13. Probability-theoretic Investigations on Inheritance. VI. Rate of Danger in Random Blood Transfusion.[1)]

By Yûsaku KOMATU.
Department of Mathematics, Tokyo Institute of Technology and
Department of Legal Medicine, Tokyo University
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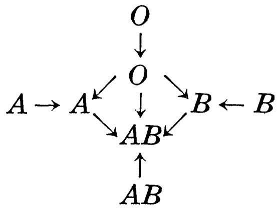
1. Preliminaries.

We insert here a short chapter concerning the rate of accidental danger in *blood transfusion*, especially in case of *random selection*. In view of the nature of problem, we concern exclusively the concrete human blood types alone. Now, it is one of the most important applications of blood types to clinical medicine, to make possible to choose a suitable type of donor in blood transfusion. That the blood transfusion shows a restoring effect against profuse hemorrhage of various kinds, has been well verified by many experiences. But, in order to ward off an accompaniable danger, it is necessary to choose a suitable donor possessing the blood-corpuscles not agglutinated as well as not dissolved by serum of the receiver. If, in future, the system of blood transfusion company or blood bank, where the blood of every type is preserved, will perhaps spread more wider, then the mistake on choice of suitable donor will be warded off. But, in an imminent case, it may possibly happen that there is no time sufficient to examine the blood type.

Let a pair of a donor and a receiver be chosen, one or both of which have unknown types. Then, at how many rate the danger will be expected? In the present chapter, we shall chiefly discuss the problem in case of *ABO* blood type. The safe directions of transfusion fitting for the above-mentioned postulation may be, as well known, denoted in the scheme.



Besides the postulate mentioned above, it is practically further desired that the serum of donor does not agglutinate or dissolve the blood-corpuscles of receiver. For that purpose, it will be safe to choose a transfused blood obtained, if necessary, by removing anti-*A* or anti-*B* agglutinin. However, we shall not touch here on such a circumstance.

1) In reference to preceding papers, cf. a foot-note of Y. Komatu, Probability-theoretic investigations on inheritance. V. Brethren combinations. Proc. Jap. Acad. **27** (1951).

2. Probability of danger.

We first consider the case where the type of receiver is known. In case of receiver of type O, donors of any types except O are unsuitable. Hence, the rate of danger at random choice of donor then becomes

$$D[O]=\overline{A}+\overline{B}+\overline{AB}=1-\overline{O}=1-r^2. \tag{2.1}$$

For receiver of type A or B, donors of types B and AB or A and AB must be avoided, respectively. Hence, the respective rates of danger then become

$$D[A]=\overline{B}+\overline{AB}=q(q+2r)+2pq=q(2-q), \tag{2.2}$$

$$D[B]=\overline{A}+\overline{AB}=p(p+2r)+2pq=p(2-p). \tag{2.3}$$

Last, for receiver of type AB, donors of any types without exception being admissible, the rate of danger vanishes, i.e.,

$$D[AB]=0. \tag{2.4}$$

Next, suppose that the type of receiver is also unknown. Then, at random choice of a pair of a donor and a receiver, the general rate of danger is evidently given by the expression

$$\begin{aligned} D_{ABO}&=\overline{O}\,D[O]+\overline{A}\,D[A]+\overline{B}\,D[B]+\overline{AB}\,D[AB] \\ &=r^2(1-r^2)+p(p+2r)q(2-q)+q(q+2r)p(2-p) \\ &=r^2(1-r^2)+2pq((1+r)^2-pq). \end{aligned} \tag{2.5}$$

The case where the type of donor alone is known can also be treated in a similar way as above. If, for a receiver of unknown type, a donor of type O, A, B or AB is chosen, the respective rate of danger is then given by

$$\varDelta[O]=0, \tag{2.6}$$

$$\varDelta[A]=\overline{O}+\overline{B}=r^2+q(q+2r)=(1-p)^2, \tag{2.7}$$

$$\varDelta[B]=\overline{O}+\overline{A}=r^2+p(p+2r)=(1-q)^2, \tag{2.8}$$

$$\varDelta[AB]=\overline{O}+\overline{A}+\overline{B}=1-\overline{AB}=1-2pq. \tag{2.9}$$

If the type of donor would also be unknown, the general rate of danger will then be given by the expression

$$\begin{aligned} \varDelta_{ABO}&=\overline{O}\varDelta[O]+\overline{A}\varDelta[A]+\overline{B}\varDelta[B]+\overline{AB}\varDelta[AB] \\ &=p(p+2r)(1-p)^2+q(q+2r)(1-q)^2+2pq(1-2pq) \\ &=r^2(1-r^2)+2pq((1+r)^2-pq). \end{aligned} \tag{2.10}$$

It is evidently seen from (2.5) and (2.10) that both quantities D_{ABO} and $\varDelta_{ABO}$ coincide each other identically. This fact is quite a matter of course, as immediately understood from their respective definitions.

On the other hand, the results obtained above can easily be extended to case where donor and receiver belong to different populations. But, such cases being of less practical importance, the detailed discussions will here be omitted and left to the reader.

We now consider the $Qq_{\pm}$ blood type, i.e., the subdivided Q blood type where the gene q is divided into q_- and q_+. Here, we distinguish q_- and q_+ characteristically by absence and existence of the anti-Q agglutinin in the serum, respectively. It is known that the gene q_+ is recessive against q_-. Let the frequencies of genes Q, q_-, q_+ be denoted by u, v_1, v_2, respectively; that of q is then $v=v_1+v_2$. We now consider the problem corresponding to that treated above in case of ABO blood type. Based upon the nature, it must be avoided to transfuse the blood the corpuscles of which contain the Q agglutinin into the blood the serum of which contains the anti-Q agglutinin, i.e., into the blood of type q_+. Hence, using similar notations as above, we get the rates of danger:

$$(2.11) \qquad D[Q]=D[q_-]=0, \qquad D[q_+]=\overline{Q}=u(1+v);$$

$$(2.12) \qquad D_{Qq\pm}=\overline{q}_+D[q_+]=v_2^2u(1+v) \qquad (v\equiv v_1+v_2).$$

It may be noticed that all the probabilities explicitly discussed in the present section are expressed merely by frequencies of phenotypes without bringing out those of genes. For practical use, it will suffice, for instance, to make use of the first equation in (2.5), (2.10) and (2.12).

3. Maximizing distribution.

In the preceding section we have derived explicit expressions for the rates of danger in case of random blood transfusion. We shall now determine the distribution of genes for which such a rate attains its maximum among all the possible values.

Now, the frequencies p, q, r of genes in ABO blood type are not quite independent, but there exists a unique identity given by

$$(3.1) \qquad p+q+r=1.$$

In view of this relation, the rate (2.5) can be regarded as a function of two independent variables p, q and may be denoted by $f(p,q)$, the range of variables being the triangle $0\leqq p,q$; $p+q\leqq 1$. We get from (2.5) and (3.1)

$$(3.2) \qquad f(p,q)=r^2(1-r^2)+2pq((1+r)^2-pq), \qquad r=1-p-q.$$

In view of the identity $pq=((p+q)^2-(p-q)^2)/4$, the values of the product pq, for any fixed value of r with $0\leqq r\leqq 1$, range over the interval $0\leqq pq\leqq(1-r)^2/4$, pq being equal to $(1-r)^2/4$ only if

$$p=q=(1-r)/2. \tag{3.3}$$

Therefore, for any fixed value of r $(0\leqq r\leqq 1)$, the expression

$$f(p,q)=r^2(1-r^2)+(1+r)^4/2-2((1+r)^2/2-pq)^2$$

attains its maximum for $pq=(1-r)^2/4$ and hence for (3.3).

Thus, the problem reduces to maximize the quantity

$$\begin{aligned}\varphi(r)&\equiv f((1-r)/2,\ (1-r)/2)\\&=r^2(1-r^2)+((1+r)^2-(1-r)^2/4)(1-r)^2/2,\end{aligned} \tag{3.4}$$

the variable r ranging over the interval $0\leqq r\leqq 1$. Differentiating this with respect to r, we get

$$8\varphi'(r)=8(d/dr)f((1-r)/2,\ (1-r)/2)=1-3r+3r^2-5r^3. \tag{3.5}$$

Since $\varphi'(0)=1/8>0$ and $\varphi'(1)=-1/2<0$, the quartic (3.4) attains its maximum at a value of r where the cubic (3.5) vanishes. The cubic equation $\varphi'(r)=0$ possesses a unique root r_0 contained in the interval $0<r<1$, which is numerically calculated as approximately equal to

$$r_0=0.3865. \tag{3.6}$$

The corresponding values of p and q, being denoted by p_0 and q_0 respectively, are given by

$$p_0=q_0=(1-r_0)/2. \tag{3.7}$$

Since we have $\varphi(r)=(-1/5+r)\varphi'(r)+(7+6r-6r^2)/20$, the maximum is equal to $\varphi(r_0)=(7+6r_0-6r^2)/20$; namely

$$(D_{ABO})^{\max}=0.4211. \tag{3.8}$$

The maximizing distribution of phenotypes is given by

$$\begin{aligned}&\overline{O}=r_0^2=0.1494, &&\overline{A}=p_0^2+2p_0r_0=0.3312,\\&\overline{B}=q_0^2+2q_0r_0=0.3312, &&\overline{AB}=2p_0q_0=(1-r_0)^2/2=0.1882.\end{aligned} \tag{3.9}$$

We next consider the case of $Qq_{\pm}$ blood type. For any fixed value of u $(0\leqq u\leqq 1)$, the quantity

$$D_{Qq\pm}=v_2^2u(1+v) \qquad (v=v_1+v_2,\ u+v=1) \tag{2.10}$$

may be regarded as a function of a variable v_2 alone ranging over the interval $0\leqq v_2\leqq v\equiv 1-u$, and attains its maximum evidently at $v_2=v=1-u$ (and hence $v_1=0$). The problem thus reduces to maximize

$$\psi(u)=(1-u)^2u(2-u), \tag{3.11}$$

the variable u ranging over the interval $0 \leqq u \leqq 1$. Since this function can be written in the form $\psi(u)=(1-u)^2(1-(1-u)^2)$, it is evidently that the maximizing value of u, say u_0, is given by $(1-u_0)^2=1/2$, i.e., $u_0=1-1/\sqrt{2}$, which implies the maximizing distribution of genes:

$$(3.12) \qquad u_0=1-1/\sqrt{2}=0.2929, \quad v_{10}=0, \quad v_{20}=1/\sqrt{2}=0.7071.$$

The maximum is then equal to

$$(3.13) \qquad (Qq_{\pm})^{\max}=\psi(u_0)=1/4=0.25.$$

The maximizing distribution of phenotypes is quite an extreme one given by

$$(3.14) \qquad \overline{Q}=1/2=0.5, \quad \overline{q}_-=0, \quad \overline{q}_+=1/2=0.5.$$