

WELCOME!

Welcome to the first edition of the AABB Relationship Testing Newsletter. My name is Mary Mount. I am the Manager of Parentage Testing Services at Memorial Blood Centers in Minneapolis, Minnesota and I am currently the Chair of the Relationship Testing Accreditation Program Unit (RTAPU).

Dr. George C. Maha is the Chair of the Relationship Testing Standards Program Unit (RTSPU).

We hope you enjoy the first edition. We plan to publish two newsletters each year. If you have any comments or suggestions or would like to submit articles please let us know by contacting Nikki Bass-Jeffrey at nikkib@aabb.org

Thank you.

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TESTING WITHOUT THE MOTHER

During the meeting of the Relationship testing special interest group (SIG) at 2005 AABB Annual Meeting (October 2005, Seattle, Washington) many laboratories were represented. These laboratories voiced a strong concern about the apparent increase in the number of clients submitting disputed paternity cases without the mother. Testing without the mother presents a number of problems. First, the relationship index is, on average, cut in half. This is particularly problematic in cases where the father is also not tested (reconstruction case). Not testing the mother also greatly reduces the ability to detect a falsely accused man, and in some cases, such as incest can easily produce false inclusions. When an apparent inconsistency (mutation) is present, it may not be possible to render an opinion of paternity without obtaining a sample from the mother.

The mother is also an important QC step. If the mother is excluded it may indicate a problem in the testing. The testing of the mother may also allow for the detection of fraud, such as welfare fraud on the part of the mother or cases where the alleged father brings a child he knows is his, but is not the child of the mother. Thus, the testing of the mother, even if maternity is not disputed, is important in evaluating the questioned relationship, it improves the chance of obtaining clear results and is a quality control check for both the scientific and legal community. The laboratories represented strongly felt that testing without the mother should only be done when the mother's location is unknown or she is deceased. Every effort should be made to test the mother.

Mutation Calculations

7th Edition of Guidance for Standards for Relationship Testing Laboratories

To obtain a FREE copy of the AABB Annual Report Summary

VISIT:

www.aabb.org > Accreditation > Parentage Testing Accreditation Program

Stay tuned for the release of the:

7th Edition of Guidance for Standards for Relationship Testing Laboratories

During the 2004 AABB Annual Meeting a presentation summarizing research among both European and American statisticians indicated general consensus that the future of mutation calculations may be the method described by Fimmers (for a discussion see, 2003 Annual Report Summary). Methods for collating data for the frequency tables that can be used with Fimmers' formulas were also discussed at the 2005 annual meeting. One aim of the annual reports on parentage testing is to obtain this data. The previous editions of the guidance document provide "guidance" and in the appendix it mentions the method of dividing the mutation rate by the average probability of exclusion (POE). This method was originally developed for use with mutations obtained with RFLP technology. The appendix has not been updated for many years. This method was necessary with RFLP technology because of sizing concerns and the continuous allele distribution. In the appendix it mentions the method of Fimmers et al as an alternative method that would give the specific mutation rate, however it could not be applied to RFLP data. With PCR-STR testing, the allele distribution is discrete, the mutational event in some instance may be maternal or paternal and importantly, data is becoming available to perform alternate calculations. The new edition of the guidance document (7th Edition, in press) updates this appendix. The appendix has a discussion of three different methods: Fimmers, Brenner and the method of dividing the mutation rate by the average POE. The guidance document suggests that the method of Fimmers would be a good method for calculating STR data.

AABB does not have any specific recommendation on what calculation to use for incorporating mutational events into the combined paternity index. AABB's only requirement is that the mutational event be incorporated. AABB provides guidance and laboratories are free to follow the guidance or use other validated methods to meet the standards. The guidance document represents a "safe harbor" in a choice of methods for your laboratory. A partial discussion of the many methods of calculating the mutation PI can be found on the AABB website in the Annual Report Summary for testing in various years (2001, 2002, 2003 & 2004).

Another addition to the new Guidance document (7th edition) is an appendix on "Non-exclusion probabilities for related brothers/fathers of included tested men". These formulas will be helpful in evaluating the chance that the tested man is falsely included in relation to an untested brother or father. While ideally, when a brother or father of the tested man is alleged he should be tested. Some clients look for this type of information prior to requesting the testing. Hopefully the membership will find these formulas useful in evaluating these types of cases.

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OF
THE 2005 SIGs
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Relationship testing SIG Saturday, October 15, 2005 2005 AABB Annual Meeting at Seattle

The session was divided into two parts, a morning and afternoon session. The morning session was devoted to administrative and accreditation issues. Dr. George Maha gave an overview and summary of information garnered from the annual report and detailed the upcoming changes in the 7th edition of the relationship testing standards. Dr. Cheryl Conley reviewed the issues and concerns revealed through the proficiency testing program of AABB Accredited Laboratories. There was a fruitful discussion with useful suggestions from participants on various administrative issues. The afternoon session was devoted to eight scientific paper presentations with the theme of unusual parentage testing cases encountered by parentage testing laboratories. Dr. David Gjertson kindly agreed to fill the spot left vacant by Dr. Amanda Sozer who, due to other engagements, could not attend the meeting. All the presentations are available at the Live Learning Center on the AABB web site, within 2005 Annual Meeting in the Technical/Clinical sessions 110 and 128 Parentage Testing I and II. The following is a synopsis of the scientific paper presentations:

Maternal Typing and Test Sufficiency in Parentage Analysis

Robert Wenk

Dr. Wenk discussed the precautions necessary in motherless parentage testing. Including the mother in the testing adds to the parental resolvability because the paternal genetic contribution can be more easily deduced. Duo or "motherless" cases have a certain amount of mathematical information that is "lost." This information loss has been supported by several published findings and involves different issues. These issues include genetic inconsistencies, STR typing errors and misrepresentations by modern parentage analysts regarding STR typing. Dr. Wenk explored the specifics of each of these issues in contemporary testing techniques.

Accredited Relationship Testing and Current Practices in the United States

David Gjertson

Dr. Gjertson presented the current status of parentage testing in the U.S., including technologies employed to perform parentage testing. He presented in detail the mutation rates observed in the most commonly used genetic markers and the implications for calculation of paternity index. He also provided a comprehensive list of future considerations for calculation of paternity index. He emphasized the need to collect more precise mutation data to improve the estimate of the paternity index in mutation cases.

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Application of Mitochondrial DNA typing for Identification of Human remains and Issues Involved with Court Admissibility

Mitchell M. Holland

Dr. Holland provided a comprehensive overview of the use of Mitochondrial DNA testing, especially in reference to identifying remains in cases of mass disaster. Mitochondrial DNA (mtDNA) is maternally inherited and is used for human identity testing. MtDNA has been used in large human identification projects where the victim remains are minimal. The World Trade Center is an example of this type of disaster scenario and one of the largest human identification projects devoted to kinship resolution. Short Tandem Repeats (STRs) are genetic markers that are used in identification tests such as paternity and kinship analysis. The World Trade Center identification project primarily used STR analysis but also utilized mitochondrial DNA as an additional discriminator when STR genetic markers did not provide sufficient informative. MtDNA, like STR markers, have their own biological admonitions, such as problems with population database integrity and locus commonality between tested participants, which affect stability and discriminating power. Dr. Holland explored these topics and how minimal their impact is on the usefulness of the mtDNA genetic markers as supplementary tools.

Alu Elements: Stable Genetic Markers for Paternity Testing

Anthony B. Carter

Alu elements are short (~300 base pairs) genetic elements, which can be found ubiquitously throughout all human populations. These elements contribute to a great deal of human genetic diversity, making them prime candidates to be used as human identification tools. There are also a number of attributes that make *Alu* elements appealing to use as genetic markers beyond the fact that they contribute to human genetic diversity. Dr. Carter discussed these attributes and how they can bolster paternity inclusion case PI. Reliagene Technologies, Inc. is designing a multiplex kit that will utilize these *Alu* elements to their full genetic extent. The utility of these additional markers to resolve cases involving mutation of STR loci was discussed.

Derivation of the “Random Grandparents Not Excluded” Statistic

Marco Scarpetta

The false “inclusion” of non-related grandparents can be a problem in the roughly 1000 grandparent cases that are conducted each year. Dr. Scarpetta introduced a derivation of a calculation called the “Random Grandparents Not Excluded” (RGPNE) statistic. This presentation clarified the hypothesis and the benefits of applying this statistic in questionable cases. It was suggested that the RGPNE statistic can flag cases which may require additional genetic markers. The goals of this study were to derive the RGPNE statistic and determine a minimum number of genetic markers to test in order to obtain a statistically strong conclusive result.

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A Caveat of Motherless Paternity Testing

Charles M. Kelly

Calculating a high probability of paternity is easier when the mother is included in the computations. Also, those cases where the participants contain more variations of applicable genetic markers are more easily resolved due to the strength this scenario contributes to the probability statistics. The paternity index is the primary paternal probability statistic, and without the mother's genetic profile, the paternity index, at best, is halved even with the optimal genetic marker scenario. The best genetic profile is obtained when both alleged father and child in question are highly diverse at all genetic markers. Dr. Kelly explored the stipulations of "motherless" cases and cautioned the possible biological contributions, which may result in a false conclusion.

A Triple Band Pattern in a Vietnamese Family

David Baumgarten

Mr. Baumgarten has encountered a case involving a Vietnamese family in which a conclusion was difficult to ascertain. The mother and child both exhibited three banded pattern at the genomic locus TPOX. The alleged father's profile was homozygous at the TPOX locus, which coincided with one of the three alleles that were present in the mother and child. Due to the low probability of paternity, the possibility of including this questionable marker was considered. This presentation delved into the search to resolve this unusual genetic matter including the investigation into the population databases and the occurrences of triple allele patterns.

Unusual Parentage Testing Cases

Sudhir K. Sinha

At the demand of the participants, Dr. Sinha presented his experience in dealing with Hurricane Katrina. A number of lessons were learned in disaster preparation, which could be of great value to testing laboratories facing similar circumstances. He emphasized that every laboratory should prepare a disaster mitigation plan. It was due to careful advance planning and preparedness that ReliaGene was able to cope with the most costly natural disaster in United States history. As a result, ReliaGene managed to save all samples, documents and electronic data without any loss. Dr. Sinha's original talk on unusual parentage cases is available on the Live Learning Center of the AABB web site.

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Accreditation Overview CAP Survey Results AABB Annual Meeting

At the 2005 AABB Annual Meeting in Seattle, Dr. Cheryl Conley, as Chair of the Parentage Testing Accreditation Program Unit (PTAPU), gave a presentation discussing CAP Survey Results and Parentage Accreditation for 2004-2005, which is available at the AABB Live Learning Center, within the 2005 Annual Meeting - Technical/Clinical session number 110. The new name for Parentage Testing is Relationship Testing and the two program units are Relationship Testing Standards Program Unit (RTSPU) and Relationship Testing Accreditation Program Unit (RTAPU).

It was noted that:

- ✓ There are 25 approved RT volunteer assessors and 3 assessor trainees.
- ✓ There are now 44 accredited Relationship Testing Labs.
- ✓ 28 labs were successfully re-accredited.
- ✓ 2 labs were reassessed.
- ✓ No labs were denied accreditation.
- ✓ There are 4 new labs applying for accreditation.
- ✓ Most of the accredited labs tested 5,000 cases or less per year.
- ✓ The number of labs doing RFLP continues to drop.

The RTSPU is unique among program units because AABB may be the only assessment conducted for some of the small independent laboratories. These facilities are CLIA exempt and unlike hospitals, blood banks and donor centers are not inspected by CAP, JCAHO or FDA. Because they are CLIA exempt RT laboratories may use their own "home-brew" tests, and are more likely to develop new and innovative technologies than other program units.

Dr. Conley discussed how a new facility applies for accreditation, how a facility applies for a variance from a Standard and what the process is when a reassessment is recommended for a facility. She also discussed the changes to the requirements of a laboratory director in the 7th Edition of the Standards for Relationship Testing Laboratories. A list of non-conformances found during the assessments performed in the last year was provided.

During the discussion of the CAP survey results for 2004 – 2005, Dr. Conley indicated that the number of labs participating in the 5 surveys reviewed in this presentation ranged from a low of 90 to a high of 106. The most common errors seen (11-12% of labs) in the surveys were the reporting of genotype instead of phenotype. The overall outcome of the 5 surveys can be found in the tables below.

Facility Guide to AABB Assessments

Now Available

A new resource is available for AABB Institutional Members to use in preparation for their AABB assessments. The *Facility Guide to AABB Assessments* was developed by the Education Advisory Subcommittee of the Accreditation Program Committee, and provides user-friendly information on such topics as:

- History of the accreditation program
- Overview of the accreditation process
- Preparation for an accreditation event
- Managing the onsite assessment
- Responding to nonconformances
- Staying current with accreditation requirements

New members, as well as those who have been previously accredited, will find the guidance, directions and suggestions found in the *Guide* helpful in achieving and maintaining AABB accreditation. The *Guide* can be found on the AABB Web site under:

www.aabb.org>Members Area > Accreditation > Assessment Guide

PARF-A 2004

	Included AF	Excluded AF
Correct Results	99%	96%
Indeterminate Results	1% RBC only*	2%
Not Tested		2%

PARF-B 2004

	Included AF	Excluded AF
Correct Results	99.1%	97.2%
Indeterminate Results	1% RBC only*	
Single Exclusion		0.9%
Not Tested		1.9%

PARF-C 2004

	Included AF	Excluded AF
Correct Results	99%	97%
Indeterminate Results	1% RBC only*	
Single Exclusion		1%
2 Exclusion (THO and vWA)		1%
Not Tested		1%

PARF-A 2005

	Included AF	Excluded AF
Correct Results	100%	100%

PARF-B 2005

	Included AF	Excluded AF
Correct Results	99%	98%
Not Tested	1%	2%

*The labs reporting RBCs only were doing STRs by the time the PARF-B 2005 survey was reported and the number of labs performing RFLP was down from 10 to 7.

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2005-2006 RTAPU Members:

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George Maha, JD, PhD

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WANTED

Assessors

Have you ever considered becoming an assessor? The AABB Relationship Testing Program is looking for assessors. Please consider becoming one.

The requirements for an assessor are as follows:

- Must hold a minimum of a bachelor's degree.
- Must be an active AABB individual member.
- Must possess the appropriate experience and training.
- Must agree to the defined commitments.
- Must possess defined attributes.
- Must agree to the defined continuing education and competence requirements.

New assessor training is held at the AABB Annual Meeting and at Regional Workshops offered during the year. For a complete workshop schedule and details on the requirements/qualifications contact, Kim Charity at kcharity@aabb.org or visit http://www.aabb.org/Content/Accreditation/Become_an_Assessor/becomeassess.htm

RTAPU or RTSPU Member

Are you currently an assessor? Would you like to be involved in planning the AABB Assessor Day Relationship Testing breakout session? Would you like to review corrective action plans for process non-conformances? Would you like to be involved in the newsletter? If these issues are of interest to you, the Relationship Testing Accreditation Program Unit would like to have you as a member.

Are you currently an AABB Member? Would you like to be involved in creating and revising the Relationship Testing Standards? Would you like to review the requests for variance from the Standards? Would you like to be involved in creating and revising the Guidance for the Standards? If these issues are of interest to you, the Relationship Testing Standards Program Unit would like to have you as a member.

Please contact Pam Lubel at the AABB National Office at plubel@aabb.org.