Letters to the Editor

GUIDELINES FOR REPORTING ESTIMATES OF PROBABILITY OF PATERNITY

To the Editor: "Some Fallacies in the Computation of Paternity Probabilities" by Mikel Aickin [1] purports to discredit the Guidelines for Reporting Estimates of Probability of Paternity (Appendix A) established by the American Association of Blood Banks [2]. Dr. Aickin's assumptions, reasoning, and statements require a response since they challenge the fundamental logic employed in the laboratories of the United States, Europe, and Scandinavia in calculations and the reporting of results in nonexclusion cases.

The recent alarming increase in illegitimate births in the United States has intensified interest in establishing paternity of these infants. Blood tests offer the best means of providing valuable objective evidence for or against paternity of men alleged to be fathers.

An international conference was convened by the American Association of Blood Banks (AABB) at Airlie, Virginia, in May 1982 under a grant from the Office of Child Support Enforcement of the U.S. Department of Health and Human Services in order to develop consensus in the method of calculating and reporting the probability of paternity when there is a failure to exclude the alleged father in paternity disputes. The AABB perceived a need for a uniform method to enhance credibility and communication to the courts. The Guidelines were developed after hearing various proposals and arguments from experts in the field. Eight experts in paternity testing from Europe, Scandinavia, and England were invited to participate together with several workers from the United States in this conference. In addition, two consultants in population genetics and biostatistics were invited to critique the presentations. These four consultants were selected because they were not involved in parentage testing and therefore could take an impartial look at what was presented and the logic of the calculations. A number of other diverse, invited experts in mathematics, jurisprudence, and genetics participated. Dr. Aickin was one of the contributors to this conference.

The invited experts were given one test case to evaluate in which there was no exclusion of the alleged father. Gene/haplotype frequency tables were supplied for the calculations. The test case involved a total of six genetic systems and included systems in which the maternal and paternal gene contributions to the child were obvious as well as systems where alternative possibilities existed. The HLA system analysis was complex since blanks existed at both the A and B loci in the child.

All 14 participants who responded to the test case obtained the *same result*

although different styles and logic were employed (Appendix B). This achievement is of great significance since it reflects international unanimity in terms of the mathematical result.

Various proposals and methods were discussed and debated during the conference. A strong case for reporting the probability of paternity based upon the failure to exclude after using multiple systems was proposed by Dr. C. C. Li [3]. This suggestion was given very deliberate consideration by the Committee and was recognized as having great merit. After a review of this and other proposals and suggestions, the Committee on Parentage Testing of the AABB developed the Guidelines for use by laboratories in the United States.

The Guidelines have been subsequently approved by the: Board of Directors, American Association of Blood Banks; Section of Family Law, American Bar Association; and Council on Scientific Affairs, American Medical Association.

These Guidelines do *not* require the reporting of any *specific* numerical expression but they do indicate that *some* mathematical estimate of the probability of paternity should be calculated from the observed phenotypes of the mother, child, and alleged father when there is a failure to exclude.

The Paternity Index (PI), referred to by Aickin as the likelihood ratio (LR), has become established as the basic mathematical expression employed by most laboratories in the United States and Europe. This value can also be transformed into a percentage expression using .5 as a prior probability value. This percentage expression, the probability of paternity, is the estimate most familiar to the legal community and the courts. The calculation is based *entirely* upon the *genetic markers* identified in the trio and does not consider any nongenetic evidence in the case such as access, impotency, sterility, and other men who could be the biological father.

Aickin's paper considered "three basic fallacies" in the probability of paternity statement used by laboratories engaged in paternity testing. Dr. Aickin's first argument is that the statement of probability of paternity is a fallacy since the "figure is not, in fact, the probability that the alleged father is the true father." The PI is a statement of probabilities in the form of a ratio that expresses the probability that a man with the *same phenotype* as the alleged father is the biological father of a child with the phenotypes observed when he is compared to an untested man from the same population. The assumption is made in one-man cases that the biological father was either the alleged father or an untested man often referred to as a random man. As Dr. Aickin points out, the PI is not exclusive for the alleged father but applies equally to all men of the same phenotype as the alleged father. Such a consideration is implicit in the definition of the PI ([2], pp. 475 and 656). However, Dr. Aickin avoids pursuing this matter to its logical conclusion. The relevant sequel to this statement is the question: How many men are there who have the same phenotype as the alleged father? The answer depends upon the *extent* of genetic testing performed in each case under consideration, but the value is frequently *less* than 1 in 100,000 ([2], p. 31).

The second criticism of Dr. Aickin involves factors that are unknown to the testing laboratory and therefore *cannot* be used in the calculation. Dr. Aickin has indicated that even in one-man cases there may be other "plausible fathers" beyond the man named by the mother, that is, the alleged father being tested. This may certainly be true, but such information is unknown to the laboratory and therefore cannot be used in a calculation. Thus, a neutral prior probability is used in the calculation. The reported probability of paternity can be adjusted up or down based upon the weight of other evidence in the case. However, such an adjustment is not in the province of the laboratory scientist. This is the responsibility of the judge or jury charged with evaluating *all* of the evidence in the case. The calculation does, however, consider *all* possible (compatible) fathers in the denominator of the PI by selecting the untested man using gene frequencies established from a large population. The gene frequencies utilized are based on the racial origin rather than geography and are used in both the numerator and denominator of the PI.

In those rare cases where more than one man is tested, experience has demonstrated that it is *usual* for all but one man to be excluded. When more than one man is not excluded in a single case, a calculation of the relative probability of paternity can be given for each nonexcluded man. Formulas for such calculations have been published by Prof. K. Hummel [4]. However, the question of access to the mother, frequency of intercourse, and potency and fertility of each plausible father constitute additional variables that would also be unknown and therefore could not be accurately quantitated.

Although the race of the biological father is unknown, it is important for the laboratory to use gene frequencies in the calculation from a carefully selected and large sample of the population of the same race claimed by the mother and alleged father. Gene frequency tables have been published by the AABB ([5], p. 29 ff.) for use by parentage testing laboratories in making these calculations.

Dr. Aickin's third challenge involves the estimation of genotype frequencies within a given phenotype when silent alleles may be present. He asserts that genotype frequency assignments within such phenotypes represent "speculation about random draws." In practice, such assignments are based upon published tables of gene frequencies that are then utilized in the Hardy-Weinberg formula to estimate genotype frequencies within phenotypes. Fundamental genetic principles are applied to the calculations of both genotype frequencies and gamete frequencies.

Dr. Aickin cites the example of a group B mother with an O child and points out that the biologic father must contribute an O gene. He then states that "whether a man additionally carries A or B or another O gene is irrelevant to paternity." While it is true that the only requirement for a man to be the biologic father is to carry an O gene, it is *not* true that the chances of men whose phenotypes are A, B, and O all have equal chances of transmitting an O gene. The PI values for these phenotypes are as Dr. Aickin indicates: 0.63 for A, 0.72 for B, and 1.51 for O. This observation clearly demonstrates that the group O alleged father is over two times more likely to contribute an O gene

than is a group A alleged father. In fact, the O alleged father cannot contribute a wrong gene while the group A alleged father has a 58% chance of transmitting an A gene that is incompatible with paternity. An obvious implication by Dr. Aickin would be that genetic counseling is of no value in instances where the phenotype does not reflect the genotype. A random woman is not equally likely to produce a hemophiliac son as is a woman known to be the sister of a hemophiliac. However, both carry normal genes. Neither are A, B, and O fathers equally likely to produce O children. Their relative chances of producng an O child can be calculated using the basic principles of population genetics. Of course, any of them could produce such a child but the probabilities are not the same. The fact that the "LR may be enormous" does not necessarily mean that it is incorrect but rather may indicate a true statement of the probabilities.

We agree that family studies would be of value in yielding an improved estimate of the probability of paternity. Such studies should not be limited to the alleged father or plausible fathers, but may also be informative and helpful when the mother's family is studied. Major problems, however, are state statutory laws, cooperation, and illegitimacy.

The principles used in the calculations for the probability of paternity require not only a knowledge of basic algebra and probability, but also the fundamentals of blood group genetics including the Hardy-Weinberg principle. Any expression from the laboratory relating to the probability of paternity should *only* by used with other evidence in the case in the resolution of the paternity dispute. The blood test results, however, do provide valuable objective evidence in these matters. Such objective evidence should not be ignored.

RICHARD H. WALKER[1]

REFERENCES

1. AICKIN M: Some fallacies in the computation of paternity probabilities. *Am J Hum Genet* 36:904–915, 1984
2. WALKER RH, ED.: *Inclusion Probabilities in Parentage Testing*. Arlington, Va., American Association of Blood Banks, 1983, p xiv
3. LI CC, CHAKRAVARTI A: On the exclusion and paternity probabilities, in ibid., pp 609–622
4. HUMMEL K: *Biostatistical Opinion of Parentage Table—Part 1*. Stuttgart, West Germany, Gustav Fischer Verlag, 1971, p 95
5. SILVER H: *Probability of Inclusion in Paternity Testing*. Arlington, Va., American Association of Blood Banks, 1982

Received October 12, 1984; revised December 27, 1984.
[1] William Beaumont Hospital, Royal Oak, MI 48072.

APPENDIX A

GUIDELINES FOR REPORTING ESTIMATES OF PROBABILITY OF PATERNITY

1. Testing of genetic markers in cases of disputed parentage should include multiple systems which will exclude most falsely accused men. If tests fail to exclude the alleged

father, an estimate of the probability of paternity should routinely be calculated from the observed phenotypes of the mother, child and alleged father.

2. One estimate that the nonexcluded alleged father could be the biologic father is a likelihood or odds ratio known as the Paternity Index (PI;X/Y). This compares the alleged father (X) with a random man (Y) in terms of their respective probabilities of providing an appropriate gene to the child in each of the genetic systems for which phenotypes have been determined.

3. The estimate of probability derived from the phenotypes of the mother, child and alleged father should also be stated as a percentage expression (Probability value: W value; Likelihood; Plausibility; Relative Chance of Paternity). Since calculations to determine this estimate include a value for the prior probability, reports must state the prior probability(ies) used.

4. Other mathematical expressions may be derived from the observed phenotypes or other data. If they are included in the report, such expressions should be defined and explained.

5. Probability calculations should consider the racial origin of the mother, alleged father and the random man. Gene frequencies should have been obtained by the examination of populations of adequate size. In some cases it may not be feasible to compare the alleged father with a random man because relevant and adequate gene frequency tables are not available.

6. Mathematical expressions of probability estimates may be accompanied by verbal predicates. If used, verbal predicates should be explained in the report.

(Appendix B follows on next page)

APPENDIX B
AIRLIE CONFERENCE PATERNITY CASE

System	Alleged father	Mother	Child
ABO	B	B	B
MNSs	Ns	MNSs	MNSs
Rh	Rh: 1,2,−3,−4,5,−8	Rh: 1,−2,3,4,5,−8	Rh: 1,2,3,4,5,−8
Duffy	Fy(a+b−)	Fy(a−b+)	Fy(a+b+)
Kell	K−k+	K+k+	K+k+
HLA A	2,x	9,29	29,x
B	12,y	7,35	35,y

Gene and haplotype frequencies:

CDe R^1 = .3905	cdE r'' = .0075	cD^ue = .0009	--- = Rare
cde r = .3998	Cde r' = .0054	CdE r^y = .0001	
cDE R^2 = .1462	CD^ue = .0020	−D− = Rare	
cDe R^0 = .0270	CDE R^z = .0013	C^wD- = Rare	
C^wDeR^{1w} = .0181	cD^uE = .0009	cD− = Rare	

HLA A-B haplotype frequencies in white Americans*

	A											
B	1	2	3	9	10	11	28	29	30 & 31	32	blank	Total
5	.003	.019	.005	.004	.004	.007	.004	0	.003	.001	.002	.052
7	.016	.039	.043	.010	.003	.002	0	.007	.004	.001	0	.125
8	.067	.019	.004	0	.003	.001	.001	.004	.002	.001	0	.102
12	.005	.061	.008	.017	.005	.004	.007	.022	.003	.014	.003	.149
13	.002	.005	.002	.001	0	0	0	0	.014	0	.003	.027
14	.005	.005	.008	.003	.003	.001	.005	.003	0	.003	.007	.043
15	.003	.026	.002	.008	0	.005	.004	.002	.003	0	0	.053
16	.003	.009	.002	.003	.008	.002	.001	0	.001	0	0	.029
17	.021	.011	.004	.003	.005	.001	.002	0	.004	0	0	.051
18	.001	.009	.006	.006	.009	.006	.001	0	.005	.003	0	.046

A_1 = .2038
A_2 = .0700
B = .0658
O = .6604

MS = .2578
Ms = .2907
NS = .0628
Ns = .3877
Mu = .0005
Nu = .0004
M^k = .0001
M^gs & M^gS = Rare

Fy^a = .4251

21.....	.001	.015	.003	.009	.007	.003	.002	0	.001	.002	0	.043	Fy^b = .5569
22.....	.003	.004	.002	.002	.001	.006	.002	.001	.001	0	.001	.023	Fy & Fy^x = .0180
27.....	0	.024	.003	.010	.003	.002	.003	.001	.003	.002	0	.051	
35.....	.001	.014	.012	.012	.005	.010	.007	.002	.001	.002	.002	.068	k = .9640
40.....	0	.026	.005	.008	.001	.002	.003	0	.012	.004	0	.061	K = .0359
Blank y....	.011	.018	.014	.010	.006	.007	.003	0	.004	0	.004	.077	K^o = .0001
Total	.142	.304	.123	.106	.063	.059	.045	.042	.061	.033	.022	1.000	

NOTE: For calculation purposes, assume a haplotype frequency of .0001 for those haplotypes which show a 0 above.
* 1,309 whites in the Los Angeles area, from the data of Albert, Mickey, and Terasaki, in *Histocompatibility Testing*, Munksgaard, 1972, p 235.

Paternity Indices (X/Y) Submitted for Airlie Conference

	Method*	ABO	MNSs	Rh	Duffy	Kell	HLA	Combined	W
Allen, New York City	B	1.88	1.41	2.50	2.26	1.00	4.37	65.4	.985
Bias, Baltimore	B	1.878	1.408	2.518	2.261	1.000	4.379	65.922	.9850
Chakraborty, Houston	A	1.878	1.406	2.502	2.261	1.000	4.434	66.239	.9851
Henningsen, Copenhagen	B	1.878	1.408	2.505	2.261	1.000	4.345	65.072	.9849
Hummel, Freiburg.....	A	1.878	1.407	2.505	2.260	1.000	4.343	65.501	.9850
Lee, Chicago	B	1.878	1.407	2.499	2.260	1.000	4.379	65.350	.9849
Martin, Berlin	A	1.878	1.408	2.516	2.260	1.000	4.379	65.87	.9850
Mayr, Vienna.....	A	1.878	1.406	2.518	2.260	1.000	4.379	65.826	.9850
Mickey, Los Angeles	B	1.878	1.407	2.505	2.261	1.000	4.352	65.131	.985
Morris, Long Beach	B	1.88	1.41	2.50	2.26	1.00	4.38	65.6	.985
Nijenhuis, Amsterdam	B	1.878	1.406	2.505	2.261	1.000	4.387	65.619	.9850
Salmon, Paris.....	B	1.878	1.406	2.505	2.261	1.000	4.378	65.815	.9850
Valentin, Göteborg	A	1.878	1.406	2.505	2.261	1.000	4.339	64.903	.9848
Walker, Detroit	B	1.878	1.407	2.504	2.260	1.000	4.352	65.076	.9849

* Methods A and B refer to two different approaches in logic employed in the calculation. See [2], p 466. X/Y = LR of Aickin ([1], p 906).