GUIDE TO LEARNING
IN REPRODUCTIVE
ENDOCRINOLOGY
AND INFERTILITY

The Division of
Reproductive Endocrinology
and Infertility

The American Board of
Obstetrics and Gynecology, Inc.

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INTRODUCTION

This *Guide to Learning in Reproductive Endocrinology & Infertility* has been prepared by members of the Division of Reproductive Endocrinology and Infertility, American Board of Obstetrics and Gynecology, Inc. to provide assistance to both the Fellow in training and the Program Director. It is intended to identify the minimal acceptable level of achievement and should not be interpreted as describing the ideal or setting upper limits on learning and achievement.

This guide is intended for several uses. Firstly, it should serve to guide the Program Director as to the areas of training required for an adequate fellowship program. Secondly, it can serve as a study guide for the fellow. Finally, this guide serves as a content list for the several examinations given by the Division of Reproductive Endocrinology & Infertility of the American Board of Obstetrics and Gynecology, Inc.

The Division regards the Fellow as a postgraduate trainee with the implied responsibility for self study and independent inquiry. However, the Program Director is responsible for providing adequate clinical experience, technical instruction, learning resources, study guidance, and regular direct personal evaluation of the fellow.

The Reproductive Endocrinologist is expected to have advanced knowledge of endocrine and fertility problems in female and male patients. He/she must have clinical competence in reproductive endocrinology and infertility and should be able to function as a consultant to obstetricians-gynecologists. Finally, this individual should be able to function effectively in the arena of basic and applied investigation in reproductive endocrinology and infertility, for only in this way does one advance the discipline and remain current in this rapidly changing field.

DEFINITION OF A REPRODUCTIVE ENDOCRINOLOGIST

A Reproductive Endocrinologist is a subspecialist in the discipline of Obstetrics and Gynecology who is capable of managing complex problems relating to reproductive endocrinology and infertility, and whose current professional activity involves the practice of reproductive endocrinology and infertility in a setting wherein essential diagnostic and therapeutic facilities are being appropriately utilized.
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I.

Mechanisms of Hormone Action
I. MECHANISMS OF HORMONE ACTION

TERMINAL OBJECTIVES: The fellow should be familiar with the mechanisms whereby hormones exert their effects at a cellular level and be able to apply these principles to reproductive physiology and disorders of reproduction.

ENABLING OBJECTIVES:
A. To accomplish this, the fellow should be able to understand and discuss:
   1. the mechanism of action for releasing hormones and other neural peptides.
   2. the mechanism of action for tropic hormones.
   3. the mechanism of action for steroid hormones.
   4. the significance of concepts involved in hormone action, including heterogeneity of hormones, desensitization, receptor replenishment, internalization, and second messengers.
   5. the nature of receptor assays and their usefulness.
   6. the nature of steroid receptor binding to DNA and initiation of transcription.
   7. steroid receptor defects, orphan receptors, and their effect on hormone action.
   8. signal transduction pathways for reproductive hormones and cofactors.
   9. molecular control of hormone and hormone receptor synthesis.
II.

Clinical Pharmacology of Hormones
II. CLINICAL PHARMACOLOGY OF HORMONES

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 reproductive endocrinology and infertility.

ENABLING OBJECTIVES:
A. The fellow should be able to:
   1. define absorption, excretion, distribution, biotransformation and bioavailability of drugs and hormones, showing knowledge of these mechanisms for transfer across membranes (e.g., placenta), into and across cells, storage, metabolism, and renal, hepatic and fecal excretion.
   2. discuss mechanisms of drug and hormone action including structure activity relationships, receptors and sites of action.
   3. characterize drug and hormone effects, including dose-responses, biologic variations, and factors that modify effects (e.g., age, sex, body weight, route of administration, tolerance and drug or hormone interactions), teratogenicity, agonist and antagonist effects.
   4. define scope and limitation of different delivery systems for steroid and glycoprotein hormones.
   5. discuss the production, availability, and advantages of recombinant glycoprotein hormones.
III.

Pathology
III. PATHOLOGY

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

ENABLING OBJECTIVES:
A. For the specific organs listed below, the fellow should be able to identify and describe for the:
   1. **vagina** the
      a. gross and microscopic findings of adenosis.
      b. pathophysiology and possible consequences of antenatal hormone exposure.
      c. mechanisms of action and effects of hormones upon the vagina and be able to interpret cytograms.
   2. **cervix** the
      a. mechanisms of action and effects of hormones.
      b. pathophysiology and possible sequences of antenatal hormone exposure.
   3. **endometrium** the
      a. histology of normal and abnormal endometrium.
      b. current data relating to estrogen and progestins and endometrial hyperplasia and adenocarcinoma.
      c. developmental stages (dating).
      d. responses to pharmacologic agents.
      e. histology of trophoblast/implantation.
   4. **myometrium** the
      a. gross and microscopic findings of adenomyosis, leiomyomata and other myometrial findings related to reproductive endocrinology.
      b. relationship of leiomyomata to infertility, including each of the different types (i.e., subserosal, intramural and submucosal).
   5. **oviduct** the
      a. gross and microscopic findings of diseases related to reproductive endocrinology (e.g., acute and chronic salpingitis, granulomatous salpingitis, salpingitis isthmica nodosa, endometriosis).
      b. natural history and clinical course of acute and chronic salpingitis as they relate to subsequent fertility.
6. **ovary** the
   a. gross and microscopic findings and the natural history of functional and neoplastic ovarian tumors as they relate to reproductive endocrinology (i.e., follicular cysts, luteoma, corpus luteum, endometrioma, granulosa-theca cell tumor, Sertoli-Leydig cell tumor, gynandroblastoma, cystic teratoma, dysgerminoma, gonadoblastoma and mixed germ cell tumors).
   b. individual compartments of the Graafian follicle (i.e., 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.
   c. histology of the polycystic ovary.
   d. specific staining techniques and cellular ultrastructure as they relate to function.
   e. gross and microscopic appearance of gonadal structures in various forms of gonadal dysgenesis and intersexuality.

7. **hypothalamus-CNS axis** the
   a. anatomy and functional relationships of the various hypothalamic centers involved in reproductive endocrine functions.
   b. other endocrinologically related central nervous system structures (e.g., third ventricle, cerebral cortex, pineal gland).

8. **pituitary** the
   a. cellular morphology of normal and neoplastic cells of the adenohypophysis.
   b. anatomy and function of the neurohypophysis.

9. **testis** the
   a. stages of normal and abnormal spermatogenesis.
   b. gross and microscopic findings in the normal testis, accessory sex organs and testicular disease.

10. **thyroid** the
    a. normal structure.
    b. thyroid lesions associated with altered reproductive function (e.g., primary hypothyroidism, Graves' disease, thyroiditis, neoplasia).

11. **adrenal** the
    a. normal structure.
    b. lesions associated with altered reproductive functions (i.e., hyperplasia, adenoma, carcinoma, pheochromocytoma).
12. placenta the
   a. structural characteristics necessary for maintenance of fetal well-being.
   b. specific cells responsible for protein and steroid hormone production.

13. peritoneum the
   a. microscopic anatomy.
   b. healing and scarring processes (pelvic adhesions).
   c. lesions associated with endometriosis.

B. For the specific organs listed above under A, the fellow should be able to use immunohistochemistry and DNA-RNA hybridization techniques to localize the site and temporal specificity of endocrine, paracrine and autocrine regulation of these tissues relating to reproductive function.
IV.

Immunology
IV. IMMUNOLOGY

TERMINAL OBJECTIVE: The fellow should be able to evaluate, diagnose and manage patients with infertility and endocrinologic diseases of immunologic origin.

ENABLING OBJECTIVES:
To accomplish this, the fellow should be able to understand and describe the:
1. essentials of basic immunology including the
   a. mechanism of antibody production.
   b. origin and function of IgA, IgM, IgG and IgE.
   c. origin and function of “T”, “B”, “helper” and “suppressor” lymphocytes.
   d. definition of and examples of autoimmune disease.
   e. mediation of cytokine immunologic signals.
   f. basic components of the immune system and their possible role in male and female reproductive failure, recurrent abortion, infertility and contraception.
   g. production, characterization of assay systems, and applications of polyclonal and monoclonal antibodies with respect to reproductive disorders.
   h. role of cytokines in the immune system with regard to reproductive function and disorders.
2. possible role of cellular and circulating antibodies in infertility with specific reference to
   a. proposed etiologies of isoimmunization against seminal antigens in the male.
   b. possible significance of sperm agglutinating and sperm immobilizing antibodies and head-to-head and tail-to-tail agglutination.
   c. premature ovarian failure.
3. clinical aspects related to infertility including the
   a. techniques and interpretation of diagnostic procedures (i.e., post-coital test, tests for antisperm antibodies).
   b. various modes of treatment for "immunologic infertility" and their limitations (e.g., condom, washed spermatozoa, donor cervical mucus) and expected results.)
   c. various sexually transmitted diseases, their diagnosis and therapy, as well as their implications for infertility in both male and female.
4. pathophysiology of autoimmune disease to gonadal failure and other endocrine dysfunction.
5. effect of active and passive immunization on hormone producing target tissues.
6. clinical features of autoimmune endocrinologic disease (i.e., thyroid, adrenal, gonad).
7. principles of immunologic contraception.
V.

EMBRYOLOGY
V. EMBRYOLOGY

TERMINAL OBJECTIVES: The fellow should be able to diagnose and manage patients with congenital abnormalities of the female internal and external genitalia as well as sexual ambiguity.

ENABLING OBJECTIVES:

To accomplish this, 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 factors thought to be involved in the control of oocyte maturation.
2. 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.
3. mechanisms for the various developmental aberrations of the reproductive tracts including müllerian and gonadal abnormalities, vaginal agenesis, transverse vaginal septums, and imperforate hymen.
4. anatomy, surgical approach, and management for vaginal agenesis, transverse vaginal septum, clitoral reduction, exteriorization of vagina, feminizing genitoplasty, and müllerian anomalies.
5. embryology and anatomy of the hypothalamic-pituitary system, thyroid gland, and adrenal gland.
VI.

GENETICS
VI. GENETICS

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

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. normal genetics, gene structure and regulation, chromosomal structure and standard cytogenetic nomenclature, and DNA diagnosis referable to reproductive endocrinology.
2. techniques of chromosomal karyotyping, DNA-RNA detection (e.g., Southern blotting, Northern blotting), techniques of gene amplification (e.g., PCR) and other assay systems (FISH, etc.).
3. abnormal genetics, including gametogenic errors, single gene disorders, cytogenetic abnormalities, and molecular mutants referable to reproductive endocrine disorders (e.g., gonadal dysgenesis, Klinefelter syndrome, congenital adrenal hyperplasia, growth hormone deficiency Type IA, Kallmann syndrome, etc.).
4. infertility and recurrent abortions and describe the roles of meiotic errors, cytogenetic abnormalities and embryonic lethal mutations.
5. routine preconceptional screening for genetic disorders in couples with reproductive problems, and prior to assisted reproduction using donor sperm or donor oocyte.
VII.

Endocrinology of Pregnancy
VII. **ENDOCRINOLOGY OF PREGNANCY**

**TERMINAL OBJECTIVES:** The fellow should be able to discuss maternal and fetal physiology and pathophysiology and diagnose and manage endocrinopathy in obstetrical patients.

**ENABLING OBJECTIVES:**

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

1. feto-placental unit as it relates to the biochemistry, physiology and pathophysiology of steroid, protein and polypeptide hormones.
2. production of endometrial/decidual hormones.
3. selection and interpretation of endocrine assays during the course of pregnancy.
4. initiation of parturition, including the role of prostaglandins, cytokines, placental steroid hormones and adrenal steroids.
5. physiology of the fetal adrenal gland.
6. endocrine pathophysiology of preeclampsia-eclampsia, including the possible role of renin, angiotensin, aldosterone and prostaglandins.
7. physiology and pathophysiology of fetal hypothalamic-pituitary-gonadal function and pancreatic function.
8. altered maternal thyroid, adrenal and pancreatic function during pregnancy.
9. placental transfer of hormones and their effects on fetal development.
10. intra and postpartum diagnosis and management of thyroid, parathyroid, pancreatic and adrenal disease.
11. intra and postpartum diagnosis and management of hypothalamic-pituitary abnormalities.
VIII

Laboratory Capability
VIII. LABORATORY CAPABILITY

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

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 and receptor assay, as well as their statistical analysis.
2. biochemical methodology, including extraction, purification, and identification of steroid and protein hormones.
3. enzyme kinetics, as they relate to steroid and protein metabolism.
4. kinetics of production, distribution, interconversion and metabolism of specific hormones.
5. experimental design, data interpretation, and statistical analysis.
6. assay validation and description of standard curve, precision, specificity, bias, sensitivity, and assay drift.
7. validation of immunohistochemical, Western blotting and Northern/Southern blotting techniques.
IX.

Statistics
IX. **STATISTICS**

**TERMINAL OBJECTIVES:** The fellow should be able to design and analyze experiments utilizing conventional 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
   a. the question examined,
   b. the hypothesis,
   c. the sampling technique (including sampling bias),
   d. the expression and correlation of raw data,
   e. significance of the results,
   f. the conclusions, and
   g. the appropriate inferences which can be obtained from the data.
4. apply the following statistical tests:
   a. T-test, paired and independent,
   b. chi-square,
   c. life table analysis and other related statistical methods (e.g., Pearl's index, person year exposure),
   d. correlation analysis, and
   e. 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. define and calculate assay variation.
8. use the least squares regression line and calculate unknowns from standards in radioimmunoassay.
9. describe the methods of performing and limitations of prospective, cohort, and retrospective case control studies. Relate these techniques to the analysis of fecundibility and conception rates in infertile couples.
10. use one-way and two-way analysis of variance.
11. define the indications and use of Non-Parametric versus Parametric Tests.
12. describe the clinical assessment of a test to include sensitivity, specificity, positive and negative predictive values and relationship to prevalence.
13. understand the principles and pitfalls of meta-analysis.
X.

Clinical Diagnostic Techniques
X. CLINICAL DIAGNOSTIC TECHNIQUES

TERMINAL OBJECTIVES: In patients with endocrinologic disease or infertility the fellow should be able to take a comprehensive medical history, perform a general physical examination in addition to a specific gynecologic history and physical examination; select, organize, accomplish and interpret the diagnostic techniques needed to establish a diagnosis; evaluate co-existing disease or factors which may have a bearing on selection of and response to treatment; and evaluate the response to therapy.

ENABLING OBJECTIVES:

To accomplish this, the fellow should be able to describe, perform (or where appropriate, obtain) and interpret results of these diagnostic techniques:
1. **operative**, including biopsies of the endometrium, laparoscopy and hysteroscopy, and laparotomy.
2. **radiographic** and **imaging**, including hysterosalpingography, sonohysterography and genitography; sella turcica radiography; 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. Be able to perform and interpret dynamic endocrinologic testing of these systems. Describe clinical conditions (e.g., pregnancy, thyroid disease) in which endocrine test results may be altered.
4. **biochemical**, including blood chemistries performed on biologic fluids.
5. **obstetrical**, including endocrinologic and genetic evaluation of the fetus.
XI.

Neuroendocrine Function and Disease States
XI. NEUROENDOCRINE FUNCTION AND DISEASE STATES

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.

ENABLING OBJECTIVES:

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

1. anatomical-functional relationships of the hypothalamus, neurovascular, and target cells of the pituitary.
2. supra-hypothalamic structures and neuronal systems relevant to regulation of reproductive processes.
3. regulatory secretory activities of the pituitary hormones, including long and short-term biorhythmicity, and their target organ feedback systems.
4. biochemical basis of the neuroendocrine interactions and the use of neuropharmacological agents.
5. the site of production, biological action and control of secretion of oxytocin, vasopressin and neurophysins (the posterior hypophysis).
6. distribution and cellular characteristics of pituitary hormone producing cells with special reference to gonadotrope, somatotrope and lactotrope.
7. anatomical arrangement of hypothalamic-hypophyseal portal circulation.
8. circumventricular organs and blood brain barrier.
9. structure and function of pituitary reproductive hormones and neuropeptides (GnRH, TRH, somatostatin, pro-opiomelanocortin family, GHRH, CRH, vasopressin, etc.)
10. sexually dimorphic nuclei.
11. biochemical basis of neuropharmacology of agonists and antagonists.
12. neuroendocrine regulation of the menstrual cycle.
13. neuroendocrine function of the fetal-placental unit.
14. hypersecretory syndromes.
15. organic lesion and/or functional disorders of the hypothalamic-pituitary system.
16. ectopic hormone producing syndromes.
17. deficiencies of the hypothalamic-pituitary system (i.e.,
panhypopituitarism, Sheehan syndrome, Kallmann syndrome
and isolated pituitary hormone deficiencies).
XII.
Ovarian Function and Disease States
XII. OVARIAN FUNCTION AND DISEASE STATES

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.

ENABLING OBJECTIVES:

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

1. hypothalamus/pituitary control of ovarian function.
2. cyclic changes in endocrine activities within the ovary.
3. events leading to the development of a normal primary oocyte, germinal vesicle breakdown and completion of meiosis I.
4. synthesis and secretion of steroid 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 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. the 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. the pathophysiology of polycystic ovary syndrome.
XIII.

Thyroid Function and Disease States
XIII. **THYROID FUNCTION AND DISEASE STATES**

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

**ENABLING OBJECTIVES:**

In order to accomplish this, the fellow should be able to understand and discuss:

1. TRH-TSH-thyroid physiology.
2. the scope, diagnostic value, and limitations of laboratory testing for thyroid function (TSH, T4, T3 uptake, T3 RIA, TBG, free T4 and reverse T3).
3. the biosynthesis, control and metabolism of thyroid hormones.
4. the clinical and pathophysiological correlates 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 chorio-carcinoma.
10. the therapy of hyperthyroidism and hypothyroidism.
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.
XIV.

Adrenal Function and Disease States
XIV. ADRENAL FUNCTION AND DISEASE STATES

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

ENABLING OBJECTIVES:

A. In order to accomplish this, the fellow should be able to understand and discuss:
   1. regulation and secretion of adrenocortical hormones.
   2. clinical and laboratory assessment of adrenocortical function.
   3. pharmacology of naturally occurring and synthetic glucocorticoids and mineralocorticoids.
   4. adrenocortical hypo- and hyperactivity (e.g., Cushing syndrome, adenoma, carcinoma).
   5. genetics and biochemistry of specific steroid pathway defects in the congenital adrenal hyperplasias.
   6. effects of aberrations of adrenocortical function on hypothalamic-pituitary-ovarian function, including Nelson syndrome.
   7. aldosterone and disorders of the renin-angiotensin system.
   8. syndromes of excess catecholamine secretion.
   9. deficiencies of the adrenal, including hypoadrenalism resulting from pituitary or adrenal disease or hormonal medications in pregnant or non-pregnant women.
   10. steroid pathway enzyme defects and their effect on gonadal, development and function (17 alpha hydroxylase deficiency, 17 ketoreductase, 17-20 desmolase, etc.).

B. The fellow should be able to diagnose and treat any of the above abnormalities, including
   1. adrenal crisis.
   2. the requirements for long-term hormone replacement.
XV.

Androgen Disorders
XV. **ANDROGEN DISORDERS**

**TERMINAL OBJECTIVES:** The fellow should be able to discuss and be able to diagnose and treat patients with androgen disorders.

**ENABLING OBJECTIVES:**

To treat such patients, the fellow should be able to:

1. define secretion, physiology, and metabolism 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 which may result in virilism.
8. relate polycystic ovary syndrome to abnormal androgen secretion and hirsutism.
9. indicate the role of hormone assays in evaluating hyperandrogenism.
10. differentiate between adrenal and ovarian etiologies of normal androgen production, including neoplasms.
11. differentiate between non-classical variants and classical adrenal hyperplasia in terms of etiology, genetic factors, genital morphology, general metabolic effects and treatment.
12. describe the treatment of androgen excess.
13. describe mechanisms of androgen production and their control in the male, particularly as it relates to spermatogenesis and sexual behavior.
14. describe radiologic and imaging procedures commonly used for diagnosis in women with hyperandrogenism.
15. 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.
XVI.
Abnormal Uterine Bleeding
XVI. ABNORMAL UTERINE BLEEDING

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

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 used to describe abnormal uterine bleeding.
3. discuss anovulation and the resultant hormonal changes, indicating effects on the endometrium.
4. discuss the molecular effects of steroids in relation to proliferation of the endometrium, secretory changes, and menstruation, including spiral arteriolar change, lysosome stability and fibrinolysis.
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 treatment for abnormal bleeding, including the pharmacology and rationale for drugs used in its treatment.
7. discuss the indications for surgical management and the possible surgical techniques.
8. relate abnormal bleeding to such intercurrent diseases as obesity, blood dyscrasias, and thyroid disorders.
9. describe the coagulation abnormalities which may produce uterine bleeding.
10. describe the role of hysteroscopy and sonohysterography.
XVII.

Amenorrhea
XVII. AMENORREA

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

ENABLING OBJECTIVES:

To diagnose and treat such patients, the fellow should be able to understand and discuss:

1. the 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 which result in amenorrhea, including pharmacological effects.
3. growth and developmental aspects of amenorrhea as they relate to puberty and the menarche.
4. the clinical manifestations of diseases associated with amenorrhea (e.g., Sheehan syndrome, polycystic ovary syndrome, hypopituitarism, Kallmann syndrome, acromegaly, etc.).
5. the physiology and pathophysiology of prolactin secretion and the diagnosis and management of patients with hyperprolactinemia.
6. the interpretation of tests utilized in the evaluation of amenorrhea.
7. a rational diagnostic and therapeutic cost-effective approach to patients with amenorrhea.
8. the techniques for and ability to carry out the evaluation and therapy of patients who require ovulation induction.
XVIII.

Puberty
XVIII. PUBERTY

TERMINAL OBJECTIVES: The fellow should be able to discuss the physiology of growth and development as it relates to normal puberty, recognize deviations from normal, develop a plan for differential diagnosis and treat patients with abnormal pubertal development.

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; 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. pathophysiology, differential diagnosis, evaluation and appropriate therapy for delayed puberty.
5. sexual precocity syndromes including the pathophysiology, differential diagnosis, evaluation and appropriate therapy.
XIX.

Female Infertility
XIX. FEMALE INFERTILITY

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.

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, knowledge related to
   a. ovulatory disorders, including: correct utilization and interpretation of basal body temperatures, plasma progesterone and endometrial biopsy; diagnoses of causes of anovulation, including polycystic ovary syndrome, syndromes of inappropriate prolactin secretion, CNS-hypothalamic-pituitary syndromes and other GnRH causes; selection of ovulation induction utilizing clomiphene, human gonadotropin, bromocryptine and other agents; appropriate monitoring of ovulation induction including estrogen determinations, ultrasound, and LH assays.
   b. tubal disorders, including correct utilization and interpretation of studies of tubal function (e.g., hysterosalpingography and laparoscopy); indications for tubal reparative procedures including the specific indications for microsurgery and laser surgery.
   c. uterine factors, including: correct utilization and interpretation of studies of the uterine cavity, such as hysteroamogram and hysteroscopy and indications and techniques for corrective procedures.
   d. endometriosis and other peritoneal causes of infertility; knowledge of the medical management of endometriosis (preservation of fertility) (i.e., pseudopregnancy, danazol, continuous progestin, androgen therapy, and GnRH and its analogs); indications for surgery for these diseases; the rationale for pharmacologic adjuncts to surgical therapy.
e. cervical factors, including the several causes of cervical infertility (e.g. chronic cervicitis, inadequate mucus production and cervical antibody formation); utilization and interpretation of the various tests of cervical mucus-sperm interaction, application of current therapeutics (e.g. estrogen, antibiotic, cryosurgery, insemination - homologous and heterologous).

f. artificial insemination (cervical and intrauterine), including the:
   (1) indications and contraindications,
   (2) evaluation of male infertility,
   (3) screening of sperm donors to exclude transmissible infection (HIV, etc.) and genetic disorders and,
   (4) proper use of sperm cryo-banking.

g. adoption, including the indications for adoption, knowledge of appropriate counseling methods; familiarity with various local agencies and legal implications dealing with adoption.

h. outcome of various managements, including the
   (1) statistics related to the effectiveness of therapies used to treat various forms of infertility, and
   (2) use of life tables and meta-analyses.

i. unexplained infertility, including knowledge and evaluation of current methods of diagnosis and therapy.

4. cite the incidence of infertility as related to age and the prognosis for treatment of infertility.
XX.

Male Infertility
XX. MALE INFERTILITY

TERMINAL OBJECTIVES: The fellow should be able to evaluate the male partner and diagnose relative and absolute infertility and evaluate and discuss patients with these problems.

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 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, vas and testicular sperm aspiration) and their limitations.
   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. normal male sexuality throughout the life cycle.
XXI.

Recurrent
Abortion
XXI.  RECURRENT ABORTION

TERMINAL OBJECTIVE: The fellow should be able to diagnose and manage patients with recurrent pregnancy wastage.

ENABLING OBJECTIVES:

The fellow should be able to 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 lethality.
4. contribution of mullerian and other anatomical anomalies, congenital or acquired, to recurrent pregnancy losses.
5. contribution of endocrine factors, including hypothalamic, pituitary, thyroid, adrenal disorders and corpus luteum defects to recurrent pregnancy losses. Outline the arguments for and against each of these factors as a cause of infertility or recurrent pregnancy loss.
6. contribution of immunologic factors, including HLA types, lupus anticoagulant and anti-cardiolipin antibodies to recurrent pregnancy losses (antiphospholipid antibody syndromes).
7. contribution of systemic disorders, including diabetes and autoimmune disorders, to recurrent pregnancy losses.
8. contribution of environmental exposure, including radiation and teratogenic exposure, to recurrent pregnancy losses.
9. diagnostic and therapeutic plan for a given patient presenting with recurrent pregnancy losses.
10. realistic prognosis for patients undergoing and not undergoing different treatments.
XXII.

Psychologic and Sexual Implications of Reproductive Disease
XXII. PSYCHOLOGIC AND SEXUAL IMPLICATIONS OF REPRODUCTIVE DISEASE

TERMINAL OBJECTIVE: The fellow should be able to discuss the psychologic and sexual implications of disease or dysfunction of the endocrine reproductive system.

ENABLING OBJECTIVES:

The fellow should be able to understand and discuss the:

1. psychodynamics of growth and development, puberty and the establishment of the gender role.
2. antenatal hormone influence on subsequent behavior and psychologic function.
3. role of psychodynamics, including stress, in amenorrhea.
4. psychologic changes associated with infertility, and recurrent pregnancy loss.
5. psychologic 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 and infertility.
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 of women throughout the life cycle, and in particularly how this relates to reproductive endocrinology.
XXIII.

Surgical Techniques
XXIII. **SURGICAL TECHNIQUES**

**TERMINAL OBJECTIVES:** The fellow should be able to discuss the indications for, identify results and perform surgical procedures appropriate to reproductive endocrinology.

**ENABLING OBJECTIVES:**

A. To accomplish this, the fellow should be able to understand, discuss and perform the following surgical procedures associated with:

1. **fertility control**, including laparoscopy and laparotomy techniques used to reverse sterilization.
2. **diagnostic and therapeutic techniques**, including hysterosalpingography and endoscopy (laparoscopy and hysteroscopy).
3. **infertility surgery**, including all techniques used for
   a. reconstruction of uterine anomalies.
   b. myomectomies.
   c. resection of uterine synechiae.
   d. restoration of cervical competence.
   e. tuboplasty.
   f. resection of pelvic adhesions.
   g. ovarian cystectomies.
   h. staging and treating endometriosis, including pre and post operative medical adjunctive therapy.
4. **developmental disorders**, including all techniques used for
   a. neovaginal construction (dilation and surgical methods).
   b. correction of imperforate hymen.
   c. removal of vaginal septae.
   d. correction of müllerian abnormalities.
5. **ambiguous genitalia**, including
   a. assignment of sex of rearing for an infant with ambiguous genitalia.
   b. indications for surgical construction of unambiguous functioning female external genitalia and vagina (e.g. vaginoplasty, clitoral reduction, exteriorization of the vagina and feminizing genitoplasty).
c. indications and techniques for prophylactic gonadectomy.

B. The fellow should be able to:
   1. recognize surgical complications, including the incidence and prevention of immediate and late complications of reproductive and infertility surgery.
   2. cite the principles of the physical modalities used in reproductive surgery.
XXIV.

Techniques of Assisted Reproduction
XXIV. TECHNIQUES OF ASSISTED REPRODUCTION

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

ENABLING OBJECTIVES:

To accomplish this objective, 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 and relate this to the method of stimulation.
4. methodology for induction of preovulatory follicles and describe methods for monitoring follicular development.
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. technique of embryo transfer.
8. selection of patients for IVF, gamete intra-fallopian tube transfer (GIFT) and related techniques and know the expected results.
9. techniques for preservation of embryos.
10 techniques for embryonic diagnosis.
11. use of donor oocytes and embryos and how micromanipulation of gametes and fertilized eggs may be useful.
12. implications of different specific diagnoses and their expected success rates with treatment.
13. impact of maternal age on all stages of ART.
14. problem of multifetal pregnancy.
15. complications of ART (multifetal pregnancy, severe ovarian hyperstimulation syndrome, intra abdominal and retroperitoneal hemorrhage, infection) and their prevention and treatment.
XXV.

Physiology and Endocrinology of the Climacteric
XXV. PHYSIOLOGY AND ENDOCRINOLOGY OF THE CLIMACTERIC

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

ENABLING OBJECTIVES:

To accomplish this end the fellow should be able to understand and discuss the:

1. earliest changes in the endocrine function of the ovary that occur in the peri-menopausal period.
2. significance of changes in the production and intermediary metabolism of estrogen with advancing age.
3. significance of changes in lipid and bone metabolism that accompany physiologic aging in the female.
4. basic clinical assessment and subsequent monitoring techniques to evaluate the effects and progression of somatic and ovarian aging.
5. scope and limitations of biochemical assessments of serum lipids.
6. techniques used to assess bone turnover and bone composition, as well as use of vitamin D and calcitonin therapy.
7. approaches used in the management of osteoporosis, including bisphosphonates, calcitonin, fluoride, etc.
8. general approaches used to ameliorate the effects of aging and estrogen deficiency with respect to risks of breast and endometrial cancer.
9. advantages and disadvantages of hormone substitution therapy in physiologic menopause or other hypogonadal states.
10. techniques used for the surveillance of cardiovascular changes, serum lipid fluctuations, accelerated bone loss, and early malignancy.
11. different forms of hormone therapy (estrogen only, estrogen plus progestin, androgens and newer synthetic estrogens), modes or protocols for administration, side effects, contraindications and alternatives to hormone therapy.
12. normal psychologic changes with increasing age, the detection of early signs of maladjustment, and the symptoms suggestive of underlying psychiatric disease.
13. direct effects of steroids on vascular endothelium.
14. hormonal, non-hormonal and lifestyle recommendations for women in their 50's, 60's and beyond.
XXVI.

Contraception
XXVI. CONTRACEPTION

TERMINAL OBJECTIVE: The fellow should be familiar with methods of contraception, and be able to select the most appropriate method for a high risk patient.

ENABLING OBJECTIVES:

To accomplish the terminal objective the fellow should be able to:

1. describe the various steroids used in contraceptive formulations, and be able to relate their chemical structure to potency, effective route of administration, intermediary metabolism, metabolic clearance, and metabolic side effects.
2. describe the advantages, disadvantages, and failure rates of the various contraceptive methods.
3. discuss the specific type 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 of male contraception.
XXVII.

Research and Thesis
XXVII. RESEARCH AND THESIS

TERMINAL OBJECTIVE: The fellow should be able to participate fully in the theoretical and technical aspects of clinical and/or basic science research projects.

ENABLING OBJECTIVES:

The fellow should write a thesis which is a scholarly publication and be able to defend it according to the following outline.

1. **Hypothesis**
   a. What are the study objectives?
   b. What is the population to be studied?
   c. What is the population to which the investigators intend to apply their findings?

2. **Design of the Investigation**
   a. Was the study an experiment, case control study, randomized clinical trial, planned observations, or a retrospective analysis of records?
   b. Are there possible sources of sample selection bias?
   c. How comparable is the control group?
   d. What is the statistical (study) power?

3. **Observations**
   a. Are there clear definitions of the terms used? (i.e., diagnostic criteria, inclusion criteria, measurements made and outcome variables)
   b. Are the observations reliable and reproducible?
   c. What is the sensitivity, specificity and predictive values of the methods?

4. **Presentation of Findings**
   a. Are the findings presented clearly, objectively, and in sufficient detail?
   b. Are the findings internally consistent? (i.e., do the numbers add up properly and can the different tables be reconciled, etc.)

5. **Analysis of the Results**
   a. Are the data worthy of statistical analysis? If so, are the methods of analysis appropriate to the source and nature of the data?
   b. Is the analysis correctly performed and interpreted?
c. Is there sufficient analysis to determine whether “significant differences” may, in fact, be due to a lack of comparability of the groups? (i.e., age, sex, clinical characteristics, or in other relevant variables)
d. Is design of the study appropriate for solving the stated problems?
e. Is there an improper use of statistical techniques?
f. Is there mention of the type of test used or the significance level?
g. Is there use of measured sensitivity without specificity?

6. **Conclusions or Summary**
   a. Which conclusions are “justified” by the findings?
   b. Are the conclusions relevant to the hypothesis?

7. **Redesign the Study**
   If the study could be improved, the candidate should suggest a revised experimental design that would provide reliable and valid information relevant to the questions under study.

8. **Breadth and Depth of Subject Matter**
   Is the candidate knowledgeable about the reference or cited material?