

**American University of Beirut Medical Center  
Fellowship Program Curriculum**

**Program Information**

Program: Clinical Fellowship in Reproductive Endocrinology and Infertility

Program Director: Johnny Awwad, M.D.

Department: Obstetrics and Gynecology

Division: Reproductive Endocrinology and Infertility

**Eligibility Criteria**

Qualified candidates must have completed a four-year residency training program in Obstetrics and Gynecology in an accredited medical school-affiliated academic clinical department listed in the International Medical Education Directory (IMED).

**Overview of Program**

The Fellowship Program is comprised of faculty from the Division of Reproductive Endocrinology and Infertility (REI) in the Department of Obstetrics and Gynecology at AUBMC. The mission of the Division of REI is to enhance the quality of care for infertile couples in Lebanon and the Middle East. To do so, it aims to provide postgraduate training fellows with a rich learning experience in the clinical and surgical management of fertility and endocrine disorders, nurturing in them the sense of advocacy and leadership. The program also aims at promoting basic and clinical research in reproductive medicine with the aim of advancing science and maintaining high standards of training to students, residents and fellows, and cutting-edge treatment to couples with infertility.

The two-year fellowship training program is structured to capitalize on the particular strengths and resources of the American University of Beirut. Infertility services and operative care are provided by the clinical services of the Women's Health Center in the Department of Obstetrics and Gynecology. Experience in the Assisted Reproductive Technologies (ART) is provided by rotation in the newly renovated, state-of-the-art AUBMC Fertility Center. Fellows also obtain medical endocrine, pediatric endocrine, and genetic clinical training through rotation on the active inpatient services of the Division of Endocrinology and Medical Genetics. In addition, outstanding formal research training is available through the Scholar in Health Research Program (SHARP). The program offers didactic courses and hands-on training in the essential disciplines to conduct quantitative research. The fellowship program is also intended to achieve synergistic interaction between the clinical services of the Medical Center and the molecular core laboratory of the Medical School, and to provide fellows with an experience and resources seldom found in the region.

## **Structure of the Clinical Training**

### **First Year Fellowship**

The first year fellow is primarily responsible for the initiation of a research project relating to the chosen thesis. It is expected that the fellow will devote 80% of time to the completion of a thesis project that will be published in a peer-reviewed journal by the end of the second year. The program is structured to allow the fellow to focus research effort (9 months of protected time) on a particular problem in order to achieve a depth of understanding which will serve as a foundation for a future independent research program. Fellows are required to take one formal graduate level research training course during this first year which has been arranged through the fully accredited sponsoring Medical School at Harvard University. This course will be managed by the Scholar in Health Research Program to train fellows on developing skills in study design, statistics, grant applications, and manuscript writing. It will be taken for a letter grade with an exam on which the fellows are expected to perform well.

Other than week-end calls, the clinical responsibilities of the first year fellow are an eight-week rotation on adult and pediatric endocrine services at AUBMC. During this experience, the fellow will be primarily responsible (under direct supervision of adult and pediatric endocrine faculty) for the evaluation and treatment of common endocrine disorders such as hyper- and hypothyroidism, premature thelarche, diabetes mellitus, growth disorders, and complications of menopause. It is this experience which permits the reproductive endocrine fellow to collaborate with faculty from other disciplines on the most challenging of endocrine cases and to deepen the fellow's understanding of evaluation of complex endocrine disorders. Following that experience, fellows rotate for four weeks in the ART laboratories at the AUBMC Fertility Center. This laboratory rotation provides the fellow with introduction to the methods used in assisted reproduction and in vitro handling and assessment of gametes and embryos. It is followed by a four-week rotation in genetics at the Division of Medical Genetics in the same institution. The genetics rotation includes training on the most recent tools for genetic research, as well as fundamental principles of genetics of relevance to REI.

### **Second Year Fellowship**

Second year fellows will complete 12 months of clinical training during the first year. In a typical rotation sequence, the fellow begins shadowing REI faculty in their clinics at the Women's Health Center. The fellow is instructed in the current evaluation and treatment of common reproductive endocrine/infertility disorders such as anovulation, hirsutism, pituitary dysfunction, amenorrhea, recurrent pregnancy loss, contraception, and pubertal disorders. While on rotation in the clinical reproductive service at the AUBMC Fertility Center, the second-year fellow is primarily responsible for the clinical management (with close supervision) of patients undergoing ovarian stimulation and assisted reproductive technologies. This is a busy clinical service with approximately 1500 cycles annually. The fellow is directly involved in all facets of assisted reproduction, including patient selection, counseling, ultrasound ovarian monitoring, hormonal measurement interpretation, intrauterine inseminations, ovum retrievals, and embryo transfers.

The fellow will also start staffing the resident's infertility clinics at both the in-campus and out-campus program facilities, developing self-directive autonomy under the indirect supervision of REI faculty members. During this exposure, the senior fellow assumes an "acting attending" level of responsibility for the execution of an ART cycle. The fellow is expected to be familiar with all aspects of patient selection, ovarian stimulation, ovum retrieval, and gamete/embryo transfer. The fellow will answer questions and deal with problems and dilemmas faced in the conduct of an ART program. During this experience the faculty will closely observe the fellow, but the emphasis will be on permitting the fellow to make decisions and function at an attending level. This experience represents the final step in a graduated level of responsibility, and will also assure that program graduates are up-to-date with the most recent advances in the changing field of assisted reproduction. The fellow participates as "primary surgeon" on all operative cases of the service under supervision and guidance of program faculty. The first year fellow receives operative training in current methods of surgical treatment of infertility including minimally invasive surgery (laparoscopy & hysteroscopy) and robotics. To provide additional depth to their clinical training, fellows will rotate for two weeks on the Male Infertility service in the Division of Urology.

### **Didactic Learning**

There are many learning opportunities, both formal and informal during the fellowship. Structured training includes a series of introductory seminars geared to the first year fellow that take place from August till May of the first year. These introductory seminars provide a basic understanding of the practice of REI. There is also a bi-monthly teaching rounds conference where challenging cases are reviewed and discussed with faculty and fellows. Regular attendance at a monthly Journal club is expected, during which recent updates in REI are critically appraised. Fellows are also expected to attend the weekly laboratory/nursing performance evaluation meetings. They should be present to departmental Grand Rounds and Morbidity & Mortality conferences.

Formal didactic lectures should cover the following topics over two years of training:

1. Neuroendocrinology of Reproduction
2. Gonadotropin Hormones and Receptors
3. Prolactin
4. Steroid hormones and actions
5. Menstrual cycle
6. Ovarian life cycle
7. Male Reproduction
8. Reproductive Immunology
9. Menopause
10. Male aging
11. Sex development
12. Puberty
13. PCOS
14. Female infertility
15. Male infertility

16. Endocrine disturbances
17. Endometriosis
18. Benign uterine disorders
19. Endocrine disorders of pregnancy
20. Breast cancer
21. Ovarian stimulation
22. ART
23. Gamete manipulation
24. Genetics of reproduction
25. Hormonal status
26. Pelvic imaging
27. Contraception

### **Practical Learning**

During their training, fellows are expected to achieve full competence in many aspects of assisted reproductive technologies. By the end of their fellowship, they are expected to submit a log book showing a minimum number of procedures performed independently under supervision to claim competency:

- Ovarian stimulation using gonadotropins: 50 procedures
- Ovum retrieval: 50 procedures
- Embryo transfer: 25 procedures
- Intrauterine insemination: 35 procedures

Fellows are expected to attend the minimally invasive workshops organized by the Division of REI to improve dexterity in laparoscopy, hysteroscopy, and Da Vinci robot-assisted surgery. Fellows should be able to:

- Perform trocar port entry, safe use of energy sources, intra-corporeal suturing/tying, and manage complications during laparoscopic procedures.
- Perform fluid management during hysteroscopy.
- Pass successfully the virtual training sessions on the Da Vinci robot consol.

### **Case List**

#### **Content**

#### **Reproductive Endocrinology Cases**

A list of 15 REI patients managed during the fellowship training years during the rotations in the Faculty and Residents Clinics must be prepared in the proper format. Individual patients who presented with any of the following problems may be listed (at least one, and no more than 2 patients in each category).

1. Contraception
2. Genetic counseling
3. Primary and secondary amenorrhea
4. PCOS, hirsutism and hyperandrogenism
5. Hyperprolactinemia
6. Endometriosis

7. Menopause/premature ovarian failure
8. Diabetes mellitus
9. Thyroid disorders
10. Adrenal Disease
11. Hypothalamic and Pituitary disorders
12. Fertility Preservation
13. Pediatric Endocrinology: abnormal differentiation and pubertal development

### **Reproductive Surgery**

A list of 10 reproductive surgical patients managed during the fellowship training years should be prepared in the proper format. Individual patients who presented with any of the following problems should be listed. (At least one and no more than 2 patients in each category).

1. Operative laparoscopy
2. Operative hysteroscopy
3. Uterine myomas
4. Asherman's syndrome
5. Endometriosis
6. Tubal reversal/tuboplasty
7. Ectopic pregnancy
8. Congenital anomaly of the reproductive tract

### **Infertility/IVF**

A list of 15 infertility/IVF patients managed during the fellowship training years during the rotations in the AUBMC Fertility Center must be prepared in the proper format (at least 3 patients in each category).

1. Female infertility
2. Male infertility
3. Recurrent pregnancy loss
4. Recurrent implantation loss

### **Case List Instructions**

The case list must include the category headings within the list above. The font size may not be smaller than 12 point. The case collection period extends throughout the two fellowship training years, at the end of which it should be submitted to the division head prior to graduation. The patient case list must be de-identified in accordance with the requirements of the Final Privacy Rule, issued by the US Department of Health and Human Services under the Health Insurance Portability and Accounting Act of 1996 (HIPAA).

### **Thesis**

A thesis is required by the Division of REI. The thesis must be published or accepted for publication before graduation. The format of the thesis must comply with the instructions for authors for *Fertility and Sterility*. The manuscript may not exceed 30 pages in length, and the pages must be numbered. The thesis must be type-written in 12 point type, single-spaced, and double-sided on standard 8 1/2 x 11 paper. The thesis must be a scholarly effort that often

should include the following sections: *Abstract, Introduction, Methodology, Statistics, Discussion, Summary, and References*. Unacceptable manuscript types include: *book chapters, case reports, reviews, and survey report*.

### **Call and Duty Hours**

Fellows perform no in-house calls during their two training years. They will average two weekend calls per month, which involve ART patient care namely sonographies and retrievals at the Fertility Center and management of complications in the main hospital. These calls are usually not in-house and are typically completed by the 2 PM on the call day. The program rigorously adheres to all ACGME-I and ABOG duty hour regulations.

### **Major Clinical and Research Interests of the Faculty**

#### **Reproductive Endocrinology and Infertility**

- Johnny Awwad, M.D. – Endometrial receptivity and implantation failure
- Antoine Hannoun, M.D. – Means of improving embryo quality
- Antoine Abu Musa, M.D. – Diagnosis and management of endometriosis
- Ghina Ghazeeri, M.D. – Characterization and management of Polycystic Ovary Syndrome

#### **Medical Endocrinology**

- Ghada Hajj Fuleihan, M.D. – Vitamin D and reproduction
- Mona Nasrallah, M.D.

#### **Pediatric Endocrinology**

- Asma Arabi, M.D.

#### **Medical Genetics**

- Chantal Farra, M.D. – Genetic markers of male and female infertility

#### **Embryologist**

- Fadi Choucair, M.D. – The effects of oxidative stress on human gametes

### **Application Information**

Qualified candidates must have completed a four-year residency program in Obstetrics and Gynecology in an accredited medical school-affiliated academic clinical department listed in the International Medical Education Directory (IMED). One position is available for each year for a total of two.

Applications are accepted 9 months before the anticipated start date and interviews are typically held approximately 6 months before the start date. Applications should be submitted online on the Graduate Medical Education (GME) website from mid-November to mid-December. Applicants from programs outside the United States and Canada are required to sit for an *English proficiency examination* that includes either TOEFL (minimum score of 573, 230, or 88 on PBT, CBT, or IBT respectively) or IELTS (minimum score of 7.0). They are also required to sit for a *General Departmental Exam* offered by GME that reflects their residency knowledge.

In addition to the materials required by the GME office, interested candidates must submit a personal statement, recent curriculum vita, three letters of reference, and medical school transcripts. Upon receipt of these materials, the applicant will be notified regarding an interview.

Questions regarding the application and status of applications may be addressed to:

**Graduate Medical Education Office**

Medical Dean's Office  
American University of Beirut  
P.O. Box: 11-0236  
Riad El Solh, Beirut 1107 2020  
Beirut – Lebanon

**Location**

Saab Medical Library Building, 1st floor, Maamari Street, Hamra, Beirut, Lebanon

**Telephone:** 00961-1-350000 ext: 4706

**Fax:** 00961-1-744489

**Email:** [gme@aub.edu.lb](mailto:gme@aub.edu.lb)

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### Fellowship Curriculum Details

Typical Monthly Block Diagram		
	Year 1 - Research	Year 2 - Clinical
<b>July</b>	Research and statistics didactic course (SHARP)	Reproductive Endocrinology and Infertility
<b>August</b>	Basic and clinical research	ART Laboratory Andrology and Male Infertility
<b>September</b>	Basic and clinical research	Pediatric Endocrinology Reproductive Endocrinology and Infertility
<b>October</b>	Basic and clinical research	Medical Endocrinology Reproductive Endocrinology and Infertility
<b>November</b>	Basic and clinical research	Medical Genetics Reproductive Endocrinology and Infertility
<b>December</b>	Basic and clinical research	ART Laboratory Reproductive Endocrinology and Infertility
<b>January</b>	Basic and clinical research	Reproductive Endocrinology and Infertility
<b>February</b>	Basic and clinical research	Reproductive Endocrinology and Infertility
<b>March</b>	Basic and clinical research	Reproductive Endocrinology and Infertility
<b>April</b>	Basic and clinical research	Reproductive Endocrinology and Infertility
<b>May</b>	Basic and clinical research	Reproductive Endocrinology and Infertility
<b>June</b>	Vacation	Vacation

<b>Typical Weekly Block Diagram</b>		
	<b>Year 1 – Research</b>	<b>Year 2 - Clinical</b>
<b>Monday</b>	Assisted Reproductive Techniques (Fertility Center 7W)	Assisted Reproductive Techniques (Fertility Center 7W)
	Resident Reproductive Clinics (OPD 6W)	Resident Reproductive Clinics (OPD 6W)
	Curriculum/Research	Assisted Reproductive Techniques (Fertility Center 7W)
	Research Meeting Division Meeting (Library 8W)	Research Meeting Division Meeting (Library 8W)
<b>Tuesday</b>	Curriculum/Research	Assisted Reproductive Techniques (Fertility Center 7W)
	Curriculum/Research	Faculty Reproductive Clinics (WHC 7W)
<b>Wednesday</b>	Department Rounds (Library 8W)	Department Rounds (Library 8W)
	Curriculum/Research	Faculty Reproductive Clinics (WHC 7W)
<b>Thursday</b>	Assisted Reproductive Techniques (Fertility Center 7W)	Assisted Reproductive Techniques (Fertility Center 7W)
	Resident Reproductive Clinics (OPD 6W)	Resident Reproductive Clinics (OPD 6W)
	Curriculum/Research	Faculty Reproductive Clinics (WHC 7W)
<b>Friday</b>	Division Meeting (Fertility Center 7W)	Division Meeting (Fertility Center 7W)
	Curriculum/Research	Reproductive Surgery (OR 7W)
	Curriculum/Research	Off-Campus Reproductive Clinics (BGUH)
<b>Saturday</b>	Scheduled Week-end Call	Scheduled Week-end Call
<b>Sunday</b>	Scheduled Week-end Call	Scheduled Week-end Call

**Statistics and Research Design Rotation**

**Final objectives:** Research design and use of biostatistical tools.

**Enabling objectives:** The fellow should be able to:

1. Differentiate population parameters and sample statistics.
2. Compute and interpret measures of comparisons of means and variations.
3. Analyze a presented experiment and construct a hypothetical experiment with respect to the: question examined, hypothesis, sampling technique, concept, and calculation of statistical power, expression and correlation of raw data, significance of the results, conclusions, and appropriate inferences which can be obtained from the data.
4. Apply the following statistical tests: t-test, paired and independent, chi-square, life table analysis and other related statistical methods (e.g. Pearl's index, person-year exposure, etc.), correlation analysis, and regression analysis.
5. Define the terms "coefficient of variation", "significance", "confidence interval", "Type I error", and "Type II error".
6. Use logarithmic and logit transformations.
7. Use the least squares regression line and calculate unknowns from standards in radioimmunoassay.
8. Describe the methods of performing and limitations of prospective, cohort, and retrospective case control studies.
9. Use one-way and two-way analysis of variance.
10. Define the indications and use of Non-Parametric versus Parametric Tests.
11. Describe the clinical assessment of a test to include sensitivity, specificity, positive, and negative predictive values, and relationship to prevalence.
12. Understand the principles and pitfalls of meta-analysis.

**Medical Genetics Rotation**

**Final Objectives:** Interpretation of pedigree data and care for patients with inherited and sporadic genetic disorders affecting the male and female reproductive systems as well as general well being.

**Enabling Objectives:** The fellow should be able to apply genetic concepts and techniques to diagnostic problems in REI and be familiar with:

1. Normal genetics, gene structure and regulation, chromosomal structure and standard cytogenetic nomenclature, and DNA diagnosis referable to REI.
2. Techniques of chromosomal analysis, DNA-RNA detection (Southern and Northern blotting, microarray analysis, etc.), gene amplification (PCR, etc.), and other assays (FISH, etc.).
3. Abnormal genetics, including gametogenic errors, cytogenetic abnormalities (Gonadal dysgenesis, Klinefelter syndrome, etc.), and molecular germ line and somatic cell mutations associated with reproductive disorders (Gonadal dysgenesis, congenital adrenal hyperplasia, Kallmann syndrome, Y chromosome microdeletion, CFTR mutations, Fragile X, etc.).

4. Recurrent implantation failure and the roles of meiotic errors, cytogenetic abnormalities, and embryonic lethal mutations.
5. Routine pre-conceptional screening for genetic disorders in couples with reproductive problems prior to gamete donation.
6. Role of preimplantation genetic diagnosis for single gene disorders, translocations, and aneuploidy.
7. The technique of comparative genomic hybridization (CGH) and its scope and limitations.
8. Ethical concerns surrounding sex selection and pre-implantation screening.

## **Medical Endocrinology Rotation**

### **Thyroid function and disease**

**Final Objectives:** Management of thyroid disorders.

**Enabling objectives:** The fellow should be able to understand and discuss:

1. The roles of TRH and TSH in regulation of thyroid physiology
2. The scope, diagnostic value, and limitations of laboratory testing for thyroid function (TSH, T4, T3 uptake, T3 RIA, TBG, free T4, reverse T3, and anti-thyroid antibodies).
3. The clinical and pathophysiological correlation of hypo- and hyperthyroidism, particularly as related to menstrual disorders, infertility, and pregnancy.
4. Pregnancy and hormone induced changes of thyroid function on the mother and fetus.
5. The effects of thyroid replacement and anti-thyroid drug therapy on the fetus.
6. The pathophysiology of thyroid autoimmune disorders.
7. Thyroid role in gynecological disorders, such as struma ovarii, molar pregnancy, and choriocarcinoma.
8. The management of hyperthyroidism, hypothyroidism, and thyroid nodules.

### **Adrenal function and disease**

**Final objectives:** Management of adrenal disorders.

**Enabling objectives:** The fellow should be able to understand and discuss:

1. Regulation and secretion of adrenocortical hormones, including circadian rhythms and the effects of stress and aging.
2. Clinical and laboratory assessment of adrenocortical function.
3. Adrenocortical hypo and hyperactivity (Cushing syndrome, adenoma, carcinoma, etc.).
4. Genetics and biochemistry of specific steroid pathway defects in congenital adrenal hyperplasia, adrenal deficiencies, and their effect on fetal and postnatal development.
5. The effects and metabolism of exogenous adrenal androgens.
6. Adrenal crisis, adrenal suppression from corticosteroid replacement, congenital adrenal hyperplasia, androgen secreting adenoma.

### **Androgen disorders**

**Final objectives:** Management of androgen disorders.

**Enabling objectives:** The fellow should be able to:

1. Define secretion, physiology, metabolism, and measurement of androgens in normal women.

2. Describe the symptoms and signs of androgen excess.
3. Describe the mechanism of androgen action, including 5 alpha reductase deficiency.
4. Discuss the physiology of normal and abnormal hair growth; and differentiate hirsutism from defeminization, virilization, and hypertrichosis.
5. Relate polycystic ovary syndrome to abnormal androgen secretion and hirsutism.
6. Discuss relationships between androgen disorders and hyperinsulinemia, including mechanisms of insulin action on theca cell androgen production.
7. Indicate the role of hormone assays in evaluating hyperandrogenism.
8. Describe the treatment of androgen excess.
9. Describe mechanisms of androgen production and their control in the male, particularly as it relates to spermatogenesis and sexual behavior.

### **Neuroendocrine physiology and diseases**

**Final objectives:** Management of neuroendocrinological disorders.

**Enabling objectives:** The fellow should be able to understand and discuss:

1. Anatomical-functional relationships of the hypothalamus and pituitary.
2. Embryonic derivation and migration of GnRH neurons.
3. Supra-hypothalamic structures and neuronal systems relevant to regulation of reproductive processes.
4. Regulatory secretory activities of the pituitary hormones, including biorhythmicity and feedback.
5. Site of production, biological action, and control of secretion of oxytocin, vasopressin, and neurophysins.
6. Distribution and cellular characteristics of pituitary hormone producing cells with special reference to gonadotrope, somatotrope, and lactotrope.
7. Function of pituitary reproductive hormones and neuropeptides (GnRH, TRH, somatostatin, pro-opiomelanocortin family, GHRH, CRH, vasopressin, etc.).
8. Biochemical basis of neuropharmacology of GnRH agonists and antagonists.
9. Neuroendocrine regulation of the menstrual cycle.
10. Neuroendocrine function of the fetal-placental unit.
11. Organic lesion and/or functional disorders of the hypothalamic-pituitary system.
12. Deficiencies of the hypothalamic-pituitary system (panhypopituitarism, Sheehan syndrome, Kallmann syndrome, etc.).
13. Genetic variants related to neuroendocrine diseases.

### **Pediatric Endocrinology Rotation**

#### **Puberty**

**Final objectives:** Management of abnormalities in growth and development, and puberty.

**Enabling objectives:** The fellow should be able to understand and discuss the:

1. Normal sequence and timing of pubertal changes in the female and male, including Tanner stages.
2. Effects of gonadal and adrenal hormones on sexual development, somatic growth, and epiphyseal closure.

3. Molecular causes of hypogonadotropic/hypogonadism and the role these genes play in normal pubertal development.
4. Sexual precocity syndromes, including the pathophysiology, differential diagnosis, evaluation, and management.
5. Delayed puberty syndromes, including investigation and management.
6. Growth problems in adolescents, including investigation and management.

### **Andrology and Male Infertility Rotation**

**Final objectives:** Management of male infertility and subfertility.

**Enabling objectives:** The fellow should be able to:

1. Take an appropriate history relevant to male infertility.
2. Evaluate an infertile male.
3. Understand and discuss spermatogenesis, including endocrinologic control, mechanisms, and abnormalities.
4. Describe the content of seminal fluid, the physiology and pathophysiology of ejaculation, abnormalities of sperm transport, including ductal obstruction and retrograde ejaculation.
5. Know medical and surgical therapies of male infertility, including microscopic procedures to facilitate fertilization (ICSI, epididymal aspiration and testicular sperm extraction).
6. Describe the biosynthesis of steroids and regulatory control of the human testis and the biological action of testosterone of men.
7. Enumerate environmental factors that may affect the endocrine and exocrine function of the testis.
8. Investigate and manage male hypogonadism.
9. Discuss normal male sexuality throughout the life cycle.
10. Know the possible role of varicocele in male infertility.
11. Discuss genetic testing in male infertility.
12. Discuss paternal age and pregnancy outcomes.
13. Be familiar with indications and regulatory issues involving sperm donation.

### **Reproductive Endocrinology and Infertility Rotation**

#### **Mechanisms of hormone action**

**Terminal objectives:** Familiarity with the mechanisms of hormone effects at cellular and molecular levels and be able to apply these principles to reproductive physiology and disorders of reproduction.

**Enabling objectives:** The fellow should be able to understand and describe the:

1. Mechanism of action for releasing hormones, tropic hormones, steroid hormones and neural peptides.
2. Significance of hormone action, including heterogeneity of hormones, post-translational modification, desensitization, receptor replenishment, internalization, and second messengers.
3. Nature of receptor assays and their usefulness.
4. Steroid receptor defects, orphan receptors, and their effect on hormone action.

5. Molecular control of hormone and hormone receptor synthesis.

### **Clinical pharmacology of hormones**

**Terminal objectives:** Management of patients receiving clinical pharmacology for the treatment of their reproductive disorders.

**Enabling objectives:** The fellow should be able to:

1. Define absorption, excretion, distribution, biotransformation, and bioavailability of drugs and hormones in reproduction.
2. Discuss mechanisms of drug and hormone action, including structure activity relationships, receptors, and sites of action, receptor heterogeneity, and post-receptor molecular events.
3. Discuss the production, availability, and advantages of recombinant glycoprotein hormones.
4. Discuss tissue specific responses to hormones, hormone analogues, and selective receptor modulators. Understand the molecular events involving hormonal interaction with receptors, DNA, and other transcription factors.

### **Pathology**

**Terminal objectives:** Knowledge of gross anatomy, microscopic histology, and immunohistochemical techniques as they relate reproductive endocrine pathology.

**Enabling objectives:** The fellow should be able to describe:

1. Vagina: Gross and microscopic findings of adenosis, consequences of antenatal hormone exposure, hormone action on the vagina.
2. Cervix: Mechanisms of action and effects of hormones, consequences of antenatal hormone exposure.
3. Endometrium: Histology of normal and abnormal endometrium, effects of estrogen and progestins, endometrial hyperplasia, adenocarcinoma, developmental stages (dating), responses to pharmacologic agents, histology of trophoblast/implantation.
4. Myometrium: Gross and microscopic findings of adenomyosis and leiomyomata, and relationship of leiomyomata to infertility.
5. Oviduct: Gross and microscopic findings of salpingitis and endometriosis, clinical course of salpingitis as a cause of infertility.
6. Ovary: Gross and microscopic findings and the natural history of functional and neoplastic ovarian tumors: follicular cysts, luteoma, corpus luteum, endometrioma, granulosa-theca cell tumor, Sertoli-Leydig cell tumor, gynandroblastoma, cystic teratoma, dysgerminoma, gonadoblastoma, and mixed germ cell tumors; individual compartments of the Graafian follicle, primordial, preantral and antral follicles; histology of the polycystic ovary, of gonadal dysgenesis.
7. Hypothalamus-CNS axis: Anatomy and functional relationships of hypothalamic centers involved in reproductive endocrine functions.
8. Pituitary: Cellular morphology of normal and neoplastic cells of the adenohypophysis, anatomy and function of the neurohypophysis.
9. Testis: Stages of normal and abnormal spermatogenesis, gross and microscopic findings in the normal testis, accessory sex organs, and testicular disease.

## Immunology

**Final objectives:** Management of patients with infertility and endocrinologic diseases of immunologic origin.

**Enabling objectives:** The fellow should be able to understand and describe the:

1. Essentials of basic immunology, including mechanisms of antibody production; origin, types, and function of the immunoglobulins; mechanisms of cell mediated immunity; definition of autoimmune diseases; diagnostic testing for autoimmune diseases; function of cytokines; basic components of the immune system and their possible role in male and female reproductive failure, recurrent abortion, infertility, and contraception; production, characterization, and application of polyclonal and monoclonal antibodies with respect to reproductive disorders.
2. Pathophysiology of autoimmune disease as it relates to gonadal failure and other endocrine dysfunction.

## Embryology

**Terminal objectives:** Diagnosis and management of congenital abnormalities of the reproductive tract.

**Enabling objectives:** The fellow should be able to understand and describe the:

1. Processes of oocyte and sperm maturation, mechanism of fertilization, including a description of morphological stages of oocyte maturation.
2. Embryonic development and anatomy of the genital tract.
3. Mechanisms for developmental aberrations of the reproductive tracts, such as müllerian and gonadal abnormalities, vaginal agenesis, vaginal septum, and imperforate hymen; and corrective surgical procedures.
4. Embryology of the hypothalamic-pituitary system, thyroid gland, and adrenal gland.
5. Human embryonic stem cell technology and applications

## Clinical Diagnostic Techniques

**Final objectives:** Comprehensive medical history, and physical examination in couples with reproductive disorders. Interpretation of diagnostic techniques

**Enabling objectives:** The fellow should be able to describe, perform, and interpret results of the following diagnostic techniques:

1. Biopsies of the endometrium, laparoscopy, hysteroscopy, and laparotomy findings.
2. Radiographic and imaging, including hysterosalpingography, sonohysterography, ultrasonography, computerized tomography, magnetic resonance imaging, arterial and venous catheterization, radioisotope scanning techniques, bone densitometry, and establishment of bone age.
3. Endocrinological hormone measurements for evaluation of the hypothalamus, pituitary, parathyroid, thyroid, adrenal, and gonadal systems, including dynamic endocrinologic testing.
4. Genetic, including preconception genetic screening and screening for known genetic disorders related to REI.

### **Ovarian Function and Disease**

**Final objectives:** Knowledge of ovarian physiologic and management of related diseases.

**Enabling objectives:** The fellow should be able to understand and discuss:

1. Hypothalamic-pituitary control of ovarian function, ovarian feedback mechanisms regulating hypothalamic and pituitary function.
2. Acquisition of oocyte developmental competence, including role of follicular hormones and events leading to the development of a normal primary oocyte, germinal vesicle breakdown, and completion of meiosis I and II.
3. Synthesis and secretion of steroid and peptide hormones by the various compartments and cell types of the ovary.
4. Atresia, recruitment, and selection of the dominant follicle and oocyte maturation.
5. Luteolysis.
6. Age-related changes in ovarian structure, function, and regulation.
7. Clinical, genetic, and pathophysiologic correlates of disorders of the human ovary.
8. Autocrine and paracrine effects of cytokines and growth factors on ovarian function.
9. Physiology and pathophysiology of primary or secondary hypogonadism, perimenopause and menopause.
10. Rationale for the use or non-use of estrogens, progestins, and other hormone therapies.
11. Pathophysiology and treatment approaches involving insulin resistance and polycystic ovary syndrome

### **Abnormal Uterine Bleeding**

**Final objectives:** Management of abnormal uterine bleeding.

**Enabling objectives:** The fellow should be able to:

1. Describe the normal menstrual cycle, changes in circulating gonadotropins, and steroid hormones. Relate hormone levels to the endometrial effects.
2. Define the new terminology to describe abnormal uterine bleeding.
3. Discuss anovulation, the resultant hormonal changes, and effects on the endometrium.
4. Discuss the molecular effects of steroids in relation to endometrial changes.
5. Discuss limits of normal menstrual blood loss, and methods of estimating blood loss, including the role of prostaglandins in the menstrual cycle and the physiology of the cessation of menstrual bleeding.
6. Describe the medical treatments for abnormal bleeding, including the pharmacology and rationale for drugs used in its treatment.
7. Discuss the indications and limitations of the techniques for surgical evaluation and management.

### **Amenorrhea**

**Final objectives:** Management of amenorrhea.

**Enabling objectives:** The fellow should be able to understand and discuss the:

1. Pathophysiology of amenorrhea as it relates to end-organ structure and function, the secretion of steroid hormones and gonadotropins, and the function of related endocrine systems.

2. Abnormalities of the hypothalamic control of pituitary function that result in amenorrhea, including pharmacological effects.
3. Growth and developmental aspects of amenorrhea as they relate to puberty and the menarche.
4. Clinical manifestations, causes, and pathophysiology of diseases associated with amenorrhea (gonadal dysgenesis, Sheehan syndrome, polycystic ovary syndrome, hypopituitarism, Kallmann syndrome, acromegaly, etc.)
5. Physiology and pathophysiology of prolactin secretion and the diagnosis and management of patients with hyperprolactinemia.
6. Interpretation of imaging modalities and tests utilized in the evaluation of amenorrhea.

### **Female Infertility**

**Final objectives:** Evaluation and management of a woman for infertility.

**Enabling objectives:** The fellow should be able to:

1. Take an appropriate history and do a physical examination oriented to infertility.
2. Describe and apply in the overall management of the infertile couple, namely correct utilization and interpretation of basal body temperatures, plasma progesterone, and endometrial biopsy, diagnosis of anovulation, selection of ovulation induction utilizing clomiphene, aromatase inhibitors, human gonadotropins, and bromocriptine; appropriate monitoring of ovulation induction, including estrogen determinations, ultrasound, progesterone assays, and ovulation predictor kits; correct utilization and interpretation of studies of tubal function (hysterosalpingography and laparoscopy), indications and contraindications for tubal reparative procedures; correct utilization and interpretation of studies of the uterine cavity, such as hysterosalpinography, sonohysterography and hysteroscopy and indications and techniques for corrective procedures.
3. Knowledge of the medical management of endometriosis (pseudopregnancy, danazol, continuous progestin, androgen therapy, aromatase inhibitors and GnRH analogs); indications for surgery and rationale for pharmacologic adjuncts.
4. Artificial insemination including indications, contraindications, and complications.
5. Evaluation of male infertility and screening of sperm donors to exclude transmissible infection and genetic disorders; proper use of sperm cryobanking.
6. Adoption, including indications, knowledge of appropriate counseling methods; Familiarity with domestic and international adoption requirements, and legal implications.

### **Recurrent Pregnancy Loss**

**Final objectives:** Management of recurrent pregnancy wastage.

**Enabling objectives:** The fellow should be able to understand and discuss the:

1. Prognosis for patients who have more than two pregnancies.
2. Genetic causes and mechanisms of cytogenetic abnormalities in embryonic loss, including prevalence at different gestational ages.
3. Advantages and limitations of preimplantation genetic diagnosis (FISH and CGH) for abnormal parental karyotypes.

4. Contribution of müllerian and other anatomical anomalies, congenital or acquired, to recurrent pregnancy loss.
5. Contribution of endocrine factors, including hypothalamic, pituitary, thyroid, adrenal, and ovarian disorders, endometrial dysfunction, diabetes mellitus, and PCOS to recurrent pregnancy loss.
6. Contribution of immunologic factors, including lupus anticoagulant, anti-cardiolipin antibodies, and anti- $\beta$ 2-glycoprotein 1 antibody to recurrent pregnancy losses (antiphospholipid antibody syndromes).
7. Contribution of thrombophilias (deficiencies of antithrombin III, protein C and protein S and Factor V Leiden mutations) to recurrent pregnancy loss.

### **Surgical Techniques**

**Final objectives:** Understanding of indications, contraindications, complications of surgical procedures appropriate to REI.

**Enabling objectives:** The fellow should be able to

1. Understand, discuss, and perform fertility restoration, including laparoscopy and laparotomy techniques used to reverse sterilization; diagnostic and therapeutic techniques, including hysterosalpingography, sonohysterography, tubal canalization, and endoscopy (laparoscopy and hysteroscopy); infertility surgery, including all techniques used for reconstruction of uterine anomalies, myomectomies, resection of uterine synechiae, cervical cerclage, tuboplasty, resection of pelvic adhesions, ovarian cystectomies, staging, and treating endometriosis.
2. Correct developmental disorders, including all techniques used for neovaginal construction, correction of imperforate hymen, removal of vaginal and uterine septae, correction of müllerian abnormalities, and ambiguous genitalia.

### **Techniques for Assisted Reproduction**

**Final objectives:** Understanding of the principles of in vitro fertilization and embryo transfer.

**Enabling objectives:** The fellow should be able to describe and discuss the:

1. Facilities and personnel required for such a program.
2. Mechanisms controlling oocyte development and maturation.
3. Physiology and methodology for recruitment of preovulatory follicles and describe methods for *in vitro* maturation and monitoring of follicular development *in vivo*.
4. Methods for oocyte retrieval.
5. Techniques for in vitro fertilization.
6. Micromanipulation of gametes and embryos.
7. Technique(s) of embryo transfer.
8. Indications and techniques for preimplantation diagnosis.
9. Use of donor oocytes and embryos.
10. Impact of maternal age on the practice of ART.
11. Complications of ART (multifetal pregnancy, severe ovarian hyperstimulation syndrome, intra-abdominal and retroperitoneal hemorrhage, infection).
12. Techniques for cryopreservation of embryos.

### **Physiology and Endocrinology of the Climacteric**

**Final objectives:** Familiarity with the physiologic and pathological changes that occur in somatic, endocrine, and psychological function with age.

**Enabling objectives:** To accomplish this, the fellow should be able to understand and discuss the:

1. Stages of reproductive aging that precede and succeed the menopausal transition.
2. Changes in somatic (non-reproductive) aging in women and the techniques useful for measuring these changes with respect to the following endocrine and related systems: somatotrophic axis; metabolic axis of insulin, glucagon, and adipose tissue signaling; skeletal system; cardiovascular system, including lipids and lipoproteins, inflammatory markers, and vascular distensibility, and the process of atherosclerosis; hypothalamic-pituitary-adrenal axis; thyroid axis; cognition and affect; sexuality.
3. Changes in production of gonadotropins and sex steroids across the menopause transition and postmenopause.
4. Changes in estrogen metabolism with aging.
5. Advantages and disadvantages of hormonal substitution therapy in natural or surgical menopause: Impact of hormone therapy on symptoms, cardiovascular disease, thrombotic risk, breast cancer, urinary incontinence, cognitive function, quality of life, and cognition.
6. Different forms and routes of hormone therapy, the rationales for their use, and their indications and contraindications.

### **Contraception**

**Final objectives:** Familiarity with the principles and methods of contraception.

**Enabling objectives:** The fellow should be able to:

1. Describe the various steroids used in contraceptive formulations and relate their chemical structure to potency, effective route of administration, intermediary metabolism, metabolic clearance, side effects, cellular targets, and mechanisms of action.
2. Describe the advantages, disadvantages, and failure rates of the various contraceptive methods.
3. Discuss the recommended types of contraceptive for high-risk subjects with histories of breast or endometrial cancer, liver disease, thromboembolic episodes, migraine, sickle cell anemia, hypertension, coronary disease, and pelvic infections.
4. Discuss potential methods and advances in male contraception.