Risk and safety management in infertility and assisted reproductive technology (ART): from the doctor's office to the ART procedure

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Risk and safety management (RSM) is receiving increasing attention in medicine, with the goals of reducing medical error and increasing quality of care. The principles and tools of RSM can and should be applied to assisted reproductive technology (ART), a field that has already made significant progress in reducing the undesirable and sometimes dangerous consequences of treatment. ART is a prime area of medicine to contribute and help to lead the application of RSM and patient safety because it has been ahead of many other fields of medicine in standardizing treatment, certifying and auditing practitioners, and reporting standardized outcomes, and because treatments are applied to otherwise healthy individuals where exposure to risk may be less acceptable. (Fertil Steril® 2013;100:1509–17. ©2013 by American Society for Reproductive Medicine.)

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When aviation took off 110 years ago in the wake of the Wright brothers' first flight at Kitty Hawk, it was not automatically destined to become the ultrasafe transportation industry we know today. Commercial aviation's evolution to safety resulted from a combination of factors, including highly effective government regulation, the industry's eventual dedication to safety, motivated by concerns of the public, the pilots whose own lives were at risk, and the survival of a risky business, whose financial success was at stake.

Medicine, in contrast, went through similar scientific advances and technologic accomplishments, but has lagged behind aviation in the quest for high reliability and safety. In large part, this difference can be explained by a lack of clarity regarding consistent definitions and the absence of a standard methodology to assess iatrogenic harm (1). Awareness is rising, however, owing primarily to several seminal publications by the Institute of Medicine documenting how unsafe medical practice is and outlining steps that must be taken to improve safety outcomes (2, 3). Despite this, the difference in the level of safety between aviation and medicine remains striking. To remedy this situation, there have been numerous attempts of exporting to medical care the safety knowledge developed in aviation and other ultrasafe industries, such as nuclear power plant and aircraft carrier operations. In this quest for a safer and more highly reliable medical industry, infertility and the assisted reproductive technology (ART) could play a particularly important role for the following reasons:

1. Women needing infertility treatment and ART are generally healthy, yet exposed to serious medical risks. For fertility disorders confined to the man, the woman assuming those risks may be entirely normal.

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2. ART, owing to greater exposure to the news media and legislative scrutiny, is accustomed to a high level of regulations and controls, having established, for example, mandatory training requirements, laboratory accreditation, and guidelines for patient care.
3. Because of the common and sometimes misleading use of intermediate outcomes (e.g., clinical pregnancy rate rather than viable delivery rate), ART has been often required to report its results to government agencies in a standardized fashion. Only several other medical activities are required to report such detailed treatment outcomes.
4. A variety of quality control processes are often mandated, because outcomes can be significantly affected by minute environmental and procedural factors.

The safety-minded actions inspired from aviation already enacted in medicine have included checklists, preprocedural briefings, and medical teamwork (4). In many, but far from all, operating rooms and intensive care units, these tools have been adopted and have been highly successful at eliminating "mega" mistakes, e.g., the "triple W" of wrong patient, wrong side, and wrong organ, where they have been implemented. In the hospital operating room, a simple preoperative checklist reduced surgical mortality by 47% worldwide at study institutions (5). These effective safety measures have not consistently entered the doctor's office and other outpatient facilities, however, where the more fundamental errors of medicine, such as wrong diagnosis or wrong surgical indication, may still be a significant problem.

In 2008 the American College of Obstetricians and Gynecologists (ACOG) established a task force to study and make recommendations for the implementation of safety tools and procedures in the outpatient setting (6). This initial effort led in part to the development of ACOG's more comprehensive Safety Certification in Outpatient Practice Excellence (SCOPE) program. The SCOPE program is designed primarily for general obstetrics and gynecology outpatient practices. The risk and safety management (RSM) process discussed herein aims to address risk and safety issues in the subspecialty of infertility, including in the doctor's office where procedures involving risks are initiated and often performed. RSM is to be seen as a complement and not a competing system to existing quality systems such as the International Organization for Standardization (ISO) certification programs (7) and other certification processes in ART. For the reasons outlined above, we think that infertility and ART may constitute an ideal field of medicine for further development and implementation of a global risk and safety management (RSM) program.

HAZARDS, RISKS, AND THEIR CONSEQUENCES

Studying risks and safety requires knowledge of the important difference between two closely related yet distinct concepts: hazard and risk. Hazards are intrinsic and "potential sources of danger" that refer to the immutable conditions of a given activity or situation. By nature, therefore, hazards can not be changed. Risks, however, refer to "the possibility that something unpleasant or unwelcome could happen." Therefore, the consequences of known risks in medical practice must be proactively prevented from happening by defense mechanisms or countermeasures. Defense mechanisms in medical practice consist of technology and procedures that minimize the probability that error will result in patient harm (8). These efforts at prevention of harm to patients and providers from the consequences of hazards and risks are the essence and primary goals of RSM.

Some features of mountain climbing can serve as an example of hazard and risk. In mountain climbing, the prevailing hazard is height, stemming from the fact that mountains are what they are, and this intrinsic hazard of height can not be rectified. Risks while mountain climbing, e.g., slipping, must be avoided, however, because the consequences may be dreadful. Defensive mechanisms and countermeasures to this risk associated with mountain climbing could be the use of anchoring pitons or tethering of team members together to reduce the risk and possible consequences of slipping.

Risks are not static events, but rather dynamic processes. When left unheeded, risks have consequences (adverse outcomes) progressing along a path of increasing severity and frequency. In our example, the consequences of slipping while climbing mountains can range from a bad scare with no damaging consequences to a potentially fatal fall. Paying attention to the risks of climbing and taking defensive actions can positively affect (decrease) both the frequency and the severity of the consequences of slipping.

With surgery, including oocyte retrievals, the primary hazards are the vascular anatomy and bacteriologic exposures of the human body, both of which are immutable facts. The risks stemming from these hazards are the possibility of hemorrhage and infection. The consequences or outcomes of these risks depend on where and how a possible vascular breach or bacteriologic intrusion occurs. As with mountain climbing, the risks incurred during oocyte retrievals are dynamic processes potentially leading to consequences of increasing severity.

MEDICAL ERRORS

Aviation has its own terminology for describing error which has become standard worldwide. Medical practice, and all health care, however, does not as yet have a uniform or universally accepted lexicon for patient safety. Medical error in the United States is usually defined as a preventable adverse effect of medical care, regardless of whether it is harmful or even evident to a patient. In the United States, several terms are used to describe the consequences of the hazards and risks of medical treatment. They are:

1) Adverse event (AE).
2) Preventable adverse event (PAE).
3) Adverse drug event (ADE).
4) Sentinel event (SE).

An AE is defined as an unexpected or unintended outcome of medical care, and a PAE is an adverse event that could have been prevented. An ADE is an adverse drug event, which is one of the most common adverse events in health care. These terms do not include the severity of any harm to the patient as part of their definitions. The Joint

Commission uses the term sentinel event to describe an AE that has resulted in significant harm or death. In Europe, the Committee of Experts on the Management of Safety and Quality in Health Care uses terms such as "accident", "active error", and "active failure", among others, to describe medical and drug errors. One of the reasons that medical practice lags behind aviation in safety technology may be the lack of a common terminology to describe and study medical error. In this article we will use AE, PAE, ADE, and SE to describe medical error in ART.

All of these unwanted AEs, regardless of the severity of consequences, should be monitored and investigated just as "near misses" (a type of AE) must be reported and investigated in aviation. Recognizing the possible consequences of risks in terms of their tendency to result in increasingly dreadful outcomes, however, is pivotal for RSM. For each AE, one should establish: 1) the recognition parameters; and 2) whether progression can be monitored and, if necessary, prevented. The latter is vital for building and positioning effective countermeasures for the most serious consequences or outcomes of risk. For AE prevention (especially SEs), robust and redundant countermeasures must be put in place.

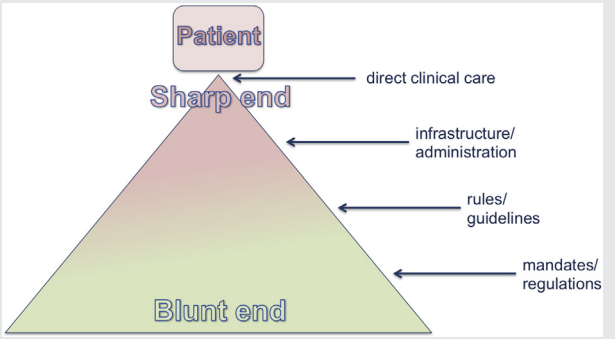
MEDICAL ERRORS AND DEFENSE MECHANISMS

It is common knowledge that errors, deviations, and procedural violations committed by pilots as well as doctors and nurses, called "active failures" in aviation and "active errors" in medical care, may adversely affect safety (9). Although these "sharp end" errors (Fig. 1) and violations do not always have significant consequences, they can be unpredictable and have immediate adverse effects. Active errors are the least predictable and the most difficult to prevent. Examples of unpreventable active errors would be a competent surgeon unintentionally entering the bladder when there are extensive adhesions or during an emergency cesarean delivery for fetal distress. Sometimes at the sharp end of care, catastrophic consequences may occur in the absence of any identified error (9). This is more common when procedures are not well defined or a definition is simply missing.

Latent errors occur toward the "blunt end" of medical care (Fig. 1). These errors are caused by system inefficiencies and are usually the most predictable and easiest to prevent. An example of a latent error leading to a possible ADE would be understaffing in the hospital pharmacy causing an incorrect dose of pain medication to be missed there and sent on to the nursing staff. There is no harm if the nurse on duty catches the error, but these kinds of system deficiencies can lead to significant adverse outcomes. Figures 2 and 3 depict the so-called "Swiss cheese theory of error" (10). Even a series of barriers or defenses against error are imperfect. In the example above, the trigger event for the error is the ordering of the wrong dose of pain medication. The understaffing in pharmacy creates one hole or defect in the care system seen in the layer of cheese. If the nursing staff misses this error (a second hole in the next layer of protective "cheese"), harm to a patient could occur (Fig. 2). On the other hand if nursing staff catches the error, the patient is protected (Fig. 3). The more layers of "protective cheese" in the system of care, the less likely that all holes will line up to allow an error to cause harm.

Obeying rules and abiding by procedures to reduce medical errors enhance safety only if the rules and procedures are intelligently conceived and continuously updated by ongoing error-reporting processes. The latter activity must be

FIGURE 1



Components of a medical care system. Doctors and nurses work at the "sharp end" of health care, where active errors can occur immediately and are generally unpredictable and unpreventable. Latent errors are system deficiencies that are often hidden in the blunt end of care and can harm patients. Latent errors are typically more predictable and preventable with adequate defenses, mindfulness, and situational awareness. (Modified from: Cook RI, Woods DD. Operating at the "Sharp End": the complexity of human error in medicine. In: Bugner S, ed. Human error in medicine. Hillsdale, New Jersey: Lawrence Erlbaum, 1994:255–310.)

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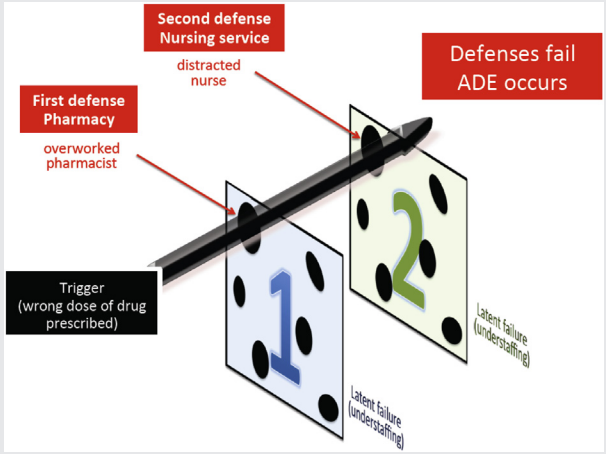
FIGURE 2



Medical care system defenses. Reason's Swiss cheese metaphor for understanding how latent errors occur. The defects in multiple layers of defenses may line up to allow latent errors to harm patients. In this illustration, the latent failure of understaffing in both the pharmacy and the nursing service allows an incorrect drug dose to be given to a patient, resulting in an adverse drug event (ADE). (Adapted from: Reason J. Human error: models and management. BMJ 2000;320:768–70.)

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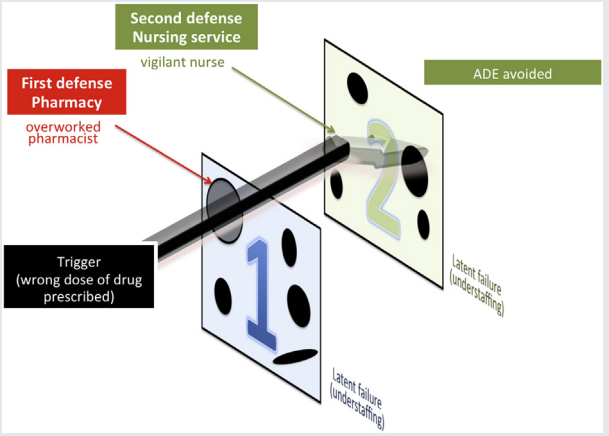
FIGURE 3



Medical care system defenses. This Swiss cheese drawing illustrates how a vigilant nurse (mindfulness and situational awareness) overcomes the latent failure of understaffing and prevents the ADE. (Adapted from: Reason J. Human error: models and management. BMJ 2000;320:768–70.)

de Ziegler. Risk and safety management (RSM). Fertil Steril 2013.

incorporated into the culture (unwritten but widely accepted normative behavior) of an organization to be effective on a sustained basis. Although identifying errors implies knowing right from wrong, most patient safety errors in hospitals and elsewhere occur because of system failures that are not usually identified until someone is harmed (1). Incompetent (not knowing the right from the wrong procedure) or negligent practitioners are responsible far less often than system failures. Communication problems are among the most common cause of medical error in health care (10). Before surgery, preoperative workups are necessary. Moreover, surgery should be performed on the right organ, right side, and right patient. Given such relatively simple scenarios, mega mistakes can be significantly reduced by sets of proper ad hoc measures such as correct patient identification, preprocedure checklists and briefings, and other tools and procedures.

The situation may be different, however in the doctor's office where diagnoses are initially made and treatments decided. The public wants to believe that all doctors inherently know what is best for their patients through the expertise of their art. A global vision of medical practitioners who are deft and capable of quickly adapting is seen as characteristic of all doctors, practicing seemingly without the need of any guidance. Reality, however, may be different. Guiding protocols and standard operating procedures (SOPs) in outpatient clinical medicine are often incomplete if not simply lacking, letting solo improvisation and individual inspiration substitute for well informed protocol-based practice. We think, however, that the embodiment of excellent medical practice—to do what is best and safest for the patient—is compatible with modern concerns for quality and safety. This RSM for ART must aim beyond the mega mistakes of medicine with the use of more comprehensive written procedures of a quality assurance system as a guiding principle to reduce and hopefully eliminate all types of preventable errors.

The highest degree of safety will not come from simply adding more rules and regulations. Rather, the path to the highest degree of safety for infertility and ART will derive from asking doctors to first "say what they should do", and then expecting them to document that they are "doing what they say they should be doing." An embedded culture of first defining correctness and then practicing correctly on a consistent and reliable basis must be established. And the culture of safe medical practice must include a commitment to ongoing measurement and systems redesign for continuous improvement.

Human Factors and Latent Conditions

Views on the root causes of aviation accidents have changed over time. In the early days of aviation, accidents resulted primarily from mechanical and technical failures (11). It was a midair collision over the Grand Canyon in the 1950s that emphasized the human factor in accidents. The pilots of the two aircraft had both tried to provide a good view of the Grand Canyon for their passengers. Their intention was good, but the human factor or critical pilot error of flying too close to each other caused the midair collision killing all on board. Mindfulness and situational awareness on the part of both pilots was lacking and was the human cause of this accident. Mindfulness and situational awareness should become important attributes and goals of safe medical practice (12).

Today, "latent conditions" (e.g., the work environment), are more often identified as the primary causes for aviation accidents. Latent conditions are potentially unsafe hazards in the environment that may cause harm. An example of the effect of latent factors is the Colgan Air flight 3407 crash near Buffalo, New York, in 2009. The post-accident investigation brought to light the fact that pilot errors can stem from a toxic work environment and other "latent conditions." Inadequately trained sleep-deprived pilots made critical landing errors, in a mechanically sound aircraft, that resulted in a catastrophic crash that killed all on board as well as one person on the ground.

As in aviation, defective work conditions in medicine, such as 12-hour or longer shifts for nurses, exhausted house staff, and missing charts in consultation suites, are latent conditions that may lead to safety lapses and errors. Finger pointing and blame for human errors does little to improve safety if latent conditions remain. As discussed later, a three-tier nonpunitive error-reporting system used in aviation for preventing future errors of the same type and remedying latent conditions should be tried in medicine, including ART.

Defensive Mechanisms

Defenses or countermeasures are built to prevent accidents or medical errors from causing harm. They consist of multiple independent layers positioned where errors (especially those with catastrophic consequences) are most likely to strike. Yet, defenses have pitfalls of their own. Two examples deserve discussing.

The Davy lamp effect. In the mining industry, the Davy lamp (a safety lamp that prevents open exposure of the flame to the highly flammable gases in mining caves) drastically reduced

the risk of igniting catastrophic explosions while mining. Soon, however, mining accidents returned back to pre–Davy lamp levels, because safer mining was extended to previously unreachable areas. Effective defenses for one risk (explosions from exposed flames) may allow for more risk-taking behavior which then introduces new risks and hazards (9). Could the antagonist protocols with GnRH trigger and deferred transfer that drastically reduce ovarian hyperstimulation syndrome (OHSS) and venous thrombotic event (VTE) risks introduce a "Davy lamp effect" in ART? Could reduction of one known risk bring on new ones through higher-dose controlled ovarian stimulation (COS) protocols and higher E_2 levels? For example, bleeding after retrieval has been associated with more aggressive COS. Could elimination of an antiseptic prep of the vagina to avoid any potential toxicity being carried over to the culture system increase the chance of pelvic infection during oocyte retrieval? While we hope not, awareness and caution for unintended consequences are appropriate through recognition of problems and the early application of new strategies and countermeasures.

Killed by your defenses: writing another safety rule. Legend has it that the French cavalry were severely disadvantaged by the weight of their very protective but excessively heavy armor during a battle with the English at Agincourt (13). They were more easily defeated mounted on horses exhausted by the weight of the heavy armor. Can excessive safety measures become the protective armor that is then too heavy for allowing safe and effective medical practice? However appealing to quality personnel, an uncontrolled "let's write another rule" approach can be a modern-age Agincourt, disabling effective safety management. Even when regulations for safer procedures abound, nothing can replace the need to first enact an intelligent design, assuring that procedures are workable before they are instituted, and building safety into the process from the beginning (14). And it must be realized that all safety protocols and procedures are dynamic and must be constantly reviewed and updated based on new medical knowledge, as well as mistakes detected in the original protocol after it has been implemented. Furthermore, no matter how good the protocol, unexpected and unintended circumstances may occur that require deviations. Mindfulness and situational awareness are extremely important for adapting to unexpected events (12).

TYPES OF AEs IN INFERTILITY AND ART

The AEs encountered in infertility and ART are generally of three types. They can be: 1) AEs due to generic risks that are associated with all invasive procedures; 2) AEs associated with the specific kinds of treatment used in ART; and 3) AEs associated with personal characteristics of a particular woman undergoing ART treatment. A few examples of generic AEs associated with ART include hemorrhage, damage to adjacent organs, and infection.

Hemorrhage

Hemorrhage is encountered in $<1\%$ of ART cases, with bleeding occurring intra- or extraperitoneally. The former causes abdominal pain and distension, typically 2–6 hours after oocyte retrieval, with abundant intraperitoneal blood seen on ultrasound examination. Retroperitoneal bleeding generates prompter and more severe symptoms. Ultrasound examination shows normal amounts of fluid and often an area of retroperitoneal distension with blurred limits and exquisite tenderness. Unless they resolve on their own, both forms of bleeding may require surgical exploration and correction.

Damage to Adjacent Organs

During oocyte retrievals, damage to the bowel, bladder, and ureter have occurred. Serious consequences can follow if early symptoms are ignored.

Infection

The risk of infection after oocyte retrievals is real, sometimes involving organisms with low pathogenicity, such as actinomycis (15), and is higher when endometriomas or cystic teratomas are present (16). In other instances, virulent organisms have even caused consumption coagulopathy (17). Clinical symptoms are variable, usually occurring a few days after the retrieval, but sometimes with late onset [weeks or months, including during pregnancy or even after delivery (18) having been described (19)]. Surgical exploration and at times adnexectomy are needed (20). Unfortunately, vaginal antisepsis and antibiotic prophylaxis are not uniformly effective defenses (21), which underscores the importance of not entering these cysts during oocyte retrieval if at all possible.

AEs Unique to ART

Examples of AEs that are due directly to treatments unique to ART include OHSS, multiple pregnancies, and disorders of placentation.

Ovarian hyperstimulation syndrome. Although the risk of OHSS has greatly decreased with antagonist protocols, its discussion is appropriate because of its emblematic place in ART complications. Anticipating COS responses based on age, body weight, menstrual cycle irregularity, and hormonal profile leads to treatment adjustments. Yet despite tailoring COS regimens, excessive responses resulting in OHSS may still occur.

During COS, the risk of OHSS is monitored by following E_2 levels. When the risk of OHSS is imminent, further development toward more serious stages can be stopped or controlled by withholding human chorionic gonadotropin (hCG) injection, coasting without medication, or deferring embryo transfer to a subsequent cycle. If OHSS still occurs, modern treatment (water and electrolyte management, repetitive paracentesis, intravenous albumen, prophylactic heparin) effectively averts the dreadful and possibly fatal consequences of thromboembolism or organ failure that characterize the SE stage (22). Significant AEs most often result from poor management of OHSS rather than from OHSS itself (23). Assuring that all cases of OHSS are properly managed (thus avoiding the severe consequences of OHSS) can be as effective for patient safety as reducing its overall incidence (22).

Based on the above, safety efforts regarding OHSS should include instructing ART patients to seek treatment in an ART

center. Likewise, institutions treating ART complications should train their emergency staff in properly recognizing and treating OHSS (and other ART-related complications). With this in mind, patients should receive written instructions urging them to seek treatment at an ART center if post-ART complications occur. We are aware of two women who had placement of chest tubes (not necessary with proper management of OHSS) for pleural fluid at facilities not accustomed to treating OHSS.

Multiple pregnancies. Today, systematically transferring two embryos carries a twin pregnancy rate of 30%–50%, whereas systematic single-embryo transfer lowers pregnancy success. Opting for elective single-embryo transfer (eSET) when all parameters are highly favorable minimizes twin pregnancy rates with a minor impact on the odds of pregnancy being achieved (24). The recent application of trophectoderm biopsy and comprehensive chromosome screening may provide an important adjunct toward this goal. As governmental and private insurers become more aware of the overall cost savings of eSET, mandates for eSET under high-risk situations are increasingly being imposed (25–27).

Placentation disorders. Several newly identified risks of ART stem from reports of increased incidences of certain obstetric complications (e.g., preeclampsia) in singleton ART pregnancies (26). Although the respective roles of ART and infertility are difficult to establish, a lower incidence of these problems is encountered after frozen-embryo transfers (FETs) (28–31).

Most if not all of the obstetrical problems encountered after ART may stem from disordered placentation due to endometrial abnormalities seen in COS but not with FETs. Finding larger placentas and higher placental weight/birth weight ratios in ART compared with spontaneous pregnancies (32) supports this concept, even if advanced paternal age may also play a role (33).

AEs That May Occur Due to Personal Characteristics

The third category of AEs encountered in ART are those that are due to the unique risks or predispositions that an individual woman about to undergo ART may already have. These conditions should always be identified and any risks mitigated beforehand when possible. Examples of AEs due to personal risks include adverse vascular events, cytogenetic abnormalities leading to AEs, and uterine defects that may lead to AEs.

Vascular AEs (venous). Certain patients may be predisposed to VTE. These individuals, typically identified by a personal and/or family history of VTE, require heparin prophylaxis during ART. Although routine checking of hemostasis-related mutations is not warranted (34), recognizing that OHSS induces a 100-fold increase in VTE risk is crucial (35). However, no increased risk is seen with FETs, further fueling the interest in deferring embryo transfers (36).

Failure to identify women at particular risk for VTE up front could be fatal, because unlike OHSS there are usually no obvious clinical signs before a VTE. Protective barriers must concentrate on not failing to identify individuals at risk who may need heparin prophylaxis during ART. Considering the seriousness of the issue, we suggest that all ART candidates should be asked the same question using the exact same terms: "Have you personally had a blood clot, or were there people in your family who died before age 50 of a heart attack or without any apparent reason?" Though not absolute, a negative answer may be more reliable when such a standardized question is used.

The risks from each of these conditions (OHSS and VTE) have different dynamics. Each risk therefore needs different protective defenses to effectively prevent their respective AEs.

Cytogenetic AEs. Chromosomal and genetic risks leading to AEs are personal conditions bearing possible threats for: 1) the child, e.g., fragile X premutation leading to fragile X mental retardation in a male offspring; or 2) the patient, e.g., Turner syndrome, possibly exposing the patient to fatal rupture of the aorta during pregnancy, an SE.

AEs due to uterine malformations. Risks due to uterine malformations, such as fibroids or earlier scars, can put the pregnancy at a higher risk for obstetrical complications, sometimes dictating eSET or surrogacy to avoid the risks. As with other personal risks, identification should occur before ART.

ERROR REPORTING AND DISCLOSURE OF ERRORS

Reporting errors, regardless of whether harm occurs, is essential to RSM. Yet it is human nature to avoid coming forward after errors are committed and/or a rule is violated. We seem to be hard wired to minimize errors and safety lapses that result in limited to no consequences, resulting in a "no harm, no foul" attitude. Neither an undue tolerance of errors seemingly without consequences nor individual blame when an error leads to significant harm enhance safety.

Errors can not be ignored and should be dealt with. As demonstrated in aviation, achieving safer medicine mandates being aware of all errors. There are three primary modes of error reporting: 1) automatic; 2) mandatory; and 3) voluntary. All three methods applied to ART should be confidential and nonpunitive.

Automatic Reporting

Automatic error reporting was instrumental in enhancing safety in aviation. The automatic nature in particular is key for counteracting the human tendency to either ignore or blame, depending on outcome. In aviation, flight recorders are set for automatically reporting certain nonordinary events, such as an excessively steep approach to landing. The first question asked generally is, what happened? Sometimes good reasons for these errors exist. More often, however, steep approaches result from ordinary blunders. The important thing to know is exactly what happened, so that individual or collective remediation can occur. The information gained from this investigation is confidentially shared with others in the industry so that all can learn from any mistakes. The fact that all crew members are exposed to similar scrutiny sets the basis for a so-called "just culture", which ultimately nurtures a voluntary mode of error reporting and treating all errors regardless of outcome as events that need to be investigated (37).

Automatic reporting is being instituted as part of the Society for Assisted Reproductive Technology (SART) reporting. For example, programs having an unusual rate of triplets are identified so that helpful steps can be taken to allow that program to improve patient safety. Although as yet rudimentary, automatic reporting aims to change the attitude about error analysis (helpful improvement rather than sanctions), making a step forward toward instituting and maintaining a "fair and just culture."

Mandatory Reporting

Certain events need to be reported and analyzed even if not usually due to errors. In ART, for example, each program should have mechanisms in place to review instances where no oocytes were retrieved or fertilization failed. These two events may not be due to medical error but rather to patient characteristics. However, when either of them occurs the clinical and laboratory processes should be reviewed. When patients undergoing ART are at higher risk (advanced age, poor responders, and male factor) for these disappointing "process outcomes" an expected result based on reported results elsewhere should be compared with the actual outcomes as a way of benchmarking the results. Benchmarking can be a powerful tool to compare results and evaluate performance, especially when error is not likely.

In the United States, disclosure of medical error to patients, including any unexpected AEs, is required by regulatory groups, such as the Joint Commission, and by some government agencies in the hospital and outpatient surgical center settings. A voluntary process for full disclosure to patients should be built into any RSM for infertility and ART.

Voluntary Reporting

Voluntary nonpunitive reporting is crucial for safe operations. A culture favoring nonpunitive reporting allows earlier discovery of medical errors and AEs and permits actions, such as systems redesign, when needed. In the United States, the Federal Aviation Agency shas enacted an "Aviation Safety Action Program" whereby a certified agent can report an incident confidentially. For many years there has been a program that allows a pilot to report an incident, such as a near miss, without any sanctions through an "Aviation Safety Reporting System." Voluntary reporting, however, will not happen out of the blue in medicine. Strong leadership and incentives for voluntary reporting and investigating all errors will be needed to establish a strong safety culture in medical practice.

SIMILARITIES AND DIFFERENCES BETWEEN MEDICINE AND AVIATION

Efficacy: A Variable in Medicine, but Not in Aviation

In aviation, efficacy is assumed and nearly invariable. An airplane going from point A to destination B will eventually get there unless an extremely rare accident occurs. Aviation safety management therefore only addresses accidents and the relevant conditions leading to them. In medical practice the situation is different, because efficacy, particularly in ART, is affected by many variables.

In ART, the single most important variable of efficacy is age. The risk of some AEs that occur with ART may be increased due to personal factors such as age or body mass index. Increased risk will be unacceptable if efficacy approaches zero because of these same risk factors. RSM in ART must therefore address the risk-efficacy ratio.

Indication: Questioned for Surgery but Not for Flying

In case of surgical complication, the first question asked is whether surgery was indicated. If surgery was not indicated, any complication, no matter how minor, is unacceptable. Aviation is different. After a crash, the reasons that led passengers to travel or generally to be on airplanes are not questioned. Safety protocols have to address the indications for ART, as illustrated in the companion review in this issue. Age limits should be defined for ART with own or donor oocytes, so that arbitrary decisions are not made to provide treatment where no meaningful chance of pregnancy exists or when the complications of treatment are too great.

More Complex Systems in Medicine

Systems in modern aviation are complex, but not nearly as complex as those in medicine. In medical care the primary source of complexity is not just the disease. Kenneth Kizer, a former head of both the U.S. Veterans Affairs Health System and the National Quality Forum, has stated that modern health care has become the most complex activity ever undertaken by humans (10). He identified "communication barriers" as a major cause of its complexity along with eight other factors (Table 1). Infertility and ART, although usually dealing with essentially normal persons, has all of these complexities and is an ideal medical activity for implementing RSM.

"SAY WHAT YOU DO": THE BASIS FOR KEEPING DOCTORS IN CHARGE

Procedures within Accepted Guidelines

A core issue in safety management is the necessity to define, standardize, and apply procedures to monitor and detect deviations. However, the art of drafting and following defined

TABLE 1

Causes of complexity in medical care.

1. Highly complicated technologies
2. Many powerful drugs
3. Differing backgrounds and training of providers
4. Often unclear lines of authority
5. Highly variable physical settings
6. Communication barriers
7. Medically diverse patients
8. Large variation in care processes
9. Time-pressured environment

Note: Modified from Kizer (10).

de Ziegler. Risk and safety management (RSM). Fertil Steril 2013.

procedures is inconsistent in clinical medicine. This has been a stumbling block for implementing safety systems going beyond the checklist level in the majority of medical fields.

Some aspects of ART practice are getting entangled in ever-tighter meshes of "top-down" rules and regulations that are expanding to the possible point of hindrance. A notable example was a California tissue bank law that prevented transfer of sperm into an intimate partner when the male had a condition such as hepatitis C. Until the law was finally amended, couples had to seek treatment in other areas of the country without this rule. All too often, regulations are excessively complex, not up to date, impractical to implement, and at times targeted toward reducing expenses. As in other industries, such measures can pave the way for unlawful deviations and violations to simply keep the system working and maintain practice flow. Further expansion of rules and regulations, however noble the safety purpose, can add insult to injury to an already entangled system. Simply adding more rules and regulations is not, as we see it, the best way toward safer ART.

Rather than just making more rules, RSM needs to invent new modes of doctor-regulator interaction that promote safety and embed reliability into the culture of practice. As discussed below, the quality systems existing in ART with reporting and oversight by physician-developed bodies such as SART are as good as or ahead of other areas of medicine for further promoting an ideal RSM system. Anesthesia is one specialty of medicine that has advanced farther than others, and ART programs can learn a great deal from what that field has already done. ACOG has a long history of education and research for patient safety, providing courses and training in safety science and quality improvement.

ART and Certification Systems

In many countries, the vulnerability and risk-exposed nature of ART motivated the supervising authorities to recommend traditional quality assurance systems. ISO certification, described in this series of views and reviews (7), is a highly formalized process containing procedures that can be used by all ART programs to work with and improve RSM.

The certification documents, such as the protocols and SOPs describing ART processes, are starting points for RSM. They offer a "say what you do" approach on which RSM can be built. Yet, risk management is not always an inherent part of quality and certification processes. RSM, with its own safety-minded agenda, will work with ISO but is not simply ISO. RSM and quality systems are like a computer program and its operating systems: They work together, but each is different.

Education with "RSM Inside"

Patient safety is a discipline in medical practice that strives to apply safety science toward achieving a trustworthy system of health care delivery. A safe health care system should minimize error and reduce harm to patients (37). Paraphrasing a widely known advertisement for a microprocessor, initial and recurrent education programs in infertility and ART should be offered with "RSM (risk and safety science) inside." Pioneering this principle, a global ART review course sponsored by the University of California at Los Angeles every July for the past 26 years in Santa Barbara, California, has included analysis of risks and AEs in ART with feedback obtained from the audience on actual experience. The use of "anonymous clickers" for confidential responses allows for a more candid disclosure of experiences. A more inclusive global program for confidential error analysis with discussion of effective countermeasures to make ART safer should be instituted.

As described above, acceptability of any risk is always relative to corresponding benefit. In aviation, simulator training markedly abbreviates the experience needed to fly a commercial aircraft safely. Key to "RSM inside" education in infertility and ART are "training-by-simulation" programs initiated whenever necessary and/or possible. Simulation is increasingly being used in medical training (38). One crucial ART procedure ideal for "training by simulation" is embryo transfer. A formal educational program using intrauterine insemination as a simulation model can effectively teach embryo transfer technique, so as to relegate the "live" learning curve principle for safe and effective embryo transfer to the dust bin. In addition to training by simulation, an effective RSM program for infertility and ART should emphasize a systems perspective where all ART team members are aware of the important processes of treatment and accept accountability for the desired outcomes of the care given. Training and working in teams improves outcomes and reduces harm to patients (4). These features of an RSM program together with prospective monitoring of actual practice results can optimize benefit as the other key factor in the risk-benefit ratio.

CONCLUSION

In spite of an urgent need for safer and more highly reliable medical practice, the path leading to it is still uncertain (1, 39). The primary stumbling block for going beyond checklists and medical team briefings is that most clinical procedures and techniques are seldom described in detail in the form of practice protocols. Infertility and ART is a prime domain for inculcating a safety culture into its practices, because the required quality systems are highly amenable to written protocols and standardization.

This article has proposed a starting blueprint for RSM in infertility and ART. It outlines the basis and the importance of: 1) defining the known hazards and risks; 2) identifying and reporting errors nonpunitively; 3) setting defenses and countermeasures; 4) enacting professionally defined protocols to "say what we do"; and then 5) monitoring to improve our care. Based on existing quality systems, the ideal RSM promotes a "bottom-up" (with ART medical team input) doctor-regulator relationship conceived within the boundaries of "top-down" clinical societies (e.g., American Society for Reproductive Medicine (ASRM)– and SART-defined guidelines and regulations). By not "weighing down" ART with unnecessary rules and letting practitioners define

appropriate practice (based on the best evidence) and write detailed protocols, RSM opens new opportunities for more productive safety-oriented doctor-regulator interactions. Designed specifically for infertility and ART, the RSM approach outlined here may offer some innovative ideas for obstetrics and gynecology and possibly medicine at large.

Reason (10) has stated that RSM, like life, is "one damn thing after another." RSM as defined here for infertility treatment and ART is no exception, making safety and risk management necessary on an ongoing basis. Although all error can never be eliminated, RSM offers a long-term "fitness program" for maintaining risk and safety awareness in infertility treatment and ART. Requiring the reporting of errors in a safe and confidential environment is essential. And providing feedback so that learning for improvement can occur without the fear of sanctions must be a part of any safety program. RSM aims to make ART safer for patients without adversely affecting creativity or patients' and their doctors' aspirations and needs.

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