thers.com, for detailed information on obstetrics & gynecology books, visit our website www.jaypeebrothers.com

JAYPEE

The Art & Science of Assisted Reproductive Technology



Editor
Sunita R Tandulwadkar

Forewords
Bomi Bhote • Togas Tulandi • Prakash Trivedi

Contents

Section 1 Setting-up an ART Laboratory

1. How to Set-up an ART Laboratory? **3**
Sunita R Tandulwadkar, Devika Chopra

Location of the Art Laboratory 3 • Construction Materials 3 • Construction Design 4 • Configuration of the Air-handling Ventilation and Filtration System 4 • Use of Ultraviolet Lamps in in vitro Fertilization Laboratory 4 • Laminar Air Flow Hoods 5 • Incubators 5 • Microscopes 5 • Centrifuges 6 • Liquid Nitrogen Cans 6

2. Quality Control in an ART Laboratory **8**
Vijay Mangoli, Ranjana Mangoli

Laboratory Personnel 8 • Procedures 9 • Culture Room 10 • Infection/Contamination Control 10 • Instructions to Patients 10 • Record Keeping 10 • Other Aspect of Quality Control 10

3. Quality Care Management in ART Clinic **12**
Madhuri Patil

Objectives of Quality Control and Assurance 12 • Minimal Physical Requirements of an ART Clinic 13 • Documentation 17 • Quality Control and Quality Assurance 18 • Discussion 20

Section 2 How to Investigate an Infertile Couple?

4. Evaluation of the Male Partner **25**
Madhuri Patil

Evaluation of Male Partner 26 • Discussion 42

5. Investigation of Infertile Female **46**
Sonia Malik, Meenakshi Dua, Vandana Bhatia

Individualized Pretreatment Assessment 46 • General Assessment 46 • History and Physical Examination 46 • Tests 47

6. Ultrasound and Doppler in Infertility **52**
Sonal Panchal, Narendra Malhotra, Jaideep Malhotra, Chaitanya Nagori

Monitoring of Treatment Cycles in Patients with Infertility 52 • Early Proliferative Scan 52 • Preovulatory Scan 53 • Luteinized Unruptured Follicle 64

7. Effect of Environment on Fertility **68**
Sunita R Tandulwadkar, Sejal Naik

Mechanism of Damage to Cell 69 • Common Compounds Detrimental to Fertility 69 • Clinical Consideration 71

Section 3 Endoscopy in Infertility

8. Fertility Enhancing Laparoscopic Surgery **77**
Sanjay Patel

Tubal Surgery 77 • Endometriosis Surgery 79 • Laparoscopic Myomectomy 83 • Laparoscopic Adenomyomectomy 83

19. Ovulation Trigger **184**
Fessy Louis T
Human Chorionic Gonadotropin 184

Section 5 Gamete Collection and Preparation

20. Oocyte Retrieval **191**
Sunita R Tandulwadkar, Sejal Naik, Devika Chopra
Primary Assessment 191 • Techniques 191 • Timing 192 • Equipment 192 • Procedure 192 • Complications 193

21. Oocyte Evaluation and Preparation **198**
Sonal Vaidya
The Oocyte 198 • Oocyte Abnormalities 199

22. Semen Analysis and Evaluation of Sperm **207**
Daniel Franken
Semen Analysis 207 • Evaluation of Sperm and Sperm Function 208

23. Semen Collection and Preparation **212**
Ashok Agarwal, Sejal Doshi
Semen Collection 212 • Commonly Used Movement-based Techniques 213 • Salient Points 218

Section 6 Micromanipulation

24. Micromanipulation: Instrument, Technique and ICSI Procedure **223**
Sunita R Tandulwadkar, Susmitha Dulipalla, Chaithra SK
Indications of Intracytoplasmic Sperm Injection 223 • Ejaculated Spermatozoa 223 • Equipment and Materials 224 • Intracytoplasmic Sperm Injection Procedure 225 • Collection and Preparation of the Oocytes 227 • Setting for the Microinjection 229 • Sperm Immobilization 230 • Penetration into the Ooplasm 230 • Evaluation of Fertilization, Embryo Development, Culture Conditions, and Embryo Replacement 231

Section 7 Enhancing Sperm, Oocyte, Embryo Quality

25. Polarized Light Microscopy **235**
Devika Chopra
Polarized Light Microscopy 235

26. IMSI in Daily Laboratory Practice: Lights and Shadows **241**
Fabien Murisier, Françoise Urner, Alain Chanson, Marc Germond, Alfred Senn
Material and Methods 241 • Results 243 • Discussion 244

27. Role of Preimplantation Genetic Diagnosis in ART **247**
Sunita R Tandulwadkar, Sejal Naik
Methods of Breaching the Zona 247 • Polar Body Biopsy 249 • Cleavage-Stage Embryo Biopsy 250 • Blastocyst Biopsy 250 • Chromosomal Aneuploidies 251 • Chromosomal Translocations 252 • Blastocyst Transfer following Biopsy 252 • Impact of PGD on IVF Outcome 252

28. Assisted Hatching of Human Embryos **254**
Sunita R Tandulwadkar, Devika Chopra

Structure and Function of Zona Pellucida 254 • Indications for Assisted Hatching 255 • Mechanism of Assisted Hatching 256 • Techniques of Assisted Hatching 256 • Laser-assisted Hatching 257 • Review of Literature 258 • Risks Associated with Assisted Hatching 258

Section 8 Culture of Embryos and Transfer

29. Culture and Evaluation of Embryos: From Fertilization to Transfer **263**
Rajvi H Mehta

Culture Media for ART 263 • Basic Composition of Culture Media for ART 263 • Sequential versus Single Step Culture Medium 265 • In Vitro Culture Conditions 265 • Evaluation of Zygotes and Embryos 266

30. Proteomics and Metabolomics in ART **271**
Devika Chopra

What are Genomics, Proteomics and Metabolomics? 271 • Proteomics in ART 271 • Proteomic Studies on the Male Reproductive System 273 • Metabolomics in ART 274

31. Time-lapse Microscopy **278**
Sunita R Tandulwadkar, Devika Chopra

Stages of Embryo Development 278 • Time-Lapse Microscopy 278 • Future Prospects 284

32. Embryo Transfer: Catheters and Techniques **287**
Hrishikesh Pai

Historical Aspects 287 • Preparatory Techniques 287 • Other Techniques 292

Section 9 Implantation

33. Endometrial Receptivity **297**
Jure Knez, Christophe Blockeel

The Process of Implantation 297 • Endometrial Receptivity 297 • The Role of Steroid Hormones 298 • Morphologic and Molecular Markers of Receptivity in Human Endometrium 298 • Non-invasive Assessment of Endometrial Receptivity 301

34. Embryo Endometrial Dialogue **305**
Sunita R Tandulwadkar, Kamala Selvaraj, Devika Chopra

Synopsis 305 • Preimplantation Embryo Development 306 • Uterine Receptivity and Implantation 306 • Implantation Window 306 • Susceptibility to Immunity 307 • Relevance of the Leptin System in the Embryo: Endometrial Dialogue 307 • Potential Molecular Signaling during Implantation 308 • Immunomodulation 308 • Cytokines 308

35. Physiology of Implantation in Natural Cycle Versus Stimulated Cycle **311**
Jana AlShalati, Togas Tulandi

Changes in Endometrium during Menstrual Cycle 311 • Early Embryo Development and Implantation 311 • Stimulated Cycle 312

36. Recurrent Implantation Failure: Strategies and Intervention **314**
Sadhana K Desai, Partha Guha Roy

Embryo as a Possible Cause of RIF: Strategies and Intervention 314 • Endometrium as Possible Cause of RIF: Strategies and Intervention 316 • Immunological Factors 317 • Adjuvant Pharmaceutical Therapies 318 • Alternative Medicines to Improve Implantation 319 • Surrogacy and Gamete Donation 320

37. Implantation and the Endometrium in Uterine Fibroid **323**
Sesh Kamal Sunkara

Fibroids and Fertility 323 • Fibroids and in Vitro Fertilization Treatment Outcome 323 • Fertility after Myomectomy 324 • In Vitro Fertilization Outcome after Myomectomy 324 • Alternative Treatments for Fibroids 324

38. Implantation in Endometriosis **326**
Sunita R Tandulwadkar, Anupama Singh

Physiology of Implantation 326 • Pathogenesis of Defective Implantation 328 • Treatment of Endometriosis 330 • Future Research Areas 330

Section 10 Cryopreservation

39. Oocyte Cryopreservation **337**
Dominic Stoop

Efficiency of Oocyte Cryopreservation 337 • Clinical Applications 338

40. Embryo Cryopreservation **341**
Yasser Orief, Engie Al Salman

Cryopreservation of Two Pronuclear Stage Zygotes 342 • Comparison of the Different Cryopreservation Techniques 343 • Future Perspectives 351

41. Cryopreservation of Ovarian Tissue **353**
Sunita R Tandulwadkar, Sejal Naik

Ovarian Cortical Tissue 354 • Whole Ovary Cryopreservation 354 • Methods of Freezing 355 • Pregnancy after Ovarian Tissue Cryopreservation 355 • Transplantation 355 • Risk of Cancer Recurrence 356 • Alternatives to Ovarian Tissue Cryopreservation 357

42. In Vitro Maturation of Oocytes **359**
Sunita R Tandulwadkar, Devika Chopra

History of In Vitro Maturation of Oocytes 360 • In Vitro Maturation of Oocytes 360 • Applications of In Vitro Maturation 360 • Disadvantages of In Vitro Maturation 360 • Animal Models for In Vitro Maturation 361 • Discussion 361

43. Semen Banking **364**
Natachandra Chimote, Bindu Chimote, Nishad Chimote

General Aspects of Semen Banking 364 • The Principal Variables of Cryopreservation: Solutions, Temperatures and Rate Changes 364 • Sperm Cryopreservation 365 • Apoptosis in Ejaculated Human Spermatozoa 365 • Mechanisms and Manifestations of Cryoinjury in Spermatozoa 365 • Apoptosis in Cryopreserved Subfertile Semen Samples 367 • Methods to Decrease Apoptosis during Sperm Cryopreservation 367 • Processing of Semen can Result in Increased Sperm Deoxyribonucleic Acid Fragmentation 368 • Effects of Cryopreservation on Human Sperm Deoxyribonucleic Acid Integrity 369 • Cancer and Fertility: Strategies to Preserve Fertility 369 • Effects of Cancer and its Treatment on Fertility 369 • Preservation of Fertility for Young Adults with Cancer 370 • Cryopreservation Techniques 370 • Male Fertility Preservation 370 • Sperm Vacuoles are not Modified by Freezing–Thawing Procedures 370 • Simple Vitrification for Small Numbers of Human Spermatozoa 371 • Protocols for Laboratory Procedures 371 • Procedures (Aspiration from Surgery) 372 • Procedure (Semen from Ejaculate) 373

44. Fertility Preservation in Cancer (Male and Female) **378**
Bina Vasan

Effects of Cancer and its Treatment on Fertility 378 • Patients' Dilemma: Coping with Cancer and Decision on Fertility Preservation 381 • Malignant Conditions Necessitating Fertility Preservation 381 • Methods of Fertility Preservation in Males 384 • Methods of Fertility Preservation in Females 386

• Special Considerations for Ovarian Stimulation in Cancer Patients 389 • Obstacles to Fertility Preservation 390 • Ethical Dilemma 390 • Current Guidelines for Fertility Preservation 390

Section 11 Luteal Phase in ART

45. Luteal Phase Support in ART **399**
Sunita R Tandulwadkar, Sejal Naik, Chaithra SK

Luteal Phase in Natural Cycles 399 • Luteal Phase Defect 399 • Luteal Phase in Stimulated Cycles 400 • Rationale Behind Luteal Support in Agonist/Antagonist Cycles 400 • Practical Options for Luteal Support 401 • Efficacy of Various Progesterone Preparations 401 • Duration of Luteal Support 402 • Adjunct Therapy for Luteal Phase Support 402 • Luteal Phase in Special Cases 402

Section 12 ART in Special Conditions

46. Endometriosis and ART **407**
Israel Ortega, Juan A García-Velasco

Medical Treatment Prior to in Vitro Fertilization 407 • Management of Ovarian Endometriomas 408 • Risks of Expectant Management and Surgery 410

47. Myomas in Infertility **413**
Sunita R Tandulwadkar, Devika Chopra

Recent Evidence 413 • Effect of Location of Myoma on IVF Outcome 413 • Effect of Size of Myoma on IVF Outcome 417 • Effect of Myomectomy on IVF Outcomes 417

48. Genital Tuberculosis and ART **421**
Neena Malhotra

Epidemiology of Genital Tuberculosis 421 • Etiopathogenesis of Infertility in Genital Tuberculosis 421 • Diagnosis of Genital Tuberculosis 422 • Endoscopy Prior to in Vitro Fertilization 423 • Indications of Assisted Reproduction Techniques 424 • Pre-in Vitro Fertilization Evaluation 424 • Medical Treatment Prior to in Vitro Fertilization 426 • Surgical Treatment Prior to in Vitro Fertilization 427 • Problems during in Vitro Fertilization 427 • Outcome of Assisted Reproduction Techniques 427

49. Poor Ovarian Response **430**
Sunita R Tandulwadkar, Parinaaz Parhar

Definition 430 • Incidence 432 • Etiology 432 • Predictors of Poor Ovarian Response 432 • Treatment 434 • Natural Cycle IVF and Modified Natural Cycle IVF 437 • Other Adjuvants 438 • Laboratory Options in Poor Response Cycles 438

50. ART in Polycystic Ovary Syndrome **444**
Jaideep Malhotra, Parul Arora

Challenges in PCOS 444 • Pathophysiology and Oocyte Abnormalities in PCOS 445 • Ovarian Stimulation Protocols for ART Cycles in PCOS 447 • Insulin Sensitizers in PCOS 450 • Complications of Ovarian Stimulation in PCOS 454 • In Vitro Maturation 457

Section 13 Third Party ART

51. Gamete Donation **463**
Abha Majumdar, Chauhan Kumudini

Sperm Donation 463 • Oocyte Donation 466 • Changing Practice of Anonymity 468 • Levels of Information Sharing 468

52. Embryo Donation **475**
Devika Gunasheela, Ashwini S, Jyothi Patil, Prathiba G

Definition 475 • History 475 • Types 475 • Source 476 • Indications for Embryo Donation 476 • Guidelines 476 • Record Keeping 477 • Protocol 478 • Success 478 • Legal Issues 478 • Ethical Issues 478 • Donor Issues, Obstacles and Dilemmas 479

53. Surrogacy **481**
Nayana Patel, Pankaj Kaingade

Indian Mythology 481 • Bible Mythology 481 • Definitions 481 • Indications for Gestational Surrogacy 481 • Steps in Surrogacy 482 • Our Experience 484

Section 14 Pregnancy and ART

54. First Trimester Screening in Pregnancies Conceived with ART **489**
Pooja Lodha

First Trimester Screening 489 • Effect of ART on First Trimester Screening 491 • Effect of FTS on ART Pregnancy 492 • Other Implications of FTS Results for ART 492 • Possible Explanations for Differences in FTS in ART Pregnancies 493

55. Obstetric Outcome Following ART **495**
Sunita R Tandulwadkar, Bhavana Mittal, Nirzari Mangeshikar

Comparison of Pregnancy Outcome in Fertile versus Subfertile Women 495 • Comparison of the Pregnancy Outcomes of Subfertile Women after Infertility Treatment and in Naturally Conceived Pregnancies 495 • Comparison of Pregnancy Outcome in Fertile Women versus ART Pregnancies in Subfertile Women 496 • Comparison of Pregnancy Outcome in Natural Conception in Subfertile Women or Use of Ovulation Induction (With or Without Intrauterine Insemination) and Use of in Vitro Fertilization 497

56. ART to Antenatal Care **499**
Sunita R Tandulwadkar, Parinaaz Parhar

First Trimester 499 • Second and Third Trimester 502

Section 15 Complications in ART

57. Ovarian Hyperstimulation Syndrome **509**
Nalini Mahajan

Pathophysiology 509 • Clinical Presentation and Classification of Ovarian Hyperstimulation Syndrome 510 • Ovarian Hyperstimulation Syndrome Prevention 512 • Management of Ovarian Hyperstimulation Syndrome 515

58. Ovarian Cancer and ART **519**
Priya Bhave Chittawar

Infertility and Ovarian Cancer Risk 519 • Drawbacks of the Studies Evaluating IVF and Ovarian Cancer Risk 521

59. Ethical and Stress Issues in ART **524**
Ian Cook

Ethical Issues 524 • Stress Issues 528 • Counseling 532

Index *535*

2 Quality Control in an ART Laboratory

Vijay Mangoli, Ranjana Mangoli

Every time an embryologist sees an in vitro fertilization (IVF) baby, he recollects its journey from gamete collection to embryo transfer. He truly experiences what Aristotle had said, *"those who see things grow from the beginning will have the finest view of them"*. An embryologist does not just observe them grow, but create them under optimum culture conditions.

Creating a human being in laboratory is indeed a responsible task that requires technical skill and adequate knowledge about the subject. IVF laboratory is a cluster of many sections, each with a specific purpose affecting final outcome. Hence, it also demands strict quality control not only for establishment, but also on a continuous basis till the program is running. It becomes responsibility of the embryologist to establish and maintain optimum standards at all time with motto of "Zero Tolerance" for mistakes and negligence. Mistakes in IVF have the potential for very serious consequences. Therefore, we should have a holistic approach of prophylactic management for prevention of errors.

Although there is a steady rise in pregnancy rate over last two decades, still there is lot of uncertainty in IVF outcome. Many times, the embryologists are surprised not because they are not getting expected pregnancy rate but because they are confused—why all of a sudden so many patients are getting pregnant. On the other hand, sometimes they wonder, in spite of everything looking perfect, why there is a sudden drop in pregnancy rate! Though there is no magic formula available as yet which can give us consistent high pregnancy rate, there are some quality control Dos and Don'ts that can prevent pregnancy rate from falling below unacceptable level. Another important aspect to keep in mind is, there can be vast differences between two assisted reproductive technology (ART) laboratories—structure wise, material wise and technique wise. Therefore, quality indices criteria should be based on basic principles of ART.

There are two main aspects of quality management: (1) quality control and (2) quality assurance. Quality control is the standardization of all techniques, tests and procedures so that the outcome becomes reproducible and not person specific, e.g. if a laboratory director has standardized a technique of semen freezing to get more than 70% post thaw survival, the protocol should be mentioned in standard operative procedure (SOP) in such a way that anybody in the laboratory doing semen freezing should get same results.

Whereas quality assurance is more expansive term that encompasses not only quality control but involves monitoring and control of the ultimate outcome of the test or technique. In the above example, quality assurance not only confirms 70% survival, but ensures that the sample is collected, processed, stored, recorded and utilized properly.

It is practically not possible to do quality control checking of all stages on a daily basis. Therefore, such monitoring is divided in durations as daily, weekly, monthly and yearly basis. These are some practical quality control points that help us getting reproducible results.

LABORATORY PERSONNEL

To maintain a good quality control program, center should have fully trained keen interested and committed staff. Apart from sound knowledge in their respected field, they should have basic knowledge about the instruments maintenance and troubleshooting. Second very important requirement is willingness to admit and rectify the mistakes. It is not a crime to make mistake, but it is a crime to hide and try to cover them. Experience, skill and ability to handle difficult situations by laboratory staff, contribute to the success of an ART center. As there is no government-recognized training centers in India at present, the person is trained "on job". It is responsibility of the project director to have adequate staff depending upon number of cases. Overburden can cause fatigue and more seriously, irreversible mistakes like specimen misidentification. It was speculated before the era of

JAYPEE BROTHERS

intracytoplasmic sperm injection (ICSI) that a center performing 100 IVF cases per year should have one embryologist and two technicians. However, in today's scenario of ICSI, intracytoplasmic morphologically selected sperm injection (IMSI) and detailed data entry, the same center needs two fully trained embryologists and three technicians. Quality control in this aspect includes upgradation of knowledge to latest developments in the field and experimentation, within permissive limits, by laboratory director. All protocols and procedures of every step involved should be in written form of SOP that can be accessed easily by each laboratory person. Any change should be immediately mentioned in SOP with date of rectification so that its effect can be analyzed. Every new person joining the team should be given adequate time to get accustomed to working conditions and protocols. Considering significance of the job, the proficiency of staff to demonstrate competency can be evaluated periodically.

PROCEDURES

Consistent results are obtained when there is uniformity in procedures irrespective of person performing. Each procedure should be available in written form near the site of performance. All protocols should be written in simple language and stepwise manner giving details of materials, equipment, solutions and disposable required. Formulae of calculation, if any, should be mentioned simply, preferably citing examples. The laboratory director should supervise performance of juniors till it is done in the same manner that gives reproducible results. It is also his responsibility to review SOPs at least annually and upgrade if required.

Air

Ambient air is an important but often ignored part in the laboratory. Air pollution often goes unnoticed because it is invisible. **Table 1** illustrates some of the sources that can contribute to air pollution. Almost all these pollutants have strong affinity for water molecule and hence can easily get dissolved in culture media, changing its composition to toxic level. In an IVF laboratory, scents, perfumes or any such volatile material are strictly prohibited.

Table 1 Common pollutants and their sources in an IVF laboratory

Pollutants	Sources
Enflurane, halothane	Anesthetic gases
Toluene, butane	Pesticides, aerosoles
Aldehydes	Paints, vinyl flooring
Freones, chloroethanes	Refrigerators, air conditioners
Ethylene oxide	Disposables
Isopropyl alcohol	Disinfectant

Culture room should have air purification class 10,000 maintained continuously with about 40 air changes/hour. It is necessary to maintain continuous positive pressure in one direction—from culture room to operating theater and outwards. Prefilters and high-efficiency particulate air filters should be changed regularly. Its frequency depends upon location of the center. Alcohols, acids or batteries of uninterruptible power supply (UPS) system should not be stored near culture room. Establishments like adjacent petrol pump or chemical godown will increase criteria air contaminants including volatile organic compounds in the culture room to very high level.

Instruments and Equipment

These are the backbones of an ART center. We depend a lot on them to achieve the goal of creating and maintaining viable embryos. In fact quality control of instruments itself is a separate topic if discussed in detail. The best way to deal with them is to give annual maintenance contract to respected companies and maintain a fix schedule for their servicing. But equal important is to counter check the readings displayed on the panel with standardized calibrating instruments on a daily basis—particularly temperature, CO_2 level, humidity of incubators and optics maintenance of microscopes. Generally major instruments like incubators, freezing machine, micromanipulators are taken care of, but temperature of dry air oven, stage warmer of microscope, refrigerator, proper steam pressure of autoclave, revolutions per minute of centrifuge are generally ignored. If instruments are in perfect working conditions, then half the job is done!

Medium

The importance of media is next to the experience of the embryologist. Embryos are cultured in micro-environments and any deviation from optimum requirements immediately reflects in their growth pattern. One should understand science and logic behind its composition. If medium is made in house, it should be checked for these three parameters—physicochemical, biological and functional. Physicochemical includes pH and osmolarity. Biological control includes proper sterilization, and testing endotoxin level. Functional tests are carried out mainly to check potential of medium through sperm survival test, mouse embryo assay, and cell culture growth such as the culture of the mouse

JAYPEE BROTHERS

hybridoma cell line. The centers using ready-made media should confirm proper handling and temperature control during transport.

Electricity

In vitro fertilization center should have a continuous power supply. There are many delicate and sensitive instruments which are calibrated with great care. Sudden fluctuations in the electric current can change the internal settings of electronic circuit completely. They may display set values, but the actual values may vary. Installation of proper stabilizer, and spike suppressor along with a good UPS system should be part of equipment.

Disposables

It is advisable to use disposables from a reputed company. They are to be rinsed before use whenever possible, e.g. before equilibrating media, oocyte pickup (OPU), sperm preparation and transfer catheters. Minimum 10 days of proper ventilation is required for ethylene oxide treated disposables because these products are known for their property called "Off-Gassing" for few days after sterilization.

CULTURE ROOM

Temperature of culture room is to be balanced between ambient air and that of incubators or ICSI platform. Proper ventilation will minimize the discomfort to embryologists. In many countries, another major problem is to get consistent medical grade CO_2. One should not use industrial grade CO_2. Purity certification should be demanded form supplier. It is advantageous to keep separate cylinders for each incubator rather than giving same connection. The gas tubing and filters should be changed regularly. User manuals of all instruments should be kept in an easily accessible manner.

INFECTION/CONTAMINATION CONTROL

As we try to create ideal conditions for the growth of embryos in the culture room, it invites unwanted growth as well. Warm, humid atmosphere inside the incubator is good for many pathogens and even normal flora like *Escherichia coli*. Source of contamination can be materials like pens, markers, spectacles, cell phones, papers, cartons, etc. Minimum material should be stored in the culture room. At the same time, care has to be taken of main storage room, which is generally overlooked, thus carrying yeast and fungal spores directly into the culture room. Source of infections can be biological fluids like semen, follicular fluid and blood, or it can be through staff. It is responsibility of clinicians to inform laboratory staff clearly about any such known infection of husband or wife. Because generally laboratory staff does not interact with patient till they come for OPU. Maintaining sterility of incubators, good awareness and personal hygiene habits of the staff can prevent both infection and contamination from spreading to the culture room.

INSTRUCTIONS TO PATIENTS

This is an extremely important aspect of quality assurance which is often underestimated. It is important to tell patient not only what to do, but equally important to instruct what not to do, e.g. husband is asked to keep abstinence from sex of 3 days but not instructed to includes masturbation and night falls as well. Similarly, patient is asked to collect sample in sterile container but not instructed that if sample is spilled on the floor, not to pick it up and put it in the collection jar. Giving proper instructions is collective responsibility of clinicians, nurses, laboratory people and even administration persons.

RECORD KEEPING

Another mandatory requirement in the quality control procedure is to maintain proper records in detail of all methodologies adopted, materials used, and account of each egg and embryo obtained through IVF. As aim of quality control is primarily to assess performance, it becomes absolutely essential to keep records of all variables, personnel, techniques and material both in favorable and adverse situations. Analysis of such data helps us to find out cause of poor results and also factors that improves pregnancy rates. For years, data has been recorded as hard copies in registers. However, for quick access and immediate analysis, data should be backed up in electronic form. This also minimizes space required to store large data for longer duration, as may be required by local authorities. The importance of paperwork is much more than we anticipate academically, research wise, for retrospective analysis and in legal issues.

OTHER ASPECT OF QUALITY CONTROL

Till now we discussed one side of quality control, which can be applied to maintain and enhance pregnancy rate. Quality control in IVF has one more perspective, which is more important than getting pregnancies. And which should be considered with highest priority that is to avoid accidents while handling human genetic material. Many types of error may occur, for example, miscommunication (putting embryos into the wrong patient), technique

JAYPEE BROTHERS

(carryover of sperm between patients), forgetfulness (leaving dishes out of the incubator, not filling nitrogen vessels), accident (dropping dishes), forced errors (due to excessive workload, interruption, inexperience), poor checking (misprogramed machines), and so on. All of these mistakes can happen, probably more than once, but most are avoidable. One role of quality assurance is to reduce the likelihood of mistakes. Nevertheless, where human being is involved, errors and mistakes are bound to occur. Moreover, there is the, thankfully rare, additional possibility of malicious or criminal activity, which is particularly difficult to guard against.

One incident in the Netherlands in March 1993 shook the whole world when a twin of different races was born to a couple undergoing IVF treatment. Similar incidents were reported in the United Kingdom in 2009 and in the United States of America in 2011. Of course, these may be some of the incidents that came into light out of numerous that we are not aware of. In any other establishment, if a mistake is found, then the product can be withdrawn from the market, or if it is a general laboratory then the reports can be canceled and tests can be repeated. But the same rule does not apply to an IVF laboratory. Once the baby is born, or even the pregnancy is established, the issue becomes much complicated ethically, emotionally and legally. Therefore, each step in all the procedures should be performed keeping this potential risk in mind. Extreme care has to be taken while processing many semen samples, distributing many patient's eggs and embryos for insemination and growth medium, preparing ICSI plates, adding sperm to the PVP droplet, during insemination and while freezing more than one patient's embryos. Each step has to be done with full concentration.

In near future, there will be more uniformity throughout global ART centers in techniques and procedures for infertility treatments to give high pregnancy rate in terms of take-home babies. This will further narrow quality control indices that can be monitored by single internationally accredited body. Till then each center should set and follow rigorous quality control program to achieve best possible results.

BIBLIOGRAPHY

1. American Society for Reproductive Medicine. Revised minimum standards for in vitro fertilization, gamete intra fallopian transfer, and related procedure. Fertil Steril. 1998;53: 225-6.
2. Hall J, Gilligan A, Schimmel T, et al. The origin, effect and control of air pollution in laboratories used for human embryo culture. Hum Reprod. 1998;13(Suppl 4):146-55.
3. Jhonson MT, Gardner DK. Embryo culture in the twenty-first century. In: Gardner DK, Rizk BRMB, Falcone T, (Eds). Human Assisted Reproductive Technology: Future trends in Laboratory and Clinical Practice. Cambridge: Cambridge University Press. 2011.
4. Lane M, Mitchell M, Cashman KS, et al. To QC or not to QC: the key to a consistent laboratory. Reprod Fertil Dev. 2008;20: 23-32.
5. McCulloh DH. Quality control and quality assurance: record keeping and impact on ART performance and outcome. Infertil Reprod Med Clin North Am. 1998;9:285-309.
6. Nijs M, Franssen K, Cox A, et al. Reprotoxicity of intra uterine insemination and in vitro fertilization–embryo transfer disposables and products: a retrospective analysis of 4 year study. Fertile Steril. 2009;92:527-35.
7. Svalander P, Anderson E, Hyllner J, et al. Quality assurance methods for production of culture media and equipment essential for high success rate. In: Maximizing the Potential of Every Embryo to Minimize Multiple Embryo Transfer. Textbook for Postgraduate Course at the Meeting of American Society for Reproductive Medicine. American society for Reproductive Medicine. San Francisco, October; 1998.pp.1-15.

JAYPEE BROTHERS

or detailed information on obstetrics & gynecology books, visit our website **www.jaypeebrothers.com**, for detaile

The Art & Science of Assisted Reproductive Technology

Learning through the experiences of others over the years can minimize the learning curve in reproductive medicine. There is a continuous pressure of high quality assisted reproductive technology (ART) services and delivering high success rate. Apart from reading the journals, the textbook will always lay the sound knowledge of foundation helping the ART consultants to optimize their success rates. Thus, the need for exchange of experience across the continents forms the basis of writing the book. The authors contributing to the book are the pioneers in the field of ART.

The book intends to cover assisted reproductive techniques in a detailed manner, and hence, the book aspires to be a reference book from the point of view of the infertility specialists, gynecologists, embryologists, and trainees at graduate and postgraduate levels. Therefore, the content should be a blend of practical aspects based on national and international guidelines with a strong foundation of theory.



Sunita R Tandulwadkar MD FICS FICOG is the Head, Department of Obstetrics and Gynecology and the Chief, IVF and Endoscopy Center, Ruby Hall Clinic, Pune Maharashtra, India. Ruby Hall IVF and Endoscopy Center is recognized for Post-doctoral Fellowship in Reproductive Medicine by the National Board of Examinations. It is the only center in India recognized for the International Fellowship of Institute of Reproductive Medicine and Endoscopic Surgery (IRMES). She also represents as Board Member, the International Society of Gynecologic Endoscopy (ISGE), the Indian Association of Gynecological Endoscopy (IAGE), and the Indian Society of Assisted Reproduction (ISAR). She was the Infertility Committee Chairperson (2011–2013) for the Federation of Obstetric and Gynaecological Societies of India (FOGSI). During her tenure as Infertility Committee Chairperson, she has conducted workshops on optimizing infertility outcomes and operative hysteroscopy workshops in more than 50 cities across the country. Her aim was to teach gynecologists basic infertility managements as well as the latest trends so as to reach out to every woman in the country.

She is the one who started the trend of laparoscopic hysterectomy and all advanced laparoscopic surgeries (1995) in Pune, Maharashtra, India. She has conducted endoscopic workshops at many places and has trained many gynecologists and surgeons across the world.

She has been awarded the *Sarvashree* award and gold medal for her pioneering work in the field of endoscopy and ART (2004). She has also been awarded Master's award for her dedication towards teaching endoscopy by IMAGES. She is also the recipient of the *PunyaShlok Ahilyabai Holkar* award by the Ministry of Women and Child Development, Government of India, for her dedication and passion towards improving women's health in India.

'Ruby Hall IVF centre is recognized for basic as well as advanced ART training as well as basic and advanced endoscopy training by FOGSI. It is also recognized for post-doctoral fellowship in reproductive medicine by the National Board of Examinations. It has achieved its name and reputation in a short span of time because of her hard work, dedication and honesty.'

Available at all medical bookstores
or buy online at www.jaypeebrothers.com

JAYPEE BROTHERS
Medical Publishers (P) Ltd.
www.jaypeebrothers.com

Join us on facebook.com/JaypeeMedicalPublishers

Shelving Recommendation
OBSTETRICS & GYNECOLOGY

ISBN 978-93-5152-475-5