Molecular immunohaematology round table discussions at the AABB Annual Meeting, Anaheim 2015

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Introduction

At an international meeting, we offered round table discussions on six topics of molecular immunohaematology: one donor-related, two patient health care-related, and three technical topics. The six issues discussed can be challenging, even controversial, among professionals in the field of blood group serology and genetics and addressed: the "gold standard" method for red blood cell antigen determination; use of next generation sequencing (NGS); replacing ABO serology with red cell genotyping; patient cohorts benefiting from cost-efficient, prophylactic red cell genotyping; justifiable additional cost and reimbursement; and centralised databases across different donor services. We provide a summary of the participants' input to our questions and then discuss the topics. Use of molecular-based immunohaematology testing is becoming more widespread in laboratories worldwide and is known to benefit patients at a level that cannot be achieved by any serological approach alone.

Organisation of the discussion rounds

An international group of transfusion medicine specialists gathered in a 1.5-hour workshop "Roundtable Discussions for Molecular Immunohematology Professionals", which was offered to any attendee of the AABB Annual Meeting & CTTXPO 2015. The format of this workshop was similar to those in the three preceding years, 2012 to 2014[1]: a group of participants at a table met sequentially with six chaperones for 10 minutes each to discuss topics in the form of a question; the participants remained at the table discussing successive questions while the chaperones moved from table to table. The chaperones, selected prior to the workshop, listened to the participants' viewpoints, clarified questions, took notes regarding the points raised and kept the discussion on track. Most chaperone pairs consisted of a US and an international expert in the field: the groups consisted of five to ten participants each at 11 tables.

During the annual meeting registration, 25 individuals signed up for the session; 65 logged in on site and actually attended the workshop, returning 18 evaluation forms after the event for a 28% reply rate (Table I). The participants came from six countries and represented a broad range of experience in serology and molecular testing. They reported working at hospital transfusion services that either outsource molecular testing or offer it as service (30%), regional blood centres including immunohematology reference laboratories that perform molecular testing (35%), commercial entities including a cell therapy company (10%) and the Food and Drug Administration (FDA) (5%). The non-US attendees (20%) represented hospitals and blood centres.

Round table results

All participants had the opportunity to provide input to the six questions. The six teams of two chaperones each provided the following summaries of their round table discussions, representing only the views of the participants.

Question 1: What constitutes the current "gold standard" method for determining red blood cell antigens: serology, molecular immunohaematology, or both?

"Both", was the spontaneous answer by the majority of participants, although most continued to use exclusively serology for their day-to-day routine testing. Molecular immunohaematology methods were being utilised when discrepancies were encountered in patient typing, such as discrepancies between the alleged phenotype and a suspected antibody. Although there was a place for serology even in recently transfused patients[2], most participants were well aware of the limitations

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Table I - Demographics of the participants.

Parameter and characteristics	Replies (n)	Percentage
Level of experience		
1-5 years	2	12
6-10 years	3	18
11-19 years	4	24
20+ years	8	47
Total	17	100
Position*		
Director/Manager	5	29
Lead/Specialist	3	18
Chief/Medical Director	2	12
Technologist/Technician	2	12
Supervisor/Coordinator	2	12
All other replies combined	3	18
Areas of specialty†		
Patient laboratory testing	7	35
Clinical practice/Patient care	3	15
Molecular testing	3	15
Administration	3	15
All other replies combined	4	20
Relevance of content		
Excellent	15	100
Good	0	0
All other (Fair/Poor)	0	0

* Other replies: Physician, Scientist/Clinical Investigator, Other (n=1 each).
† Other replies: Blood collection, Cellular therapy, Research/Development, Other (n=1 each). Multiple replies possible. Replies may not sum up to 18, because some fields were not answered on all forms.
Recorded countries of origin: USA, Canada, Brazil, Spain, United Kingdom, and New Zealand.

facing serology and, despite the very best efforts, its relatively frequent misleading results[3]. One participant stated, "We can go through a lot of heroics getting a phenotype and in the end you might be incorrect". The "marriage" of serological and molecular testing is where hospitals and blood centres should be heading. Hospitals with donor programmes and large blood centres used red cell genotyping to identify unique, often rare, blood group patterns, needed to support patients[4] and particularly in sickle cell programmes[5].

What are the relevant criteria? While reliability of the assay method ought to be paramount, the availability for patients' care is also critical if delays are unacceptable. The participants reported a wide disparity in the turnaround time for the commonly requested red cell genotyping panels. At some blood centres, one or two runs per week were performed, while others complete their red cell genotyping within 3 days of receiving the samples and have sufficient staffing to complete "STAT" tests within 24 hours, if requested. Participants from hospitals, who have to send out any molecular testing, reported waiting times of 1 to 2 weeks and, consequentially, have to rely on their serological testing for most patient care, while molecular testing, recognised as the more definitive approach, is deferred to later transfusions or subsequent hospital admissions (Chaperones: DAW & FP).

Question 2: How should we characterise blood group genes and alleles so that patients will benefit most from next-generation sequencing data?

Many of the participants were not familiar with the technical details of NGS. A few acknowledged NGS would increase single nucleotide polymorphism coverage, improve sequencing accuracy, and resolve some allele haplotypes better. However, most concern was raised about the longer turnaround time and the need for additional equipment and training (Table II). Almost everyone agreed that our community was not adequately prepared to interpret, store, and share the large amount of data generated by any NGS-based assays and, at this time, many felt NGS would best be dealt with at a national or regional level rather than at each institution.

Participants also raised questions about the relevance of sequencing all blood group genes and alleles, because much of the information would be irrelevant or unreferenced in known alleles. If all the genes and alleles are sequenced, what will define a match?

Table II - Challenges and solutions toward establishing routine next-generation sequencing for red cell genotyping.

Challenges	Solutions
Turnaround time (TAT)	TAT continues to become shorter. In addition, results of NGS performed once may be used later, which will be the most cost effective way for any red cell genotyping.
Cost of NGS	The cost continues to decrease. Eventually, whole genome sequencing will become so economical that most patients will have it done for routine medical use. Transfusion medicine should be prepared to utilise such data for secondary use in antigen prediction and matching.
Ethics of genomic sequencing	Ethical considerations concerning genomic testing are not unique to red cell genotyping, which is known to be free of many ethical concerns rightfully raised in genomic testing. As NGS will become common place, many of the concerns raised will be worked out by the larger medical community. Transfusion medicine should be positioned to contribute in that process.
Clinical interpretation	The large scale nature of the data will require the development of software and algorithms that can automate red cell matching (dry matching)[18] and aid in the clinical interpretation.

NGS: next generation sequencing.

How will the clinically significant information be defined and interpreted, and how will the seemingly insignificant information be used and managed? All but five participants expressed concern regarding the ethical implications of characterising all blood group genes and alleles, especially if part of a larger NGS assay including whole genome data. Most informed consent documents were designed in the past without specifically addressing the use of NGS. There was also concern that widespread use of NGS might cause more individuals to feel coerced to donate because more "rare" blood typing results may be expected.

Opinions differed greatly over which patients or donors should undergo NGS. The cost may only be warranted for specific patient populations, identified for additional red cell genotyping in a previous survey in 2012 (Thesis 4)[6]. One participant suggested it would be cost effective to use NGS for all patients as the sample cost might decrease the more it is performed, and another participant noted that NGS was the future of antigen evaluation and that the transfusion community could only gain if we embrace NGS and move to using NGS as soon as possible (Chaperones: NS & WJL).

Question 3: What advances are required to enable red cell genotyping to replace serology for typing ABO antigens?

Using diverse platforms to type for ABO antigens by serology (Table III), the majority of participants experienced discrepancies only rarely or occasionally (Table IV). Some commonly cited causes of failures and discrepancies in ABO serology included ABO-mismatched haematopoietic progenitor cell transplantation, massive out-of-type red cell transfusion, cold autoantibodies, and underlying diagnoses influencing ABO antigen expression or ABO antibodies, such as acute myeloid leukaemia and immunodeficiency disorders. Virtually all of such serological ABO discrepancies could be resolved by ABO genotyping. Many participants indicated that they had employed ABO genotyping for just this purpose.

A large percentage of the participants (45%, Table IV) indicated that their primary ABO platform rarely failed despite the wide variety of clinical issues that can affect ABO testing. Nonetheless, 34% (18 out of 53) stated having utilised genetic methodologies to aid in ABO typing. No participant from hospitals or donor facilities reported using ABO genotyping on a routine basis. One common indication for ABO genotyping was to resolve or confirm a serologically suspected A or B antigen variant. Most facilities reporting use of ABO genotyping (83%, 15 out of 18 participants) sent their ABO genotyping request to specialised reference laboratories.

Table III - ABO typing methods currently used as standard approach.

ABO typing methods	Participants (n)
Tube and gel	16
Tube only	11
Tube and solid phase	7
Gel only	6
Solid phase only	5
Tube, gel and solid phase	2
Gel and solid phase	1
Other*	5
Total	53

* Not specified. Several ABO genotyping assays currently in development by participants from industry or research facilities.

Table IV - Perceived discrepancy rates for the currently used ABO typing methods.

Incidence of ABO discrepancies and failures	Participants (n)
Frequent	2
Occasional	17
Rare	24
Other*	10
Total	53

* Not known, unclear, not reported, not applicable.

Which technical and scientific advances are needed and why? As to what is impeding adoption of ABO genotyping, the most widely shared view among participants was that current serological methods are inexpensive, rapid and easy to perform, so the routine use of ABO genotyping is not perceived as practical at present. However, many participants indicated that the development of faster and cheaper ABO genotyping technologies would move the field forward and allow for eventual consideration of routine ABO testing by molecular techniques. Some participants pointed to blood group O red cells as a readily available option for patients with an ABO discrepancy. For donors, time constrains being of lesser concern, ABO genotyping could become a viable alternative and ABO serological testing might be completely abandoned one day. Only a few participants raised concerns related to rare or unknown ABO gene variants and the known interfering genes.

Another concern was the general inexperience of participants with ABO genotyping, seen as relatively complex compared to a more straightforward molecular assessment of most non-ABO antigens. Some participants felt that community and even academic hospitals lacked personnel capable of performing or interpreting ABO genotyping. The development of commercial FDA-approved kits was identified as a supportive advancement for molecular ABO methods to bridge the perceived knowledge and experience gaps.

A few participants considered that the management and communication of large amounts of data generated by ABO genotyping are obstacles that can be overcome by improved computer software and automated analysis programmes (Chaperones: CAT & FFW).

Question 4: Is antibody generation still observed after transfusion of antigen-matched red blood cells? For which selected patient groups would you consider prophylactic red cell genotyping to be cost efficient? Do you use red cell genotyping for such patients?

Participants were virtually unanimous in responding that blood group antibody generation was still observed, even when transfusions were extensively matched by serology. The majority also reported that their matching for Rh and K for patients with sickle cell disease resulted in reduced alloimmunisation, although antibodies to Rh antigens and low prevalence antigens were still observed. There was consensus that prophylactic red cell genotyping was cost-efficient for chronically transfused patients, especially patients with sickle cell disease (Table V). One participant commented that it could be even more cost-efficient, if it were possible to limit genotyping to antibody "responders", who unfortunately cannot yet be distinguished from non-responders. Some participants volunteered the observation that genotyping reduced personnel time in complex serological cases, with one stating that it "avoids days of work-up". Some participants also advocated that it would be cost-efficient to genotype all premenopausal females to reduce the future risk of haemolytic disease of the foetus and newborn. The participants did not support prophylactic red cell genotyping to reduce alloimmunisation and delayed haemolytic transfusion reactions in general hospital patients, because cost-benefit data are insufficient at present.

Table V - Cost-efficient indications for red cell genotyping.

Indication considered cost-efficient	
by 75% to 100% of participants	*by 50% to 75% of participants*
Patients with chronic transfusion	Patients with non-haematological malignancy
Patients with multiple alloantibodies	Patients with suspected RH variants
Patients with autoimmune haemolytic anaemia	Foetus in a mother with an alloantibody
Patients with an alloantibody to a high-prevalence antigen	Pregnant women with weak D or partial D phenotypes
Specimen with phenotyping discrepancy or difficulty	Paternal *RHD* zygosity
Search for antigen-negative red cells when serological reagents are unavailable or rare	Search for donors to obtain reagent blood cells for development and testing
Search for donors with rare phenotypes	

Many participants reported that in their current practice red cell genotyping is applied for chronically transfused patients, patients with autoimmune haemolytic anaemia, and patients with multiple antibodies or with antibodies to high prevalence antigens[7]. One hospital-based participant indicated that her facility genotypes patients for virtually all indications listed in Table V. Participants representing several donor centres indicated that they currently use red cell genotyping to screen for donors with rare phenotypes[8] (Chaperones: GS and LC).

Question 5: Some molecular test kits are available for use in the transfusion service laboratory. Do you think additional cost to perform red cell genotyping is justified? What do you know about reimbursement for such testing?

There was broad consensus that the use of red cell genotyping is becoming widespread and standard in immunohaematology reference laboratories. The prime utility was seen in resolving indeterminate or discrepant serological results and in finding the best matched blood for patients with haematological diseases and those undergoing haematopoietic progenitor cell transplantation, who are often recently and multiply transfused (see also Question 4). Red cell genotyping for many non-ABO antigens is evolving from a "reflex" test in complex serological work-ups, to a test routinely used by policy[9].

Blood centre participants noted that their hospital customers are becoming familiar and comfortable with molecular typing results, and are starting to request genotyping for patients felt to benefit from extended antigen typing, and in fact many larger hospitals are beginning to routinely order red cell genotyping for patients by category such as those with sickle cell disease[5], thalassaemia[2], and warm auto-immune haemolytic anaemia. Some large hospital transfusion services are performing such tests in-house for the same categories of patient[10]. In many instances, blood collection agencies are routinely using red cell genotyping to increase the characterisation of their blood donors to improve the availability of blood for patients with complex red cell antigen requirements[4,8].

The cost for red cell genotyping was reported to range from $ 150 to 400[11,12], with additional costs associated with complex serological work-ups. Immunohaematology reference laboratories often did not charge separately for molecular typing, and included those costs in their reference laboratory overall charges to the referring hospital. For instance, hospitals in Canada were not billed for red cell genotyping, and it was acknowledged that billing decisions were based on the healthcare financing systems. Knowledge of the specific Current Procedural Terminology (CPT) codes

was still limited while, for example in the USA, some Medicare Administrative Contractors have released local coverage determinations for specific red cell genotyping platforms and applications[13].

Some participants felt that blood centres should charge separately for red cell genotyping to encourage hospitals to bill patients for those tests. Indeed, some reference laboratories charged referring hospitals and some hospitals attempted to bill the patients, though there was little knowledge of the payments relative to the charges. Although a recent joint statement from the AABB and CAP[9] was discussed at some local Medicare Advisory Committees recommending red cell genotyping in certain groups of patients[14], the proposition and its discussion were not generally known to most participants.

Participants felt that the increased cost for molecular typing was justified based on the capacity of extended typing to prevent alloimmunisation, to improve availability of matched blood in a timely fashion for alloimmunised patients, and potentially to reduce subsequent serological work-ups in patients who receive matched blood (Chaperones: EBK & WALH).

Question 6: Is a centralised database across different donor services useful for red cell genotypes?

Easy data access and overall cost savings were seen as the advantages of a national or centralised donor registry, while concerns focused on issues of privacy, management and cost burden at the blood centres (Table VI). Who should manage such a database, when few centres are currently performing red cell genotyping? Who would release the data and based on what need, such as prophylactic matching *vs* suspected alloantibodies; who would manage or resolve discrepancies[15,16]; and who would answer questions or release data to hospitals when a donor becomes a patient? Transparent donor data could cause competition for rare donors. Policies would be needed to decide which patient should receive a rare unit over another patient.

Logistic complexities involved the number of test platforms, some licensed and some not, with different resolutions and lack of a standard and consistently updated blood group allele nomenclature[17]. How should data be handled from older test versions when technologies evolve rapidly? Information technology challenges include data security and portability among different databases, which could be addressed with data exchange standards and national donor identification numbers. The translation from genotype to phenotype would need to be standardised, although this issue is less critical in dry matching[18].

In the USA, the Health Insurance Portability and Accountability Act defines the requirements for securing personally identifiable information, such as that found in electronic health records. Privacy and ethics were seen as a major barrier to a donor database, especially for immigrants who might stop donating out of fear. Some participants noted that a national database might be seen as negative to donors who want their blood to be used in their local community. Such issues could be addressed by policies and education.

The American Rare Donor Program was cited as an existing effort to localise donors with rare blood groups[19]. The National Marrow Donor Program was noted as a long-standing US programme that houses large genetic data sets used for matching donors and patients[20]. The Canadian Blood Service has two locations for molecular testing, and three hospitals (Ottawa, Toronto and Calgary) also perform testing in Canada. In New Zealand, 26 blood banks shared a database for donor serological blood group information.

Generally, the participants felt that a red cell genotype database would be difficult to implement at this time, with prohibitive costs without any prospect for funding sources. Most participants put a higher priority

Table VI - Centralised databases across different donor services for donor red cell genotypes.

Utility	Concerns	Technical issues and solutions
Portability	Privacy of genetic data - Who is responsible for data release?	Code for Personally Identifiable Information - follow HIPAA in the USA
Standardisation - donor databases may be an easier objective than patient databases	Data integrity - Who will be keeping the data current? Information technology standardisation - red cell genotype data exchange standards - national donor identification number	Varying degree of molecular resolution - among different platforms - over time even within a given platform Algorithms for red cell genotyping - How to resolve discrepancies? - confirmation by serology or second genotyping? - licensed *vs* unlicensed tests
Cost - savings anticipated for the overall health care system	Cost burden - for the participating blood centres - caused by establishing a database, its maintenance and ongoing use	Coordinated action - among insurers, hospitals and blood centres - heavily dependent on healthcare financing system

HIPAA: Health Insurance Portability and Accountability Act.

on a registry for patients with red cell antibodies and transfusion histories to avoid delays from repeat testing, especially in critical care hospitals where prompt access to results is paramount, and to cut down costs in the hospitals (Chaperones: MAK & MSL).

Discussion

The participants at the round tables represented a cross-section with diverse experience in immunohaematology. It is the perception of experienced specialists which will shape the adoption of molecular immunohaematology in the future. Collating data on currently held views is useful for developing this field, discussed here by the authors.

Topic 1. Gold standard method

If there is no complication known before or encountered during blood group testing, almost every participant recognised serology as the gold standard method today. Serology also continues to be the only practical method in emergency situations. Molecular testing is the gold standard for complex problems, including suspected variants of blood group antigens and phenotypes obscured by recent transfusions or a positive direct antiglobulin test. There was enough confidence in red cell genotyping to replace serology, if molecular techniques become more readily available with a faster turnaround time, and more affordable. The reported actual turnaround times were in stark contrast to the clinically desired times preferred by the participants of our session in 2014 (Question 4)[1].

Topic 2. Next-generation sequencing

NGS is a widely applied method in research and also in clinical routine for DNA sequencing by repeatedly sequencing DNA stretches of several hundred base pairs, thus yielding precise results over large segments of the genome[21-24]. Starting in 2011[25], NGS has been successfully applied to blood group genes[26,27] and viewed as a promising development[22,24]; red cell antigen prediction is feasible using whole genome sequencing data derived by NGS[28].

Some participants highlighted several benefits of NGS, such as allowing more single nucleotide polymorphisms to be evaluated, improved haplotype determination, and resolving discrepant serology results; all potentially contributing to better matched products with decreased alloimmunisation. A significant proportion of transfusion medicine specialists who are not used to NGS may indeed be convinced that NGS is able to determine haplotypes. Some kinds of haplotype studies may sometimes be possible, to determine whether two or more single nucleotide polymorphisms are located on the same chromosome, such as single nucleotide polymorphisms that are rather close within the same exon - this is also true for standard genomic DNA sequencing when using appropriate primers. However, current NGS technology cannot determine haplotypes if single nucleotide polymorphisms are in distant exons or different gene loci. For instance, NGS is unfortunately not suitable for determining *RHD/RHCE* or *GYPA/GYPB* haplotypes at this time.

Many concerns were raised, including the costs, the ability to interpret the data, longer turnaround times, and ethical considerations of genomic sequencing. The current turnaround time for NGS is several days, but once done it can clearly be used for future transfusions. The required informed consent documents must be checked and, if needed, updated to address the extent of red cell genotyping covered by NGS. No donor must feel coerced to donate; while more "rare" blood typing result may be expected with NGS, the established ethical approach will not change. Participants of our session in 2014 considered identifying "rare" donors as a legitimate donor motivation, retention and recruitment tool (Question 5 and Table VI[1]).

A personal lack of knowledge and how to interpret NGS data were of general concern. Several participants indicated an urgent need for more NGS education targeted to the transfusion medicine community; this education could include social media activities such as a set of NGS questions in the popular Transfusion News Question of the Day (see Web Resources). Although the participants raised many concerns, transfusion medicine specialists can address these challenges and pioneer the implementation of NGS in our field (Table II). The initial steps are a good start[22,24]. In exons and introns alike we will find many single nucleotide polymorphisms that do *not* affect blood group antigens, but identifying those polymorphisms will still be worthwhile because they help to ascertain allele identification by NGS.

Topic 3. ABO genotyping

We noted with some surprise that more than one-third of the participants had employed ABO genotyping in the past to help resolve an ABO discrepancy or overcome a failure in ABO serology. A highly reliable prediction of the ABO phenotype by red cell genotyping is a challenging mission[29]. Any incorrect prediction, such as a group O patient assigned as group A or a red blood cell unit of group A labelled as group O, will frequently cause a devastating clinical outcome[30]. Current single nucleotide polymorphism-based methodology is unlikely to provide the necessary safety margin, because this technology cannot cover unanticipated molecular variations that cause diverse, sporadic, or non-functional alleles[24]. This principal limit to the applicability of single nucleotide polymorphism-based methods has recently

been overcome by molecular genetics methods, such as NGS[22,23], which cover whole genes including relevant regulatory sequences[21]. There are also approaches to account for epistasis (modification of the ABO gene effect by another gene, such as the H transferase enzyme[31], transcription factors[32] and microRNA[33]) and epigenetics (DNA modification at the ABO gene locus[34], such as by DNA methylation[29]). From a technical perspective, ABO genotyping seems to be within reach with the potential to equal and eventually exceed the reliability of current ABO serology.

Considering the rapid progress of molecular techniques with shrinking turnaround times[1] and declining costs, ABO genotyping may become worthwhile sooner than expected: The first commercial red cell genotyping platform has been resulting ABO groups as a "by-product" without relevant additional cost[35]. The participants expected several advancements, such as the development of more rapid and inexpensive platforms and improved knowledge of interpreting ABO genotyping results, before ABO serology will eventually be replaced. Anticipating these technological advances, it was reassuring to learn the participants' concerns focused on practical limitations of current methods and not on categorical doubts that ABO genotyping can become highly reliable and safe for patient care.

Topic 4. Cost efficient red cell genotyping

Virtually all participants were aware of the limitations of serological testing in chronically transfused patients and patients with warm autoantibodies, and agreed that prophylactic red cell genotyping should be used for such patients (Table V)[2,36,37]. Moreover, genotyping appears to have been further incorporated into the daily practice at hospitals and blood centres compared to our previous survey in 2012 (Thesis 4[6]). Even though the majority of participants were applying the prophylactic strategy of Rh and K antigen-matched transfusions for patients with sickle cell disease, they still observed antibody generation; as such, the participants' responses remained consistent with published observations[5]. This feedback demonstrated a need for clinical trials including a cost-effectiveness study to guide further expansion of red cell genotyping.

Several studies, in fact, have provided the beginnings of such an evidence-based approach. In particular, one study demonstrated cost savings for genotyping pregnant, non-Hispanic, Caucasian females with serological weak D by identifying those individuals who do not require Rh immunoprophylaxis[12]. In addition, a randomised trial[38] and a cost-effectiveness analysis[11] of antigen matching (by serology) have indirect relevance, and are prototypes of the cost-effectiveness studies needed for red cell genotyping. According to the participants, more evidence supporting a reduction in alloimmunisation and haemolytic transfusion reactions were still needed to convince administrators, rather than physicians, that prophylactic red cell genotyping was generally cost-efficient. Identifying donors with rare phenotypes or rare combinations of a large number of antigen-negative types using red cell genotyping is now routine at large blood centres[16] and has been shown to be economically preferred[4].

Topic 5. Cost and reimbursement

It has been widely agreed that more research establishing further clinical benefit of molecular typing is crucial[11,12,39-41]. Transfusing physicians must be educated regarding the applications and benefits of molecular typing (Table V)[3], which will lead to increased ordering of such tests[2]. Insurers also require education[41] about potential savings related to the prevention of alloimmunisation and timely availability of blood[4,40], and physicians are key players in this process, as noted before by the participants of our session in 2013 (Discussion 5[42] and Table III[42]). The American Medical Association recently approved addition of a new analyte for CPT code 81403 (tier 2 molecular pathology procedure, level 4) for *RHD* genotyping (see CPT Editorial Summary in Web Resources)[14], and some payers are setting reimbursement rates for the tier 2 code[13].

Topic 6. Donor genotype databases

We followed up on the feasibility of databases involving different blood donor services, a question raised at our session in 2012 (Thesis 3[6]). The participants were interested in exploring the prospect of a national or centralised donor registry but quick to identify many challenges impeding its implementation (Table VI). Although we think the overall cost-saving within any health care system could be shown, the participants were at a loss to detail the fair sharing of the management and costs of such a database. Most participants thought that a higher priority was to form a centralised registry for patients with alloantibodies. We propose that the legal, ethical and technical challenges of a centralised database should be explored, as this discussion raised multiple substantive issues that will need to be resolved before either a donor or a patient database can be successfully implemented.

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Authorship contributions

GAD directed and WAF moderated the workshop; both designed the topic statements. The six teams of two chaperones, who volunteered to participate, each wrote the summaries of their discussion rounds. WAF compiled and wrote the report.

Disclosure of conflicts of interest

CAT holds a research grant from Terumo BCT. FFW and WAF are inventors of patents owned by the German Red Cross Blood Service Baden-Württemberg-Hessen. GAD is the inventor of patents on red cell genotyping owned by the Canadian Blood Services and on the speakers' bureau of Grifols. GS receives research support from Immucor. LC is on the Transfusion Advisory Board of Grifols. MAK is on the speakers' bureau of Agena Bioscience. WAF holds intellectual property rights for RHD genotyping applications. WALH is a consultant for Cerus Corporation and Seres Therapeutics. WJL receives support from Wiley Publishing for educational activities related to the Transfusion News Question of the Day. The remaining authors declared that they have no competing financial interests relevant to this article.

Statement of disclaimer

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The first molecular immunohematology assay for blood group genotyping was approved by the US Food and Drug Administration in 2014, while several *Conformité Européenne* (CE)-labelled test kits have been available for more than 10 years; the CE label certifies that a test kit may be used for *in vitro* diagnostic purposes in the European Union. If Laboratory Developed Tests, which may employ commercial kits for Research Only Use, are used for patient care in the USA, such tests will come under the authority of the Clinical Laboratory Improvement Amendments, categorised as tests of either "high" or "moderate" complexity[1].

Web resources

- CPT Editorial Summary of Panel Actions, 2015 October (Tab. 35): www.ama-assn.org/ama/pub/physician-resources/solutions-managing-your-practice/coding-billing-insurance/cpt/cpt-summary-panel-actions.page. Accessed on 28/12/2015.
- Globe Newswire. 2015, July 9: globenewswire.com/news-release/2015/07/09/750924/0/en/Palmetto-GBA-Finalizes-Local-Coverage-Determination-LCD-for-Immucor-PreciseType-TM-HEA-Test.html. Accessed on 30/12/2015.
- Transfusion News Question of the Day: transfusionnews.com/path-questions/. Accessed on 07/01/2016.
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