

**GUIDE TO LEARNING  
IN  
REPRODUCTIVE ENDOCRINOLOGY  
AND INFERTILITY**



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## I. INTRODUCTION

The *Guide to Learning in Reproductive Endocrinology and Infertility* (REI) has been developed by The American Board of Obstetrics and Gynecology, Inc. (ABOG) to assist both the fellow in training and the Program Director. The basic educational needs that lead to appropriate achievement are presented; however, this description should not be misinterpreted as outlining the ideal or setting limits on learning or achievement.

This *Guide* is comprised of educational objectives serves as:

1. The curriculum for an adequate fellowship training program, and
2. A study guide for the fellow during their fellowship and when sitting for the ABOG Subspecialty Certification Examinations.
  - a. This *Guide* is the content list for the examinations given by the ABOG Division of REI.

The Division regards the fellow as a graduate student with the implied responsibility for self-study and independent inquiry. The Program Director is responsible for providing adequate clinical experience, technical instruction, learning resources, study guidance, and periodic direct personal evaluation. The Program Director should review with the fellow an outline of study at least on an annual basis.

## II. DEFINITION OF A REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY SUBSPECIALIST

An REI subspecialist is an obstetrician/gynecologist who provides consultation and/or comprehensive care for women with complex problems related to REI. This activity requires additional education and training to acquire advanced knowledge of the most current diagnostic and therapeutic approaches available. It also requires the practice of REI where all essential modalities are available and used appropriately.

Additionally, an REI subspecialist is expected to have knowledge of endocrine and fertility problems in male patients and should be able to function effectively in the arena of basic and applied investigation in REI, for only in this way does one advance the discipline and remain current in this rapidly changing field.

## III. OBJECTIVES

This *Guide* has two objectives. First, the terminal objectives describe what the fellow should know and be able to perform by the end of the fellowship. These objectives principally refer to problem-solving skills needed to make a diagnosis and implement management programs. Second, the enabling objectives describe the skills the fellow must acquire in order to accomplish the terminal objectives.

## IV. GENERAL CONSIDERATIONS

The practice of Obstetrics and Gynecology and REI requires a commitment to professionalism as well as personal growth. In addition to practicing technical skills, physicians should cultivate the ability to expand and apply those skills. Knowledge of ethical principles, communication skills, and the ability to acquire and continually update information are important components of professional development. The Accreditation Council on Graduate Medical Education (ACGME) identified six core competencies that should be incorporated into REI subspecialty fellowship programs (see full definitions at [www.acgme.org](http://www.acgme.org)). The fellow should demonstrate competence at the level of a new REI practitioner in the following:

1. *Patient Care*: Provide patient care that is compassionate, appropriate, and effective for the treatment of health problems and the promotion of health.
2. *Medical Knowledge*: Demonstrate knowledge of established and evolving biomedical, clinical, epidemiological, and social-behavioral sciences relevant to REI practice, and apply this knowledge to patient care.

3. *Practice-based Learning and Improvement*: Demonstrate the ability to investigate and evaluate patient care, to appraise and assimilate scientific evidence, and to continuously improve patient care based on constant self-evaluation and life-long learning.
4. *Interpersonal and Communication Skills*: Utilize outstanding interpersonal and communication skills that result in the effective exchange of information and collaboration with patients, their families, and other health professionals.
5. *Professionalism*: Maintain a high level of commitment to the completion of professional responsibilities and an adherence to ethical principles.
6. *Systems-based Practice*: Cultivate an awareness of and responsiveness to the larger context and system of health care as well as the ability to call effectively on other resources in the system to provide optimal health care.

## **V. MECHANISMS OF HORMONE ACTION**

### **A. TERMINAL OBJECTIVES:**

The fellow should be familiar with the mechanisms whereby prohormones are metabolized to active ligands, how hormones exert their effects at cellular and molecular levels and be able to apply these principles to reproductive physiology and disorders of reproduction.

### **B. ENABLING OBJECTIVES:**

The fellow should be able to understand and describe the:

1. Mechanism of action for releasing hormones and other neural peptides.
2. Signaling via G-protein coupled receptors.
3. Mechanism of action for steroid hormones, vitamins and eicosanoids.
4. Significance of concepts involved in hormone action, including heterogeneity of hormones, post-translational modification, desensitization, receptor replenishment, internalization, and second messengers.
5. Nature of receptor assays and their applications.
6. Nature of steroid receptor binding to DNA, recruitment of co-factors, including co-activators and co-repressors, RNA polymerase and initiation of transcription.
7. Steroid receptor defects, orphan receptors, and their effects on disease.
8. Mechanisms of hormone action, including structure activity relationships, sites of action, receptor heterogeneity, and post-receptor molecular events.
9. Genomic and genetic regulation of hormone and hormone receptor synthesis.

## **VI. CLINICAL PHARMACOLOGY OF HORMONES**

### **A. TERMINAL OBJECTIVE:**

The fellow should be able to evaluate clinically and manage patients with problems related to the clinical pharmacology of hormones as related to REI.

### **B. ENABLING OBJECTIVES:**

The fellow should be able to:

1. Define absorption, distribution, biotransformation, and bioavailability and excretion of drugs and hormones, showing knowledge of these mechanisms for transfer across membranes (e.g., placenta, blood brain barrier, etc.), into and across cells, including storage, metabolism, and renal, hepatic and fecal excretion.
2. Discuss mechanisms of drug action, including structure activity relationships, receptors, and sites of action.

3. Characterize drug and hormone agonist and antagonist effects, including dose-responses, time courses, and biologic variations that modify effects (e.g., age, sex, body weight, route of administration, tolerance, clearance and drug-drug, drug-herb interactions, etc.).
4. Define advantages and limitations of different delivery systems for steroid and protein hormones.
5. Discuss the production, availability, and advantages of recombinant glycoprotein hormones.
6. Discuss tissue specific responses to hormones, hormone analogues and selective receptor modulators, including receptor affinity, receptor isoforms, co-factors, post-receptor activity, and interaction with binding proteins. Understand the molecular events involving hormone interactions with receptors, DNA, and transcription and post-transcription factors.
7. Discuss mechanisms by which drugs may alter hormone sensitivity (e.g. insulin sensitizing agents, etc.).
8. Discuss teratogenicity and FDA pregnancy categories of pharmaceutical agents.

## VII. PATHOLOGY

### A. TERMINAL OBJECTIVE:

The fellow should have knowledge of gross, microscopic histology, and immunohistochemical techniques as they relate to the diagnosis and further clarification of reproductive endocrine pathology.

### B. ENABLING OBJECTIVES:

The fellow should be able to:

1. Identify and describe these specific organs:
  - a. Vagina
    - 1) Gross and microscopic findings of adenosis and atrophy
    - 2) Pathophysiology and possible consequences of antenatal hormone exposure
    - 3) Mechanisms of action and effects of hormones upon the vagina
  - b. Cervix
    - 1) Mechanisms of action and effects of antenatal hormone exposure, HPV, and environmental factors (e.g., smoking)
  - c. Endometrium
    - 1) Histology of normal and abnormal endometrium (including endometrial dating)
    - 2) Current data relating to the effects of estrogen and progestins on endometrial hyperplasia and adenocarcinoma
    - 3) Histology and cell biology of trophoblast invasion/implantation
  - d. Myometrium
    - 1) Gross and microscopic findings of adenomyosis, leiomyomata, and other myometrial findings related to reproductive endocrinology
    - 2) Relationship of leiomyomata to infertility, including each of the different types (e.g., subserosal, intramural, and submucosal)
    - 3) Endocrine regulation of onset of parturition
  - e. Oviduct
    - 1) Gross and microscopic findings of anatomical segments and diseases related to infertility (e.g., acute and chronic salpingitis, granulomatous salpingitis, salpingitis isthmica nodosa, and endometriosis)
    - 2) Natural history and clinical course of acute and chronic salpingitis and their treatment as they relate to subsequent fertility and IVF success
    - 3) Contribution of tubal epithelium to ovarian and peritoneal cancers
  - f. Ovary
    - 1) Gross and microscopic findings and the natural history of functional and neoplastic ovarian tumors as they relate to reproductive endocrinology (e.g., follicular cysts, luteoma, hyperreactio luteinalis, corpus luteum, OHSS, endometrioma, granulosa-

- theca cell tumor, Sertoli-Leydig cell tumor, cystic teratoma, dysgerminoma, gonadoblastoma, and mixed germ cell tumors)
  - 2) Individual compartments of the Graafian follicle (e.g., oocyte, granulosa cells, theca, and adjacent stroma) and the primordial, preantral and antral follicles, including the dynamic, changes which occur in the ovary from embryonic life to menopause
  - 3) Histology of the polycystic ovary
  - 4) Specific staining techniques and cellular ultrastructure as they relate to function
  - 5) Gross and microscopic appearance of gonadal structures in various forms of gonadal dysgenesis and intersexuality
  - 6) Stage of oocyte, zygote and preimplantation embryo development as they pertain to IVF
  - g. Hypothalamic-CNS axis
    - 1) Anatomy and functional relationships of the various hypothalamic centers involved in reproductive endocrine functions
    - 2) Other endocrinologically related central nervous system structures (e.g., third ventricle, cerebral cortex, and pineal gland)
  - h. Pituitary
    - 1) Cellular morphology of normal and neoplastic cells of the adenohypophysis
    - 2) Anatomy and function of the neurohypophysis
    - 3) Regulation of prolactin production
    - 4) Physiological changes associated with pregnancy
    - 5) Medical, surgical and radiological interventions for pituitary pathology
  - i. Testis
    - 1) Stages of normal and abnormal spermatogenesis
    - 2) Gross and microscopic findings in the normal testis, accessory sex organs, and testicular disease
    - 3) Genetic and anatomical defects associated with congenital absence of the vas deferens
  - j. Thyroid
    - 1) Normal structure
    - 2) Thyroid lesions associated with altered reproductive function (e.g., primary hypothyroidism, Graves' disease, thyroiditis, thyroid storm, and neoplasia)
    - 3) Embryonic and fetal thyroid development and related pregnancy complications
  - k. Adrenal
    - 1) Normal structure in fetal and adult life
    - 2) Contributions of fetal adrenal to hormones of pregnancy
    - 3) Lesions associated with altered reproductive functions (e.g., hyperplasia, adenoma, carcinoma, and pheochromocytoma)
  - l. Placenta
    - 1) Structural characteristics necessary for maintenance of fetal well-being
    - 2) Specific cells and enzymes responsible for protein and steroid hormone production
    - 3) Functional histology of the maternal-fetal interface
  - m. Peritoneum
    - 1) Microscopic anatomy
    - 2) Pelvic adhesions and angiogenesis
    - 3) Endometriosis
2. Understand the use and limitations of *in situ* hybridization and immunohistochemistry for the specific organs listed in section VII.B.1.

## VIII. IMMUNOLOGY

### A. TERMINAL OBJECTIVE:

The fellow should understand the unique immunology of early pregnancy and the maternal-fetal interface; be able to evaluate, diagnose, and manage patients with infertility and endocrinologic diseases of immunologic origin; and be able to manage patients with immunologic disorders that affect the reproductive systems.

**B. ENABLING OBJECTIVES:**

The fellow should be able to distinguish the cell types and contributions of the innate and adaptive immune systems and understand and describe the:

1. Essentials of basic immunology, including the:
  - a. Cell type and mechanisms for antibody production
  - b. Origin, types, and function of the immunoglobulins
  - c. Production, characterization, and application of polyclonal and monoclonal antibodies with respect to reproductive disorders
  - d. Mechanisms of cell mediated immunity, including cell types
  - e. Definition of and examples of autoimmune diseases
  - f. Diagnostic testing for autoimmune diseases (e.g., source and function of cytokines and chemokines)
  - g. The possible role of the immune system in male and female reproductive failure, recurrent abortion, and primary ovarian insufficiency
2. Pathophysiology of autoimmune disease as it relates to gonadal failure and other endocrine dysfunction.
3. Effect of active and passive immunization on hormone producing target tissues.
4. Clinical features, diagnostic testing, and progression of autoimmune endocrinologic disease states (e.g., thyroid, adrenal, and gonad).

**IX. EMBRYOLOGY**

**A. TERMINAL OBJECTIVES:**

The fellow should understand fundamental aspects involving early human embryo development and be able to diagnose and manage patients with congenital abnormalities of the reproductive tract.

**B. ENABLING OBJECTIVES:**

The fellow should be able to understand and describe the:

1. Processes of oocyte and sperm maturation and the mechanism of fertilization, including a description of morphological stages of, and factors involved in the control of, oocyte maturation (including gametogenesis and the progression of meiosis for both male and female gametes).
2. Developmental stages of the post-fertilization zygote and embryo, and the timing and anatomic location of those events relative to *in vivo* and *in vitro* conception.
3. Embryonic development and anatomy of the genital tract, including factors controlling the development of the gonadal primordia, accessory reproductive structures, and external genitalia in the male and female.
4. Indications and complications of blastomere and trophectoderm biopsy for PGD.
5. Mechanisms for the various developmental aberrations (including exposure to toxins and teratogens) of the reproductive tract, including intersex disorders, müllerian and gonadal abnormalities, vaginal agenesis, vaginal septum (transverse, longitudinal), and imperforate hymen.
6. Anatomy, surgical approach, and management for vaginal agenesis, vaginal septum (transverse, longitudinal), clitoral reduction, exteriorization of vagina, feminizing genitoplasty, and müllerian anomalies.
7. Embryology and anatomy of the hypothalamic-pituitary system, thyroid gland, and adrenal gland.
8. Imaging procedures to diagnose and characterize abnormalities of the reproductive tract.
9. Methods used to derive human embryonic stem cells (hESC), induced pluripotent stem cells (iPSC), and a general knowledge of their potential clinical application.

## **X. GENETICS**

### **A. TERMINAL OBJECTIVES:**

The fellow should be able to interpret pedigree data and care for patients with inherited and sporadic genetic, somatic, and epigenetic disorders affecting the male and female reproductive system.

### **B. ENABLING OBJECTIVES:**

The fellow should be able to apply (use) genetic concepts and techniques to diagnostic problems in reproductive endocrinology and be familiar with:

1. Genomics and genetics, gene structure and regulation, chromosomal structure and standard cytogenetic nomenclature, and DNA diagnosis referable to reproductive endocrinology.
2. Techniques of chromosomal analysis, including distinguishing features of current tests and their proper application for management and screening for heritable disorders (including whole-exome sequencing, whole genome sequencing, comparative genomic hybridization (CGH), etc.), techniques of gene amplification (e.g., PCR, etc.), and other assay systems (e.g. FISH, etc.).
3. Differences between DNA versus RNA detection (e.g., Southern and Northern blotting, cDNA microarray analysis).
4. Epigenetic inheritance as it relates to reproduction, fundamental mechanisms and relevance to assisted reproductive technologies.
5. Abnormal genetics, including gametogenic errors, cytogenetic abnormalities (e.g. gonadal dysgenesis, Klinefelter syndrome, etc.) and molecular germ line and somatic cell mutations associated with reproductive endocrine disorders (e.g. gonadal dysgenesis, congenital adrenal hyperplasia, growth hormone deficiency, McCune Albright syndrome, Kallmann syndrome, microdeletion of the Y chromosome with azoospermia, etc.).
6. Role of abnormal genetics in recurrent miscarriage (including Robertsonian translocation and complex chromosomal rearrangements).
7. Role of aneuploidy in infertility and ovarian aging (including the roles of meiotic errors, cytogenetic abnormalities, and embryonic lethal mutations).
8. Routine preconceptional screening for genetic disorders in couples with reproductive problems and prior to assisted reproduction using donor sperm or donor oocyte.
9. Role and management of preimplantation genetic diagnosis for single gene disorders, translocations, and aneuploidy.
10. Indications and complications of blastomere and trophectoderm biopsy for PGD.
11. Ethical concerns surrounding sex selection and pre-implantation screening.

## **XI. ENDOCRINOLOGY OF PREGNANCY**

### **A. TERMINAL OBJECTIVES:**

The fellow should be able to discuss maternal-fetal physiology/pathophysiology and develop a management protocol of endocrinopathies in obstetrical patients.

### **B. ENABLING OBJECTIVES:**

To care for such patients, the fellow should be able to understand and discuss the:

1. Signaling between the endometrial and blastocyst compartments that facilitate or hinder the process of implantation, including the production of endometrial/decidual hormones and growth factors in the non-pregnant uterus.
2. First trimester and perinatal consequences of impaired trophoblast invasion.
3. Maternal endocrine adaptations to pregnancy, including general physiological changes that



- impact virtually every endocrine system as well as specific changes in thyroid, adrenal, and pancreatic function:
- a. Interpretation of endocrine assays in pregnancy
  - b. Diagnosis and management of thyroid, parathyroid, adrenal, and pancreatic disease in pregnancy and postpartum
  - c. Intra- and postpartum management of hypothalamic-pituitary disease
4. The maternal-fetal-placental unit as a cooperative source of steroid hormones.
  5. Steroid, protein, polypeptide hormone, and eicosanoid production by the placenta and decidua.
  6. Fetal endocrinology:
    - a. Ontogeny and physiology of the fetal adrenal and thyroid glands
    - b. Ontogeny and physiology of fetal hypothalamic-pituitary-gonadal function
    - c. Placental transfer of hormones and their effect on fetal development
  7. Initiation of parturition, including the roles of prostaglandins, cytokines, placental steroids, and adrenal hormones.
  8. Endocrine physiology of fetal lung maturation and pathophysiology of preeclampsia.
  9. Evaluation and management of endocrine disorders in pregnancy (thyroid, hirsutism, r/o Cushing's disease, etc.).

## **XII. LABORATORY CAPABILITY**

### **A. TERMINAL OBJECTIVES:**

The fellow should be able to discuss the nature, application, and methodology of hormone assays in reproductive endocrinology.

### **B. ENABLING OBJECTIVES:**

The fellow should be able to explain the scope and limitations, interpret, and where appropriate carry out laboratory elements of clinical and basic reproductive endocrinology, including:

1. Specific techniques for hormone assays of various types, including immunoassay, bioassay, receptor assay, chromatography and mass spectroscopy as well as their statistical analysis.
2. Biochemical methodology, including extraction, purification, and identification of steroid and protein hormones.
3. Enzyme and receptor binding kinetics, as they relate to steroid and protein hormone and metabolism.
4. Kinetics of production, distribution, interconversion, and metabolism of specific hormones.
5. Concept, associated clinical presentation, and detection of anti-heterophile antibodies.
6. Experimental design, data interpretation, and statistical analysis of biochemical assays.
7. Assay validation and description of standard curve, precision, specificity, bias, sensitivity, and assay drift.
8. Validation and application of immunohistochemical techniques.
9. Specific techniques in RNA and DNA analysis (e.g. PCR, RT-PCR, real time PCR, Northern and Southern blotting, cloning, vectors, deep sequencing databases for location of genes on chromosomes, etc.).
10. Concepts and clinical applications of genomics (e.g. DNA micro- and macro-arrays), proteomics (e.g., mass spectrometry and 2D gels), and pharmacogenetics (e.g. polymorphisms, pharmacokinetics and drug responses).
11. Specific techniques in protein analysis and the proteome (e.g. immunoblot, etc.).

### XIII. STATISTICS

#### A. TERMINAL OBJECTIVES:

The overarching goal is for the fellow to understand how to read an article in the literature and determine if its findings are based upon a proper study design with appropriate statistics. The fellow should then be able to design a study of their own using these guidelines.

#### B. ENABLING OBJECTIVES:

The fellow should know about the concepts and uses of each test.

1. Describe the null hypothesis:
  - a. Define the hypothesis
  - b. How do you reject or accept the null hypothesis
  - c. Discuss differences in analysis if a 2-tailed vs. 1-tailed test
  - d. Discuss what is meant by a type 1 (or a) error vs. a type 2 (b) error
  - e. Discuss power and how to perform a power analysis for a given study
2. Types of data:
  - a. Describe the difference between the sample and the population
  - b. Describe and categorize types of variables: continuous vs. discrete, independent vs. dependent
  - c. Discuss if data is normally distributed and how you test for it
  - d. Describe characteristics of parametric vs. nonparametric data including use of standard deviation (parametric) and median (nonparametric)
3. Describe retrospective, cohort, prospective studies, and randomized controlled trials:
  - a. How to conduct each type of study
  - b. Discuss benefits and limitations of each type of study
  - c. Discuss sampling methods, bias, blinding, and randomization
  - d. Discuss data analysis and statistical testing
4. Describe how to compare two samples and what tests are used:
  - a. Normally distributed (means): t- test
    - 1) Paired vs. unpaired
  - b. Not normally distributed (medians):
    - 1) Paired – Wilcoxon signed rank test or sign test
    - 2) Unpaired – Mann Whitney rank sum test
5. Describe how to compare >2 samples and what tests are used:
  - a. Normally distributed (means): Analysis of variance (ANOVA)
    - 1) Unblocked (independent): 1-way ANOVA
    - 2) Blocked or Paired (from same subjects/specimens): 2-way ANOVA
    - 3) Understand need for post-hoc test to determine which samples are different (Dunnett's vs. control; otherwise, pairwise Newman-Keuls test)
  - b. Not normally distributed (medians):
    - 1) Unblocked (independent) – Kruskal-Wallis
    - 2) Blocked (same subjects/specimens – Friedman
    - 3) Need for post-hoc test
6. Discuss how to compare proportions and specifically understand:
  - a. Chi-square
  - b. Fisher exact test
  - c. Adjusting for multiple comparisons
7. Discuss screening tests and understand each of the following:
  - a. Sensitivity
  - b. Specificity
  - c. Positive predictive value
  - d. Negative predictive value
  - e. False positive, false negatives
  - f. Receiver operator characteristic (ROC) curve

8. Discuss the difference between correlation and regression:
  - a. Define correlation and its use for association of two variables
  - b. Define linear regression for prediction of dependent variable from a given independent variable
  - c. Logistic regression use (when one variable is categorical)
  - d. Discuss odds ratio vs. relative risk (and confidence intervals)
  - e. Discuss ANCOVA (analysis of covariance), a type of regression used for baseline and follow up measurements
9. Discuss how to determine measurement error:
  - a. Discuss why correlation and regression may not be appropriate for measurement error, observer variation, and level of agreement
  - b. Discuss an appropriate method such as levels of agreement, Cohen's kappa, intraclass correlation coefficient, or limits of agreement
10. Discuss statistics related to hormone assays:
  - a. Understanding of precision in linear part of curve
  - b. Lower limits of detection
  - c. Sensitivity
  - d. Coefficient of variation
  - e. Hook Effect
11. Discuss Life table (survival) analysis:
  - a. Discuss Kaplan-Meier curves – indications, assumptions, limitations
  - b. Discuss the use of Cox proportional hazards model – indications, assumptions, limitations
12. Discuss meta-analysis vs. systematic review including the following topics:
  - a. Define meta-analysis and systematic review
  - b. Benefits and limitations of meta-analysis
  - c. For meta-analysis, discuss the role of:
    - 1) Locating studies to include
    - 2) Quality assessment of studies
    - 3) Calculating effect sizes
    - 4) Checking for publication bias – funnel plot
    - 5) Sensitivity analysis
    - 6) Data presentation – Forest plot; heterogeneity

#### **XIV. CLINICAL DIAGNOSTIC TECHNIQUES**

##### **A. TERMINAL OBJECTIVES:**

In patients with endocrinologic disease or infertility, the fellow should be able to:

1. Take a comprehensive medical history, perform a general physical examination in addition to a specific gynecologic history and physical examination.
2. Select, organize, accomplish, and interpret the diagnostic techniques needed to establish a diagnosis.
3. Evaluate co-existing disease or factors which may have a bearing on selection of and response to treatment.
4. Evaluate the response to therapy.

##### **B. ENABLING OBJECTIVES:**

The fellow should be able to describe, perform, or where appropriate obtain and interpret results of these diagnostic techniques:

1. Operative surgical samples, including biopsies of the endometrium, at laparoscopy, hysteroscopy, and laparotomy.
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. Endocrinologic, including the measurement of hormones in biological fluids for evaluation of the hypothalamus, pituitary, parathyroid, thyroid, adrenal, and gonadal systems:
    - a. Be able to perform and interpret dynamic endocrinologic testing of these systems.
    - b. Describe clinical conditions (e.g., pregnancy, thyroid disease, etc.) in which endocrine test results may be altered.
  4. Biochemical, including blood chemistries performed on biologic fluids.
  5. Genetic, including preconception genetic screening and screening for known genetic disorders related to reproductive endocrinology and infertility.
  6. Obstetrical, including endocrinologic and genetic evaluation of the fetus.

## **XV. NEUROENDOCRINE FUNCTION AND DISEASE STATES**

### **A. TERMINAL OBJECTIVES:**

The fellow should be able to discuss neuroendocrine physiology and function and to diagnose and manage patients with diseases originating in the neuroendocrinologic system.

### **B. ENABLING OBJECTIVES:**

The fellow should be able to understand and discuss

1. Anatomical-functional relationships of the hypothalamus, neurovascular, and target cells of the 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 long and short-term biorhythmicity, and their target organ feedback systems.
5. Biochemical basis of the neuroendocrine interactions and the use of neuropharmacological agents.
6. Site of production, biological action, and control of secretion of oxytocin, vasopressin, and neurophysins (the posterior hypophysis).
7. Distribution and cellular characteristics of pituitary hormone producing cells with special reference to gonadotrope, somatotrope, and lactotrope.
8. Anatomical arrangement of hypothalamic-hypophyseal portal circulation.
9. Circumventricular organs and blood brain barrier.
10. Structure, half-life, and function of pituitary reproductive hormones and neuropeptides (e.g., GnRH, TRH, somatostatin, pro-opiomelanocortin family, GHRH, CRH, vasopressin, etc.)
11. Sexually dimorphic nuclei.
12. Biochemical basis of neuropharmacology of agonists and antagonists.
13. Neuroendocrine regulation of the menstrual cycle.
14. Neuroendocrine function of the fetal-placental unit.
15. Hypersecretory syndromes.
16. Organic lesion and/or functional disorders of the hypothalamic-pituitary system.
17. Ectopic hormone producing syndromes.
18. Deficiencies of the hypothalamic-pituitary system (e.g., panhypopituitarism, Sheehan syndrome, Kallmann syndrome, and isolated pituitary hormone deficiencies).

19. Interactions between the different hypothalamic-pituitary-target gland endocrine axes.
20. Genetic variants related to neuroendocrine disease states.

## **XVI. OVARIAN FUNCTION AND DISEASE STATES**

### **A. TERMINAL OBJECTIVES:**

The fellow should be able to discuss ovarian physiologic processes including folliculogenesis, ovulation, corpus luteum development, maintenance and regression, and steroidogenesis, and to diagnose and manage patients with diseases involved in these systems.

### **B. ENABLING OBJECTIVES:**

The fellow should be able to understand and discuss:

1. Hypothalamic-pituitary control of ovarian function and ovarian feedback and feed-forward mechanisms regulating hypothalamic and pituitary function.
2. Cyclic changes in endocrine activities within the ovary.
3. 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.
4. Synthesis and secretion of steroid and peptide hormones by the various compartments and cell types of the ovary.
5. Mechanisms of protein/steroid hormone action in the ovary, including apoptosis.
6. Atresia, recruitment and selection of the dominant follicle and oocyte maturation.
7. Hetero-autoregulation of hormone receptors and down-regulation.
8. Luteolysis.
9. Age-related changes in ovarian structure, function, and regulation.
10. Ovarian activity during gestation.
11. Hormone producing tumors of the ovary.
12. Clinical, genetic, and pathophysiologic correlates of disorders of the human ovary (structure and function).
13. Autocrine and paracrine effects of cytokines and growth factors on ovarian function and on the oocyte.
14. Testing procedures needed in primary or secondary hypogonadism, including its physiology and pathophysiology as well as the management of patients during the perimenopause and menopause.
15. Various therapies for primary or secondary hypogonadotropic patients and the rationale for the use or non-use of estrogens, progestins, and other therapies.
16. Pathophysiology and treatment approaches involving insulin resistance and polycystic ovary syndrome.

## **XVII. THYROID FUNCTION AND DISEASE STATES**

### **A. TERMINAL OBJECTIVES:**

The fellow should be able to discuss thyroid function and physiology and diagnose and treat patients with thyroid disorders.

### **B. 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 biosynthesis, control, and metabolism of thyroid hormones.
4. The clinical and pathophysiological correlation of hypo- and hyperthyroidism, particularly as related to menstrual disorders, infertility, and pregnancy.
5. Pregnancy and hormone induced changes of thyroid function in the mother and the effect of abnormal maternal thyroid function on the fetus.
6. Fetal and newborn thyroid physiology.
7. The effects of thyroid replacement and anti-thyroid drug therapy on the fetus.
8. The pathophysiology of autoimmune disorders involving the thyroid.
9. Thyroid function in struma ovarii, molar pregnancy, and choriocarcinoma.
10. The evaluation and therapy of hyperthyroidism, hypothyroidism, and thyroid nodules.
11. The pharmacology of thyroid medications.
12. Deficiencies of the thyroid, including hypothyroidism in pregnant or non-pregnant women and women on various hormonal medications, including the differentiation of hypothyroidism resulting from thyroid, pituitary, or hypothalamic disease.
13. Use of various radionuclides in the management of thyroid disease.

## **XVIII. ADRENAL FUNCTION AND DISEASE STATES**

### **A. TERMINAL OBJECTIVES:**

The fellow should be able to discuss adrenal function and physiology and be able to diagnose and treat patients with adrenal disorders.

### **B. ENABLING OBJECTIVES:**

The fellow should be able to:

1. Understand and discuss:
  - a. Regulation and secretion of adrenocortical hormones, including circadian rhythms and the effects of stress and aging
  - b. Clinical and laboratory assessment of adrenocortical function
  - c. Pharmacology and physiological effects of naturally occurring and synthetic glucocorticoids and mineralocorticoids
  - d. Adrenocortical hypo and hyperactivity (e.g., Cushing syndrome, adenoma, carcinoma, etc.)
  - e. Genetics and biochemistry of specific steroid pathway defects in the congenital adrenal hyperplasias
  - f. Explain management of the couple at risk for CAH (classical and late-onset) in their offspring
  - g. Effects of aberrations of adrenocortical function on hypothalamic-pituitary-ovarian function, including Nelson syndrome
  - h. Aldosterone and disorders of the renin-angiotensin system
  - i. Syndromes of excess catecholamine secretion
  - j. Deficiencies of the adrenal, including hypoadrenalism resulting from pituitary or adrenal disease or hormonal medications in pregnant or non-pregnant women
  - k. Genetics and biochemistry of steroid pathway enzyme defects and their effect on fetal and postnatal development
  - l. The zona reticularis, the androgens it produces, and the kinetics of their metabolism before and after menopause and in various reproductive disorders
  - m. The effects and metabolism of exogenous adrenal androgens (e.g. DHEA)
2. Diagnose and treat any of the abnormalities in section XVIII.B.1., including:
  - a. Adrenal crisis

- b. Adrenal suppression from long-term corticosteroid replacement
- c. Congenital adrenal hyperplasia
- d. Androgen secreting adenoma
- e. Requirements for long-term glucocorticoid and mineralocorticoid hormone replacement

## **XIX. ANDROGEN DISORDERS**

### **A. TERMINAL OBJECTIVES:**

The fellow should be able to discuss and be able to diagnose and treat patients with androgen disorders.

### **B. ENABLING OBJECTIVES:**

To treat such patients, 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.
5. Differentiate hirsutism from defeminization, virilization, and hypertrichosis.
6. Discuss ovarian tumors, benign and malignant, which may be androgen secreting.
7. Describe those benign stromal changes in the ovary that may result in virilism.
8. Relate polycystic ovary syndrome to abnormal androgen secretion and hirsutism.
9. Discuss relationships between androgen disorders and hyperinsulinemia, including mechanisms of insulin action on theca cell androgen production.
10. Indicate the role of hormone assays in evaluating hyperandrogenism.
11. Differentiate between adrenal and ovarian etiologies of normal androgen production, including neoplasms.
12. Differentiate between non-classical variants and classical adrenal hyperplasia in terms of etiology, genetic factors, genital morphology, general metabolic effects, and treatment.
13. Describe the treatment of androgen excess.
14. Describe mechanisms of androgen production and their control in the male, particularly as it relates to spermatogenesis and sexual behavior.
15. Describe radiologic and imaging procedures commonly used for diagnosis in women with hyperandrogenism.
16. Describe the indications for and the use of CT and MRI imaging as well as the use for selective catheterization of the ovarian and/or adrenal veins.

## **XX. ABNORMAL UTERINE BLEEDING**

### **A. TERMINAL OBJECTIVES:**

The fellow should be able to discuss the problems of and diagnose and manage patients with abnormal uterine bleeding.

### **B. ENABLING OBJECTIVES:**

To treat such patients, 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 of estrogen, progesterone, and androgen.

2. Define the terms and classification system used 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.
8. Relate abnormal bleeding to such intercurrent diseases as obesity, blood dyscrasias, and thyroid disorders.
9. Describe the management and etiologies of coagulation abnormalities that may produce uterine bleeding.
10. Describe the role of hysteroscopy and sonohysterography in the diagnosis of abnormal bleeding.

## **XXI. AMENORRHEA**

### **A. TERMINAL OBJECTIVES:**

The fellow should be able to diagnose and treat patients with amenorrhea.

### **B. ENABLING OBJECTIVES:**

To diagnose and treat such patients, 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 (e.g., 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.
7. Rational diagnostic and therapeutic cost-effective approach to patients with amenorrhea.
8. Techniques for and ability to carry out the evaluation and therapy of patients who require ovulation induction.

## **XXII. PUBERTY**

### **A. TERMINAL OBJECTIVES:**

The fellow should be able to discuss the physiology of growth and development as it relates to normal puberty. The fellow should:

1. Recognize deviations from normal.
2. Develop a plan for a differential diagnosis.



3. Treat patients with abnormal pubertal development.

**B. ENABLING OBJECTIVES:**

The fellow should be able to understand and discuss the:

1. Hormonal changes relative to the reproductive cycle from intrauterine life to the development of normal reproductive cycles (e.g., gonadotropin secretion in the fetus and neonate, sensitivity of the feedback system during fetal and neonatal life and childhood, central control mechanisms for the initiation of puberty and modulation of GnRH neuron activity, the role of adrenal androgens, and the effects of weight changes).
2. Normal sequence and timing of pubertal changes in the female and male, including Tanner stages.
3. Effects of gonadal and adrenal hormones on sexual development, somatic growth, and epiphyseal closure.
4. Molecular causes of hypogonadotropic/hypogonadism and the role these genes play in normal pubertal development.
5. Disorders of sexual development, including classification, sexual precocity syndromes, the pathophysiology, differential diagnosis, evaluation, and appropriate therapy of disorders of sexual development.
6. Delayed puberty syndromes, including the pathophysiology, differential diagnosis, evaluation, and appropriate therapy.
7. Growth problems in adolescents, including evaluation and appropriate therapy.

### **XXIII. FEMALE INFERTILITY**

**A. TERMINAL OBJECTIVES**

The fellow should be able to evaluate a woman for infertility and be able to develop and carry out an appropriate plan for management of the infertile woman.

**B. ENABLING OBJECTIVES:**

The fellow should be able to:

1. Take an appropriate history and do a physical examination oriented to infertility.
2. Evaluate an infertile female.
3. Describe and apply in the overall management of the infertile couple, as related to:
  - a. Ovulatory disorders, including:
    - 1) Correct utilization and interpretation of tests of ovulation
    - 2) Diagnosis of causes of anovulation, including polycystic ovary syndrome, syndromes of inappropriate prolactin secretion, CNS-hypothalamic-pituitary syndromes, and other GnRH causes
    - 3) Selection of ovulation induction utilizing clomiphene, aromatase inhibitors, human gonadotropins, bromocriptine, and other agents
    - 4) Appropriate monitoring of ovulation induction, including estrogen determinations, ultrasound, progesterone assays, and ovulation predictor kits
  - b. Tubal disorders, infectious in origin or not, including:
    - 1) Correct utilization and interpretation of studies of tubal function (e.g., hysterosalpingography and laparoscopy)
    - 2) Indications and contraindications for tubal reparative procedures, including the specific indications for microsurgery
  - c. Uterine factors, including correct utilization and interpretation of studies of the uterine cavity, such as hysterosalpinography, sonohysterography, and hysteroscopy, and the indications and techniques for corrective procedures

- d. Endometriosis and other peritoneal causes of infertility – knowledge of the medical management of endometriosis (e.g., pseudopregnancy, danazol, continuous progestin, androgen therapy, aromatase inhibitors and GnRH analogs):
    - 1) Indications for surgery for these diseases
    - 2) The rationale for pharmacologic adjuncts to surgical therapy
  - e. Cervical factors, including the treatment of chronic cervicitis and cervical conization that accompany infertility
  - f. Artificial insemination including the:
    - 1) Indications, contraindications, and complications
    - 2) Evaluation of male infertility
    - 3) Screening of sperm donors to exclude transmissible infection (HIV, etc.) and genetic disorders
    - 4) Proper use of sperm cryobanking
  - g. Unexplained infertility, including knowledge and evaluation of current methods of diagnosis and therapy
  - h. Adoption, including:
    - 1) The indications for adoption, knowledge of appropriate counseling methods
    - 2) Familiarity with domestic and international adoption requirements, and legal implications dealing with adoption
  - i. Outcome of various managements, including the:
    - 1) Statistics related to the effectiveness of therapies used to treat various forms of infertility
    - 2) Use of life tables and meta-analyses as they relate to the effectiveness of infertility treatment
4. Cite the incidence of infertility as related to age and the prognosis for treatment of infertility and understand the methods of testing for ovarian reserve.
    - a. Explain indications for consideration of egg donor
    - b. Explain indications for oocyte cryopreservation for medical and social reasons
  5. Describe appropriate preconceptional counseling and screening and explain further diagnostic and therapeutic approaches for couples carrying dominant, X-linked, or recessive disorders.

## XXIV. MALE INFERTILITY

### A. TERMINAL OBJECTIVES:

The fellow should be able to evaluate the male partner and diagnose sub-fertility and absolute infertility and evaluate and discuss patients with these problems.

### B. ENABLING OBJECTIVES:

The fellow should be able to:

1. Take an appropriate history oriented to infertility.
2. Evaluate an infertile male.
3. Understand and discuss:
  - a. The cycle of spermatogenesis, including endocrinologic control, mechanisms, and its abnormalities
  - b. The formation and content of seminal fluid
  - c. The physiology and pathophysiology of ejaculation, including diseases which inhibit it
  - d. Abnormalities in sperm transport, including ductal obstruction and retrograde ejaculation
  - e. The medical and surgical therapies of male infertility, including microscopic procedures to facilitate fertilization (ICSI, epididymal aspiration and testicular sperm extraction) and their limitations, and prognosis for vasectomy reversal
  - f. The biosynthesis of steroids and regulatory control of the human testis and the biological action of testosterone in man

- g. Methods of evaluating semen quality and fertilizing capabilities
- h. Environmental factors, including drugs that may affect the endocrine and exocrine function of the testis
- i. Male hypogonadism
- j. Management of azospermic male with hypogonadism secondary to inappropriate steroid use
- k. Normal male sexuality throughout the life cycle
- l. The relationship of varicocele in male infertility
- m. Genetic testing in male infertility
- n. Infectious etiologies of male infertility
- o. Paternal age and pregnancy outcomes
- p. Indications for and regulatory issues involving donor sperm

## **XXV. RECURRENT PREGNANCY LOSS (RPL)**

### **A. TERMINAL OBJECTIVE:**

The fellow should be able to diagnose and manage patients with recurrent pregnancy loss.

### **B. ENABLING OBJECTIVES:**

The fellow should be able to properly define PRL, understand, and discuss the:

1. Prognosis for patients who have lost one, two, three, four, or more pregnancies.
2. Causes of euploidic and aneuploidic abortion (sporadic or recurrent), including their relative incidence.
3. Genetic causes and mechanisms of cytogenetic abnormalities in embryonic loss, including prevalence at different gestational ages.
4. Advantages and limitations of preimplantation genetic diagnosis (FISH, CGH, high density SNP arrays and whole-exome and whole genome sequencing) for abnormal parental karyotypes.
5. Contribution of müllerian and other anatomical anomalies, congenital or acquired, to recurrent pregnancy losses.
6. Contribution of endocrine factors, including hypothalamic, pituitary, thyroid, adrenal, and ovarian disorders, endometrial dysfunction, diabetes mellitus, and PCOS to recurrent pregnancy losses.
7. Contribution of immunologic factors, including lupus anticoagulant, anti-cardiolipin antibodies, and *anti-β<sub>2</sub>-glycoprotein 1* antibody to recurrent pregnancy losses (antiphospholipid antibody syndromes).
8. Relationship of thrombophilias (e.g., deficiencies of antithrombin III, protein C and protein S and Factor V Leiden mutations) to recurrent pregnancy losses and data regarding MTHFR.
9. Contribution of environmental exposure, including radiation and teratogenic exposure, to recurrent pregnancy losses.
10. Advantages and limitations of genetic analysis of aborted fetal tissue, including karyotyping, FISH, SNP and CGH arrays, and PCR.
11. Outline the arguments for and against each of these factors as a cause of infertility or recurrent pregnancy loss.
12. Diagnostic and therapeutic plan for a given patient presenting with recurrent pregnancy losses.
13. Realistic prognosis for patients undergoing various management options, including observation, for recurrent pregnancy loss.

## **XXVI. PSYCHOLOGICAL, SEXUAL, AND ETHICAL IMPLICATIONS OF REPRODUCTIVE DISEASE**

- A. **TERMINAL OBJECTIVE:**  
The fellow should be able to discuss the psychological, sexual, and ethical implications of management of reproductive diseases or dysfunctions of the endocrine reproductive system.
- B. **ENABLING OBJECTIVES:**  
The fellow should be able to understand and discuss the:
1. Psychodynamics of *in utero* and pubertal sexual growth and development, the correlation between sex assignment and gender identity, and the establishment of gender identity.
  2. Antenatal hormone influence on subsequent behavior and psychological function.
  3. Role of psychodynamics, including stress in amenorrhea.
  4. Psychological changes associated with infertility and recurrent pregnancy loss.
  5. Psychological and sexual changes associated with hormonal therapy.
  6. Psychodynamics of premenstrual tension and menopause and the therapy of these problems.
  7. Effects of infertility diagnosis on well-being of individuals, and couples.
  8. General concepts of normal and abnormal sexual function.
  9. Psychological changes associated with the puerperium.
  10. Pathophysiology of erectile dysfunction and its psychological, medical, and surgical treatment.
  11. Sexuality throughout life.
  12. Diagnosis and management of endocrine issues related to hormone therapy in transgender individuals.
  13. Fundamental ethical principles that apply to decisions of reproductive care and choice.
  14. The legal and ethical aspects of assisted reproduction technologies (including access to care, reporting of results, fertility preservation, gamete donation, surrogacy, etc.).

## **XXVII. SURGICAL TECHNIQUES**

- A. **TERMINAL OBJECTIVES:**  
The fellow should be able to discuss the indications and contraindications, complications of, and expected results as well as perform surgical procedures appropriate to reproductive endocrinology.
- B. **ENABLING OBJECTIVES:**  
The fellow should be able to:
1. Understand and discuss in detail the surgical techniques, risks, and complications of the following surgical procedures:
    - a. Fertility restoration, including laparoscopy and laparotomy techniques used to reverse sterilization
    - b. Diagnostic and therapeutic techniques, including hysterosalpingography, sonohysterography, tubal canalization, and endoscopy (laparoscopy and hysteroscopy)
    - c. Infertility surgery, including all techniques used for:
      - 1) Reconstruction of uterine anomalies
      - 2) Myomectomies
      - 3) Resection and postoperative management of uterine synechiae
      - 4) Resection of pelvic adhesions
      - 5) Ovarian cystectomies
      - 6) Staging and treating endometriosis, including pre and postoperative medical adjunctive therapy

- 7) Reversal of sterilization procedures of the fallopian tube, surgery of the fallopian tube and salpingectomy
- d. Developmental disorders, including all techniques used for:
  - 1) Neovaginal construction (dilation and surgical methods)
  - 2) Correction of imperforate hymen
  - 3) Removal of vaginal and uterine septae
  - 4) Correction of müllerian abnormalities
- e. Ambiguous genitalia, including:
  - 1) Counseling of family members regarding ambiguous genitalia
  - 2) Evaluation and assignment of sex of rearing for an infant with ambiguous genitalia
  - 3) Construction of unambiguous functioning female external genitalia and vagina (e.g. vaginoplasty, clitoral reduction, exteriorization of the vagina, and feminizing genitoplasty)
  - 4) Techniques and timing of prophylactic gonadectomy
2. Recognize surgical complications, including the incidence and prevention of immediate and late complications of reproductive and infertility surgery.
3. Cite correctly the principles of the physical and energy modalities used in reproductive surgery.
4. Discuss the rationale, indications, techniques, and materials available for adhesion prevention.
5. Discuss the rationale, techniques, and materials available for surgical hemostasis.

## XXVIII. TECHNIQUES OF ASSISTED REPRODUCTION

### A. TERMINAL OBJECTIVE:

The fellow should understand the principles of extracorporeal fertilization and embryo transfer.

### B. ENABLING OBJECTIVES:

The fellow should be able to describe and/or discuss the:

1. Facilities and personnel required for such a program.
2. Mechanisms controlling oocyte development and maturation.
3. Appearance of the mature compared with an immature oocyte while relating this to the method of stimulation.
4. Physiology and methodology for recruitment of preovulatory follicles and describe methods for *in vitro* maturation and monitoring of follicular development *in vivo*.
5. Methods for oocyte retrieval, including ultrasound directed transabdominal, transvesical, and transvaginal oocyte recovery.
6. Techniques for extracorporeal fertilization and *in vitro* growth of embryos.
7. Micromanipulation of gametes and embryos.
8. Techniques of embryo transfer.
9. Proper selection of patients for IVF and ICSI, gamete intra-fallopian tube transfer (GIFT) and related techniques, and know the expected outcomes.
10. Indications and techniques for preimplantation genetic diagnosis.
11. Use of donor oocytes and embryos.
12. Implications of different specific diagnoses and their expected success rates with treatment.
13. Impact of maternal age on the practice of ART.
14. Problems associated with multifetal pregnancy and methods to prevent multifetal pregnancy.

15. Complications of ART (multifetal pregnancy, severe ovarian hyperstimulation syndrome, intra-abdominal and retroperitoneal hemorrhage, infection) and their prevention and treatment.
16. Techniques for cryopreservation of embryos.
17. Indication, techniques, and success of preservation of oocytes, ovarian, and testicular tissue.
18. Derivation of stem cells and their potential clinical application.
19. Psychological, genetic, and infectious disease screening requirements recommended by ASRM and those imposed by the FDA and state regulations for sperm and ovum donation.

## **XXIX. PHYSIOLOGY AND ENDOCRINOLOGY OF THE CLIMACTERIC**

### **A. TERMINAL OBJECTIVE:**

The fellow should be familiar with the physiologic and pathological changes that occur in somatic, endocrine, and psychological function with age.

### **B. 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:
  - a. Somatotrophic axis
  - b. Metabolic axis of insulin, glucagon, and adipose tissue signaling
  - c. Skeletal system
  - d. Cardiovascular system, including lipids and lipoproteins, inflammatory markers, and vascular distensibility and the process of atherosclerosis
  - e. Hypothalamic-pituitary-adrenal axis
  - f. Thyroid axis
  - g. Cognition and affect
  - h. 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 or other hypogonadal states:
  - a. Comparison and contrast of results from observational and cohort studies to those of randomized, clinical trials
  - b. Impact of hormone therapy on symptoms
  - c. Impact of hormone therapy on cardiovascular disease, thrombotic risk, breast cancer, urinary incontinence, and cognitive function
  - d. Impact of hormone therapy on quality of life and cognition
6. Different forms and routes of hormone therapy, the rationales for their use, and their indications and contraindications.

## **XXX. CONTRACEPTION**

### **A. TERMINAL OBJECTIVE:**

The fellow should be familiar with the principles and methods of contraception and able to select the most appropriate method for a high-risk patient.

### **B. 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, including LARCs and intrauterine devices.
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, pelvic infections, etc.
4. Discuss potential methods and advances in male contraception.

### **XXXI. THESIS REQUIREMENTS**

A thesis is required by the Division of Reproductive Endocrinology and Infertility. For a list of requirements, refer to the *Bulletin for Subspecialty Certification* on the ABOG website.