SIERR update

Focus on details
Continuous
improvement in IVF

Cryo-management & Safety

Achilleas Papatheodorou

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Embryolab Academy Board Member

Next Gen IVF

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Conflict of Interest:

None

Vitrification

Kuwayama M. Highly efficient vitrification for cryopreservation of human oocytes and embryos: the Cryotop method. Theriogenology. 2007

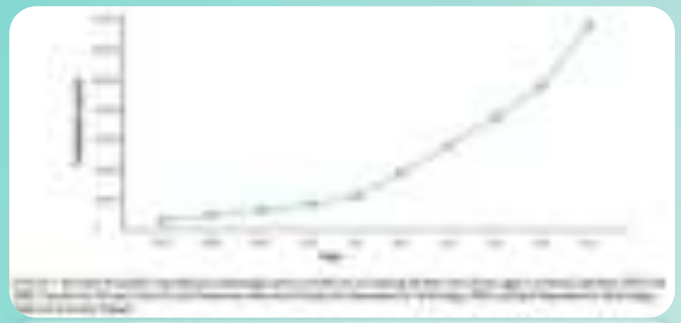
Vitrification soon Transformed Our Routine Practices …

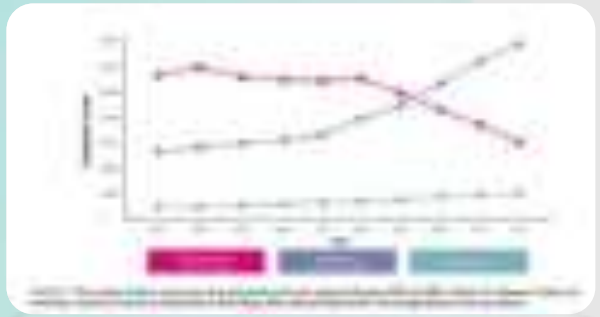
Elective Freeze All Strategies

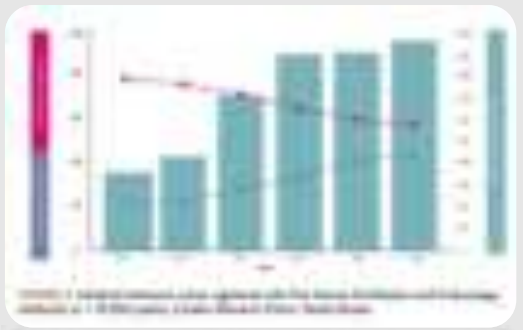
- High Responders – OHSS
- Low Responders – Embryo Banking

- All patients ?

Embryo Vitrification







Embryo cryopreservation and utilization in the United States from 2004–2013

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Objective: To evaluate the quantity and use of embryos cryopreserved at assisted reproductive technology (ART) clinics in the United States from 2004 through 2013 and to characterize trends in ART cycles in which all embryos were cryopreserved.
Design: Retrospective analysis.
Setting: Not applicable.
Patient(s): Registry data from the Society for Assisted Reproductive Technology.
Intervention(s): Historical cohort of U.S. ART cycles reported to the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System between 2004 and 2013.
Main Outcome Measure(s): Number of embryos cryopreserved and factors associated with having cryopreserved embryos.
Result(s): The percentage of fresh cycles in which all embryos were frozen increased dramatically each year after 2010: 15.6% (2010), 19.9% (2011), 30.7% (2012), and 40.7% (2013). During 10 years, 1,954,548 embryos were cryopreserved and 717,345 embryos were transferred. In freeze-only cycles from 2004 to 2013, there was a significant increase in the percentage of women with diminished ovarian reserve (19.9% to 34.1%) and in those who used preimplantation genetic testing (3.2% to 6.9%). During the 10-year period, there were 294,575 fresh cycles with embryo transfer and at least one embryo cryopreserved. Overall, 52.5% (n = 154,543) did not undergo a subsequent frozen embryo transfer, 29.5% (n = 40,462) were left with no frozen embryos, 50.4% (n = 68,875) had one-five embryos, and 20.0% (n = 27,396) had ≥ six. Factors associated with having excess embryos included donor oocyte cycles and increased antimullerian hormone levels.
Conclusion(s): There has been a sharp increase in U.S. ART cycles in which all embryos are frozen and this may result in more embryos in storage. [Fertil Steril Rep® 2020;1:71–7. ©2020 by American Society for Reproductive Medicine.]
Key Words: Embryo cryopreservation, embryo disposition, in vitro fertilization

Discuss: You can discuss this article with its authors and other readers at https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/xfre19-00001

With the evolution of techniques in human assisted reproductive technology (ART), many more fertilized eggs and early embryos are created than can be safely transferred to a woman's uterus. To avoid the morbidity of multiple gestation, embryo cryopreservation has developed as a routine practice among U.S. ART clinics (1). Despite the clinical advantages that embryo cryopreservation provides, it also presents new ethical, legal, and healthcare policy challenges. As a result of the prevalent practice of embryo cryopreservation, in 2003 it was estimated that at least 400,000 cryopreserved embryos were in storage at that time in the United States (2). Couples primarily have five choices regarding disposition of supernumerary embryos: save the embryos for a future embryo transfer cycle, donate embryos for research, thaw and discard, donate their embryos to another intended parent, or continue to store embryos. Evidence suggests, however, that many embryos remain in storage with no specific plan for future use because the majority of patients delay the final disposition decision (3).

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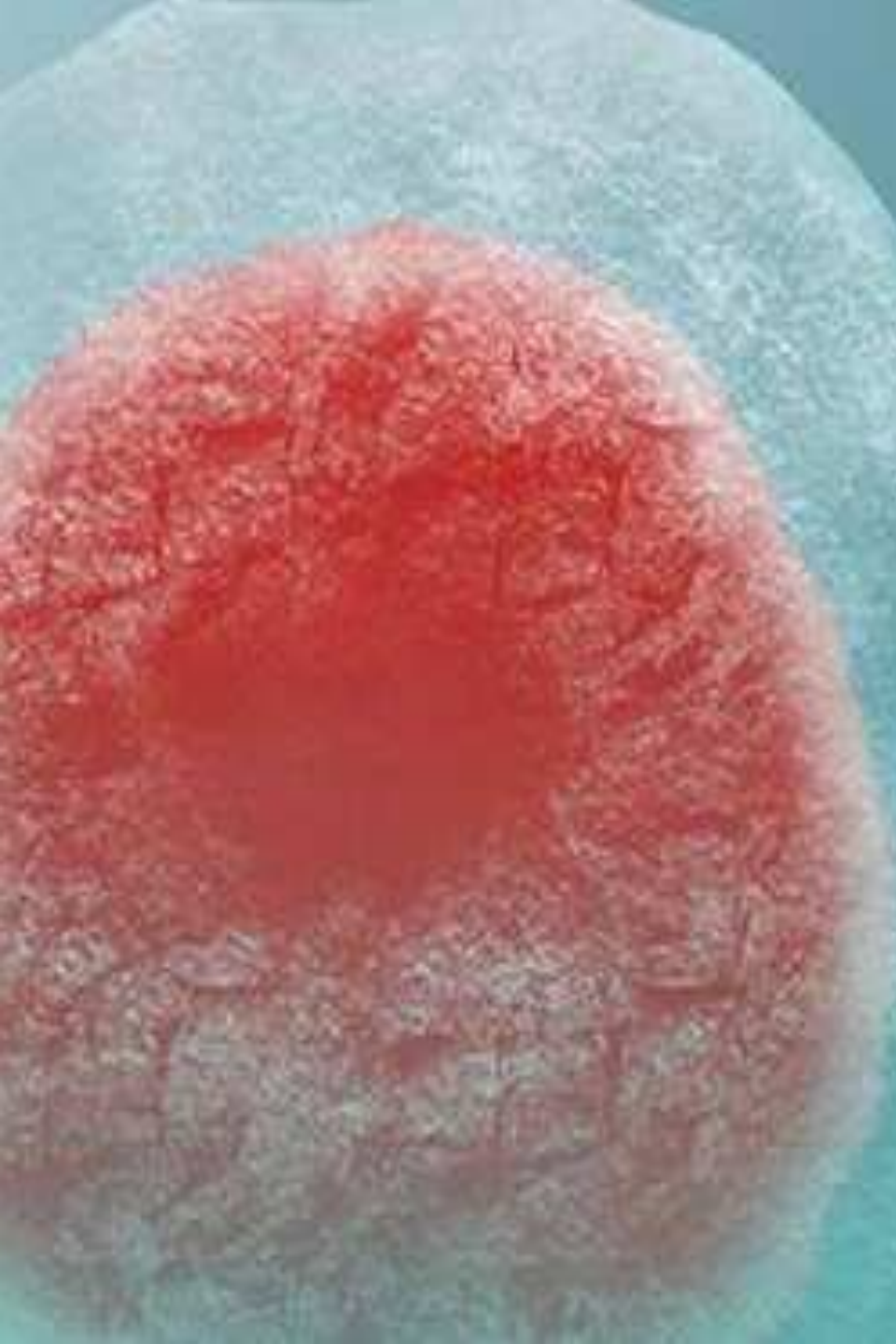
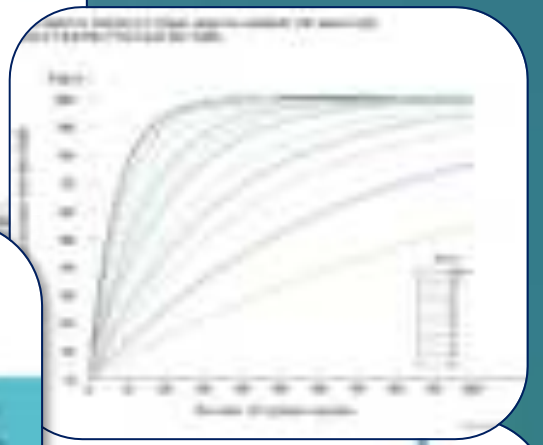
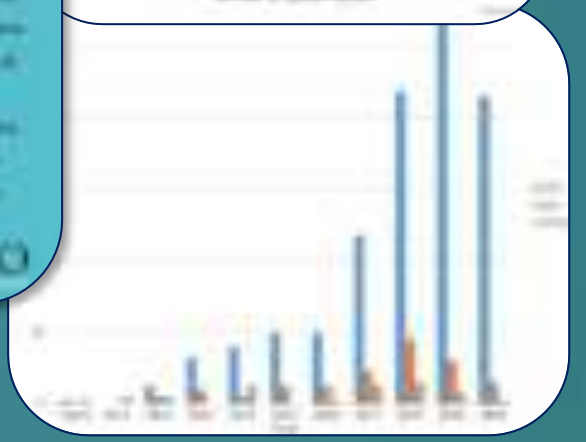
https://doi.org/10.1016/j.xfre.2020.05.010

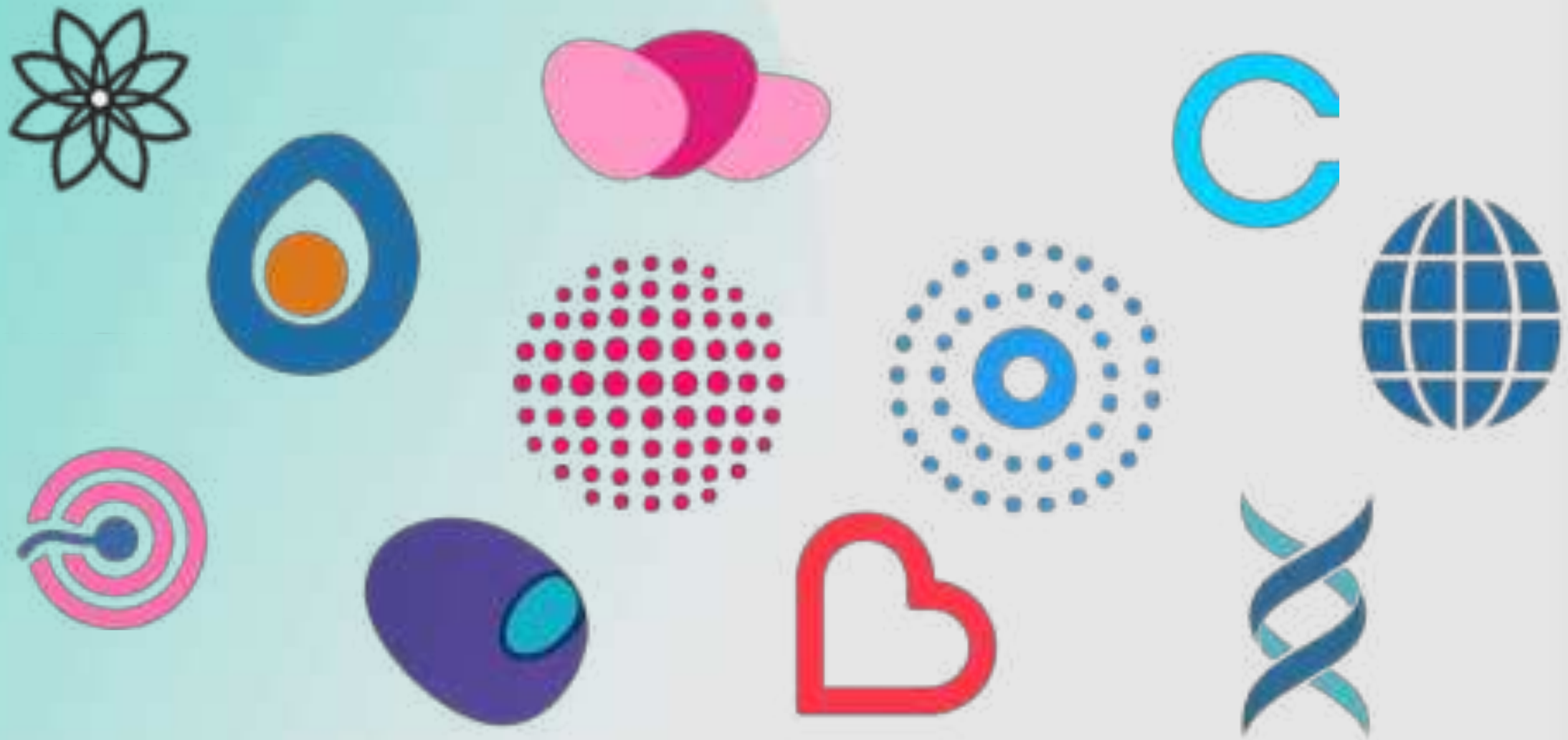
Planned Oocyte Cryopreservation (POC)







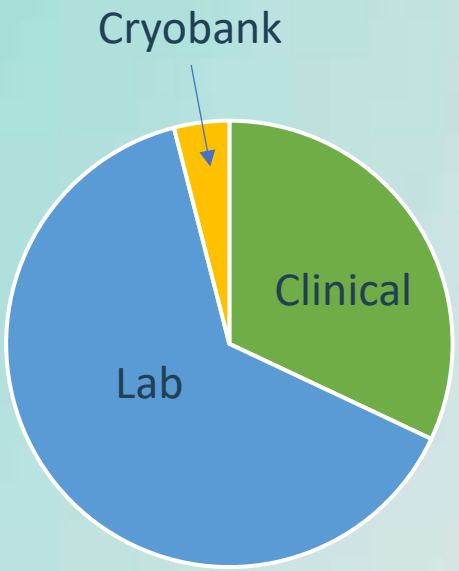
Donor Oocyte Banking



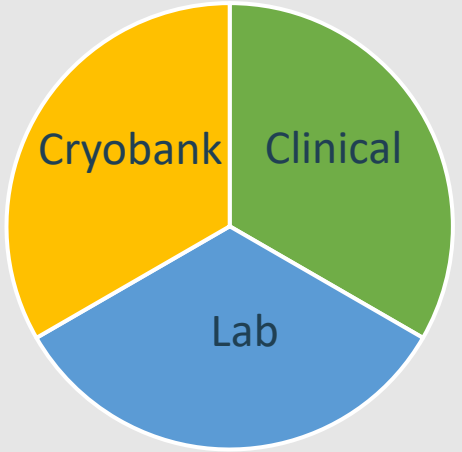
Additional Contributory Factors

- Improved Culture Systems
- Increasing use of SET
- 1 embryo per carrier system
- More than >10 MII for POC
- Two-three oocytes per carrier system
- Prolonged storage
- Mosaic embryos
- Abnormal Embryos & Bioethical dilemmas
- Unused and unclaimed Embryos/Oocytes
- Advancements in PGT

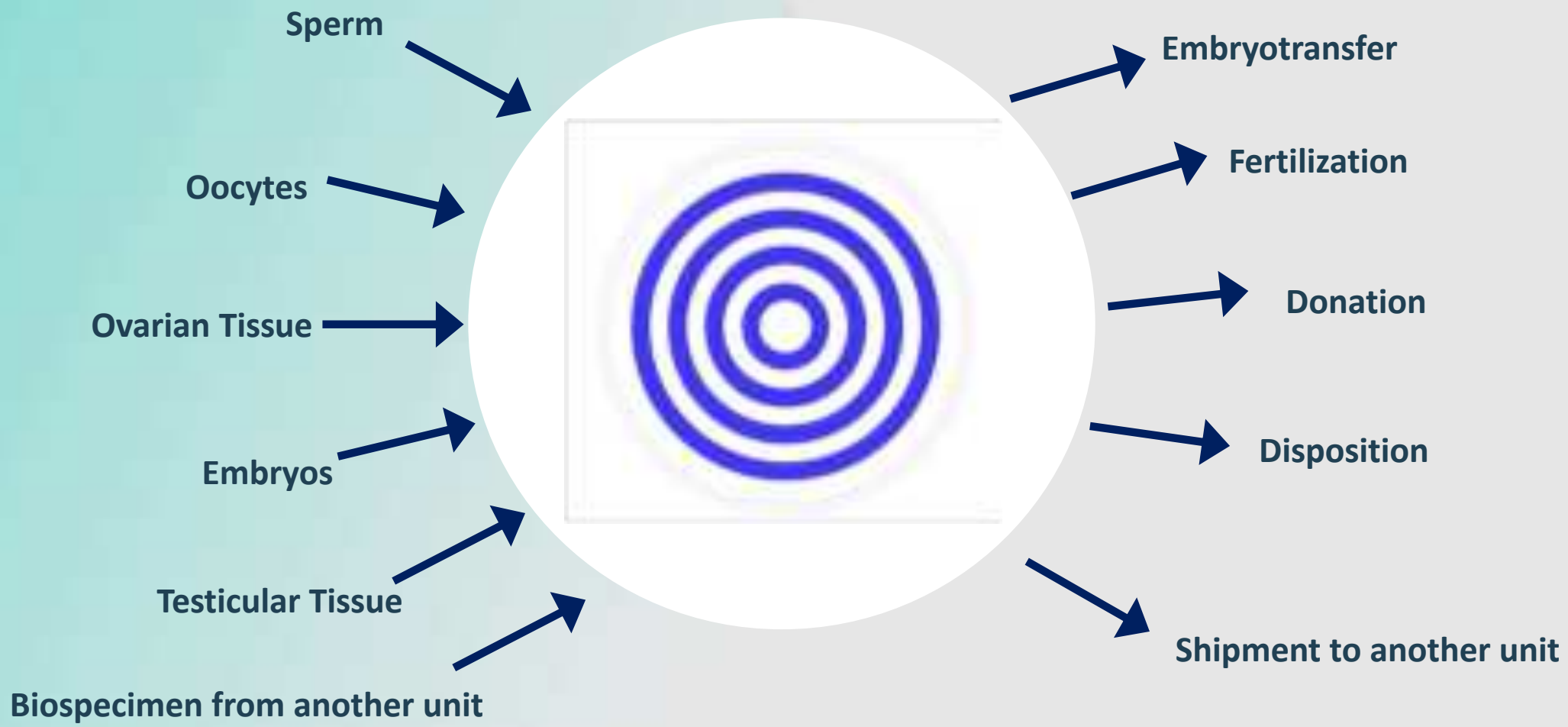
Cryobanks in 2000



Cryobanks in 2025



CRYOBANKS in Next Gen ART Units




Cryostorage of reproductive tissues in the in vitro fertilization laboratory: a committee opinion


TQM
TOTAL QUALITY MANAGEMENT

Quality Systems

- ✓ **Mandatory** (Legal requirement, Professional guideline)
- ✓ **Voluntary** (Good practice)

TÜV AUSTRIA
EAOT EN 15224:2017

*..It is in the interest of **competent laboratories** that **OUR** competence is verified through a process of inspection and compared against appropriate standards as a confirmation of **OUR** good standing..*

ISO 9001

"In an IVF lab, frozen sperm, oocytes or embryos **are absolutely priceless** and quite rightly patients who consent to storage, they expect the **best possible condition**.

It is therefore imperative that patients and other users of the services such as oncologists, gynecologists and general practitioners are reassured that **quality systems are in place** to look after their samples for the entire storage period, which, of course may be many years".

Tomlison M., HR, 2005

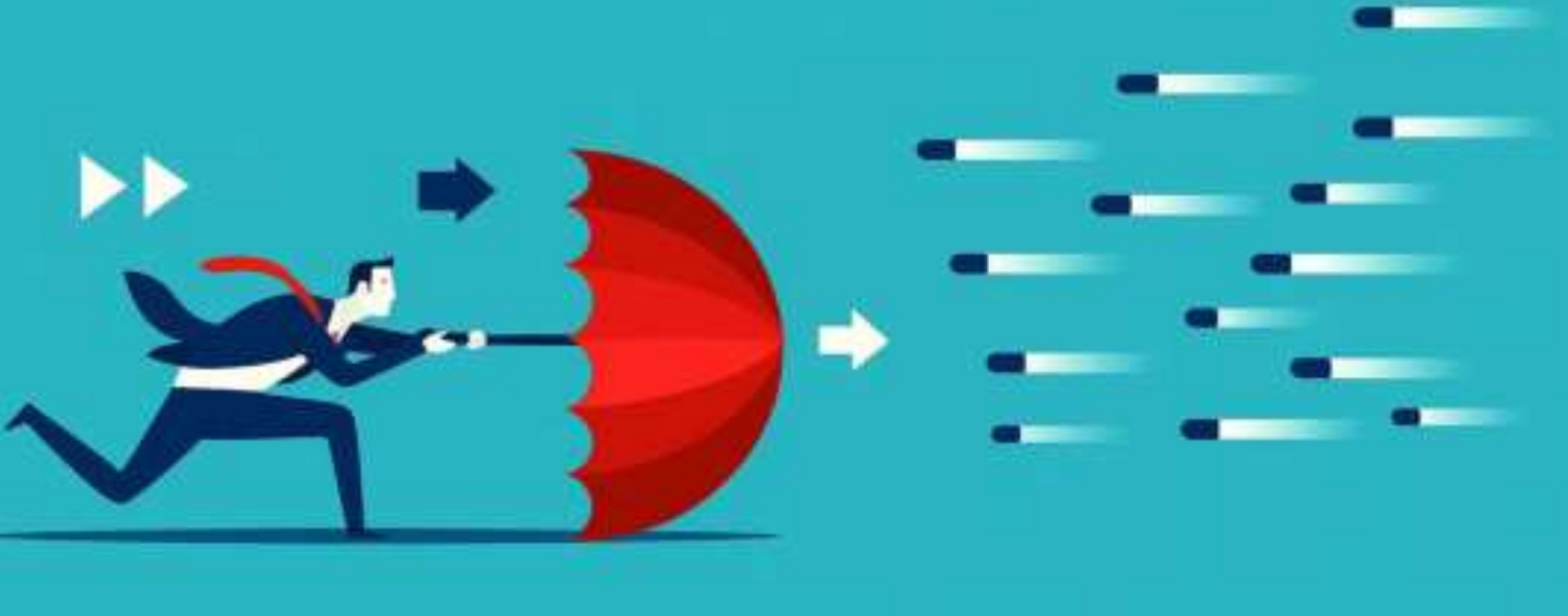

MONITORING
ANALYZE
ACTION
CONTROL
IDENTIFY
RISK
MANAGEMENT

Risk Management makes THE difference

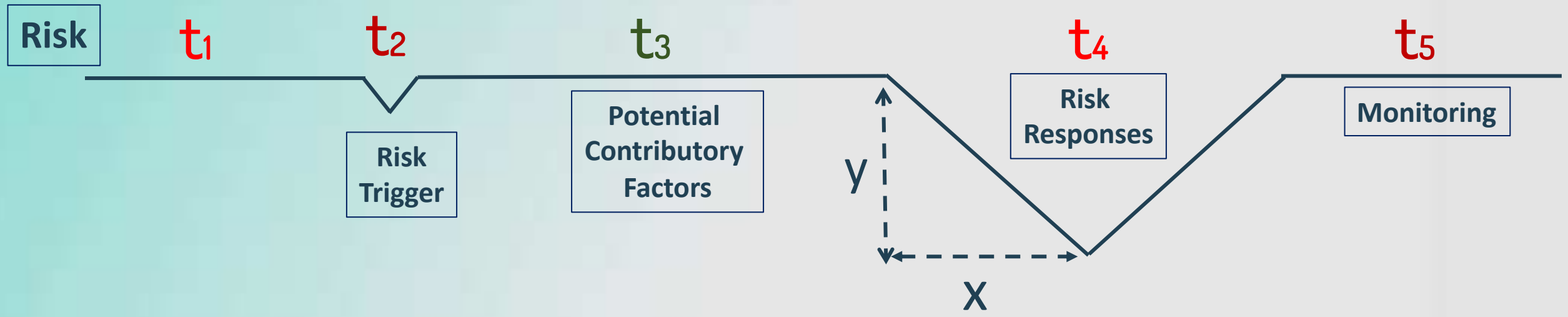
System not prepared when an unforeseen event occurs!
System crashes!

All the risks are actively assessed, managed, prevented corrected and eliminated

Cryobank: A Risk Averse System with ZERO Tolerance to Errors!!



The Anatomy of Each Cryo-Risk



Cryobanks in Next Gen ART Units: The Operational Axes

- Equipment & Maintenance
- Techniques, Procedures & SOPs
- Sample Safety & Traceability
- Personnel & Training
- Personnel Safety
- Sample Transportation
- Emergency plan
- Litigation
- Data Safety
- Lessons learned
- Management of unused embryos
- Human factor

1. Equipment & Maintenance

Dewars

Alarm Systems

Monitoring Systems

Equipment

1. Your Decisions will determine the Profile of your Cryobank

- Type of Dewars
- Storage Conditions
- Carrier System
- Storage Location
- Monitoring System
- Alarm systems

2. Each Decision brings Different Risks into your Cryobank!

3. Risks you need to Address and mitigate

Storage Capacity

- Larger Tanks
- Re-design Extend Cryo-room
- Increase LN2 Supply
- Increase and minimum storage LN2 quantity
- Central installation and LN2
- LN2 production system
- External storage for long term samples

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Maintenance

- Daily /Periodic/Continuous Monitoring- QC
- Alarm systems
- Refiling of LN2 procedure
- Visual inspection of the Dewars
- Cleaning Protocols (dewars, cannisters, goblets etc)
- Dewar Validation Protocols
- Replacement of old or a Malfunctioning Dewar
- Cleaning/Validations of a new Dewar
- Emergency plan in case of a tank failure
- Measures Sample Contamination

Techniques, Procedures & SOPs

- Consent forms
- Carrier systems-consumables
- Cryopreservation media
- Cryopreservation protocols
- Labeling system
- Infectious samples
- Samples received from other units
- Resources
- Administration
- Training
- SOPs

- Storage vessels
- LN_2 monitor system
- LN_2 supply system
- Alarms
- Traceability
- Storage of infectious samples
- Vessel maintenance
- Replacement- Cleaning
- Storage duration
- Training
- SOPs

- Thawing protocols
- Thawing media
- Consumables
- Consent form
- Samples shipped to other units
- KPIs
- Culture post thaw
- Discard samples
- Training
- SOPs

Techniques, Procedures & SOPs

Safe and High Performing Processes!

<u>Processes must be</u> :

Optimized

Standardized

Monitored

Sample Safety & Traceability During Storage


Human Reproductive Cell Cryopreservation, Storage, Handling, and Transport: Risks and Risk Management

Abstract

- ✓ Prolonged Storage
- ✓ Storage conditions & Temperature Fluctuations
- ✓ Unintended warming:
  - *Human error*
  - *Equipment Failure*

Sample Safety & Lessons Learned

Lawsuit frequency and claims basis over lost, damaged, and destroyed frozen embryos over a 10-year period

Management of Unused and Unclaimed Embryos/Oocytes

- Educate patients
- Informed Consent Forms
- Clear Disposition Options
- Regular contact with the patient
- Good billing practices
- Recruitment of a 3rd party service

Personnel Safety

Oxygen monitoring with Alarm

Forced ventilation

Training of staff

Nitrogen is odorless, colorless, and tasteless and may produce asphyxia

1 Liter LN_2 produce
700 liters Nitrogen gas

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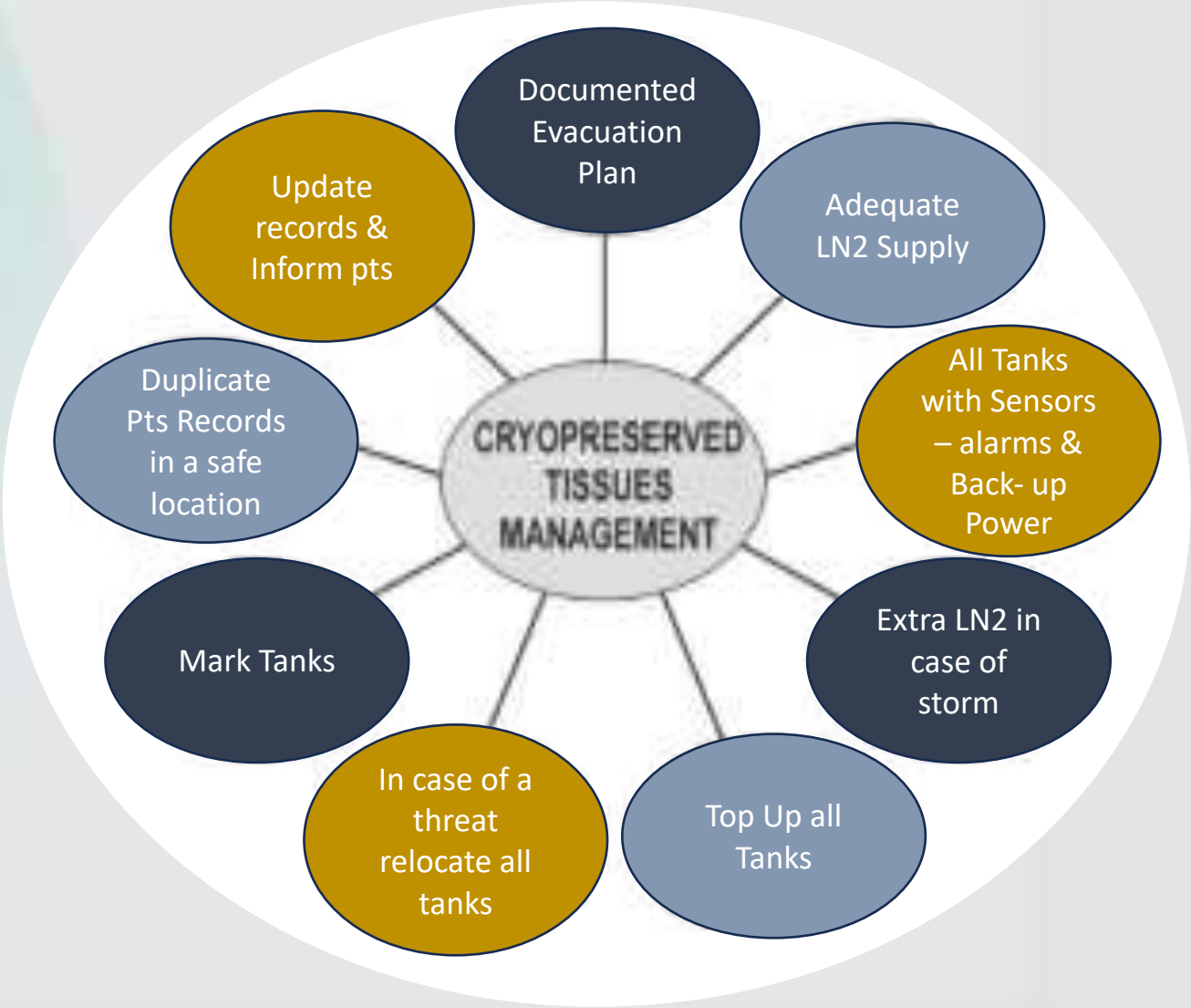
Emergency Plan

Development of an emergency plan for in vitro fertilization programs: a committee opinion

Disaster preparedness in assisted reproductive technology

Emergency Plan - When Disaster Strikes



Sample Transportation

Human Reproductive Cell Cryopreservation, Storage, Handling, and Transport: Risks and Risk Management

Sample Transportation

Storage, transport, and disposition of gametes and embryos: legal issues and practical considerations

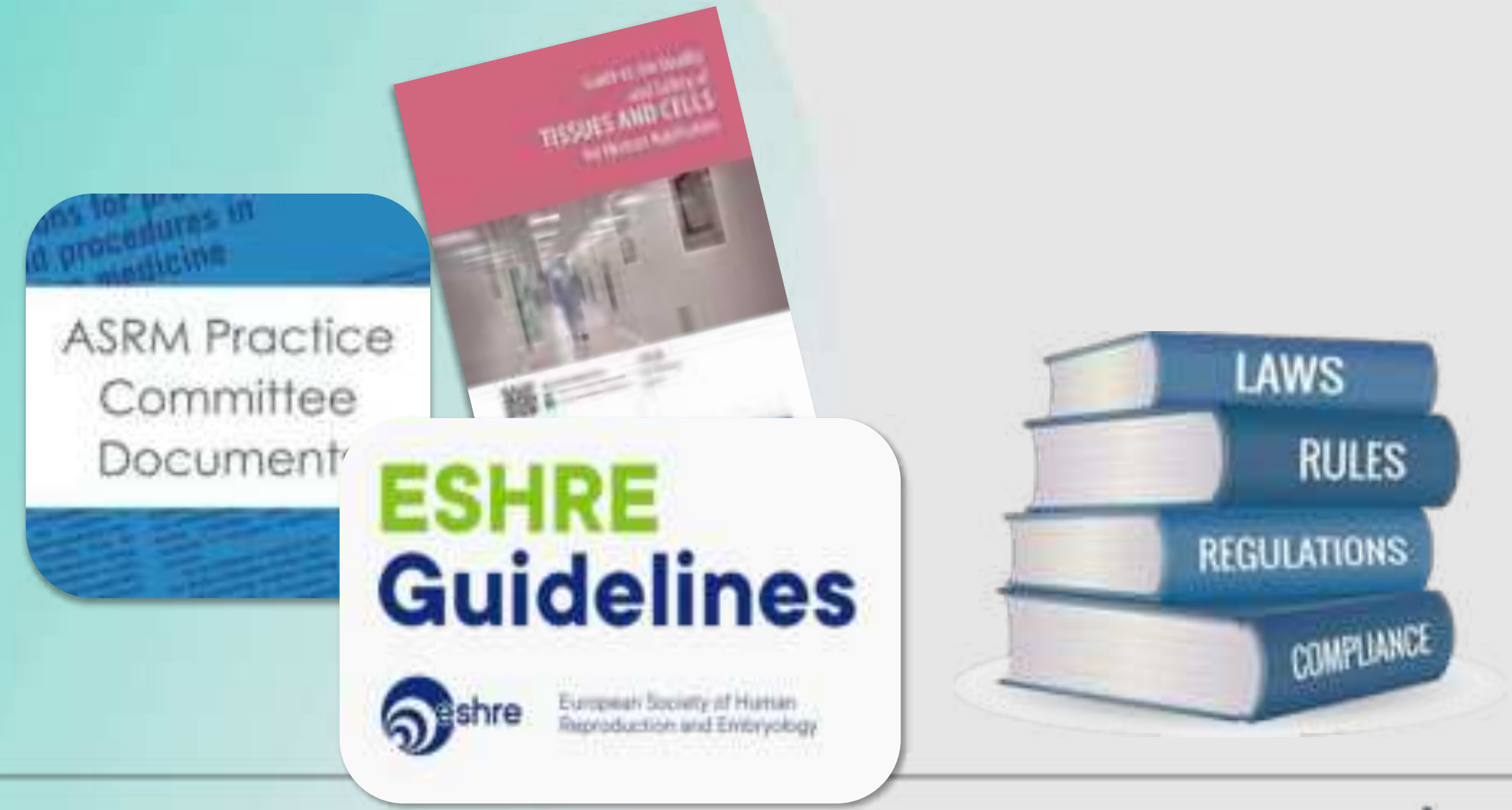
Data Safety

HACK BRIEF: HACKERS ARE HOLDING AN LA HOSPITAL'S COMPUTERS HOSTAGE

AUTHOR: BRIAN BARRETT.
SECURITY DATE OF PUBLICATION: 02.16.16.
TIME OF PUBLICATION: 5:26 PM

- ✓ Role/user based access
- ✓ Fire walls
- ✓ Internet Filter
- ✓ No USB policy
- ✓ Antivirus programs
- ✓ AntiSpyware and AntiMalware
- ✓ Monitored Network Attached Storage (NAS)
- ✓ Several daily back ups
- ✓ Several Back up Servers

Law-Regulations-Guidelines



Personnel Training

- Cryobiology Principles
- Procedures
- Logbook
- Audits and DOPs
- External Quality Assessment

- ✓ Cryo protocols
- ✓ Labelling
- ✓ Positioning
- ✓ Emergency plans
- ✓ Safe use of LN2
- ✓ LN2 Monitoring
- ✓ Tank Validation
- ✓ Sample Transportation
- ✓ Administration
- ✓ Cryo sample disposition
- ✓ Patient Counselling

Staffing in Next-Gen Cryobanks

Cryobank Adverse Events

"If the policy outcomes mandated under this decision stand, the consequences will be profound. Modern fertility care will be unavailable to the people of Alabama, needlessly blocking them from building the families they want... Clinics will be forced to choose between providing sub-optimal patient care or shutting their doors."

ASRM President Dr. Paula Amato, MD

ESHRE statement

March 2024

ESHRE condemns the recent Alabama supreme court ruling

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The Future Of Cryostorage

Automation

Digitalization

The Next Generation Lab & Clinics

Innovation

Robotics

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AI - Automation - Robotics

Cryobanks & The Human Factor

- Vision
- Mission
- Commitment
- Leadership
- Improvement Opportunities
- Effective Inter and intra department communication
- Process Monitoring
- Process improvement
- Data & Issue Reporting

The role - position - recognition of Clinical Embryologists

Thank you for your attention!