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Biostatistical evaluation of blood group, HLA and DNA findings in Jeffreys' immigrant test-case using special kinship and DNA algorithms

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Summary. In the immigration case cited by Jeffreys et al. (1985), the biostatistical evaluation of blood group findings in 16 systems and of HLA-A,B findings for the mother and child, using a special kinship algorithm developed by Ihm and Hummel (1975), produced a probability of maternity of the Ghanaian-born putative mother of W = 6%; the probability of maternity for her sister was W = 94%. Using the DNA multilocus probes 33.15 and 33.6 and the bandsharing technique, the authors analysed band patterns from the putative mother and child as well as another 3 children of the same woman. It was concluded that the putative mother was the mother of all 4 children. An evaluation of the band patterns using the multi-di-allelism model and the kinship algorithm in accordance with the Essen-Möller principle produced: W = 99.99999999999999991%, or, if the "-----" constellations were not considered, W = 99.99998%.

Key words: Probability of maternity – Biostatistics: Blood groups, HLA, DNA

Zusammenfassung. Die biostatistische Auswertung der in dem bekannten Immigrantenfall [Jeffreys et al. (1985)], bei Mutter und Kind ermittelten Blutgruppenbefunde in 16 Systemen und der HLA-A,B-Befunde unter Verwendung eines speziellen Kinship-Algorithmus von Ihm und Hummel (1975) brachte zugunsten leiblicher Mutterschaft der aus Ghana stammenden Putativmutter W = 6%; W = 94% ist die Mutterschaftswahrscheinlichkeit für deren Schwester. Anhand der Bandenmuster von Mutter und Kind sowie weiterer 3 Kinder dieser Frau, erhalten mit den DNA-Multilocus-Sonden 33.15 und 33.6, kamen die Autoren – unter Anwendung des Band-sharing-Verfahrens – zum Schluß, *alle* 4 Kinder stammten von der Putativ-Mutter. Die Auswertung der Bandenmuster unter Anwendung des Modells multipler Diallelie und des Kinship-Algorithmus brachte nach dem Prinzip von Essen-Möller W = 99,99999999999999991%, ohne "-----" Konstellation W = 99,99998%.

Schlüsselwörter: Mutterschaftswahrscheinlichkeit – Blutgruppengutachten – HLA-Gutachten – DNA-Gutachten

Biostatistical evaluation of blood group and HLA findings in Jeffreys' case

The question in the immigration test-case of Jeffreys et al. (1985) is whether Ms Sa. is the *mother* or the *aunt* of the child A.G. Dr. L. calculated the exclusion expectation for nonmothers from blood group and HLA findings[1] provided by Mr. R. However, the figure is not relevant to the present case, because if Ms Sa. is *not* the mother of A.G., her *sister* is, and non an *arbitrary* woman from the same population.

From the blood group and HLA (A and B loci) findings for Ms Sa. and A.G., we have calculated the probabilities that:

a) Ms Sa. is the mother of A.G., and
b) that the sister of Ms Sa. is the mother of A.G.

We have assumed that the cohabitant in case a) is *not* the same man as the cohabitant in case b).

The null hypothesis (X in Essen-Möller's formula: Essen-Möller 1938) has the pedigree X (Fig. 1).

The alternative hypothesis (Y in Essen-Möller's formula) has the pedigree Y (Fig. 2).

The probability that Ms Sa. is the mother, is then

$$W_{Sa} = \frac{f(X)}{f(X) + f(Y)}$$

and the probability that her sister is the mother, is

$$W_{Au} = \frac{f(Y)}{f(Y) + f(X)} = 1 - W_{Sa},$$

where f(X) denotes the frequency of pedigree X and f(Y) that of pedigree Y.

The formulae for W_{Sa} and W_{Au} fulfil the conditions of Bayes' Theorem, including Bayes' Postulate (i.e., a neutral prior probability of 0.5).

[1] I wish to thank Professor Alex Jeffreys, Leicester, England, for these data

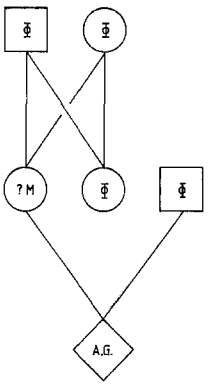

Fig. 1. Pedigree for the case that Ms Sa. is the mother of child A.G.

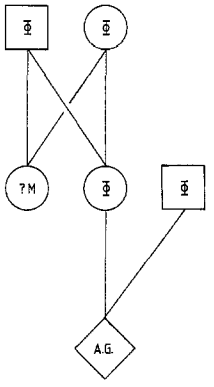

Fig. 2. Pedigree for the case that the sister of Ms Sa. is the mother of the child A.G. ⊕ denotes persons for whom there are no findings

We used the "kinship algorithm" of Ihm and Hummel (1975) to calculate f(X) and f(Y) from the blood group findings. We used the same algorithm for the HLA-A,B findings, modified for an "ad hoc" system (Hummel and Conradt 1990).

Expressed as EM = lg [f(Y)/f(X)] + 10, the findings in 16 blood group systems (using North African negro frequencies wherever possible) gave:

$$EM = 11.4996.$$

For the HLA,A,B findings (again using North African negro haplotype frequencies)

$$EM = 9.7042.$$

Combining the two values gives

$$EM = 11.2039,$$

from which $W_{Sa} = 6\%$,
and $W_{Au} = 94\%$.

The explanation for the large value of W_{Sa} lies in the *negative* influence of the *Hp* constellation on the findings for Ms Sa. and A.G. (Ms Sa.: Hp 2; A.G.: Hp 1).

Excluding the Hp results,

$$EM = 9.1469,$$

from which $W_{Sa} = 87\%$,
and $W_{Au} = 13\%$.

The biostatistical values from the serotypes (blood groups and HLA-A,B) leave the question of maternity of Ms Sa. open. The results would have been *less equivocal* if other systems had also been typed, e.g., Tf-sub, Hp-sub, PLG, PGP, ORM_1, F13B, A2HS, C3, C6, Bf, and 6-PGD. A greater drawback is the lack of blood group and HLA findings for the 3 children of Ms Sa.: these data would almost certainly have settled the case.

Biostatistical evaluation of band patterns, revealed by multilocus probes 33.15 and 33.6 in Jeffreys' case

Jeffreys et al. (1985) ultimately achieved the desired result with the evidence of 2 multilocus probes, principally because this examination *did include* the *three other children* of Ms Sa.

For the *DNA analysis* Jeffreys et al. (1985) used the multilocus probes 33.15 and 33.6, reporting their mean band frequency as

$$a = 0.26.$$

The mean number of bands per person is probably in the region of

$$n = 58$$

(determined from the band patterns of the mother and those of the four children[2]). The number of bands revealed by both probes is

$$N = 58/0.26 = 223.$$

We treated every visible band in the pherogram as the manifestation of an allele *A in a di-allele system, to which must be allotted an antithetical "silent" allele (= *nonA) (Honma and Ishiyama 1989; Hummel et al. 1990). The bands were assumed to be mutually independent.

To evaluate the band patterns biostatistically we again used the kinship algorithm (Ihm und Hummel 1975). The two hypotheses are H_X and H_Y. H_X, the null hypothesis, says that Ms Sa. is the mother of all 4 children, H_Y, the alternative hypothesis, that she is the mother of 3 children and her sister is the mother of the fourth child. For each of these hypotheses there is a pedigree containing 10 individuals (Fig. 3a, b).

For any band pattern one can calculate the frequencies X and Y for the respective pedigrees. The so-called EM value gives the ratio of the frequencies:

$$EM = \log Y/X + 10.$$

For the 5 persons in the pedigrees for which findings (+ or −) were available, there are a total of 27 different patterns of varying frequency. An EM value can be calculated for each pattern.

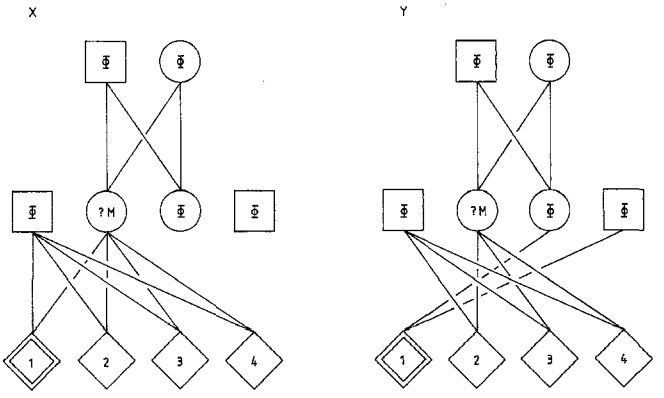

Fig. 3a. Pedigree for the case that Ms Sa. is the mother of the 4 children. **b** Pedigree for the case that Ms Sa. is the mother of the 4 children and the sister of Ms Sa. is the mother of child A.G. (= 1)

[2] I am grateful to Professor Jeffreys for providing this data

Table 1. Frequency of the 27 different types of band patterns found in the quintuple *4 children and Ms Sa.* and the derived EM-values

Running no. of band patterns	Band patterns					Frequency of band patterns	EM-value
	K_1	K_2	K_3	K_4	M		
1	+	+	+	+	+	15	6.9531
2	+	+	+	−	+	4	9.4578
3	+	+	−	+	+	4	9.4578
4	+	+	−	−	+	3	9.6881
5	+	−	+	+	+	4	9.4578
6	+	−	+	−	+	4	9.5842
7	+	−	−	+	+	6	9.3763
8	+	−	−	−	+	4	9.6425
9	−	+	+	+	+	4	11.3409
10	−	+	+	−	+	3	10.3919
11	−	+	−	+	+	2	10.3919
12	−	−	+	+	+	4	10.2613
13	−	−	+	−	+	1	10.3699
14	−	−	−	+	+	2	10.0925
15	−	−	−	−	+	2	10.1536
16	+	+	+	+	−	2	8.9151
17	+	+	+	−	−	6	7.6108
18	+	+	−	+	−	1	9.6018
19	+	−	+	+	−	2	9.2036
20	+	−	+	−	−	5	8.0090
21	+	−	−	+	−	2	9.2036
22	−	+	+	−	−	1	10.2042
23	−	+	−	+	−	3	10.6125
24	−	+	−	−	−	4	10.8167
25	−	−	+	−	−	2	10.4084
26	−	−	−	+	−	4	10.8167
27	−	−	−	−	−	128	−1.3007

Because it is assumed that the bands are mutually independent, the overall EM value can be obtained by adding together the EM values for the individual constellations:

$$EM_{sum} = \sum_{i=1}^{n} EM_i - 10(n-1).$$

The frequency of the constellation "−−−−−" is relevant to the null hypothesis. However, it cannot be established by observation and counting, but by *calculation* using N = 223. This circumstance has led some experts to recommend a "conservative" approach, and ignore this frequency. To take this view into account, we present 2 sets of biostatistics, one including and one excluding the constellation "−−−−−".

All 27 constellations together give

EM = −9.2783,
from which W_M = 99.99999999999999998%,
where W_M = probability that Ms Sa. is the mother of all four children.

Without the "−−−−−" constellations
EM = 2.0224,
from which W_M = 99.999999%.

Combined with EM = 11.4996 from the blood group findings
and EM = 9.7042 from the HLA-A,B findings

one obtains *with* "−−−−−"
EM = −8.0745,
from which W_M = 99.99999999999999991%,

and *without* "−−−−−"
EM = 3.2262
from which W_M = 99.99998%.

As demonstrated, an evaluation of the blood group and HLA findings for just 2 of the persons concerned, Ms Sa. an A.G., produced a probability of maternity of only W = 6%, or, if Hp is excluded, of W = 87%. By contrast, the evaluation of the band patterns of five persons, Ms Sa. and four children, using 2 MLPs produced a probability of W = 99,99998% that Ms Sa. is the mother of A.G. (and the other 3 children). The reason for this difference lies in the number of people included in the respective calculations: only *two* − mother and A.G. − in the bloodgroup and HLA opinions, but *five* − mother, A.G. as well as another three children − in the DNA analysis.

Discussion

The immigration case of Jeffreys et al. (1985), in which the question was whether a Ghanaian woman was the *mother* or the *aunt* of a particular child, is one of a group of *special cases* that blood group experts rarely have to deal with. It is a "deficiency case" because there are no results for the child's father in the X pedigree (associated with the hypothesis "mother") and no results for either parent in the Y pedigree (associated with the hypothesis "aunt"). A further complication is the need to distinguish between close kin, namely 2 sisters. Finally, the origins of the persons involved, in this case North African Negros, have to be taken into account.

In statistical terms, the question is the probabilities of motherhood and aunthood. The sum of the two probabilities is 1 (= 100%) as *no other* hypothesis is involved. Applying the kinship algorithm (Ihm and Hummel, 1975) to the availalbe blood group and HLA findings, one can obtain the frequencies of the 2 pedigrees [f(X); f(Y)], and from these calculate the probabilities W_M and W_A with the Essen-Möller formula:

$W_M = 1/[1+f(Y)/f(X)]$;
$W_A = 1-W_M$.

Blood grouping results in 16 systems together with HLA-A and B findings for the child and the putative mother produced a probability of motherhood of only 6%. Correspondingly, the probability that the woman in question is the child's *aunt*, W_A, is 94%. These W values are deceptive. The reason lies in the constellation in the Hp system (= opposite homozygosity between the child and the putative mother).

To solve the case, Jeffreys et al. used 2 multilocus DNA probes and included 3 other children of the wife

which were without doubt her real children. Biostatistically – as our evaluation using the model of multiple diallelism (Honma and Ishiyama, 1989; Hummel et al. 1990) demonstrates – this will *always* produce W_M values of more than 99.73%, i.e., the predicate "maternity practically proven".

Even if DNA band patterns are available only for the child and putative mother, the W value should be convincingly high. *Including* the "––" constellation, we obtained W = 99.9992% (= maternity "practically proven") for the case of Jeffreys et al. In this case the number of visible bands common to both putative mother and child is very high: 70% (44 out of 62 bands).

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