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Consider This

IVF errors: Is this only the tip of the iceberg?

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Abstract:

ART errors are fortunately a rare occurrence. but humans are fallible and mistakes are inevitable. As social media sensationalizes these events, we, as infertility specialists, must be vigilant in reviewing existing risk management systems and consider other options to minimize/eliminate these events. ART programs should work emphasize honesty and transparency to improve quality of care.

Consider This:

Given the recent flurry of sensational "mix-ups" involving IVF (in vitro fertilization) and IUI (intrauterine insemination), public trust in the field of assisted reproductive technology (ART) has undoubtedly been shaken. None of these acts are comforting; some display human error, and others are outright egregious. While human error is a constant variable in any facet of medicine, recent reports involving misplaced embryos; the failure of cryopreservation tanks that destroyed more than 4,000 oocytes and embryos, and the use of erroneous gamete/embryo transfers do not appear to be simple mistakes.[1-5] To further exacerbate patient outrage, several physicians have been accused of inseminating patients using their own sperm or sperm from a hospital employee instead of the intended father without informing their patients.[6,7]

Most of us are overcome with horror and profound disappointment when we hear of these events. At best, these incidents suggest major disregard for protocol; at worst, they hint at outright deception, rather than simply confusing sperm samples that are being simultaneously processed in the laboratory. These missteps strike fear into the hearts of reproductive physicians and scientists, the vast majority of whom dedicate their careers to avoiding such errors.

Furthermore, these acts inspire news stories that cause patients to be distrustful of ART services and providers. Yet our cognitive biases predispose us as physicians and staff to perceive that we could never commit such acts, intentionally or unintentionally. Thus, as

professionals, we are compelled to address these incidents through a "warts and all" approach.

Since the birth of birth of Louise Brown, now over 40 years ago, more than one in 10 women end up seeking fertility-related services from 480 U.S. clinics, resulting in 69,000 IVF live births a year – nearly 2 percent of all children born annually. More complex IVF procedures have evolved, including micromanipulation and pre-implantation genetic testing (PGT), cryopreservation of eggs and embryos, and non-traditional family units including not only intended parents but also egg and sperm donors and gestational carriers. Furthermore, IVF requires the involvement of medical, nursing, paramedical staff, ultrasonography, and embryology, and has an ever-expanding volume of cases. Current estimates posit that the number of ART cycles reported on the Society of Assisted Reproductive Technology ("SART") website (http://sart.org) have doubled between 2003 and 2017.

Over the years, this has led fertility clinics to adopt stringent control measures to minimize errors and ensure that ART practitioners meet the standard of care, with the goal of ensuring optimal care for infertility patients. The impact of errors, or non-conformances, in laboratory medicine has a reported range from 2.7% to 12%.[8] More recently, Sakkas et al. reported non-conformance rates were significantly lower. Out of over 36,000 fresh and frozen IVF cycles involving almost 182,000 laboratory procedures, 99.9% of procedures proceeded with no errors. Moreover, they observed no major grade non-conformances, errors with an extreme patient impact, such as a confirmed pregnancy or birth following misidentification of sperm, egg or embryo, or a tank failure affecting multiple patients.[9] Letterie reported on medical malpractice claims from a single carrier covering 10 of the roughly 480 ART practices in the U.S. between 2006 and 2015. While claims were rare (0.00095%, 176 in 184,015 IVF cycles), misdiagnosis and lack of informed consent accounted for 76% of award dollars, but errors in handling of embryos were most frequent, accounting for 38% percent of claims paid.[10]

Despite these rare major grade non-conformances, some have questioned whether there is enough oversight in the ART industry. Attorneys specializing in reproductive medicine malpractice have deemed this field the 'Wild West' of medicine—a realm where almost anything goes and almost no one knows what has gone on." [11] Arguments point out that, while these mistakes are tracked and publicly reported in other fields of medicine, there is no mechanism for reporting them in ART.

But reproductive medicine *has* adopted stringent control measures. Oversight frameworks were passed in 1992, when Congress passed the Fertility Clinic Success Rate and Certification Act (FCSRCA) mandating standard definitions and reporting of ART cycle data to the Centers for Disease Control and Prevention (CDC).[12] This information is used to generate an annual report from individual and aggregated clinics on infertility

procedures and their success rates to provide greater disclosure. As a result of FCSRCA, the CDC developed a model program for certifying embryology laboratories in 1999, including requirements for a state continuing certification program, quality assurance and control standards, an inspection system, and conditions under which certification can be suspended or revoked. In 2005, the FDA assumed comprehensive jurisdiction over screening and testing of reproductive tissues, such as the eggs and sperm that will be transferred into human recipients.[13] Agency regulations mandate strict protocols for egg and sperm donors, including thorough medical histories, identification controls, freedom from infectious diseases, and rigorous inspection of the facilities in which these tissues are handled.

Today, regulations, inspections, and guidelines all help to ensure that ART practitioners uphold standards of care. ASRM (http://asrm.org) describes the field of ART as "one of the most highly regulated of all medical practices in the U.S." The College of American Pathologists (CAP) accreditation program ensures that reproductive laboratories conform to high national standards of quality. On the federal level, three agencies regulate ART, including the CDC, the FDA, and the Centers for Medicare and Medicaid Services.[14] Additionally, ASRM's affiliate, SART, strictly monitors member clinics for adherence to ASRM guidelines, accreditation of their embryology labs, qualification of their staff, and submission of data to the CDC to ensure that reproductive laboratories conform to national standards. ASRM and SART also continually establish and revise ethical and practice guidelines and membership requirements, including guidelines on minimal standards for providing ART.[15]

Fortunately, adverse events leading to death are extremely rare in our medical specialty. However, in our industry, the most egregious harms are when gametes/embryos are given to the wrong patients during a reproductive treatment cycle or when reproductive tissue is inadvertently destroyed.[16] These incidents can have significant emotional, psychological, relational, and legal ramifications.

Although the vast majority of physicians and scientists possess the utmost integrity (unlike those who purposefully use others' gametes without the consent of progenitor or recipient), we must acknowledge that such errors are possible in our industry.[17] While these severe non-conformances are generally not fatal, they cause immeasurable psychological distress and lead to highly publicized events, including embryo misidentifications leading to a child's birth from different genetic parents, or gametes or embryos that are inadvertently destroyed.

So what more can be done to eliminate these incidents? Various professionals have suggested additional precautions, including enhanced quality assurance (QA) initiatives, modifications in laboratory staffing, biologic labelling, and perhaps a transparent public ranking system.

With respect to QA, Quality Management Systems (QMS), including the IOS 900, utilized in business organizations, have been implemented in the arena of ART programs. Alper has reported on the utilization of a QMS ISO 9001:2008 system (now a newer version ISO 9001:2015) that was adapted to an ART program.[18] These QMS systems allow practitioners to control documents, clearly delineate staff member responsibilities , document numerous processes and procedures, improve error tracking and reduction, and exercise better systems control. Most importantly, practitioners have suggested that QMS systems can provide transparency within the organization and promote continual improvement. Perhaps national implementation of these systems will, as Alper suggests, "encourage data-driven decisions as opposed to emotional ones, will have (internal) metrics to prove it…other than pregnancy rates."

There continues to be dramatic changes in ART practice including increasing numbers of ART procedures, use of embryo "freeze-all," and pre-implantation genetic testing. As such, safe and efficient operation of the ART laboratory has become increasingly complex, including the myriad responsibilities associated with maintaining proficiency and documentation. Alikani et al. reported that the time required to complete a contemporary ART cycle has increased significantly, requiring up to 20.2 person hours as compared with the same requirements for the ''traditional cycle'' of the 1980s and 1990s (roughly 9.1 person hours).[19] Today's ART cycles take longer because they involve more complex technologies and have more procedural steps with suggested laboratory witnessing requirements. Moreover, although guidelines suggest that safe and efficient ART laboratory operation requires one embryologist for every 90 –150 ART cycles per year,[20,21] estimates suggest that this falls short of the average recommended staffing, introducing additional risks.[22] Perhaps it is also necessary to implement strict workloads, reducing each laboratory staff member's hours to include mandatory work breaks. At a minimum, each clinic should assess its staff numbers, work volume, and ratio of senior to junior embryologists to determine appropriate staffing. Alikani et al. have proposed an interactive Personnel Calculator to better help determine staffing needs.[19.] Interestingly, Boone and Higden have described "typical" and "optimal" work environments for ART facilities, and suggest the CDC should add annual survey questions to compare time and staffing requirements to pregnancy and live-birth rates. Perhaps such measures as these could also lead to greater transparency and appropriate workload allocation.[23]

Outside of personnel matters, proper reproductive sample identification is fundamental to eliminate the risk of gamete and embryo mismatches. Labeling all labware and implementing manual double witnessing or electronic witnessing protocols, undoubtedly minimizes the risk of sample mismatching due to human error. WGA biofunctionalized barcodes have been used to identify mouse and human embryos so long as it does not significantly affect embryo preimplantation developmental and quality;[24,25] previous studies have clearly demonstrated no effect on full-term development in mice; however,

the potential effects on human embryo implantation and post-implantation development is undetermined. Cell labeling with dyes or retroviral vectors in mouse embryos has yielded important information about the embryonic origin of cell lineages, and could possibly serve as an appropriate identification method.[26.] Genetic fingerprinting may also prove an important tool given a suspected incorrect embryo transfer; fetal genotypes could be compared to the pre-screened genotypes of the appropriate embryo cohort.[27]

Improvements in cryotank malfunction and troubleshooting are also necessary. Some tank alert systems feature a scale underneath each tank to monitor weight changes and detect issues with the liquid nitrogen. Others use online platforms giving staff real-time access to cryogenic tank temperature. Creating mandatory industry standards would help prevent such catastrophies.

Our intent in this piece is not to focus on the willful failure to disclose medical errors or knowingly misusing embryos or gametes, but on the medical (human) risk of error that is present in all medical fields. How we handle these errors matters enormously. Simply acknowledging errors and how they occur can spur identification of solutions. Admitting mistakes is devastating to both the patient and the IVF team, but our patients' safety and outcomes are the highest priority. To paraphrase Proverbs 16:18, "pride makes excuses, and humility makes adjustments." Thus, we must continue and adjust risk management strategies to ensure that we continue to deserve patients' trust. Consequently, a publicly accessible clinic rating system based on adherence to error reduction and patient safety measures could provide patients valuable data.

Patients clearly deserve better. Entrusting one's gametes or embryos to laboratory personnel can be a fearful process. Though incidence rates are extremely low, news of these errors may prompt already stressed infertility patients to discontinue treatments that are highly likely to succeed. We as an industry must improve our self-regulation and monitor compliance with legal, ethical, and safety standards. Errors must be immediately disclosed to patients, and practitioners must immediately apologize and seek a resolution.[9] No error can be undone, but early disclosure will build trust, strengthen patient-provider relationships, and likely decrease malpractice claims. Lack of transparency invites independent parties, including governmental regulators and tort lawyers, into clinics to monitor and enforce standards. Only through acknowledging that these warts exist can we begin the process of removing them.

References:

1. https://www.vox.com/the-highlight/2019/6/26/18744249/fertility-clinic-destroyed-embryos-lawsuits
2. https://www.courthousenews.com/gay-couple-sue-fertility-clinic-for-sperm-mix-up/

3. https://www.today.com/health/couple-suing-ivf-clinic-after-mix-led-another-couple-having-t158142
4. https://www.theindychannel.com/news/call-6-investigators/victims-hopeful-new-law-will-protect-against-fertility-fraud
5. https://www.cincinnati.com/story/news/2019/08/07/cincinnati-fertility-clinic-sued-swapping-out-husbands-sperm/1935344001/
6. https://www.newsweek.com/fertility-doctor-ob-gyn-sperm-lawsuit-dr-john-boyd-coates-dna-genetic-test-1274540
7. https://www.wcbe.org/post/central-ohio-family-files-fertility-lawsuit-after-shocking-dna-results.
8. Plebani M. The detection and prevention of laboratory errors in medicine. Ann Clin Biochem 2010;47:101–110.
9. Sakkas D, Barrett CB, and Alper MM. Types and frequency of non-conformances in an IVF laboratory. Hum Reprod 2018;33:2196–204.
10. Letterie G. Outcomes of medical malpractice claims in assisted reproductive technology over a 10-year period from a single carrier. J Assist Reprod Genet. 2017;34:459–463.
11. https://www.nytimes.com/roomfordebate/2011/09/13/making-laws-about-making-babies/fertility-industry-is-a-wild-west
12. Fertility Clinic Success Rate and Certification Act of 1992: Public Law 102-493. US Statute Large. 1992 Oct 24;106:3146-52
13. Center for Biologics Evaluation and Research. Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) - Small Entity Compliance Guide. August 2007. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/regulation-human-cells-tissues-and-cellular-and-tissue-based-products-hctps-small-entity-compliance
14. American Society for Reproductive Medicine Oversight of Assisted Reproductive Technology. 2010. https://www.asrm.org/globalassets/asrm/asrm-content/about-us/pdfs/oversiteofart.pdf.
15. Practice Committee of the American Society for Reproductive Medicine, Practice Committee of the Society for Assisted Reproductive Technology, and Practice Committee of the Society of Reproductive Biology and Technology. Revised Minimum Standards for Practices Offering Assisted Reproductive Technologies: A Committee Opinion. Fertil Steril 2014;102:682-6.
16. Toft B. Independent review of the circumstances surrounding four adverse events that occurred in the Reproductive Medicine Units at The Leeds Teaching Hospitals NHS Trust, West Yorkshire. Available from Department of Health. 2004, pp 1-179.
17. Kohn LT, Corrigan JM, Donaldson MS, editors.To Err is Human: Building a Safer Health System.Institute of Medicine (US) Committee on Quality of Health Care in America; Washington (DC): National Academies Press (US); 2000.
18. Alper MM. Experience with ISO quality control in assisted reproductive technology. Fertil Steril! 2013;100:1503–8.

19. Alikani M, Go KJ, McCaffrey C, McCulloh DH. Comprehensive evaluation of contemporary assisted reproduction technology laboratory operations to determine staffing levels that promote patient safety and quality care. Fertil Steril 2014;102:1350–1356.
20. Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology. Revised guidelines for human embryology and andrology laboratories. Fertil Steril 2008;90(Suppl):S45–59.
21. Federal Register. Implementation of the Fertility Clinic Success Rate and Certification Act of 1992—a model program for the certification of embryo laboratories: notice. Fed Regist 1999;64(139):1–42.
22. McCulloh DH. Quality control: Maintaining stability in the laboratory. In: Gardner D, Weissman A, Howles CA, Shoham Z, eds. Textbook of assisted reproductive techniques. 4th ed., Vol. 1. London/New York: Informa Healthcare; 2012. 2. P
23. Boone WR. and H. Lee Higdon HL III, Defining the typical work environment for assisted reproductive technology laboratories in the United States Fertil Steril 2005;84:618
24. Novo S, Barrios L, Santalo´ J, Gomez-Martınez R, Duch M, Esteve J, PlazaJ A,Nogues C, Ibanez E. A novel embryo identification system by direct tagging of mouse embryos using silicon-based barcodes. Hum Reprod 2011;26:96–105.
25. Novo S , Penon O , Barrios L , Nogues C, Santalo J, Duran S, Gomez-Matınez R , Samitier J, Plaza JA, Perez-Garc´ıa L, Elena Ibanez. Direct embryo tagging and identification system by attachment of biofunctionalized polysilicon barcodes to the zona pellucida of mouse embryos Hum Reprod. 2013;28(6):1519–1527.
26. Hiriart E, van Vliet P, Dirschinger RJ, Evans SM, Puceat M. Cell labeling and injection in developing embryonic mouse hearts. J Vis Exp. 2014;86:51356
27. Scott RT, Su J, Tao X, Forman EJ, Hong KH, Taylor D, Treff NR. Trophectoderm DNA fingerprinting by quantitative real-time PCR successfully distinguishes sibling human embryos. J Assist Reprod Genet 2014; 31:1421–1425

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