RELATIONSHIP TESTING NEWS

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In This Issue

Proposed Parentage Calculations in Cases with a Chimera

| **Robert E. Wenk MD, Debra Davis PhD and Michael Baird PhD**

This article is part 3 of 3, continued from the Volume 13, Number 2 Edition of RT News

V. Statistical Logic for a Paternity Case With an Alleged Father Chimera

The ordinary child's maternal obligate allele (MOA) is determined at each locus and the paternal obligate allele is deduced. Two different visible alleles indicate the mother is heterozygous and one visible allele indicates she is homozygous, assuming she doesn't

carry a silent allele. An alleged father chimera's paternity may be excluded if he fails to carry the child's POA at more than one locus.

Probabilistic evidence that a chimeric AF is the child's biologic father (BF) is less than an ordinary AF. First, if the chimera AF carries four different (visible) alleles and one is the POA, there is a probability of 0.5 that the child inherited the POA from the DZ genome that carries it and second, there is an independent probability of 0.5 that the child would inherit the visible POA and not the second allele of that locus. The combined probability of the two independent probabilities is 0.5 x 0.5 = 0.25.

Since the probability that the child inherited the POA from a RM is the POA's frequency, which is a constant (p), the LR for a locus would be lower than is usual for a non-chimera case. Intuitively, however, one would expect that an AF composed of two genomes should have an LR that is higher than that of an ordinary AF. Thus, the probabilities that a child would inherit any duplicate POAs of the chimera AF are added to 0.25 in the LR numerator. The probability that the child inherited an invisible copy of the POA is included in calculation, unlike the case of a chimeric child in the simpler calculation presented in Scenario 2 of Section IV.

Scenario 1. AF exhibits only 1 visible allele and it is the child's POA.

AF is comprised of POA-homozygous DZ twins (P/P & P/P). The probability that AF would transmit two P alleles to the child is 1.0 (certainty). The conditional probability that a RM would transmit P to his child is p. LR = 1.0/p.

Scenario 2. AF's phenotype exhibits 4 visible alleles and 1 is the child's POA.

The probability that AF would transmit the POA to his child is 0.25. The probability that a RM transmitted the P allele = p. LR = 0.25/p.

Scenario 3. AF's phenotype exhibits 3 visible alleles, including the POA.

The single invisible allele could be an invisible copy of the POA in AF's 4-allele genotype. The conditional probability that the visible POA is transmitted to the child is 0.25. The probability that AF's invisible allele is transmitted is also 0.25 and the probability that the invisible allele is a duplicate of the POA is 0.33 because it could be any one of AF's three visible alleles. (It has a one-in-three chance of being a duplicate of the visible POA.) The joint probability that the child would inherit the invisible allele and that the allele is a duplicate of the POA is 0.25 x 0.33 = 0.08. The total probability that a visible AF POA or an invisible copy of the POA would be transmitted to the child is 0.25 + 0.08 = 0.33. The locus LR = 0.33/p.

Scenario 4. AF's phenotype exhibits 2 visible alleles, including the POA.

The probability that the visible POA of AF is transmitted to the child = 0.25. Either invisible allele in AF's genotype could be a copy of the POA. The probability that one invisible allele is a duplicate POA = 0.5 because it is one of the two visible alleles. The

probability that an invisible allele is transmitted to the child is 0.25. The joint probability that the child's POA is an invisible POA and is transmitted to the child is 0.5 x 0.25 = 0.125. The joint probability that the child's other invisible allele is a copy of the POA and is transmitted to the child is 0.5 x 0.25 = 0.125. The total probability that the visible POA or an invisible copy of the POA is transmitted from the chimera to his child = 0.25 + 0.125 + 0.125 = 0.5. The probability that a RM would transmit the POA (P) is the allele's frequency (p). The LR = 0.5/p.

Table 2 summarizes the four scenarios of a chimera father and ordinary child.

VI. An Excluded AF and A Mother Who Insists AF is the Father

A chimeric AF is a composite of DZ twins. If buccal cells contain the DNA of only the non-paternal twin, the sampling problem will falsely exonerate AF. On the other hand, the child's mother may desire child support from the AF even if he is not her child's biologic father.

The laboratory that performed the paternity test can help to resolve the problem by reusing the genetic test results to evaluate for an avuncular relationship between AF and the child. If no avuncular relationship is evident, AF is probably not a chimera. If the non-paternal genome bears an avuncular (second-degree) relationship to the child, that is evidence that AF is a chimera and a search should be made of AF's tissues to find the child's paternal obligate alleles (POAs). Semen is the most important tissue that may be sampled non-invasively. Alternately, AF's parents may volunteer for genetic testing to find POAs.

REFERENCES

Wenk RE. Paternity Probabilities when an alleged father is a congenital chimera. Transfusion. 2018 Jan;58(1):273

Table 2. Probabilities that an AF chimera would transmit the POA to his child.

Phenotypes of:		Probability that AF	
AF Chimera	Child	Transmitted POA	Likelihood Ratio
P, Q, R, S	P, T	.25	.25/p
P, Q, R	P, T	.25 + .25(.33)	.33/p
P, Q	P, T	.25 + (2).25(.5)	.5/p
P	P, T	(4).25	1/p
P, Q	P, Q	1.0	1/p + q

POA = P. The frequency of allele P = p and the frequency of allele Q = q.

Using Caution in the Reporting of Second Degree Relationships

| Kelly Beatty

DNA testing of STRs is often requested to provide evidence for a number of hypothesized biological relationships. It is not always possible to distinguish between some of these relationships by STR technology alone. True second-degree relatives (half-sibling, aunt/uncle, nephew/niece, and grandparent) can share one allele by descent or no alleles. For this basic discussion, we will focus on these two possibilities within a two-person comparison and the transmission of DNA for different second-degree relationships.

Let us consider two individuals with autosomal results of 13,15 and 9,13 at one locus.

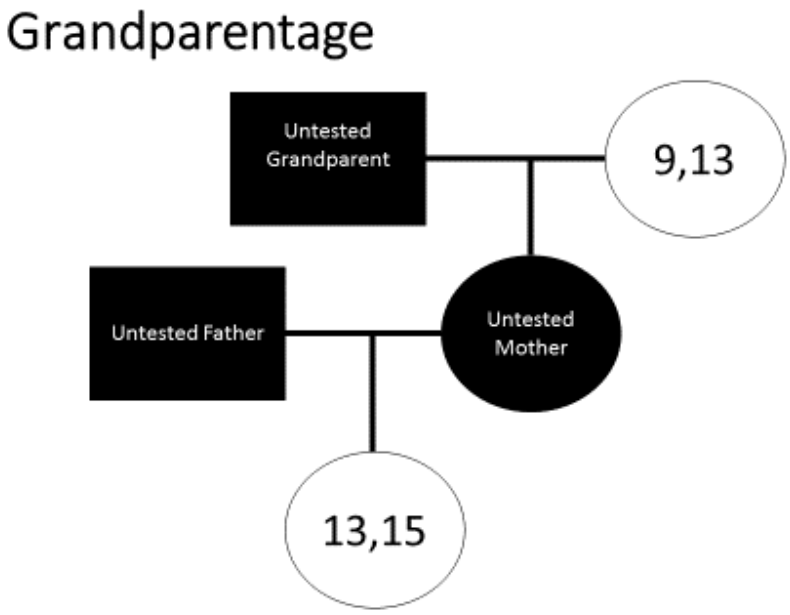

Figure 1.

Represents a pedigree in which the two individuals are questioned as grandparent/grandchild. Although results for only one alleged grandparent are present, the untested grandparent has two alleles as well, leading to four total alleles at the grandparent level. A grandparent/grandchild assessment will ask the likelihood of the observed 13 being identical by descent (IBD), thus sharing 25% of the grandparental DNA by descent or no alleles being shared since the individual in the grandchild position could have inherited by descent an allele from the untested grandparent.

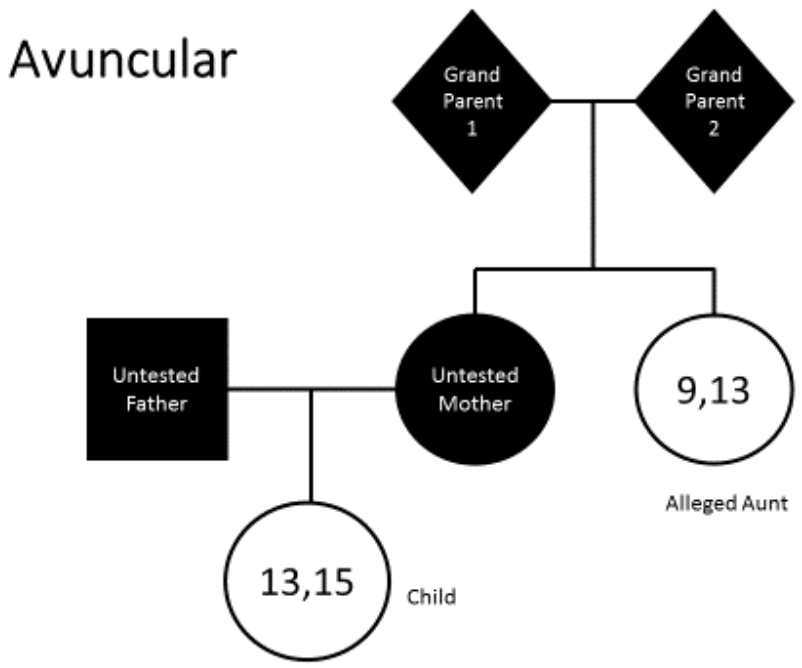

Figure 2.

Represents a pedigree in which the two individuals are questioned as aunt/niece. Assuming Mendelian inheritance, the individual in the aunt position has two of the four alleles present at the grandparent level, one from each untested grandparent. Using the alleged aunt as a reference, the avuncular comparison will ask the likelihood of the observed 13 being identical by descent (IBD), thus sharing 25% of the grandparental DNA by descent with the aunt or no alleles being shared since the individual in the niece position could have inherited an allele not identical to the 13 observed allele, just as in Figure 1.

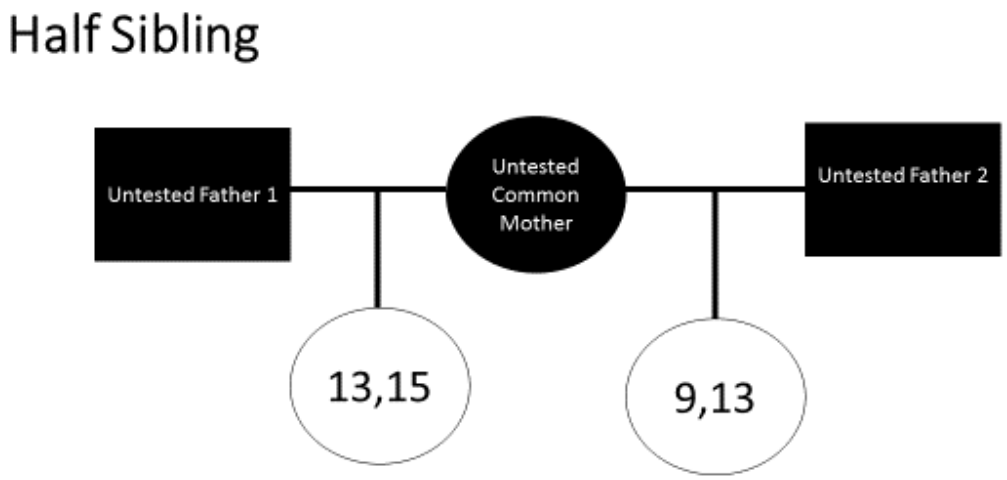

Figure 3.

Represents a pedigree in which two individuals are questioned as half-siblings. In a half-sibling comparison, there is only one shared parent, resulting in only being able to share one of four parental alleles. In a pairing of the shared mother and untested father 1, there are four parental alleles including 13 and 15. In a pairing of the shared mother and untested father 2, there are four parental alleles including 9 and 13. Again, just as in the previous examples, the assessment will take into consideration the sharing of 25% (the 13 allele by descent) or sharing no DNA and still sharing one parent.

Care should be taken in reporting these relationships as the statistic generated for a half-sibling comparison would be the same statistic generated for any other second-degree relationship. Laboratories may want to consider conclusion statements which not only include the original questioned relationship but all second-degree possibilities.

New AABB Approved Test Method

An accredited AABB laboratory submitted a variance request for using single nucleotide polymorphisms (SNP) in relationship testing, specifically as it relates to standard 5.5.3.1. After review by the AABB Relationship Testing Standards Committee, it was determined that the algorithm used to evaluate the SNP test meets AABB requirements for the

performance of the test and reporting of results, and it could therefore be included in the scope of the laboratory's accreditation. ***The forthcoming 14th edition of Standards for Relationship Testing Laboratories will include requirements for the use of these tests.***

AABB Relationship Testing Code of Conduct

REVISED 2019

AABB is a professional organization dedicated to leadership, education, service, and professional integrity in the practice of blood procurement, transfusion therapy, and all fields related to transfusion medicine, cellular therapy and relationship testing. This role mandates ethical conduct. Accordingly, all AABB accredited relationship testing laboratories hereby pledge to adhere to the following canons:

1. Provide and promote the highest quality of service and testing in accordance with current scientific knowledge and established standards of practice.
2. Provide general information to other organizations engaged in the various aspects of relationship testing when expertise or services are requested.
3. Observe the confidentiality of all communication and laboratory results including secure transmission or storage of electronic or paper documents generated as part of the testing process.
4. Provide general information, upon request, about the availability of additional or repeat testing.
5. Provide information about the laboratory's tests, services, and/or status of accreditation by AABB that is neither misleading nor unsubstantiated.
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Calculating a Relationship Index with Linked Genes

Director : David Baugmgarten
Recorded Date: Tuesday, May 7, 2019

Program Description

The presenter discusses theoretical examples related to calculating a relationship index with linked genes. This program is intended only for lab directors or others who will prepare or sign relationship testing reports.

RT Publication

Title : Relationship Testing 1.0
Author : Robert Wenk, MD

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Bethesda, MD: AABB Press, 2018

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AABB and the American Association for Laboratory Accreditation (A2LA) have joined forces to offer the AABB/A2LA Accreditation Program to the relationship testing and forensics communities.

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1-301-644-3221 or rquerry@A2LA.org

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If you have given a talk or presentation in the last 2-3 years on a topic that you think may be of interest to the relationship testing community, share your content as part of AABB's 2019 RT Webinar Series. If you decide to submit your content, you can choose to moderate the audio conference or we can assign a speaker for you.

For more information or to submit your content, email us at nikkib@aabb.org

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Articles

Do you have an interesting case or question you would like to share through this newsletter?

Or is there a topic or issue you would like us to write about? Email us at nikkib@aabb.org

RT Accreditation Committee and RT Standards Committee

- Are you interested in ensuring that assessment/audit procedures are in consistent with AABB policies established by the AABB Accreditation Program Committee?
- Are you interested in working with U.S. Citizenship and Immigration Service and/or the Dept. of State as it relates to RT?
- Are you currently an AABB Member?
- Would you like to be involved in creating and revising the Relationship Testing Standards?

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- Would you like to be involved in creating and revising the Guidance for the Standards?

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