99. *Probability-theoretic Investigations on Inheritance. XIII₁. Estimation of Genotypes.*[1]

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1. Problems to be discussed.

If there exist dominance relations among genes of an inherited character, a genotype of an individual cannot necessarily be determined uniquely from its phenotype alone. In fact, an individual representing a dominant character may be homozygotic as well as heterozygotic. A clue of deciding its genotype is to examine the characters of its descendants.

For instance, in case of the *ABO* blood type, if an individual of homozygote *AA* is accompanied by a spouse *O*, then any child is necessarily of the type *A*(=*AO*), while if an individual of heterozygote *AO* is accompanied by a spouse *O*, then its child is either of *A*(=*AO*) or *O*. Hence, if an individual of phenotype *A* accompanied by a spouse *O* produces at least one child *O*, then it is decided to be of the heterozygote *AO*. But, even when an individual of phenotype *A* accompanied by *O* produces merely the children of type *A*, it is of course yet impossible to decide its genotype as the homozygote *AA*. However, in the latter case, it will be expected that the more the children *A* increase, the more probable the individual is to be of *AA*.

Similar circumstances will also arise without reference to the type of a spouse of an individual. For instance, if an individual is of homozygote *AA*, then its child cannot have the type *O* or *B*, while if an individual is of heterozygote *AO*, then its child can have the type *O* or *B* provided its spouse is of a type containing the

1) Y. Komatu, Probability-theoretic investigations on inheritance. I. Distribution of genes; II. Cross-breeding phenomena; III. Further discussions on cross-breeding; IV. Mother-child combinations; V. Brethren combinations; VI. Rate of danger in random blood transfusion; VII. Non-paternity problems; VIII. Further discussions on non-paternity; IX. Non-paternity problems concerning mother-children combinations; X. Non-paternity concerning mother-child-child combinations; XI. Absolute non-paternity; XII. Problem of paternity. Proc. Japan Acad., **27** (1951) I. 371-377; II. 378-383, 384-387; III. 459-465, 466-471, 472-477, 478-483; IV. 587-592, 593-597, 598-603, 605-610, 611-614, 615-620; V. 689-693, 694-699; **28** (1952), VI. 54-58; VII. 102-104, 105-108, 109-111, 112-115, 116-120, 121-125; VIII. 162-164, 165-168, 169-171; IX. 207-212, 213-217, 218-223, 224-229; X. 249-253, 254-258, 259-264; XI. 311-316, 317-322; XII. 359-364, 365-369.

gene O or B respectively. Consequently, if an individual of phenotype A produces at least one child O or B, then it is decided to be the heterozygote AO; and so on.

In the present chapter, we shall discuss the *problems of estimating the genotype of an individual by means of the phenotypes of its own and its descendants with or without reference to the type of its spouse.* More concretely stated, *given an individual of a dominant character and its descendants of known phenotypes, we shall compute the probability a posteriori of a possible genotype of the individual. A lower bound for the number of the descendants of favorable types will then be determined, in order that an individual is presumed to be homozygotic with an assigned probability.* The main tool of attack is the *Bayes' theorem* referred to passim; cf. the end of §1 in IV. The related problems concerning probabilities a posteriori have also be discussed in the preceding chapters; cf. X, XI, XII.

2. Estimation with reference to spouse.

We first consider, as an illustrative model, the simplest case, *the Q blood type.* Let an individual of phenotype Q be given, and let its spouse be of phenotype Q. Then, the type q of its child is possible only if the individual (as well as its spouse) is heterozygotic. In other words, if at least one child is of the type q, then the individual is surely heterozygotic. Hence, we may restrict ourselves to the case where all the children are of the type Q. In this case, when the number of children is n, we denote by $\Pr\{Q=QQ\mid\times Q\to Q^n\}$ and $\Pr\{Q=Qq\mid\times Q\to Q^n\}$ the probabilities a posteriori of the individual to be of homozygote QQ and of heterozygote Qq, respectively, which will be determined in the following lines.

Now, the probabilities a priori of QQ and Qq among Q, may be regarded as $\overline{QQ}/\overline{Q}=u/(1+v)$ and $\overline{Qq}/\overline{Q}=2v/(1+v)$, respectively, the ratio being $u:2v$. The mating $QQ\times Q$ produces Q alone, and the mating $Qq\times QQ$ produces also Q alone, while the mating $Qq\times Qq$ produces Q and q with probabilities 3/4 and 1/4, respectively. Among the matings $Qq\times Q$, the matings $Qq\times QQ$ and $Qq\times Qq$ occur with probabilities $u/(1+v)$ and $2v/(1+v)$, respectively. Thus, we get, in view of Bayes' theorem, the desired probabilities

$$\Pr\{Q=QQ\mid\times Q\to Q^n\}=\frac{u\cdot 1^n}{u\cdot 1^n+2v\left(\dfrac{u}{1+v}+\dfrac{3}{4}\dfrac{2v}{1+v}\right)^n} \tag{2.1}$$

$$=\frac{2^{n-1}u(1+v)^n}{2^{n-1}u(1+v)^n+v(2+v)^n},$$

$$\begin{aligned}\Pr\{Q=Qq\,|\times Q\to Q^n\}&=1-\Pr\{Q=QQ\,|\times Q\to Q^n\}\\ &=\frac{v(2+v)^n}{2^{n-1}u(1+v)^n+v(2+v)^n}.\end{aligned}\tag{2.1'}$$

Next, let an individual Q accompanied by a spouse q be given. If there is at least one child q, then the individual must be heterozygotic. But, if all of n children are of Q, the individual can be homozygotic as well as heterozygotic. In this case, the respective probabilities a posteriori be denoted by $\Pr\{Q=QQ\,|\times q\to Q^n\}$ and $\Pr\{Q=Qq\,|\times q\to Q^n\}$. The mating $QQ\times q$ produces Q alone, while the mating $Qq\times q$ produces Q and q with equal probabilities. Thus, we get

$$\Pr\{Q=QQ\,|\times q\to Q^n\}=\frac{u\cdot 1^n}{u\cdot 1^n+2v(\frac{1}{2})^n}=\frac{2^{n-1}u}{2^{n-1}u+v},\tag{2.2}$$

$$\Pr\{Q=Qq\,|\times q\to Q^n\}=1-\Pr\{Q=QQ\,|\times q\to Q^n\}=\frac{v}{2^{n-1}u+v}.\tag{2.2'}$$

The probabilities obtained in (2.1) and (2.2) are the desired ones. Those obtained in (2.1′) and (2.2′) are respectively the complementary probabilities of them.

We now proceed to deal with *the ABO blood type*. Let an individual of phenotype A be given, and let its spouse be of phenotype O. Then, the type O of its child is possible only if the individual is heterozygotic. Hence, we have only to consider the case, where all the n children are of the type A. In this case, since the probabilities a priori of AA and AO have the ratio $p:2r$ and since the matings $AA\times O$ and $AO\times O$ produce A with respective probabilities 1 and 1/2, we obtain the probability a posteriori of the individual to be homozygotic in the form

$$\Pr\{A=AA\,|\times O\to A^n\}=\frac{p\cdot 1^n}{p\cdot 1^n+2r(\frac{1}{2})^n}=\frac{2^{n-1}p}{2^{n-1}p+r},\tag{2.3}$$

which, replacing p, r by u, v, coincides just with (2.2).

Let an individual A accompanied by a spouse A be given. If all the n children are of the type A, then probability a posteriori of the individual to be homozygotic is given by

$$\begin{aligned}&\Pr\{A=AA\,|\times A\to A^n\}\\ &=\frac{p\cdot 1^n}{p\cdot 1^n+2r\left(\frac{p}{p+2r}+\frac{3}{4}\frac{2r}{p+2r}\right)^n}=\frac{2^{n-1}p(p+2r)^n}{2^{n-1}p(p+2r)^n+r(2p+3r)^n}.\end{aligned}\tag{2.4}$$

Next, let an individual A accompanied by a spouse B be given. The matings $AA\times BB$ produces AB alone and the mating $AA\times BO$ produces AB, A with equal probabilities, while the mating $AO\times BB$ produces AB, B with equal probabilities and the mating $AO\times BO$ produces AB, A, B, O with respective probabilities 1/4, 1/4, 1/4, 1/4.

Hence, if there exists at least one child of the type B or O, then the individual must surely be heterozygotic. If, among all the n children, there are ν children A and $n-\nu$ children AB, then we denote by $\Pr\{A=AA\,|\times B\rightarrow A^{\nu}\cap AB^{n-\nu}\}$ the probability a posteriori of the individual to be homozygotic, which is computed in the form

$$(2.5)\quad \Pr\{A=AA\,|\times B\rightarrow A^{\nu}\cap AB^{n-\nu}\}$$
$$=\frac{\overline{AA}(\frac{1}{2}\overline{BO})^{\nu}(\overline{BB}+\frac{1}{2}\overline{BO})^{n-\nu}}{\overline{AA}(\frac{1}{2}\overline{BO})^{\nu}(\overline{BB}+\frac{1}{2}\overline{BO})^{n-\nu}+\overline{AO}(\frac{1}{4}\overline{BO})^{\nu}(\frac{1}{2}\overline{BB}+\frac{1}{4}\overline{BO})^{n-\nu}}=\frac{2^{n-1}p}{2^{n-1}p+r},$$

the value being really independent of ν, $0\leqq\nu\leqq n$.

Similarly, if a spouse in the last case is replaced by AB, the corresponding probability a posteriori becomes

$$(2.6)\quad \Pr\{A=AA\,|\times AB\rightarrow A^{\nu}\cap AB^{n-\nu}\}$$
$$=\frac{\overline{AA}(\frac{1}{2})^{\nu}(\frac{1}{2})^{n-\nu}}{\overline{AA}(\frac{1}{2})^{\nu}(\frac{1}{2})^{n-\nu}+\overline{AO}(\frac{1}{2})^{\nu}(\frac{1}{4})^{n-\nu}}=\frac{2^{n-\nu-1}p}{2^{n-\nu-1}p+r},$$

which, contrary to (2.5), is dependent on ν.

The probabilities obtained in (2.3) to (2.6) are the desired ones in case where the type of a given individual is A. Their complementary probabilities are immediately obtained; for instance,

$$(2.3')\quad \Pr\{A=AO\,|\times O\rightarrow A^{n}\}$$
$$=1-\Pr\{A=AA\,|\times O\rightarrow A^{n}\}=\frac{r}{2^{n-1}p+r}.$$

The corresponding probabilities with respect to an individual of type B can also be immediately written down. In fact, we have only to replace A, B, p by B, A, q, respectively. Thus, we get, corresponding to (2.3) to (2.6), the following expressions:

$$(2.7)\quad \Pr\{B=BB\,|\times O\rightarrow B^{n}\}=\frac{2^{n-1}q}{2^{n-1}q+r},$$

$$(2.8)\quad \Pr\{B=BB\,|\times B\rightarrow B^{n}\}=\frac{2^{n-1}q(q+2r)^{n}}{2^{n-1}q(q+2r)^{n}+r(2q+3r)^{n}},$$

$$(2.9)\quad \Pr\{B=BB\,|\times A\rightarrow B^{\nu}\cap AB^{n-\nu}\}=\frac{2^{n-1}q}{2^{n-1}q+r},$$

$$(2.10)\quad \Pr\{B=BB\,|\times AB\rightarrow B^{\nu}\cap AB^{n-\nu}\}=\frac{2^{n-\nu-1}q}{2^{n-\nu-1}q+r}.$$

By the way, we add the following remarks. Let an individual A accompanied by a spouse B be given. If all the n children are known merely as either A or AB, then the probability a posteriori of the individual to be homozygotic is given in the form

$$(2.11)\quad \Pr\{A=AA\,|\times B\rightarrow (A\cup AB)^{n}\}=\frac{\overline{AA}\cdot 1^{n}}{\overline{AA}\cdot 1^{n}+\overline{AO}(\frac{1}{2})^{n}}=\frac{2^{n-1}p}{2^{n-1}p+r},$$

which is coincident with (2.5). On the other hand, if a spouse in the last case is replaced by AB, the corresponding probability a posteriori becomes

$$\text{(2.12)} \quad \begin{aligned}&\Pr\{A=AA|\times AB\rightarrow(A\cup AB)^n\}\\ &=\frac{\overline{AA}\cdot 1^n}{\overline{AA}\cdot 1^n+\overline{AO}(\frac{3}{4})^n}=\frac{4^n p}{4^n p+3^n\cdot 2r}.\end{aligned}$$

Similarly, we get, by interchanging A and B, the corresponding probabilities

$$\text{(2.13)} \quad \Pr\{B=BB|\times A\rightarrow(B\cup AB)^n\}=\frac{2^{n-1}q}{2^{n-1}q+r},$$

$$\text{(2.14)} \quad \Pr\{B=BB|\times AB\rightarrow(B\cup AB)^n\}=\frac{4^n q}{4^n q+3^n\cdot 2r}.$$

It would be noticed that the inequalities

$$\text{(2.15)} \quad \begin{cases}\Pr\{A=AA|\times AB\rightarrow A^n\}<\Pr\{A=AA|\times AB\rightarrow(A\cup AB)^n\}\\ \qquad\qquad<\Pr\{A=AA|\times AB\rightarrow AB^n\},\\ \Pr\{B=BB|\times AB\rightarrow B^n\}<\Pr\{B=BB|\times AB\rightarrow(B\cup AB)^n\}\\ \qquad\qquad<\Pr\{B=BB|\times AB\rightarrow AB^n\}\end{cases}$$

hold good except for the trivial distribution with $pqr=0$.

The cases of other inherited characters can also be discussed in quite a similar manner. We give here, making use of the notations of the same nature as above, the results on *the $Qq_\pm$ blood type*.

$$\text{(2.16)=(2.1)} \quad \Pr\{Q=QQ|\times Q\rightarrow Q^n\}=\frac{2^{n-1}u(1+v)^n}{2^{n-1}u(1+v)^n+v(2+v)^n},$$

$$\text{(2.16}'\text{)} \quad \Pr\{Q=Qq_-|\times Q\rightarrow Q^n\}=\frac{v_1(2+v)^n}{2^{n-1}u(1+v)^n+v(2+v)^n},$$

$$\text{(2.16}''\text{)} \quad \Pr\{Q=Qq_+|\times Q\rightarrow Q^n\}=\frac{v_2(2+v)^n}{2^{n-1}u(1+v)^n+v(2+v)^n};$$

$$\text{(2.17}'\text{)} \quad \Pr\{Q=Qq_-|\times Q\rightarrow Q^\nu\cap q_-^{\,n-\nu}\}=\frac{v^{n-\nu}}{v^{n-\nu}+v_2 v_1^{\,n-\nu-1}} \qquad (\nu<n),$$

$$\text{(2.17}''\text{)} \quad \Pr\{Q=Qq_+|\times Q\rightarrow Q^\nu\cap q_-^{\,n-\nu}\}=\frac{v_2 v_1^{\,n-\nu-1}}{v^{n-\nu}+v_2 v_1^{\,n-\nu-1}} \qquad (\nu<n);$$

$$\text{(2.18)} \quad \Pr\{Q=QQ|\times q_-\rightarrow Q^n\}=\frac{2^{n-1}u}{2^{n-1}u+v},$$

$$\text{(2.18}'\text{)} \quad \Pr\{Q=Qq_-|\times q_-\rightarrow Q^n\}=\frac{v_1}{2^{n-1}u+v},$$

$$\text{(2.18}''\text{)} \quad \Pr\{Q=Qq_+|\times q_-\rightarrow Q^n\}=\frac{v_2}{2^{n-1}u+v};$$

$$\text{(2.19}'\text{)} \quad \Pr\{Q=Qq_-|\times q_-\rightarrow Q^\nu\cap q_-^{\,n-\nu}\}=\frac{v_1(v+v_2)^{n-\nu}}{v_1(v+v_2)^{n-\nu}+v_2 v^{n-\nu}} \quad (\nu<n),$$

$$\text{(2.19}''\text{)} \quad \Pr\{Q=Qq_+|\times q_-\rightarrow Q^\nu\cap q_-^{\,n-\nu}\}=\frac{v_2 v^{n-\nu}}{v_1(v+v_2)^{n-\nu}+v_2 v^{n-\nu}} \quad (\nu<n);$$

$$(2.20)\quad \Pr\{Q=QQ|\times q_+\to Q^n\}=\frac{2^{n-1}u}{2^{n-1}u+v},$$

$$(2.20')\quad \Pr\{Q=Qq_-|\times q_+\to Q^n\}=\frac{v_1}{2^{n-1}u+v},$$

$$(2.20'')\quad \Pr\{Q=Qq_+|\times q_+\to Q^n\}=\frac{v_2}{2^{n-1}u+v};$$

$$(2.21)\quad \Pr\{q_-=q_-q_-|\times Q\to q_-^{\nu}\cap Q^{n-\nu}\}=\frac{2^{\nu-1}v_1v^{\nu}}{2^{\nu-1}v_1v^{\nu}+v_2(v+v_1)^{\nu}},$$

$$(2.21')\quad \Pr\{q_-=q_-q_+|\times Q\to q_-^{\nu}\cap Q^{n-\nu}\}=\frac{v_2(v+v_1)^{\nu}}{2^{\nu-1}v_1v^{\nu}+v_2(v+v_1)^{\nu}};$$

$$(2.22)\quad \Pr\{q_-=q_-q_-|\times q_-\to q_-^{n}\}=\frac{2^{n-1}v_1(v+v_2)^n}{2^{n-1}v_1(v+v_2)^n+v_2(2v+v_2)^n},$$

$$(2.22')\quad \Pr\{q_-=q_-q_+|\times q_-\to q_-^{n}\}=\frac{v_2(2+v_2)^n}{2^{n-1}v_1(v+v_2)^n+v_2(2v+v_2)^n};$$

$$(2.23)\quad \Pr\{q_-=q_-q_-|\times q_+\to q_-^{n}\}=\frac{2^{n-1}v_1}{2^{n-1}v_1+v_2},$$

$$(2.23')\quad \Pr\{q_-=q_-q_+|\times q_+\to q_-^{n}\}=\frac{v_2}{2^{n-1}v_1+v_2}.$$

By the way, we further notice the following probabilities:

$$(2.24)\quad \Pr\{Q=QQ|\times Q\to(Q\cup q_-)^n\}=\frac{2^{n-1}u(1+v)^n}{2^{n-1}(u+2v_1)(1+v)^n+v_2(2+v+v_1)^n},$$

$$(2.24')\quad \Pr\{Q=Qq_-|\times Q\to(Q\cup q_-)^n\}=\frac{2^{n}v_1(1+v)^n}{2^{n-1}(u+2v_1)(1+v)^n+v_2(2+v+v_1)^n},$$

$$(2.24'')\quad \Pr\{Q=Qq_+|\times Q\to(Q\cup q_-)^n\}=\frac{v_2(2+v+v_1)^n}{2^{n-1}(u+2v_1)(1+v)^n+v_2(2+v+v_1)^n};$$

$$(2.25)\quad \Pr\{Q=QQ|\times q_-\to(Q\cup q_-)^n\}=\frac{2^{n-1}u(v+v_2)^n}{2^{n-1}(u+2v_1)(v+v_2)^n+v_2(2v+v_2)^n},$$

$$(2.25')\quad \Pr\{Q=Qq_-|\times q_-\to(Q\cup q_-)^n\}=\frac{2^{n}v_1(v+v_2)^n}{2^{n-1}(u+2v_1)(v+v_2)^n+v_2(2v+v_2)^n},$$

$$(2.25'')\quad \Pr\{Q=Qq_+|\times q_-\to(Q\cup q_-)^n\}=\frac{v_2(2v+v_2)^n}{2^{n-1}(u+2v_1)(v+v_2)^n+v_2(2v+v_2)^n};$$

$$(2.26)\quad \Pr\{q_-=q_-q_-|\times Q\to(q_-\cup Q)^n\}=\frac{2^{n-1}v_1(1+v)^n}{2^{n-1}v_1(1+v)^n+v_2(2+v+v_1)^n},$$

$$(2.26')\quad \Pr\{q_-=q_-q_+|\times Q\to(q_-\cup Q)^n\}=\frac{v_2(2+v+v_1)^n}{2^{n-1}v_1(1+v)^n+v_2(2+v+v_1)^n}.$$

— To be continued —