Editorial

Patients with red cell antibodies: registries improve patient care by increasing patient safety, reducing costs, and enabling health information exchange

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Some countries or regions have registries for sharing data of patients with a history of red cell antibodies, usually on a voluntary basis. Most countries, however, lack a comprehensive national database. The need used to be pressing for patients with antibodies to rare antigens, when only one individual or less among 1,000 donors has compatible blood, and the patients themselves were in the past the main pool for potential donors[1]. This donor pool became restricted by more stringent donor criteria and has mostly been replaced by efficient red cell genotyping among healthy donors without antibodies[2,3,4].

The focus has since shifted to a registry for patients with any allo-antibody against red cell surface antigens[5]. And the registries' purpose has morphed to primarily servicing the patients' needs. Much time is gained, and costs are saved, when antibody detection can build on a patient's transfusion and antibody history, instead of starting an antibody identification from scratch. Of course, antibody evanescence[6] requires ready access to past data for any patient, because no serologic test can discover antibodies that are not detectable anymore while still being clinically relevant.

A 10 year follow-up documented 9,048 patients in a voluntary registry for patients with red cell allo-antibodies in Korea[7], which was established in July 2013[8,9]. Any patient antibody that remained unresolved locally could be sent to a "case archive"[10], similar to an immunohematology reference laboratory. The antibody results were deposited in the registry database[7]. Such systematic collation of the data allowed reliable estimates for the need of red cell units that are negative for distinct antigens and combinations thereof[7], thus guiding the efforts for red cell genotyping in donors[9]. Purists may quickly note that no outcome evidence was provided in this issue's publications on registries[7,10] to support the claims in the title of this editorial, and limited evidence has been published in this spirit of evidence-based medicine before[11,12]. Although these critics may have a point, they might consider: not every question that can be researched needs to be researched, certainly not beyond a sufficient degree of evidence.

Opinions what constitutes "sufficient evidence", even when shared by most experts, could sometimes be wrong; in most instances, they are correct. The available clinical evidence in support of establishing national registries may well be considered sufficient for many years[13-18]. Publications of case reports[16,19] and case series are still

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needed and encouraged. National registries might be an example of a path not taken[20] in a long time, reflecting the lack of acceptance in the field. Instead of asking for more evidence, in an attempt to delay the obvious albeit inconvenient or unprofitable tasks, transfusion medicine could have adopted the concept decades ago.

Or was the concept implemented a long time ago? Mostly, it has been applied to patient care even before transfusion services became computerized[21]. Immunohematologists did an admirable job in taking care of this patient safety aspect –within the limits of their services and technical support– using paper index cards since before the 1960s. They painstakingly transferred all such data into computerized databases beginning in the mid 1980s[22], often adding to their ongoing full-time routine jobs while being denied clerical support for their extra work. Mergers of blood services prompted the growth of electronic databases as part of an electronic health record (EHR).

The exchange between the databases remained sluggish, however, as exemplified by record fragmentation[23,24], which is continuing. Growing databases is expensive, including maintenance on an ongoing bases, web development and legal fees[25]. Many learned to live with imperfections of the health information exchange (HIE), because no alternative methods existed or were accessible. Still, some may be too complacent with their learnt technologies, reluctant for an unduly long time to introduce new technologies in their laboratories. They thus refrained from applying the latest novel techniques for the benefit of patient care[17]. This situation ought to change rapidly.

Often seemingly legitimate reasons prevailed, such as being unable to obtain sufficient funding or reasonable return-on-investment. The gradual implementation of databases and HIE may reflect technology and other resources available to transfusion medicine at any given time. The discipline will utilize its resources for immediate patient care first, before apportioning monies, if any are remaining, to topics of delayed benefit. To achieve faster implementation, funds needed to be increased and specifically directed to "prophylactic" measures, such as HIE in transfusion medicine.

South Korea's registry[7] would serve its 52 million inhabitants, which is an impressive number for a voluntary transfusion recipient registry. Some services elsewhere may come close or even exceed this number, despite covering only a small fraction of their more populous countries. Services in countries without national health care systems, the US[14] and EU countries such as Italy[26] and Germany[2,27], come to mind. The puzzle remains: "*Few countries have registries for automatic sharing of antibody data. What is the main reason?*"

Exactly this question was posted on X, formerly known as Twitter, in July 2023. The poll received 60 votes in these days of social media. Such unsupervised queries, open to all users and certainly not representative, can still be a starting point for online discussions. They may reach professionals and generate interest early in their careers[28]. Close to a majority voted "lack of financial incentives" as the main reason (48.3%), followed by "privacy concerns" (35%), and "too much competition" (5%), while the remaining 11.7% of voters claimed: "other reasons". And these may well be the key elements to move registries forward. How can financial viability be offered to the data providers and registries while privacy will be maintained at all times? Hospitals are paid for their current patient service, rarely for future eventualities in the patient's care that is served so well by uploading data to a patient antibody registry. Instead of asking, often implicitly expecting or requiring, the data providers to absorb the costs now for possible patient care savings in the future, hospitals and reference laboratories could be incentivized and reimbursed for their data management and data uploading to registries.

The registries may be non-profit[18] or for profit[29], provided that the patients' data themselves are not proprietary. Current databases can constitute a substantial asset for their proprietors. While data sharing must be offered by the database owners, the technical means provided may be cumbersome, slowing the exchange with potential health care competitors. Seamless, eventually automatic, data sharing between various platforms in a marketplace, once incentivized, would quickly become the norm. Secure, yet accessible, database maintenance causes significantly more costs

than a basic searchable database; these costs will only increase with cybersecurity concerns. Health informatics standards are being developed for blood group data[30], which will be applied to this HIE[31] and facilitate interoperability between registries[32]. User agreements or legal requirements by health care systems can ensure compliance with automatic and inexpensive data sharing. And the patient who is ultimately the customer and payer shall retain ownership of her data.

Privacy concerns need to be taken seriously. They do not differ from any other Health Insurance Portability and Accountability Act of 1996 (HIPAA) regulated health information[25] in the US, and solutions to protect personally identifiable information (PII) are constantly being improved. The need to mobilize healthcare information electronically across organizations, enabled by portability, within a country or region is understood[5,18,33]. A choice would consider the strongest long-term data protection regulations, which may for some countries be found abroad. Access will be constantly monitored, limited to the extent needed and controlled by health ID or government ID cards that the patient carries. Transfusion medicine should be prepared to latch on as these emerging technologies become available.

The patient, her physician or health insurance can take the initiative, control her data, submit to any database of her choice, and build her online health information portfolio, of which red cell antibody and transfusion history is a critical, yet small component. A distributed data curation with highly interactive data exchange may be the future for an electronic health record.

Transfusion medicine is watching the establishment and growth of voluntary registries for patient antibody data in many countries[7,11,12,14]. Eventually, this discipline will go beyond regional, national, voluntary or even comprehensive registries and merge the utilization of data, distributed among a variety of database suppliers and locations, on a provided-as-needed basis, transcending national and language borders.

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