A Note on the Detection of Interchanged Children[1]

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INTRODUCTION

IN man and pedigreed domestic animals it is frequently desired to test certain hypotheses concerning the relationship between two or more individuals. For this purpose blood groups have been found ideally suited because of their precise genetic behavior and not too unequal population gene ratios. Also well known in both man and animals is the use of blood groups for diagnosis of zygosity in twins and larger litters. This latter application may be regarded as another example of the general problem, namely that of distinguishing between two or more hypotheses regarding relationship.

For any given serological or other genetic system, one can specify the probability that the system will furnish disproof of hypothesis R_1 (say), when R_1 is false and when relationship is actually in accord with a second hypothesis, R_0. For example, we may be interested in knowing the probability of excluding paternity (hypothesis R_1) when tests are made on a man and a child who are actually "unrelated" (hypothesis R_0). Or, we may wish to state the chance of excluding monozygosity (R_1) for a pair of twins which are full-sib dizygotic twins (R_0). In each case, hypothesis R_0 is needed in order to supply the probability distribution of the various combinations of phenotypes, some of which may be taken as disproof of R_1.

For most of the common situations arising in medicolegal work, and for most of the simpler blood group systems known in man prior to the Rh era, Wiener (1930–1935) has derived general formulae for the probabilities of exclusion, these being functions of the gene frequencies. Such formulae are of interest in showing how the usefulness of the system for any given problem will vary according to the population gene ratio. One of the objects of the present note is that of bringing together and comparing graphically such gene frequency functions, appropriate to the several kinds of problem. In doing so, the author will introduce distinctions between certain "classes" of exclusion which seem useful in understanding the interconnections between the various problems and which facilitate in particular the discussion of one of the more complex problems, namely, the detection of interchange between children belonging to two families.

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The treatment will be restricted to autosomal two-gene systems with or without dominance, as exemplified by the human "secretor" and M-N factors, respectively. Derivations of the various gene frequency functions will not be given, as these can be easily found by applying a tabular method recently described by Fisher (1951), which lends itself both to the subdivisions and extensions of medicolegal problems considered in this note.

TESTS INVOLVING TWO INDIVIDUALS

When tests are made on only two individuals, a and b, only two hypotheses concerning relationship are capable of absolute disproof, irrespective of the number and complexity of the genetic systems available, so long as we are limited to autosomal genetic factors. In specifying "absolute" disproof, we ignore, of course, the possibility of exceptional genetic events, such as mutation. The requirement for excludability of R_1 is that the relationship must demand that at least one gene of common origin be shared by the two relatives. Neglecting complex relationships made possible through inbreeding, only two classes of relationship meet this requirement: parent-child relationship and monozygosity (or identity). Consequently, the three kinds of medicolegal problem involving but a single pair of individuals are the following:

	Hypothesis R_1	*Hypothesis* R_0
(1)	Identity ($r = 1$)	"Unrelated" ($r = 0$)
(2)	MZ twinning ($r = 1$)	DZ full-sib twinning ($r = \frac{1}{2}$)
(3)	Parent-child ($r = \frac{1}{2}$)	"Unrelated" ($r = 0$)

In problem (1) we wish to ask how often the genetic system will exclude identity when bloods of two unrelated individuals are tested. Designating this probability by I, we may easily find $1 - I$ by summing the squares of the phenotype frequencies, as noted by Fisher (1951). Thus, if p and q are the frequencies of two allelic autosomal genes, and if $\theta = pq$, the expected frequency of exclusions of identity is

$$I' = 1 - (p^2)^2 - (2pq)^2 - (q^2)^2 = 4\theta - 6\theta^2$$

for two-gene systems lacking dominance, and

$$I'' = 1 - (1 - q^2)^2 - (q^2)^2 = 2\theta q(1 + q)$$

for two genes showing dominance. (Throughout this note, a prime (′) attached to any probability symbol will denote application to 2-gene systems without dominance; a double prime indicates application to 2-gene systems with dominance.) Maximal chances for exclusion of identity are as follows: max $I' = 0.625$ at $\theta = \frac{1}{4}$, or when $p = q = \frac{1}{2}$; and max $I'' = 0.50$ at $p = 0.29289$ or at dominant trait (antigen) frequency $p(2 - p) = \frac{1}{2}$ (fig. 1). In general, for any genetic system, the chances for exclusion of identity must be greater than

for any other problem, since we are discriminating between two extremes of relationship (coefficient of relationship $r = 1$ or 0).

For exclusion of monozygosity in dizygotic full-sib twins derived from unrelated parents, the corresponding probabilities are smaller quantities, namely

$$J' = 2\theta - \tfrac{3}{2}\theta^2$$

and

$$J'' = \tfrac{1}{2}\theta q(3 + q),$$

as shown by Wiener (1935) and by Rife (1938). They have the following maxima: max $J' = 0.40625$ at $\theta = \frac{1}{4}$, and max $J'' = 0.27233$ at $p = 0.31386$ or at dominant trait (antigen) frequency $p(2 - p) = 0.52921$ (fig. 1).

Ordinarily, in human disputed paternity investigations, tests are made on at least three individuals, a man (A), a child (a), and the assumed mother of the child (A'). When the mother refuses examination, is dead, or is for any other reason unavailable for testing, or when maternity itself is unknown or doubtful, decisions about the paternity of a must be based solely on tests performed on A and a. Similar conditions may obtain in cases involving a disputed maternity of A' for a. We therefore wish to ask how often a given genetic system will exclude parent-child relationship when A and a are actually unrelated. For two genes lacking dominance, only two combinations of phenotypes (MM—NN or NN—MM) are capable of disproving parent-child relationship, and each of these will occur, on hypothesis R_0, with frequency p^2q^2 or θ^2. If, for any genetic system, we let C stand for the probability of such exclusions, then

$$C' = 2\theta^2$$

for two gene systems lacking dominance, and this function has a maximal value of 0.125 at $\theta = \frac{1}{4}$, or when $p = q = \frac{1}{2}$ (fig. 1). For two genes showing dominance, no combination of phenotypes is capable of disproving parent-child relationship, so that we may write $C'' = 0$.

EXCLUSION OF PATERNITY

Suppose that three individuals are tested: a man (A) falsely represented as father of a child (a), and the latter's mother (A'). We assume that A and A' are unrelated, and similarly for A and a. For any given serological system, we can now distinguish three kinds of conclusion permitted by the test results:

$A\mathbf{F}a$	"A may be father of a"
$A\bar{\mathbf{F}}a$	"A is not father of a, whoever is mother of a"
$AA'\bar{\mathbf{P}}a$	"A is not father of a, if A' is mother of a"

Examples of test results permitting the three statements may be illustrated

for M and N blood group reactions:

$A \epsilon MM \quad A' \epsilon MN$	$A \epsilon MM \quad A' \epsilon MN$	$A \epsilon MM \quad A' \epsilon MM$
$a \epsilon MN$	$a \epsilon NN$	$a \epsilon MN$
$(A\mathbf{F}a)$	$(A\bar{\mathbf{F}}a)$	$(AA'\bar{\mathbf{P}}a)$

The first example of exclusion illustrated here $(A\bar{\mathbf{F}}a)$ may be termed *unconditional exclusion* of paternity; the denial of A's paternity for a in no way rests upon the test result for A' nor on the assumption that A' is actually mother of a. In fact, A' might as well have remained untested, and it is therefore clear that, for any genetic system, $P(A\bar{\mathbf{F}}a) = C$.

The symbol $(AA'\bar{\mathbf{P}}a)$ may be regarded as an abbreviated notation for the statement $A\mathbf{F}a \,.\, A'\mathbf{M}a \,.\, AA'\bar{\mathfrak{P}}a$, to be read in general: "A may be father of a, and A' may be mother of a, but A and A' are not jointly parents of a." This, of course, is a kind of negation of "A is father of a, and A' is mother of a" and allows three possible interpretations. Under certain conditions the result $(AA'\bar{\mathbf{P}}a)$ may be taken as disproof of maternity alone, as, for example, in a one-sire herd where paternity can be considered indisputable. In the following section we shall mention situations in which $(AA'\bar{\mathbf{P}}a)$ may be accepted as evidence of non-parentage for both A and A'. But, in connection with disputed paternity investigations, $AA'\bar{\mathbf{P}}a$ may be said to provide a *conditional exclusion of paternity*, the condition being that we accept A' as mother of a. Ordinarily, such exclusions will be considered just as forceful as unconditional exclusions of paternity, and the distinction is therefore primarily of interest from the view that $AA'\bar{\mathbf{P}}a$ can have different interpretations under varying circumstances.

As shown by Wiener *et al.* (1930), $P(AA'\bar{\mathbf{P}}a) = \theta - 3\theta^2$ for two genes lacking dominance, while $P(AA'\bar{\mathbf{P}}a) = \theta q^3$ for two genes with dominance. Hence, if we let $(A\bar{\mathfrak{F}}a)$ stand for either unconditional or conditional exclusion of paternity, i.e.

$$A\bar{\mathfrak{F}}a \equiv A\bar{\mathbf{F}}a \wedge AA'\bar{\mathbf{P}}a,$$

and let $D = P(A\bar{\mathfrak{F}}a)$ on the hypothesis of this section, we have

$$D' = C' + \theta - 3\theta^2 = \theta(1 - \theta)$$

and

$$D'' = C'' + \theta q^3 = \theta q^3.$$

These functions have the following maximal values: max $D' = 0.1875$ at $\theta = \frac{1}{4}$, and max $D'' = 0.08192$ at $p = 0.2$ or at dominant trait (antigen) frequency $p(2 - p) = 0.36$ (fig. 1).

In reference to maternity, we may use symbols $(A'\mathbf{M}a)$, $(A'\bar{\mathbf{M}}a)$ and $(A'\bar{\mathfrak{M}}a)$ with meanings analogous to the three statements concerning paternity, and

it is evident that we could write $C = P(A'\overline{\mathbf{M}}a)$ and $D = P(A'\overline{\mathfrak{M}}a)$ under conditions in which A and A' are reversed in the statement of the hypothesis of this section.

EXCLUSION OF JOINT PARENTAGE

Suppose that tests are made on three individuals, a man (A), a woman (A') and a child (a), A and A' being unrelated to each other and to the child a. For any given serological system, test results will permit any one of five possible statements, with probabilities as shown:

Conclusion	*For two-gene systems lacking dominance:*	*For two-gene systems with dominance:*
$A\tilde{\mathbf{F}}a \,.\, A'\overline{\mathbf{M}}a$	$\theta^2 - 2\theta^3$	0
$A\mathbf{F}a \,.\, A'\mathbf{M}a$	$\theta^2 + 2\theta^3$	0
$A\mathbf{F}a \,.\, A'\overline{\mathbf{M}}a$	$\theta^2 + 2\theta^3$	0
$AA'\bar{\mathbf{P}}a$	$2\theta - 8\theta^2 + 4\theta^3$	$\theta q^3(1 + q)$
$AA'\mathfrak{P}a$	$1 - 2\theta + 5\theta^2 - 6\theta^3$	$1 - \theta q^3(1 + q)$

Although only one of these statements definitely denies parentage for both A and A', there are a number of medicolegal situations in which we are willing to accept any one of the first four statements as evidence that hypothesis R_0 is true and that, accordingly, neither A nor A' is parent of a. Hence, we may define

$$AA'\bar{\mathfrak{P}}a \equiv (A\bar{\mathbf{F}}a \,.\, A'\overline{\mathbf{M}}a) \wedge (A\bar{\mathbf{F}}a \,.\, A'\mathbf{M}a) \wedge (A\mathbf{F}a \,.\, A'\overline{\mathbf{M}}a) \wedge (AA'\bar{\mathbf{P}}a),$$

that is, as any one of the first four outcomes, and let E stand for the probability of $AA'\bar{\mathfrak{P}}a$ for any system. As is shown above, we have

$$E' = 2\theta - 5\theta^2 + 6\theta^3$$

and

$$E'' = \theta q^3(1 + q)$$

for two-gene systems, without or with dominance, respectively. These functions have maxima as follows: max $E' = 0.28125$ at $\theta = \frac{1}{4}$, and max $E'' = 0.14815$ at $p = 0.18350$ or at antigen frequency $p(2 - p) = \frac{1}{3}$ (fig. 1).

Examples of medicolegal situations which conform to the hypothesis of this section and which also generally permit $AA'\bar{\mathfrak{P}}a$ to be accepted as a "solution" are the following:

1) A couple, A and A', falsely claim a as their lost, strayed or kidnapped child;

2) Individual a falsely claims A and A' as parents, in order to gain a legal inheritance;

3) The couple, A and A', correctly disclaim a as their child, alleging hospital interchange of two infants;

4) A woman, A', accuses A of paternity of the child a, which is neither the offspring of A or of A'.

Wiener (1945) relates an instance of the last-mentioned situation, in which the MN blood types revealed that $A \epsilon MN$, $A' \epsilon NN$ and $a \epsilon MM$, a result of the type $A\mathbf{F}a \,.\, A'\overline{\mathbf{M}}a$, which led to the disclosure that A' had obtained the child from an orphanage.

It may be noted that the general problem dealt with in this section has been referred to by Fisher (1951) as the problem of "interchange," but as this term seems descriptive of but one of the situations mentioned above, I prefer the expression "exclusion of joint parentage" and will use "interchange" in reference to the more complicated problem to be considered next, and one which has been previously dealt with under the same title by Wiener (1931).

DETECTION OF INTERCHANGE

We may now consider the problem wherein two children, a and b, have been assigned through error to parents A and A' and B and B', respectively, a being the child of B and B', and b being the child of A and A'. We assume further that no two of the four parents (A, A', B, B') are related. Tests on the six individuals will now permit any one of four general conclusions:

$$
\begin{aligned}
g_{ab} &\equiv AA'\overline{\mathfrak{P}}a \,.\, BB'\overline{\mathfrak{P}}b \,.\, AA'\mathfrak{P}b \,.\, BB'\mathfrak{P}a \\
g_{a} &\equiv AA'\overline{\mathfrak{P}}a \,.\, BB'\mathfrak{P}b \,. \quad '' \quad '' \\
g_{b} &\equiv AA'\mathfrak{P}a \,.\, BB'\overline{\mathfrak{P}}b \,. \quad '' \quad '' \\
g_{0} &\equiv AA'\mathfrak{P}a \,.\, BB'\mathfrak{P}b \,. \quad '' \quad ''
\end{aligned}
$$

Denoting the probabilities of these four outcomes by G_{ab}, G_a, G_b, and G_0, respectively, we find, for the case of two genes lacking dominance:

$$
\begin{aligned}
G'_{ab} &= 4\theta^2 - 8\theta^3 + 2\theta^4, \\
G'_{a} &= 2\theta - 9\theta^2 + 14\theta^3 - 2\theta^4, \\
G'_{b} &= 2\theta - 9\theta^2 + 14\theta^3 - 2\theta^4, \\
G'_{0} &= 1 - 4\theta + 14\theta^2 - 20\theta^3 + 2\theta^4,
\end{aligned}
$$

and, for the case of two genes showing dominance:

$$
\begin{aligned}
G''_{ab} &= 0, \\
G''_{a} &= \theta q^3(1 + q), \\
G''_{b} &= \theta q^3(1 + q), \\
G''_{0} &= 1 - 2\theta q^3(1 + q).
\end{aligned}
$$

We may note first the obvious relations

$$G'_{ab} + G'_{a} = G'_{ab} + G'_{b} = 2\theta - 5\theta^2 + 6\theta^3 = E'$$

and

$$G''_{ab} + G''_{a} = G''_{ab} + G''_{b} = \theta q^3(1 + q) = E''$$

which connect the present problem with that of the preceding section. However, it is also apparent that the exclusions of parentage are not independent for a and b. For two genes with dominance, "bilateral" exclusions are impossible, i.e. $G_{ab} = 0$, whereas for two genes without dominance G'_{ab} exceeds E'^2 by the quantity

$$G'_{ab} - E'^2 = 12\theta^3 - 47\theta^4 + 60\theta^5 - 36\theta^6,$$

which is positive for all positive values of θ. In general, for any genetic system, we should expect that $G_{ab} \neq E^2$. This non-independence is clearly a result of the two restrictions $P(AA'\mathfrak{P}b) = P(BB'\mathfrak{P}a) = 1$, and it accounts for the fact that Fisher's "interchange" probabilities alone are insufficient for answering the two-child problem here considered.

Now, Wiener (1931) adopts the view that we may accept as evidence of interchange of a and b a result excluding parentage for *either one or both* of the assigned pairs of parents, and he therefore takes

$$*G' = G'_{a} + G'_{b} + G'_{ab} = 4\theta - 14\theta^2 + 20\theta^3 - 2\theta^4$$

and

$$*G'' = G''_{a} + G''_{b} + G''_{ab} = 2\theta q^3(1 + q)$$

as the chances of "reaching a solution" of such problems by means of two-gene systems, by which is evidently implied a recommendation for reversal of a and b.

One can indeed imagine circumstances in which one might be willing to assume that if, for example, a has been shown to be not the child of A and A', then b must be the proper child of this couple, even though tests fail to establish that b is not the child of B and B'. Such an assumption could be made if, in a certain maternity hospital, only two mothers were confined at the time, and if introduction of a third baby from the outside could be dismissed as a possibility. Also, a unilateral exclusion might be considered sufficient if the two children, a and b, were found to have identification tags bearing the family names "B" and "A", respectively, as happened in a case described by Wiener (1931). But, considering the more usual circumstances in maternity hospitals, and the fact that such alleged interchanges are frequently contested by one couple involved, it would seem more reasonable to demand in general a bilateral exclusion of the type $AA'\mathfrak{P}a \cdot BB'\mathfrak{P}b$.

Suppose, for instance, that A and A' correctly disclaim a as their child but incorrectly name b as their rightful child, whereas b has in fact been assigned to its real parents, B and B'. Tests performed on the six individuals would now

permit 8 possible conclusions, which, for the case of two genes lacking dominance, have probabilities as shown:

(1)	$AA'\overline{\mathfrak{P}}a \,.\, BB'\overline{\mathfrak{P}}a \,.\, AA'\mathfrak{P}b \,.\, BB'\mathfrak{P}b$	$2\theta^3 - 4\theta^4 + 8\theta^5$
(2)	$AA'\overline{\mathfrak{P}}a \,.\, BB'\overline{\mathfrak{P}}a \,.\, AA'\mathfrak{P}b \,.$ "	$2\theta - 15\theta^2 + 40\theta^3 - 27\theta^4 - 2\theta^5$
(3)	$AA'\overline{\mathfrak{P}}a \,.\, BB'\mathfrak{P}a \,.\, AA'\overline{\mathfrak{P}}b \,.$ "	$6\theta^2 - 18\theta^3 + 6\theta^4 - 8\theta^5$
(4)	$AA'\mathfrak{P}a \,.\, BB'\overline{\mathfrak{P}}a \,.\, AA'\overline{\mathfrak{P}}b \,.$ "	$2\theta^2 - 4\theta^3 + 3\theta^4 - 14\theta^5$
(5)	$AA'\overline{\mathfrak{P}}a \,.\, BB'\mathfrak{P}a \,.\, AA'\mathfrak{P}b \,.$ "	$4\theta^2 - 18\theta^3 + 25\theta^4 + 2\theta^5$
(6)	$AA'\mathfrak{P}a \,.\, BB'\overline{\mathfrak{P}}a \,.\, AA'\mathfrak{P}b \,.$ "	$8\theta^2 - 32\theta^3 + 28\theta^4 + 8\theta^5$
(7)	$AA'\mathfrak{P}a \,.\, BB'\mathfrak{P}a \,.\, AA'\overline{\mathfrak{P}}b \,.$ "	$2\theta - 13\theta^2 + 26\theta^3 - 5\theta^4 + 14\theta^5$
(8)	$AA'\mathfrak{P}a \,.\, BB'\mathfrak{P}a \,.\, AA'\mathfrak{P}b \,.$ "	$1 - 4\theta + 8\theta^2 + 4\theta^3 - 26\theta^4 - 8\theta^5$

The ideal solution would be to acknowledge couple A's non-parentage of a, but search elsewhere for their misplaced child, and such a conclusion would be forced by outcomes (1), (2) and (3), with probability $2\theta - 9\theta^2 + 24\theta^3 - 25\theta^4 - 2\theta^5$, which has a maximal value of 0.21289 at $\theta = \frac{1}{4}$. A less fortunate solution would be to dismiss A's claim altogether, as recommended by (4), (6), (7) and (8), with probability $1 - E'$, having a minimal value of 0.71875. But, in outcome (5) we have a result identical with g_a in the list of outcomes on the hypothesis of interchange, which, if we were to accept unilateral exclusions of parentage, would recommend reversal of a and b. Misfortune might then be compounded, and *three* babies would now be assigned to the wrong parents.

The initial probability of result (5) is small on the hypothesis of interchange of a and c, having a maximal value of 0.06836 for two genes lacking dominance. But, supposing that couple A and A' have already been excluded as parents of a—a fact which would certainly urge hospital authorities to test other children and their assigned parents and might well encourage participation of couples who originally had no reason to suspect interchange involving their child—the probability is now

$$\frac{4\theta - 18\theta^2 + 25\theta^3 + 2\theta^4}{2 - 5\theta + 6\theta^2}$$

that tests for the same two-gene system would yield the result $AA'\mathfrak{P}b \,.\, BB'\mathfrak{P}a$ for any non-involved child and its parents. At $p = 0.10$ this function has the value 0.14547, and it reaches a maximum of 0.24306 at $\theta = \frac{1}{4}$. In like manner, any other genetic system giving the result $AA'\overline{\mathfrak{P}}a$ would have its usefulness curtailed for the simultaneous cross-exclusions, although, by taking several genetic systems, the probability of (5) could doubtless be made quite small.

When there is reason to doubt the supposition that only one possible child could have been substituted for a, it would therefore seem desirable, if not essential, to require bilateral exclusions, i.e. exclusion of joint parentage for *both* pairs of assigned parents. This greatly reduces the chance for "detection" of interchange, if we consider any single serological system. As already mentioned, $G''_{ab} = 0$ for two genes showing dominance, and the corresponding value for genes lacking dominance is $G'_{ab} = 4\theta^2 - 8\theta^3 + 2\theta^4$, which has a maximal value of 0.13281 at $\theta = \frac{1}{4}$. By contrast, the corresponding maxima are max $*G'' = 0.29630$ and max $*G' = 0.42969$, if one were prepared to accept unilateral as well as bilateral exclusions (fig. 1).

The situation is considerably improved, however, when we take into consideration two or more genetic systems, since, in addition to bilateral exclusions obtained through tests for any single system, we shall also have complementary unilateral exclusions obtained through any two or more systems. For example, if $g_{ab.1}$, $g_{a.1}$, $g_{b.1}$, $g_{0.1}$ and $g_{ab.2}$, $g_{a.2}$, $g_{b.2}$, $g_{0.2}$ represent the four possible outcomes with respect to two genetic systems, a bilateral exclusion would now be furnished by any of the following combined outcomes:

$g_{ab.1} \cdot g_{ab.2}$	$g_{ab.1} \cdot g_{a.2}$	$g_{ab.1} \cdot g_{b.2}$	$g_{ab.1} \cdot g_{0.2}$
$g_{a.1} \cdot g_{ab.2}$		$g_{a.1} \cdot g_{b.2}$	
$g_{b.1} \cdot g_{ab.2}$	$g_{b.1} \cdot g_{a.2}$		
$g_{0.1} \cdot g_{ab.2}$			

With three or more systems, we would also have favorable outcomes of the sort: $g_{a.1} \cdot g_{b.2} \cdot g_{0.3} \cdots$, etc.

In general, if we have s genetically independent systems, and denote by $G_{ab.i}$, $G_{a.i}$, $G_{b.i}$, $G_{0.i}$ the probabilities of the four outcomes for any (ith) system, the total probability of detecting interchange by means of bilateral exclusions of parentage will be given by

$$G_s = 1 - 2\prod_{i=1}^{s}(1 - E_i) + \prod_{i=1}^{s} G_{0.i},$$

where $1 - E_i = G_{a.i} + G_{0.i} = G_{b.i} + G_{0.i}$. This may be compared with

$$*G_s = 1 - \prod_{i=1}^{s} G_{0.i},$$

the corresponding probability, suggested by Wiener, appropriate for exclusions of one or both pairs of assigned parents, and with

$$E_s^2 = \left\{1 - \prod_{i=1}^{s}(1 - E_i)\right\}^2,$$

which would be the appropriate probability if the exclusions of parentage were independent for a and b for all systems.

Some idea of the effectiveness of multiple genetic systems in raising the probability of bilateral parentage exclusions (G_s) can be seen from table 1, where we assume s genetically independent 2-gene systems, each lacking dominance and each having ideal gene ratios for exclusions of parentage ($\theta_i = \frac{1}{4}$, for all systems). This probability can be designated as max G'_s, and the corresponding value appropriate to unilateral and/or bilateral exclusions as max $^*G'_s$. Numerical values are given for $s = 1, 2, \cdots 6$, and we may note that 3 ideal 2-gene systems lacking dominance would insure about 81 per cent exclusions of parentage for one or both children, but only 44 per cent bilateral exclusions. These figures are probably not far different from what would be expected using the M-N, A-B-O and Rh blood types in the United States, assuming Rh-classifications employing the four most commonly available antibodies.

TABLE 1. MAXIMAL PROBABILITIES FOR DETECTION OF INTERCHANGE, ASSUMING s INDEPENDENT TWO-GENE SYSTEMS, WITH OR WITHOUT DOMINANCE

	PARENTAGE EXCLUSIONS (NO DOMINANCE)		PARENTAGE EXCLUSIONS (DOMINANCE)		MATERNITY EXCLUSIONS (NO DOMINANCE)	
s	max G'_s	max $^*G'_s$	max G''_s	max $^*G''_s$	max H'	max $^*H'_s$
1	0.13281	0.42969	0	0.29630	0.03125	0.21875
2	0.29205	0.67474	0.04390	0.50480	0.07910	0.38965
3	0.44288	0.81450	0.11218	0.65153	0.13699	0.52316
4	0.57203	0.89421	0.19208	0.75478	0.20017	0.62747
5	0.67670	0.93967	0.27544	0.82744	0.26522	0.70896
6	0.75867	0.96559	0.35722	0.87857	0.32978	0.77263

An even more stringent criterion might sometimes be used in judging the occurrence of interchange. In the above discussion we have assumed that any one of the four kinds of exclusion of joint parentage, *viz.*

$$AA'\overline{\mathfrak{P}}a \equiv (A\bar{\mathbf{F}}a \,.\, A'\,\overline{\mathbf{M}}a) \wedge (A\mathbf{F}a \,.\, A'\overline{\mathbf{M}}a) \wedge (A\bar{\mathbf{F}}a \,.\, A'\mathbf{M}a) \wedge (AA'\overline{\mathbf{P}}a)$$

would be acceptable as evidence for the misassignment of child a, and similarly for child b. However, hospital authorities, when charged with the responsibility for interchanging two infants, might be unwilling to accept exclusions of the last two sorts as evidence for interchange, since such findings could be equally explained by extramarital conceptions.

We shall therefore consider next the probability of detecting interchange under conditions in which we require an unconditional exclusion of maternity for both of the assigned mothers, A' and B', in respect to two unrelated interchanged children, a and b. These probability functions will, of course, also apply when tests have been made on only four individuals, as, for example, in cases involving two cows and their interchanged calves, the sires being as-

sumed to be uncertain (though not identical or related) or, for any reason, untested. As before, we assume that no two of the four parents are related.

TABLE 2. TWO-GENE SYSTEMS LACKING DOMINANCE. MAXIMAL EXCLUSION FOR A SINGLE SYSTEM, AND NUMBERS OF IDEAL SYSTEMS REQUIRED FOR EXCLUSIONS OF SPECIFIED FREQUENCY

†KIND OF EXCLUSION	MAXIMAL EXCLUSION at $\theta = \frac{1}{4}$	‡NUMBER OF IDEAL SYSTEMS REQUIRED FOR EXCLUDING AT LEAST: 50%	70%	90%	95%	99%
Identity (I')	0 625	1	2	3	4	5
Monozygosity (J')	0.40625	2	3	5	6	9
Parent-child (C')	0.125	6	10	18	23	35
Paternity (D')	0.1875	4	6	12	15	23
Joint Parentage (E')	0.28125	3	4	8	10	14
In interchange of a and b:						
Parentage for both (G'_b)	0.1328125	4	6	9	12	17
Parentage for a and/or b ($*G'$)	0.4296875	2	3	5	6	9
Maternity of both (H'_{ab})	0.03125	9	14	23	28	40
Maternity of a and/or b ($*H'$)	0.21875	3	5	10	13	19

† For explicit statement of the hypothesis and assumed requirements for exclusion, see text in relation to the indicated probability function, I', J', C', etc.

‡ By "ideal" system is meant one giving maximal exclusion, with $p = q$, or $\theta = \frac{1}{4}$.

We require, therefore, the probabilities corresponding to the four conclusions:

$$h_{ab} \equiv A'\bar{\mathbf{M}}a \,.\, B'\bar{\mathbf{M}}b \,.\, A'\mathbf{M}b \,.\, B'\mathbf{M}a$$

$$h_a \equiv A'\bar{\mathbf{M}}a \,.\, B'\mathbf{M}b \,. \quad " \quad "$$

$$h_b \equiv A'\mathbf{M}a \,.\, B'\bar{\mathbf{M}}b \,. \quad " \quad "$$

$$h_0 \equiv A'\mathbf{M}a \,.\, B'\mathbf{M}b \,. \quad " \quad "$$

Denoting these, in general, by H_{ab}, H_a, H_b, H_0, we have, for two genes lacking dominance:

$$H'_{ab} = 2\theta^3,$$

$$H'_a = 2\theta^2 - 2\theta^3,$$

$$H'_b = 2\theta^2 - 2\theta^3,$$

$$H'_0 = 1 - 4\theta^2 + 2\theta^3.$$

Again we may note that the exclusions of maternity for the assigned mothers of a and b are not independent, and that $H'_{ab} > C'^2$ for all positive values of θ. But, even at the ideal gene ratio ($p = q = \frac{1}{2}$) the probability for bilateral exclusion of maternity is only: max $H'_{ab} = 0.03125$. If, however, we were will-

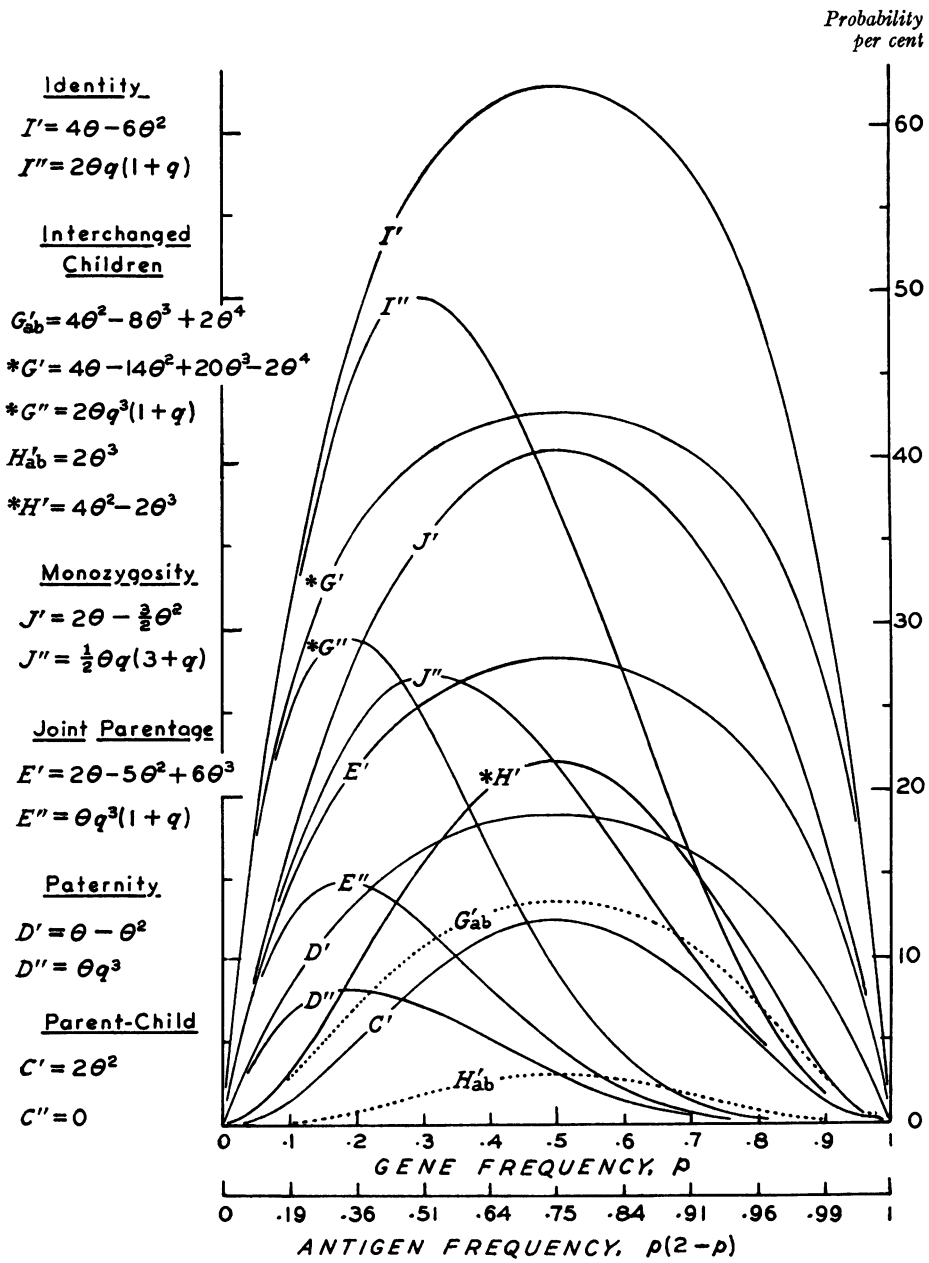

FIG. 1. Probabilities of exclusion of certain specified relationships under six situations commonly arising in medicolegal problems. Symbols C', D', $\cdots$ J' stand for probabilities using a 2-gene system lacking dominance (e.g. M-N types), while C'', D'', $\cdots$ J'' are the corresponding probabilities for two genes with dominance (e.g. any single antigenic factor, with gene frequency p), and $\theta = pq$. "Parent-child" refers to unconditional exclusion of paternity (or maternity); for description of the other situations, see text.

ing to accept unilateral as well as bilateral exclusions of maternity as evidence for interchange, we would have

$$*H' = 1 - H'_0 = 4\theta^2 - 2\theta^3,$$

having max $*H' = 0.21875$ at $\theta = \frac{1}{4}$ (fig. 1). Maximal exclusion frequencies for s independent and ideal 2-gene systems without dominance, i.e. max H'_s and max $*H'_s$, are given in table 1, being found by application of

$$H_s = 1 - 2\prod_{i=1}^{s}(1 - C_i) + \prod_{i=1}^{s} H_{0.i}$$

and

$$*H_s = 1 - \prod_{i=1}^{s} H_{0.i}.$$

Since $C'' = 0$, it is clear that $H''_{ab} = H''_a = H''_b = 0$ and that 2-gene systems showing dominance are useless for establishing interchange on the basis of maternity exclusions, however many such systems we may employ.

Table 2 summarizes, for each of the several problems discussed, the maximal frequency of exclusion attainable with a single two-gene system lacking dominance. Also listed are the numbers of ideal systems of this type which would be needed to insure an expected exclusion rate of at least 50, 70, 90, 95 or 99 per cent.

A final word might be added concerning the acceptance of hypothesis R_1 or R_0. The principle that "blood groups can disprove paternity but can never prove paternity" has been widely quoted. Similarly, it is apparent that monozygosity or identity can be disproved by a single observed difference, but cannot be proved in an absolute sense.

It also follows that when R_1 has been disproved, we cannot say that R_0 has been proved to the exclusion of all conceivable alternatives. Thus, we may be willing to assume that virtually all pairs of twins which are not monozygotic (R_1) will be dizygotic full-sibs, and this assumption provides the basis for the probability problem considered above. But disproof of monozygosity, in any instance, does not prove that a and b are full-sib twins, or even twins of any kind; it can be said to do so only if we are willing to dismiss further possibilities, such as half-sib twins, individuals falsely represented as twins, etc. In relation to interchange problems, even an outcome satisfying the most rigorous criterion—disproof of maternity for both assigned mothers—can be said to prove interchange of a and b, only if we are willing to overlook more complicated situations, such as substitutions involving three or more children.

SUMMARY

Depending on conditions surrounding different cases of alleged interchange of two children, one may adopt various criteria for the establishment of interchange, for example: (1) exclusion of joint parentage for both assigned pairs

of parents, (2) exclusion of joint parentage for at least one of the two pairs of parents, (3) exclusion of maternity for both assigned mothers, or (4) exclusion of maternity for at least one assigned mother. Probability functions are given, assuming suitable serological or other genetic factors dependent upon two allelic autosomal genes, with or without dominance, and the general procedure for compounding the probabilities for several genetic systems is indicated.

REFERENCES

FISHER, R A. 1951. Standard calculations for evaluating a blood-group system. *Heredity*, 5: 95–102.

RIFE, D. C. 1938. Simple modes of inheritance and the study of twins. *Ohio.J Sc.* 38: 281–293.

WIENER, A. S. 1931. Chances of detecting interchange of infants, with special reference to blood groups. *Zschr. indukt. Abstamm.* 59: 227–235.

WIENER, A. S. 1935. Heredity of the agglutinogens M and N of Landsteiner and Levine. IV. Additional theoretico-statistical considerations. *Human Biol.* 7: 222–239.

WIENER, A. S. 1945. *Blood Groups and Transfusion.* Third edition. Springfield, Ill.: Thomas. Pp. 438.

WIENER, A. S., LEDERER, M., & POLAYES, S. H. 1930. Studies in isohemagglutination. IV. On the chances of proving non-paternity; with special reference to blood groups. *J. Immun.*, Balt. 19: 259–282.