

## **ANNEX I**

### **CURRICULUM OF THEORETICAL KNOWLEDGE**

#### **(ALREADY AVAILABLE IN THE EXISTING ESHRE CERTIFICATION OF CLINICAL EMBRYOLOGISTS)**

Applicants for ESHRE exam in Clinical / Senior Clinical Embryology will be expected to have a knowledge of the following aspects of clinical embryology.

**Last updated by the EmCC: 20 January 2020**

#### **1. Basic Cell Biology**

##### 1.1 The cell

- Internal organisation
- Cell cycle control, checkpoints
- Mitosis and meiosis
- Reproductive cells: spermatozoa and oocytes

##### 1.2 Cell-cell interaction

- Membrane receptors: function, type, regulation
- Signalling
- Junctions

##### 1.3 Basic genetics of the cell

- DNA chromatin and chromosomes
- Concept of a gene
- Mutations
- Epigenetics

##### 1.4 Basic gene regulation

- Translation
- Transcription
- Expression
- Imprinting

#### **2. Genetics**

##### 2.1 Basic genetics principles

- Genotype and phenotype
- Basic Mendelian inheritance patterns
- Monogenic diseases
- Mutations, copy number variation (CNV), de novo mutations
- Chromosomal abnormalities: numerical, structural
- Interpretation of an inheritance / family tree / pedigree

##### 2.2 Genetic analysis and diagnosis

- How and why is it performed
- Diagnostic methods: cytogenetics (e.g. karyotyping, FISH), molecular genetics (e.g. PCR, array CGH, NGS)

### **3. Developmental Biology**

- 3.1 Embryonic stem cells
  - Origins, definitions, characteristics
- 3.2 The fetal ovary
  - Factors regulating development
  - Primordial germ cells
  - Cell migration
  - Time scale (days / week)
- 3.3 The fetal testis
  - Factors regulating development
  - Primordial germ cells
  - Cell migration
  - Time scale (days / week)
- 3.4 Gamete interaction – until 1st cleavage
  - Fertilisation
  - Acrosome reaction
  - Sperm- oocyte signaling
  - Sperm decondensation
  - Oocyte activation
  - Meiosis II, pronuclei and spindle formation
- 3.5 Embryo development - from first cleavage to implantation
  - Metabolism, cell positions, embryonic axis
  - Kinetics, timing, regulation
  - Apoptosis
- 3.6 Implantation
  - Hatching, adhesion, invasion, endometrium
- 3.7 Post-implantation embryology
  - Gastrulation
  - Organogenesis
  - Sex differentiation
- 3.8 Early pregnancy
  - hCG production, biochemical and ongoing pregnancy
  - Implantation, ultrasound (sacs, heartbeat)
  - Extra uterine pregnancies
  - Spontaneous abortions
  - Embryo factors vs. uterine factors in implantation/implantation failure

### **4. Female Reproduction**

- 4.1 Anatomy and function of the female reproductive system
  - Role of accessory systems
  - Function of the organs

#### 4.2 Oogenesis

- Regulating factors
- Hypothalamus, pituitary, gonad axis
- Endocrine regulation
- Theca & granulosa cells
- Maturation biochemistry and metabolism of the oocyte
- Oocyte morphology/structure
- Function of each structure

#### 4.3 The oocyte: markers of competence

- Nuclear maturity
- Cytoplasm
- Polar bodies
- Zona pellucida
- Cumulus cells

#### 4.4 Clinical workout

- Evaluation of (in)fertility: aetiology, medical/physical aspects, genetic diagnosis, hormonal evaluation, treatment options, etc.
- Definitions, primary infertility, secondary infertility
- Serological screening for patients and/or donors
- Effects of treatment
- Oocyte donation

#### 4.5 Ovarian hyperstimulation

- Basic principles
- Types of medication
- Stimulation regimes (types, rationales)
- Complications of treatment

### **5. Male Reproduction**

#### 5.1 Anatomy and function of the male reproductive system

- Role of accessory systems
- Function of the organs

#### 5.2 Spermatogenesis

- Regulating factors
- Hypothalamus, pituitary, gonad axis
- Endocrine regulation
- Leydig & Sertoli cells
- Differentiation and maturation
- Biochemistry and metabolism of the sperm cell
- Sperm morphology/structure
- Function of each structure

#### 5.3 Diagnosis of male infertility

- Semen analysis (functional analysis, microscopic analysis)
- WHO & ESHRE guidelines
- CASA systems

#### 5.4 Clinical workout

Evaluation of (in)fertility: aetiology, medical aspects, genetic diagnosis, hormonal evaluation, physical aspects, treatment options, etc.

Definitions, primary/secondary infertility

Serological screening for patients and/or donors

Sperm donation

### 6. ART Laboratory Procedures

#### 6.1 Strategies for choosing fertilization procedures

IUI, IVF or ICSI, criteria

IVM

PESA, TESA, TESE

Donor sperm in relation to serological tests (different handling and storage)

#### 6.2 The sperm sample: preparation methods

Gradient centrifugation, swim-up, swim-out, etc

Advanced diagnostic tests (evaluation of DNA damage, chromatin condensation, etc)

When to use what, why, differences

#### 6.3 ART techniques

Practicalities for IUI, IVF and ICSI (timing, preparation procedures, materials, etc)

Pick-up, oocyte handling

IVF insemination

Denudation prior to ICSI

ICSI procedure

#### 6.4 Embryo scoring, Day 1 - 6

PN scoring

Morphology criteria

Kinetics, genetics, physiology (e.g. amino acids, oxygen metabolism)

Time-lapse

Destination of embryos: selection criteria for transfer, cryopreservation, biopsy, etc

#### 6.5 Embryo transfer

Identity check

Selection and criteria for number of embryos to be transferred

Catheter loading and transfer procedure

Assisted hatching: pros-cons, evidence

#### 6.6 PGT

Timing of biopsy

Tubing techniques

Zona opening (pros and cons)

Different biopsy types, number of cells to evaluate

Techniques used for evaluation of the cells biopsied

Results and recommendations upon transferring embryos after PGT

## 6.7 Culture conditions

- Media
- Type of culture systems
- Requirements for consumables
- Physiochemical parameters (temperature, pH, osmolality)
- Stage specific requirements

## 6.8 Non-routine methods:

- Examples of non-routine methods, e.g. in vitro maturation, polar body evaluation, assisted hatching, etc

## **7. Cryopreservation**

### 7.1 Principles of cryopreservation

- Basic cryobiology
- Cryoprotectants, additives
- Slow freezing
- Vitrification
- Advantages/disadvantages with different methods
- Fertility preservation in oncology cases

### 7.2 Cryopreservation of sperm

- Theory and practice

### 7.3 Cryopreservation of oocytes

- Theory and practice

### 7.4 Cryopreservation of embryos

- Theory and practice

### 7.5 Cryopreservation of ovarian tissue

- Theory and practice

### 7.6 Cryopreservation of testicular tissue

- Theory and practice

### 7.7 Equipment

- Machines
- Straws/ampoules
- Contamination risk from storage medium
- Minimal safety requirements
- Security

### 7.8 The cryopreservation-thawed/warmed embryo treatment cycle

- Monitoring and timing of the thawing/warming cycle
- Controlled and natural cycles

## **8. Laboratory and Quality Management**

### **8.1 Patient data**

- Identity check
- Confidentiality
- Keeping records
- Safety, storage of data
- Single European Code

### **8.2 Type and treatment choices**

- Surgical
- Hormone stimulation
- Insemination IVF / ICSI
- Use of fresh or frozen gametes
- Gamete and embryo donation

### **8.3 Treatment outcome**

- The health of the children
- Risk factors
- Maternal factors
- Paternal factors
- Multiple pregnancies
- Chromosomal factors
- Malformations
- Imprinting

### **8.4 Quality assurance**

- Identification procedures
- Laboratory and clinical KPIs
- Standard operating procedures
- Traceability of samples/material
- Validation procedures
- Risk analysis
- Logbooks
- Introducing new methods

### **8.5 Equipment and facilities**

- Calibrations
- Validation, monitoring, logbooks, maintenance and control
- Microscopes
- Principals of optical system, calibrations, maintenance and control
- Technical requirements in a ART lab facility

### **8.6 Statistical analysis**

- Sample size evaluation
- Study design
- Statistical variance
- Interpretation of results

## 8.7 Legislation

- ESHRE guidelines
- Ethical considerations
- Code of practice
- European rules and regulations related to ART practice
- EU Tissue and Cells Directives (EUTCDs)

## 8.8 Reducing risks/ dealing adverse events/ troubleshooting

- Contaminated samples
- Processing and storage of contaminated samples with contagious agents
- Personal protective equipment (PPE)
- Hygiene and disinfectants used at ART lab
- Protective measures (alarm, sensors, etc)
- Actions upon injury
- Risk of mix-up of gametes, loss or damage during handling
- Transfer of wrong embryos
- Breakdown of equipment, back-up strategies