67$
$\overline{X}_1 = p_1^2 = 0{,}22^2 = 0{,}0484$ $\overline{Y}_1 = 0{,}67^2 = 0{,}4489$
$\overline{X}_2 = 2\,p_1p_2 = 2 \times 0{,}22 \times 0{,}05 = 0{,}0220$
$\overline{X}_3 = 2\,p_1\,r = 2 \times 0{,}22 \times 0{,}67 = 0{,}2948$

$$P[A_1, O, 2A_1] = \frac{(0{,}0484 \times 1 + 0{,}0220 \times 0{,}5^4 + 0{,}2948 \times 0{,}5^4) \times 0{,}4489}{(0{,}0484 \times 1 + 0{,}0220 \times 0{,}5^2 + 0{,}2948 \times 0{,}5^2) \times 0{,}4489}$$

$$= \frac{0{,}682}{0{,}1276} = 0{,}535$$

$$P[A_1, O, 1A_1] = \frac{(0{,}0484 \times 1 + 0{,}0220 \times 0{,}5^2 + 0{,}2948 \times 0{,}5^2) \times 0{,}4489}{(0{,}0484 \times 1 + 0{,}0220 \times 0{,}5 + 0{,}2948 \times 0{,}5) \times 0{,}4489}$$

$$= \frac{0{,}1276}{0{,}20685} = 0{,}616$$

Case 2 $X_1 = A_1O$ $Y_1 = OO$ $Z = A_1$ fr $(1,1) = 0{,}5$

$P[A_1, O, 2A_1] = 0{,}5^2 = 0{,}25$
$P[A_1, O, 1A_1] = 0{,}5$

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MNS

Case 1 $X_1 = MS/NS$ $Y_1 = MS/NS$ $Z = MNS$
$X_2 = MS/Ns$ $Y_2 = MS/Ns$
$X_3 = Ms/NS$ $Y_3 = Ms/NS$

$f(1,1) = 0,5$ $f(2,1) = 0,5$ $f(3,1) = 0,5$
$f(1,2) = 0,5$ $f(2,2) = 0,5$ $f(3,2) = 0,25$
$f(1,3) = 0,5$ $f(2,3) = 0,25$ $f(3,3) = 0,5$

Gene frequencies: $MS = 0,22$ $Ms = 0,30$ $NS = 0,08$, $Ns = 0,40$

$\overline{X}_1 = \overline{Y}_1 = 2 \times MS \times NS = 2 \times 0,20 \times 0,08 = 0,0352$
$\overline{X}_2 = \overline{Y}_2 = 2 \times MS \times N\overline{S} = 2 \times 0,20 \times 0,40 = 0,1760$
$\overline{X}_3 = \overline{Y}_3 = 2 \times M\overline{S} \times NS = 2 \times 0,30 \times 0,08 = 0,0480$

$$P[MNS+, MNS+, 2\,MNS+] = \frac{0,0352^2 \times 0,5^4 + 0,352 \times 0,1760 \times 0,5^4 + \ldots. \text{ etc.}}{0,0352^2 \times 0,5^2 + 0,352 \times 0,1760 \times 0,5^2 + \ldots. \text{ etc.}}$$

$$= \frac{0,0032}{0,0136} = 0,236$$

$$P[MNS+, MNS+, 1MNS+] = \frac{0,0352^2 \times 0,5^2 + 0,0352 \times 0,1760 \times 0,5^2 + \ldots. \text{ etc.}}{0,0352^2 \times 0,5 + 0,0352 \times 0,1760 \times 0,5 + \ldots. \text{ etc.}}$$

$$= \frac{0,0136}{0,0292} = 0,465$$

Case 2: child 1 shows that one of the parents is MS/Ns, the other MsNS; $fr(1,1) = 0,25$.

$P[MNS+, MNS+, 2MNS+] = 0,25^2 = 0,0625$
$P[MNS+, MNS+, 1MNS+] = 0,25$

Blood factor P case 1

$X_1 = PP$ $Y_1 = PP$ $Z = P+$ $f(1,1) = 1,0$ $f(2,1) = 1,0$
$X_2 = Pp$ $Y_2 = Pp$ $f(1,2) = 1,0$ $f(2,2) = 0,75$
$\overline{X}_1 = \overline{Y}_1 = P^2 = 0,25$ Gene frequencies: $P\,(= P_1) = 0,50$
$\overline{X}_2 = \overline{Y}_2 = 2\,Pp = 0,50$ $p\,(= P_2 + p) = 0,50$

$$P(P+, P+, 2\,P+) = \frac{0,25 \times 0,25 \times 1,0 + 0,25 \times 0,50 \times 1,0 + \ldots.. + 0,50 \times 0,50 \times 0,75^4}{0,25 \times 0,25 \times 1,0 + 0,25 \times 0,50 \times 1,0 + \ldots.. + 0,50 \times 0,50 \times 0,75^2}$$

$$= \frac{0,3916}{0,4530} = 0,865$$

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$$P(P+, P+, 1P+) = \frac{0{,}25 \times 0{,}25 \times 1{,}0 + 0{,}25 \times 0{,}50 \times 1{,}0 + \ldots 0{,}50 \times 0{,}50 \times 0{,}75^2}{0{,}25 \times 0{,}25 \times 1{,}0 + 0{,}25 \times 0{,}50 \times 1{,}0 + \ldots 0{,}50 \times 0{,}50 \times 0{,}75}$$

$$= \frac{0{,}4530}{0{,}5000} = 0{,}906$$

Case 2

$$P(P+, P+, 5P+) = \frac{0{,}25 \times 0{,}25 \times 1{,}0 + 0{,}25 \times 0{,}50 \times 1{,}0 + \ldots + 0{,}50 \times 0{,}50 \times 0{,}75^7}{0{,}25 \times 0{,}25 \times 1{,}0 + 0{,}25 \times 0{,}50 \times 1{,}0 + \ldots + 0{,}50 \times 0{,}50 \times 0{,}75^5}$$

$$= \frac{0{,}3459}{0{,}3719} = 0{,}930$$

$$P(P+, P+, 4P+) = \frac{0{,}25 \times 0{,}25 \times 1{,}0 + 0{,}25 \times 0{,}50 \times 1{,}0 + \ldots + 0{,}50 \times 0{,}50 \times 0{,}75^5}{0{,}25 \times 0{,}25 \times 1{,}0 + 0{,}25 \times 0{,}50 \times 1{,}0 + \ldots + 0{,}50 \times 0{,}50 \times 0{,}75^4}$$

$$= \frac{0{,}3719}{0{,}3916} = 0{,}950$$

Rhesus

Case 1 $X_1 = CDe/cde = Y_1 \quad Z = CcDee$
$X_2 = CDe/cDe = Y_2$
$X_3 = Cde/cDe = Y_3$

$fr(1,1) = fr(1,2) = fr(2,1) = fr(2,2) = fr(2,3) = fr(3,2) = fr(3,3) = 0{,}50$
$fr(1,3) = fr(3,1) = 0{,}25$

Gene frequencies: CDe = 0,41 cDe = 0,02 Cdc = 0,01 cde = 0,40

$\overline{X}_1 = \overline{Y}_1 = 2\ CDe \times cde = 0{,}3280$
$\overline{X}_2 = \overline{Y}_2 = 2\ CDe \times cDe = 0{,}0164$
$\overline{X}_3 = \overline{Y}_3 = 2\ Cde \times cDe = 0{,}0004$

Because X_3 and Y_3 are unlikely to occur, we do not take in account those possibilities. Their influence on the values of P would be too small.

Therefore fr (i,i) = 0,50 and now $P[CcDee, CcDee, 2\ CcDee] = 0{,}50^2 = 0{,}25$ and $P[CcDee, CcDee, 1\ CcDee] = 0{,}50$

Case 2

Child 2 shows that both parents have genotype $X_1 = Y_1 = CDe/cde$; $f(1,1) = 0{,}50$

As in case 1 $P[CcDee, CcDee, 2CcDee] = 0{,}50^2 = 0{,}25$
$P[CcDee, CcDee, 1CcDee] = 0{,}50$

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Kell cases 1 and 2:

$X_1 = Y_1 = Z = kk = f(1,1) = 1{,}0$

$P[K—, K—, 2K—] = P[K—, K—, 1K—] = 1{,}0$

Duffy cases 1 and 2 : $Z = Fy(a—)$
$X_1 = Y_1 = Fy^aFy^b \qquad f(1,1) = 0{,}25$
$P[Fy(a+), Fy(a+), 2Fy(a—)] = 0{,}25^2 = 0{,}0625$
$P[Fy(a+), Fy(a+), 1\,Fy(a—)] = 0{,}25$

Probability of monozygosis of the twin (3):

Case 1:

$$P = \frac{0{,}30 \times 0{,}616 \times 0{,}465 \times 0{,}906 \times 0{,}50 \times 1{,}0 \times 0{,}25}{0{,}30 \times 0{,}616 \times 0{,}465 \times 0{,}906 \times 0{,}50 \times 1{,}0 \times 0{,}25 + 0{,}70 \times 0{,}50 \times 0{,}530{,}236 \times 0{,}865 \times \overline{0{,}25 \times 1{,}0 \times 0{,}0625}}$$

$$= \frac{0{,}00974}{0{,}00974 + 0{,}00060} = 0{,}941$$

Case 2:

$$P = \frac{0{,}30 \times 0{,}50 \times 0{,}25 \times 0{,}950 \times 0{,}50 \times 1{,}0 \times 0{,}25}{0{,}30 \times 0{,}50 \times 0{,}25 \times 0{,}950 \times 0{,}50 \times 1{,}0 \times 0{,}25 + 0{,}70 \times 0{,}50 \times 0{,}25 \times 0{,}0625 \times 0{,}93 \times \overline{0{,}25 \times 1{,}0 \times 0{,}0625}}$$

$$= \frac{0{,}00445}{0{,}00445 + 0{,}00008} = 0{,}983$$

Summary

When calculating the chance of monozygosis from the results of a blood group study in a twin-family, it is desirable to use the complete information that is presented by these results and not only part of it.

A calculation-method in which the complete genetic-information is used is presented.

The use of the formulas is demonstrated by calculating the probability of monozygosis in two examples.

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RIASSUNTO

Quando si calcola la probabilità di monozigotismo dai risultati di uno studio sui gruppi sanguigni in una famiglia di gemelli, è bene utilizzare tutti i dati forniti dallo studio e non soltanto una parte.

Viene presentato un metodo di calcolo in cui vengono utilizzati tutti i dati genetici al completo.

L'uso delle formule è dimostrato mediante il calcolo delle probabilità di monozigotismo in due esempi.

RÉSUMÉ

Lorsqu'on calcule la probabilité de monozygotisme moyennant les résultats d'une étude sur les groupes sanguins dans une famille de jumeaux, il est préférable d'utiliser tous les résultats et non pas une partie.

L'on présente une méthode de calcul dans laquelle toutes les données génétiques ont été utilisées.

L'utilisation des formules est démontrée par le calcul des probabilités de monozygotisme dans deux examples.

ZUSAMMENFASSUNG

Als man die Eineiigkeitswahrscheinlichkeit durch die Ergebnisse einer Blutgruppen-Analyse in einer Zwillingsfamilie rechnet, ist es besser alle Ergebnisse, und nicht nur einige, zu verwerten.

Man stellt eine Rechnungsmethode dar, in welcher alle genetische Ergebnisse verwertet werden.

Die Verwertung der Formeln wird durch einer Rechnung der Eineiigkeitswahrscheinlichkeits in zwei Beispiele beweist.