TYPES OF EXCLUSION AND EFFICIENCY CRITERIA FOR PATERNITY TESTINGS.

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More than a hundred different genetic systems suitable for paternity testings have been described in man. This fact, being a remarkable achievement in itself by the very high exclusion efficiency that can be attained in the expertises, is at the same time a source of problems. Indeed, no laboratory is able to perform (at least routinely) all of them, and - on the other hand - besides technical problems, the cost of such an investigation would be prohibitive.

Therefore, it is necessary to select from the available list of polymorphisms some to be included in a practical routine battery of genetic tests. Two kinds of criteria can be used for this choice: a) technical / economical costs or b) potential information content.

The analysis of the first type of criteria being outside the purpose of this work, we shall discuss only the ways to mesure the usefulness of genetic systems in paternity expertises under the assumption of identical costs. In fact, we do not believe that a standardized cost for any phenotyping can be calculated, even inside the same country, due to the enormous differences in personal, equipment and management between the different laboratories.

THE MEASUREMENT OF THE USEFULNESS OF A GENETIC SYSTEM

The usefulness of a genetic system in the field of paternity expertising has been measured by the exclusion power (exclusion efficiency or "a priori" probability of exclusion. The concept can be extended to a battery of tests, and is then defined as the probability of obtaining at least one exclusion, given a random mother-child pair and a random non-father. This parameter has been used under the assumption of equal costs and technical difficulties as a basis of decision for the elaboration of the list of genetic markes to be included in an optimized battery of tests (SALMON et al., 1980).However, this parameter overlooks the different reliability of the two types of exclusion according to LANDSTEINER's rules. In short words, it would make no sense to organize a battery of genetic tests in which most of exclusions are expected to be unique and by the second rule; in most cases, then, a reasonable doubt on the possible presence of a silent gene would prevent a veredict of true exclusion.

Thus, we made an atempt to study the properties of the distribution probabilities of the two types of exclusion together with the total power of exclusion in codominant systems.

1st AND 2nd RULE EXCLUSION: DISTRIBUTION PROPERTIES

The calculation of the total power of exclusion of a genetic system with k codominant alleles with frequencies p_1, p_2 ... p_k has been derived, for instance, by SELVIN (1980). Following the approach of this author, the expression for the probability of exclusion by the second rule is easily derived, since these can only occur in one mother/child type: AX / AA where X represents any of the k alleles, including A. If the frequency of this mother/child pair is given by p_1^2 and the corresponding excludable man by: $p_2^2 + p_3^2 + \ldots + p_k^2$. Therefore the general formula for second order exclusion probability in codominant system can be written as

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$$\sum_{i=1}^{k} \left(pi^2 \times \sum_{\substack{j=1 \\ j \neq i}}^{k} pj^2 \right)$$

For 2-allele systems, the results are easily visualized in the graphic form (Fig. 1).

The main fact to underline from this distribution is that while total power of exclusion is maximum for equally frequent alleles, first rule exclusion reach a maximum when the alleles have very assymetric frequencies, decreasing afterwords.

DISCUSSION AND CONCLUSIONS

From these results it turns out obvious that the choice of the genetic systems to be included in a battery of genetic tests is a much more delicate operation than just ordering them by their total power of exclusion. Indeed, it is contradictorious to construct a battery of tests optimized on the basis of the total power of exclusion, if a single exclusion by the second rule (or, according to some authors, two) is not considered sufficient. Therefore it seems justified to use the formula derived above, to materialize another criterion for optimization of a sequence of markers: the exclusion efficiency by the first rule.

In order to demonstrate the contradiction between the two criteria, in Table 1 we compare the ordination of some polymorphic systems currently used in paternity testings, according to each of them. It is symptomatic that only 2 of the systems do not change their position in the sequences, those with both maximum and minimum total and 1st rule exclusion powers. However, the practical implications of the distribution properties of total and 1st rule exclusion chances are only realized when the "optimized" sequence excludes some of the technically available markers.

In order to simplify the calculations we assumed a very ideal situation in which 20 polymorphic markers can be freely chosen (i.e without technical or financial limitations) from systems with maximum power either total or according to the 1st rule.The results of the application of the referred oposite strategic choices are shown in Table 2. Again it is clear that optimization based in the total exclusion efficiency has a serious drawback: the low reliability of many of the obtained exclusions. On the other hand, when the oposite criterion is used, an apparent decrease in the total exclusion power, is compensated by the high reliability of the obtained exclusions.

Thus it seems to us that the only unambiguous criterion for optimization of a sequence of genetic markers for paternity testings is the exclusion power by the first rule.

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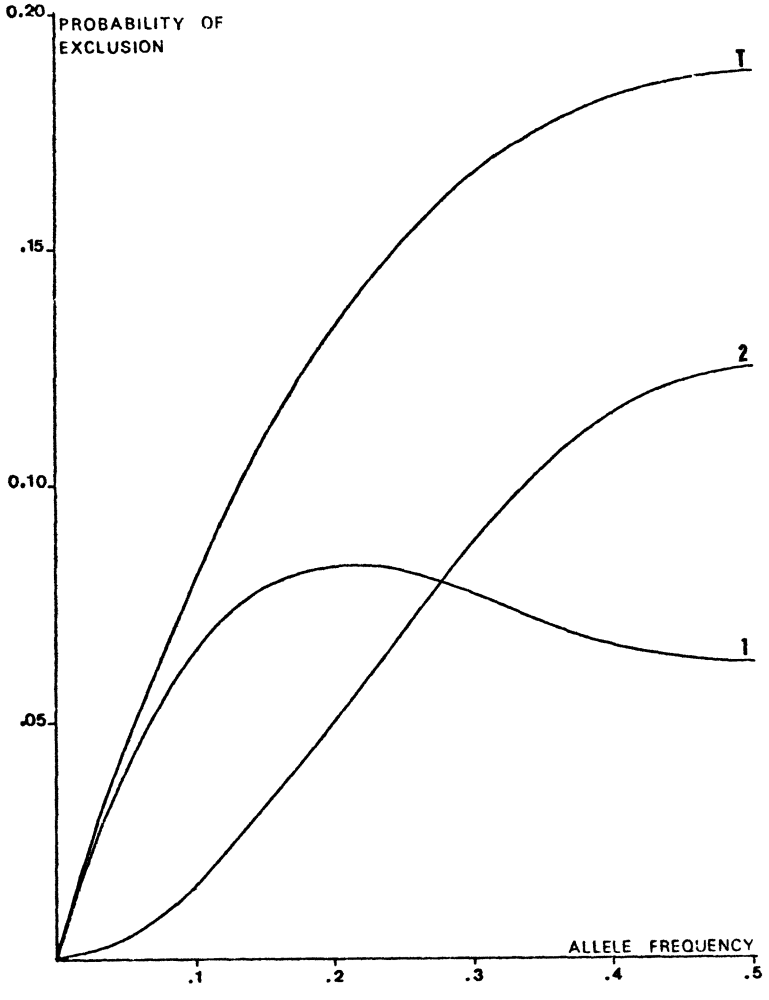

Fig. 1. Probabilities of exclusion in codominant 2-allele systems. (T: total; 1: first rule and 2: 2nd rule probabilities of exclusion)

TABLE 1

Optimized sequences of some genetic markers used routinely in our Institute, according to total and 1st rule exclusions

	Exclusion powers (%)		Ordination according to	
System	Total	1st rule	Total	1st rule
ACP1	22.69	15.45	1	1
GPT	20.03	8.03	2	5
GLO	18.54	6.45	3	9
HP	18.28	6.69	4	8
ME2	18.19	6.76	5	7
PGM3	14.64	8.29	6	4
C3	12.80	9.11	7	3
ESD	12.33	9.14	8	2
PGP	8.66	7.90	9	6
ADA	3.35	3.11	10	10

TABLE 2

Examples of outcomes from classical and first rule exclusion strategies in the choice of genetic systems for paternity testings.

Nr.of systems with maximum total excl. power	Nr.of systems with maximum excl.power by 1st rule	Total exclusion probability Pex (%)	1st rule excl.prob. P1 (%)	P1/Pex
20	0	98	72	.73
15	5	98	75	.77
10	10	97	78	.80
5	15	96	80	.83
0	20	95	82	.86