

Endocrinology, Diabetes and Metabolism Fellowship Program Curriculum

OVERALL GOALS AND OBJECTIVES

Goals

This subspecialty training program in endocrinology, diabetes and metabolism is designed to provide advanced training and experience that will allow the trainee to acquire the knowledge, skills, attitudes and experience required to satisfy the competencies needed by a consultant in this field. The program is designed to fulfill the needs of those trainees who anticipate their future activities to be solely the clinical practice of endocrinology, those who expect to function as clinician-educators and those who intend to pursue careers in clinical and/or basic endocrine research. The program recognizes that some trainees may evolve into specialists whose activities encompass more than one of the above career paths. The teaching environment and educational experiences for trainees will equip them to become strong clinicians, educators and investigators.

Specific Competency-Based Goals and Objectives

Our program aims to provide training that supports each fellow's development of the five ACGME Competencies:

- Patient Care and Procedural Skills
- Medical Knowledge
- Practice-based Learning and Improvement
- Interpersonal and Communication Skills
- Professionalism
- Systems-based Practice.

Expectations for each of these are delineated clearly in the ACGME Program Requirements for Graduate Medical Education in Endocrinology, Diabetes and Metabolism. (See attachment showing section IV.A.5)

Fellows are expected to show increasing competency in each of these areas in year 1 and throughout year 2 such that by the end of year 2 the trainee will be prepared for independent practice as a consultant in endocrinology, diabetes, and metabolism.

Specific competency based objectives of our program include (but are not limited to):

A. Patient care

The program will provide training in diagnosis and management of endocrine diseases including:

1. History and physical examination with emphasis on examination of the thyroid, feet, breast, and male and female reproductive organs and other physical exam elements specific to endocrine disorders
2. Selection and interpretation of endocrine biochemical tests
3. Selection and interpretation of imaging procedures such as sonography, radionuclide scans, computerized axial tomography, magnetic resonance imaging, positron emission tomography, etc.
4. Performance of Fine needle aspiration of the thyroid and interpretation of cytology and pathology (year 2).
5. Management of insulin pump therapy in patients with diabetes mellitus and interpretation of continuous glucose monitor downloads.
6. Appropriate use and interpretation of skeletal dual photon absorptiometry.
7. Understanding pharmacotherapy for endocrine disorders and appropriate use of surgery, radiation therapy, treatment with radioisotopes, etc. of relevant endocrine disorders.
8. Selection and management of patients for whole organ or islet cell transplantation.

B. Medical Knowledge.

The program will provide training in:

1. Endocrine biochemistry, genetics, developmental biology, physiology and pathophysiology.
2. Hormone action including signal transduction pathways as well as the biology of hormone receptors and feedback inter-relationships
3. Diagnosis and management of disorders in endocrinology, diabetes and metabolism

Details of the scope of medical knowledge expected to be gained by fellows is delineated in the Program Curriculum which can be found on our program webpage.

C. Professionalism

The program will provide training in professionalism, including peer interactions, communication with patients, their families and other health care providers, confidentiality and avoidance of conflict of interest. Professional behavior will be demonstrated by faculty in the program and expectations are also set out during fellow orientation.

D. Practice-Based Learning

1. The trainee will begin a clinical or basic research project in Endocrinology, Diabetes and Metabolism in year 1, and provide a written report and oral presentation of rationale and results by the end of year 2.
2. The program will provide training in the understanding of existing and emerging endocrine literature.
3. Ongoing mentoring and semi-annual reviews will encourage self-reflection and personal goal setting on the part of the fellow.

E. Systems-Based Learning

1. The program will provide training in the transition of diabetes care between the outpatient and inpatient settings.
2. The trainees will participate in quality improvement projects and committees during their training.

ADRENAL

INTRODUCTION

A complete understanding of normal physiology and the pathologic diseases affecting the adrenal gland is essential for the endocrinologist and should be part of education curriculum and training for fellows. Adrenal disorders can originate at various functional levels (e.g., hypothalamus, pituitary, adrenal) and be caused by genetic or environmental factors. Adrenal disorders may be associated with overproduction or underproduction of adrenal hormones and/or nonfunctioning (benign or malignant) neoplastic lesions. Comprehensive appreciation of adrenal pathophysiology also includes recognizing how adrenal dysfunction affects other body systems, including the potential effects on endocrine and nonendocrine systems (e.g., metabolic, musculoskeletal, dermatologic, cardiovascular), some of which may be life-threatening. Fellows should be competent in the diagnosis and treatment of adrenal disorders.

MEDICAL KNOWLEDGE

Fellows must demonstrate knowledge about established and evolving biomedical, clinical, and cognate (eg, epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.

Topic	Fundamental	Advanced
BASIC PHYSIOLOGIC PRINCIPLES, ADRENAL BIOLOGY		
Explain adrenal gland embryology, anatomy, and zonation.	√	
Describe steroid biosynthetic pathways, including specific enzymatic steps.		√
Describe steroid metabolism.		√
Explain regulation of the hypothalamic-pituitary-adrenal axis, including normal patterns of corticotropin and cortisol secretion.	√	
Describe the renin-angiotensin-aldosterone system and regulation of mineralocorticoid secretion.	√	
Explain regulation of adrenal sex steroid production, secretion, and extraglandular metabolism of adrenal sex steroids.		√
Describe catecholamine biosynthesis, secretion, and metabolism.	√	
List factors that affect measured levels of adrenal regulatory hormones (eg, corticotropin, renin), steroids, and catecholamines and their metabolites (eg, in plasma, urine, and saliva).	√	
Explain the molecular and cellular mechanisms, as well as physiologic effects, of glucocorticoids, mineralocorticoids, sex steroids, and catecholamines.		√

GLUCOCORTICOIDS

Cushing Syndrome

Clinical Presentation

Summarize the symptoms and signs of Cushing syndrome resulting from chronic exposure to excess glucocorticoid, including progressive obesity, dermatologic manifestations, menstrual irregularities, signs of adrenal androgen excess, proximal muscle wasting and weakness, bone loss, glucose intolerance, cardiovascular disease, thromboembolic events, neuropsychological changes and impaired cognition, and infection and impaired immune function.

√

Differential Diagnosis (Adrenal vs Ectopic vs Pituitary vs Exogenous vs Physiologic)

Perform the differential diagnosis of Cushing syndrome to determine the source of cortisol excess, which could be adrenal, ectopic, or pituitary.

√

Diagnostic Tests

Select and interpret results from appropriate case-detection (screening) tests, which may include measurement of 24-hour urinary cortisol excretion, late-night salivary or serum cortisol measurement, or 1-mg overnight dexamethasone suppression.

√

Select and interpret results from appropriate diagnostic tests to determine the source of glucocorticoid excess, which may include measurement of corticotropin, inferior petrosal sinus sampling, diurnal serum cortisol measurement, corticotropin-releasing hormone stimulation testing, vasopressin stimulation testing, and/or dexamethasone suppression testing (with or without corticotropin-releasing hormone).

√

Discuss the diagnostic challenge of glucocorticoid excess in the setting of pregnancy.

√

Determine when genetic testing is appropriate in the setting of familial hypercortisolism.

√

Select the appropriate imaging modality on the basis of the biochemical profile.

√

Exogenous Cushing Syndrome (Iatrogenic or Factitious)

Obtain a careful history to evaluate for exogenous glucocorticoid intake as the source of hypercortisolism (eg, prescribed glucocorticoid, surreptitious intake of glucocorticoid, medications that decrease glucocorticoid metabolism).

√

Pseudo-Cushing Syndrome

Distinguish physiologic hypercortisolism that can occur in disorders other than Cushing syndrome (eg, in patients with physical or psychological stress, severe obesity, malnutrition, or chronic alcoholism) from Cushing syndrome itself.		√
<i>Adrenal Neoplasm</i>		
Evaluate for adrenal adenoma, carcinoma, and micronodular and macronodular hyperplasia.	√	
<i>Ectopic Corticotropin/Corticotropin-Releasing Hormone</i>		
Evaluate for tumors associated with the ectopic ACTH (corticotropin) syndrome or the ectopic CRH (corticotropin-releasing hormone) syndrome.	√	
<i>Treatment</i>		
Depending on the etiology of Cushing syndrome, recommend the best initial treatment, which may include cessation of exogenous glucocorticoid, surgical excision of tumors, unilateral or bilateral adrenalectomy, or in certain circumstances, medical therapy.		√
Recommend appropriate long-term management depending on the initial treatment strategy and resolution of signs and symptoms, which may include postoperative glucocorticoid therapy, mineralocorticoid replacement, medical therapy, as well as therapy for associated complications (osteoporosis, etc).		√
Adrenal Insufficiency		
<i>Primary Adrenal Insufficiency</i>		
Summarize the symptoms and signs of acute adrenal crisis, including shock, abdominal tenderness, fever, weight loss, and electrolyte abnormalities.	√	
Summarize the symptoms and signs of chronic primary adrenal insufficiency, including signs of glucocorticoid, mineralocorticoid, and androgen deficiencies; chronic malaise; lassitude; fatigue; generalized weakness; anorexia; weight loss; gastrointestinal complaints; psychiatric manifestations; hypotension; hyperpigmentation; vitiligo; electrolyte abnormalities; and hypoglycemia.	√	
Recognize that adrenal insufficiency can be a sign of adrenoleukodystrophy.	√	
Recommend treatment approaches for acute adrenal crisis and chronic adrenal insufficiency, which includes choice of glucocorticoid and the appropriate regimen and mineralocorticoid replacement.	√	
<i>Secondary/Tertiary Adrenal Insufficiency</i>		
Summarize the symptoms and signs of secondary adrenal insufficiency, which are similar to those of primary adrenal insufficiency (except for	√	

the absence of hyperpigmentation, dehydration, and hyperkalemia) and which may include severe headache and/or vision disturbances and/or cranial nerve abnormalities.		
Evaluate for other pituitary hormone deficiencies in patients with secondary adrenal insufficiency.	√	
Recommend treatment approaches for secondary adrenal insufficiency depending on etiology.	√	
<i>Diagnosis</i>		
Guide the diagnosis of adrenal insufficiency, which may include measurement of cortisol, corticotropin, renin, and aldosterone; corticotropin stimulation test; metyrapone test; insulin-induced hypoglycemia test, and corticotropin-releasing hormone test.	√	
Glucocorticoid Therapy		
Describe glucocorticoid and mineralocorticoid efficacy of pharmacologically available agents (hydrocortisone, prednisone, dexamethasone, etc).	√	
Guide appropriate tapering regimens for cessation of glucocorticoids.	√	
Diagnose steroid withdrawal syndrome.		√
<i>Stress Doses</i>		
Recognize the importance of medical alert identification.	√	
Outline sick-day protocols with increased oral dosages of glucocorticoid.	√	
Guide the use of parenterally administered glucocorticoids for adrenal crisis or surgical procedures.	√	
Glucocorticoid Resistance		
Summarize the symptoms and signs of glucocorticoid resistance, including hypertension and hypokalemic alkalosis, hirsutism, male-pattern baldness, menstrual abnormalities and infertility in females, isosexual precocious puberty, and abnormal spermatogenesis and infertility in males.		√
Recommend management approaches for glucocorticoid resistance.		√
MINERALOCORTICOIDS		
Hyperaldosteronism		
<i>Primary Hyperaldosteronism</i>		
Summarize the symptoms and signs of primary aldosteronism, including hypertension, variable presence of hypokalemia, and lack of edema.	√	

Distinguish between the most common subtypes of primary hyperaldosteronism—aldosterone-producing adenomas and bilateral adrenal hyperplasia.	√	
<i>Pseudohyperaldosteronism</i>		
Differentiate among other causes of hypertension and hypokalemia such as Liddle syndrome, licorice ingestion, 17 α -hydroxylase deficiency/17,20-lyase deficiency, and 11 β -hydroxylase deficiency.		√
<i>Diagnostic Tests</i>		
Recommend case-detection testing in appropriate patients (those with hypertension and hypokalemia, severe hypertension or drug-resistant hypertension, hypertension with adrenal incidentaloma, hypertension and family history of early-onset hypertension, all hypertensive first-degree relatives of patients with primary aldosteronism).	√	
Explain the initial case-detection approach (plasma aldosterone concentration, plasma renin activity, and ratio of plasma aldosterone concentration to plasma renin activity).	√	
Differentiate among the tests used for diagnosis confirmation (saline infusion test, oral sodium loading, fluorocortisone suppression test, captopril challenge test).	√	
Describe the tests used for subtype diagnosis, including adrenal computed tomography and adrenal venous sampling.	√	
Determine when genetic testing is appropriate in the setting of familial hyperaldosteronism.		√
<i>Treatment</i>		
Recommend treatment strategies for hyperaldosteronism, which may include laparoscopic adrenalectomy, mineralocorticoid receptor antagonist therapy, and potassium-sparing diuretics.	√	
Manage hyperaldosteronism in the context of pregnancy.		√
Hypoaldosteronism		
Summarize the clinical manifestations of hypoaldosteronism, including hyperkalemia and mild hyperchloremic metabolic acidosis.	√	
Differentiate among disorders of reduced aldosterone production (eg, hyporeninemic hypoaldosteronism, primary adrenal insufficiency, congenital isolated hypoaldosteronism, pseudohypoaldosteronism type 2) vs aldosterone resistance (eg, potassium-sparing diuretics, antibiotics, pseudohypoaldosteronism type 1).	√	
Recommend appropriate diagnostic testing, including measurement of plasma renin activity, serum aldosterone, and serum cortisol after administration of a loop diuretic.		√

Recommend treatment strategies for hypoaldosteronism, which may include mineralocorticoid therapy and glucocorticoid therapy, depending on the cause of the hormone deficiency.	√	
ADRENAL ANDROGENS		
Congenital Adrenal Hyperplasia		
Differentiate among the 3 main phenotypes of 21-hydroxylase deficiency: classic salt-losing, classic non-salt-losing, and nonclassic (late-onset).	√	
Explain the genetics of 21-hydroxylase deficiency due to <i>CYP21A</i> mutations.	√	
Differentiate among the less common forms of congenital adrenal hyperplasia due to 11β-hydroxylase deficiency, 17α-hydroxylase deficiency/17,20-lyase deficiency, and 3β-hydroxysteroid dehydrogenase deficiency.		√
Guide the diagnosis of congenital adrenal hyperplasia with measurement of 17-hydroxyprogesterone and electrolytes, as well as 11-deoxycortisol, 17-hydroxypregnenolone, cortisol, androstenedione, and dehydroepiandrosterone to define the metabolic defect.		√
Appropriately recommend genetic testing and genetic counseling.		√
Recommend appropriate treatment for congenital adrenal hyperplasia (in pregnant and nonpregnant individuals), which includes providing adequate glucocorticoid to reduce hyperandrogenemia and excessive corticotropin-releasing hormone and corticotropin secretion, as well as mineralocorticoid when indicated..		√
ADRENAL INCIDENTALOMA		
Recall the prevalence of adrenal masses identified incidentally on imaging performed for other reasons.	√	
Radiographic Appearance		
Identify the imaging phenotype of benign adenomas, pheochromocytomas, adrenocortical carcinomas, and adrenal metastases, taking into account size, shape, computed tomography attenuation value (Hounsfield units), rapidity of contrast washout, signal intensity, and homogeneous or inhomogeneous density.	√	
Diagnostic Studies		
Guide the appropriate evaluation for an adrenal incidentaloma, which may include assessment for hormonal secretion (eg, plasma fractionated	√	

metanephrines), dexamethasone suppression testing, measurement of plasma aldosterone concentration and plasma renin activity, and fine-needle aspiration biopsy.		
ADRENAL MEDULLA		
Pheochromocytoma		
<i>Clinical Presentation</i>		
Summarize the signs and symptoms of catecholamine-secreting tumors, which include sustained or paroxysmal hypertension, episodic headaches, sweating, and tachycardia.	√	
<i>Diagnostic Tests</i>		
List indications for testing (eg, patients with classic signs and symptoms, hyperadrenergic spells, early-onset hypertension, resistant hypertension, adrenal incidentaloma, family history of a syndrome that predisposes to catecholamine-secreting tumors).	√	
Evaluate for pheochromocytoma by biochemical confirmation of catecholamine hypersecretion, followed by localization of the tumor with imaging studies.	√	
Identify which medications can interfere with interpretation of biochemical testing for catecholamine-secreting tumors and should be discontinued before diagnostic evaluation.	√	
Select and interpret results from biochemical tests, which may include fractionated catecholamines and metanephrines in a 24-hour urine collection and plasma fractionated metanephrines.	√	
Apply available imaging techniques appropriately to localize pheochromocytoma, including computed tomography, magnetic resonance imaging, meta-iodobenzylguanidine scintigraphy, fluorodeoxyglucose positron emission tomography, and 68-Ga-DOTATATE PET.		√
Recommend genetic testing and genetic counseling in appropriate clinical situations.		
<i>Treatment</i>		
Guide treatment of pheochromocytoma, including medical preparation for surgery with α - and β -adrenergic blockade and adrenalectomy.		√
Manage acute hypertensive crises.	√	
Manage pheochromocytoma in the context of pregnancy.		√
<i>Familial Disorders Associated With Pheochromocytoma</i>		

Diagnose and manage familial disorders associated with pheochromocytoma such as von Hippel–Lindau syndrome, multiple endocrine neoplasia type 2, and neurofibromatosis type 1.		√
Recommend genetic testing and genetic counseling in appropriate clinical situations.		√
Extra-Adrenal Catecholamine-Secreting Paragangliomas		
Distinguish pheochromocytoma from catecholamine-secreting paragangliomas.		√
Evaluate for catecholamine-secreting paragangliomas by biochemical confirmation of catecholamine hypersecretion, followed by localization of the tumor with imaging studies.		√
Diagnose and manage familial disorders associated with paragangliomas such as familial paraganglioma (<i>SDH</i> mutations) and rarely neurofibromatosis type 1, multiple endocrine neoplasia type 2, von Hippel–Lindau syndrome, and Carney-Stratakis dyad.		√
Recommend genetic testing and genetic counseling in appropriate clinical situations.		√
ADRENAL CANCER		
Distinguish adrenocortical adenomas from adrenocortical carcinoma.		√
Identify hereditary cancer syndromes associated with adrenocortical cancer, including Li-Fraumeni syndrome, Beckwith-Wiedemann syndrome, and multiple endocrine neoplasia type 1.		√
Summarize the symptoms and signs of adrenocortical carcinoma, including clinical syndromes of hormone excess (eg, Cushing syndrome, virilization) and manifestations related to tumor growth (eg, abdominal or flank pain).	√	
Guide the evaluation for adrenocortical carcinoma, which may include hormonal evaluation and radiographic studies.		√
Describe various staging systems used for adrenocortical carcinoma.		√
Recommend treatment of adrenocortical carcinoma, which includes initial surgery and possibly adjuvant medical and/or radiation therapy.		√
ADRENAL IMAGING AND PROCEDURES		
Imaging		
Differentiate among imaging techniques for adrenal disease, including computed tomography, magnetic resonance imaging, meta-		√

iodobenzylguanidine scintigraphy, indium-labeled pentetreotide scintigraphy, fluorodeoxyglucose positron emission tomography, and 68-Ga-DOTATATE PET.		
Interpret imaging phenotype to predict the histologic type of adrenal disease.	√	
<i>Benign Adenomas</i>		
Identify the imaging characteristics of benign adrenal adenomas, including round shape, homogenous density, diameter <4 cm, unilateral location, low unenhanced computed tomography attenuation values (<10 Hounsfield units), rapid contrast medium washout, and isointensity with the liver on T1- and T2-weighted magnetic resonance imaging.	√	
<i>Pheochromocytomas</i>		
Identify the imaging characteristics of pheochromocytomas, including variable size, sometimes bilateral location, high unenhanced computed tomography attenuation values (>20 Hounsfield units), increased vascularity, delayed contrast medium washout, high signal intensity on T2-weighted magnetic resonance imaging, and cystic and hemorrhagic changes.	√	
<i>Adrenocortical carcinoma</i>		
Identify the imaging characteristics of adrenocortical carcinoma, including irregular shape, inhomogeneous density, tumor calcification, diameter >4 cm, unilateral location, high unenhanced computed tomography attenuation values (>20 Hounsfield units), delayed contrast medium washout, hypointensity compared with liver on T1-weighted magnetic resonance imaging and intermediate signal intensity on T2-weighted magnetic resonance imaging, evidence of local invasion or metastases, and elevated standardized uptake value on fluorodeoxyglucose positron emission tomography.	√	
<i>Adrenal metastases</i>		
Identify the imaging characteristics of adrenal metastases, including irregular shape, inhomogeneous density, tendency to be bilateral, high unenhanced computed tomography attenuation values (>20 Hounsfield units), delayed contrast medium washout, isointensity with the liver (or slightly less intense) on T1- and T2-weighted magnetic resonance imaging, and elevated standardized uptake value on fluorodeoxyglucose positron emission tomography.		√
Procedures		
List indications for computed tomography-guided adrenal fine-needle aspiration biopsy.		√

List indications for adrenal venous sampling for aldosterone.		√
Interpret results from adrenal venous sampling (with or without cosyntropin stimulation).		√

TEACHING METHODS AND EVALUATION

Much teaching occurs one-on-one with attendings during outpatient clinics and on inpatient hospital rounds. Active learning occurs as fellows participate in patient care under the supervision and guidance of the attending. In addition, a full range of topics are reviewed in didactic sessions at weekly conferences and in the core curriculum/board review weekly sessions. Fellows are also expected to engage in self-directed study guided by the curriculum. Evaluation includes attending review of fellows knowledge base and medical reasoning during clinic and hospital rounds. In addition, the in-training exam taken in February of every year provides a loose benchmark of medical knowledge progression through the fellowship.

SUGGESTED READING

Asterisks denote references that are designated for residents, students, or endocrine fellows early in their training. While some of the references are organized under “Diagnosis” and “Management” subheadings, please note there may be overlapping content.

GENERAL READING, PHYSIOLOGY, EPIDEMIOLOGY	
*Melmed S, Polonsky KS, Larsen PR, Kronenberg HM, eds. <i>Williams Textbook of Endocrinology</i> . 13th ed. Philadelphia, PA: Saunders; 2015.	Textbook
*Jameson JL, De Groot LJ, de Kretser DM, Giudice LC, Grossman AB, Melmed S, Potts JT Jr, Weir GC, eds. <i>Endocrinology: Adult and Pediatric</i> . 7th ed. Philadelphia, PA: Elsevier Saunders; 2010.	Textbook
*Snyder PM. Minireview: regulation of epithelial Na ⁺ channel trafficking. <i>Endocrinology</i> . 2005;146(12):5079-5085.	Article
*Herrmann M. Standard and molecular cytogenetics of endocrine tumors. <i>Am J Clin Pathol</i> . 2003;119(Suppl):S17-S38	Article
*The adrenal cortex and the adrenal medulla. In: Grossman A, ed. <i>Clinical Endocrinology</i> . 2nd ed. London: Blackwell Science Ltd; 1998.	Textbook
*Disturbances in control of body fluid volume and composition. In: BM Brenner, ed. <i>Brenner and Rector's The Kidney</i> . 5th ed. Philadelphia, PA: WB Saunders; 1996.	Textbook
*Adrenal cortex. In: DeGroot LJ, Besser M, Burger HG, Jameson JL, Loriaux DL, Marshall JC, Odell WD, Potts JT Jr, Rubenstein AH, eds. <i>Endocrinology</i> . 3rd ed. Philadelphia, PA: WB Saunders; 1995.	Textbook

*Loriaux L. The adrenal glands. In: Becker KL, Bilezikian JP, Bremner WJ, Hung W, Kahn CR, Loriaux DL, Nysten ES, Rebar RW, Robertson GL, Wartofsky L, eds. <i>Principles and Practice of Endocrinology and Metabolism</i> . 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins Publishers; 1995.	Textbook
GLUCOCORTICOIDS	
Cushing Syndrome: Diagnosis	
*Nieman LK, Biller BM, Findling JW, et al. The diagnosis of Cushing's syndrome: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab</i> . 2008;93(5):1526-1540.	Clinical Practice Guideline
*Lacroix A, Feelders RA, Stratakis CA, Nieman LK. Cushing's syndrome. <i>Lancet</i> . 2015;386(9996):913-927.	Article
Beuschlein F, Fassnacht M, Assié G, et al. Constitutive activation of PKA catalytic subunit in adrenal Cushing's syndrome. <i>N Engl J Med</i> . 2014;370(11):1019-1028.	Article
Kirschner LS. Medicine. A unified cause for adrenal Cushing's syndrome. <i>Science</i> . 2014;344(6186):804-805.	Article
Assié G, Libé R, Espiard S, et al. <i>ARMC5</i> mutations in macronodular adrenal hyperplasia with Cushing's syndrome. <i>N Engl J Med</i> . 2013;369(22):2105-2114.	Article
Lacroix A. Heredity and cortisol regulation in bilateral macronodular adrenal hyperplasia. <i>N Engl J Med</i> . 2013;369(22):2147-2149.	Article
Louiset E, Duparc C, Young J, et al. Intraadrenal corticotropin in bilateral macronodular adrenal hyperplasia. <i>N Engl J Med</i> . 2013;369(22):2115-2125.	Article
Anselmo J, Medeiros S, Carneiro V, et al. A large family with Carney complex caused by the S147G PRKAR1A mutation shows a unique spectrum of disease including adrenocortical cancer. <i>J Clin Endocrinol Metab</i> . 2012;97(2):351-359.	Article
Almeida MQ, Harran M, Bimpaki EI, et al. Integrated genomic analysis of nodular tissue in macronodular adrenocortical hyperplasia: progression of tumorigenesis in a disorder associated with multiple benign lesions. <i>J Clin Endocrinol Metab</i> . 2011;96(4):E728-E738.	Article
Chiodini I. Clinical review: diagnosis and treatment of subclinical hypercortisolism. <i>J Clin Endocrinol Metab</i> . 2011;96(5):1223-1236.	Article
Sharma ST, Nieman LK. Cushing's syndrome: all variants, detection, and treatment. <i>Endocrinol Metab Clin North Am</i> . 2011;40(2):379-391.	Article
Libé R, Coste J, Guignat L, et al. Aberrant cortisol regulations in bilateral macronodular adrenal hyperplasia: a frequent finding in a prospective study of 32 patients with overt or subclinical Cushing's syndrome. <i>Eur J Endocrinol</i> . 2010;163(1):129-138.	Article

Morelli V, Masserini B, Salcuni AS, et al. Subclinical hypercortisolism: correlation between biochemical diagnostic criteria and clinical aspects. <i>Clin Endocrinol (Oxf)</i> . 2010;73(2):161-166.	Article
Lacroix A. ACTH-independent macronodular adrenal hyperplasia. <i>Best Pract Res Clin Endocrinol Metab</i> . 2009;23(2):245-259.	Article
Carroll T, Raff H, Findling JW. Late-night salivary cortisol measurement in the diagnosis of Cushing's syndrome. <i>Nat Clin Pract Endocrinol Metab</i> . 2008;4(6):344-350.	Article
Findling JW, Raff H. Cushing's Syndrome: important issues in diagnosis and management. <i>J Clin Endocrinol Metab</i> . 2006;91(10):3746-3753.	Article
Newell-Price J, Bertagna X, Grossman AB, Nieman LK. Cushing's syndrome. <i>Lancet</i> . 2006;367(9522):1605-1617.	Article
Findling JW, Raff H. Newer diagnostic techniques and problems in Cushing's disease. <i>Endocrinol Metab Clin North Am</i> . 1999;28(1):191-210.	Article
Graham KE, Samuels MH, Nesbit GM, et al. Cavernous sinus sampling is highly accurate in distinguishing Cushing's disease from ectopic adrenocorticotropin syndrome and in predicting intrapituitary tumor location. <i>J Clin Endocrinol Metab</i> . 1999;84(5):1602-1610.	Article
Newell-Price J, Trainer P, Besser M, Grossman A. The diagnosis and differential diagnosis of Cushing's syndrome and pseudo-Cushing's states. <i>Endocr Rev</i> . 1998;19(5):647-672.	Article
Raff H, Raff JL, Findling JW. Late-night salivary cortisol as a screening test for Cushing's syndrome. <i>J Clin Endocrinol Metab</i> . 1998;83(8):2681-2686.	Article
Yanovski JA, Cutler GB Jr, Chrousos GP, Nieman LK. The dexamethasone-suppressed corticotropin-releasing hormone stimulation test differentiates mild Cushing's disease from normal physiology. <i>J Clin Endocrinol Metab</i> . 1998;83(2):348-352.	Article
Stratakis CA. Genetics of adrenocortical tumors: Carney complex. <i>Ann Endocrinol (Paris)</i> . 2001;62(2):180-184.	Article
Cushing Syndrome: Management	
Fleseriu M. Medical treatment of Cushing disease: new targets, new hope. <i>Endocrinol Metab Clin North Am</i> . 2015;44(1):51-70.	Article
Chiodini I, Morelli V, Salcuni AS, et al. Beneficial metabolic effects of prompt surgical treatment in patients with an adrenal incidentaloma causing biochemical hypercortisolism. <i>J Clin Endocrinol Metab</i> . 2010;95(6):2736-2745.	Article
Mitchell IC, Auchus RJ, Juneja K, et al. "Subclinical Cushing's syndrome" is not subclinical: improvement after adrenalectomy in 9 patients [published correction appears in <i>Surgery</i> . 2008;143(2):302]. <i>Surgery</i> . 2007;142:900-905.	Article
Adrenal Insufficiency: Diagnosis	

*Bancos I, Hahner S, Tomlinson J, Arlt W. Diagnosis and management of adrenal insufficiency. <i>Lancet Diabetes Endocrinol.</i> 2015;3(3):216-226.	Article
Betterle C, Morlin L. Autoimmune Addison's disease. <i>Endocr Dev.</i> 2011;20:161-172.	Article
*Grossman AB. Clinical Review#: the diagnosis and management of central hypoadrenalism. <i>J Clin Endocrinol Metab.</i> 2010;95(11):4855-4863.	Article
Bratland E, Bredholt G, Mellgren G, Knappskog PM, Mozes E, Husebye ES. The purification and application of biologically active recombinant steroid cytochrome P450 21-hydroxylase: the major autoantigen in autoimmune Addison's disease. <i>J Autoimmun.</i> 2009;33(1):58-67.	Article
Husebye E, Løvås K. Pathogenesis of primary adrenal insufficiency. <i>Best Pract Res Clin Endocrinol Metab.</i> 2009;23(2):147-157.	Article
*Salvatori R. Adrenal insufficiency. <i>JAMA.</i> 2005;294(19):2481-2488.	Article
Betterle C, Greggio NA, Volpato M. Clinical review 93: autoimmune polyglandular syndrome type 1. <i>J Clin Endocrinol Metab.</i> 1998;83(4):1049-1055.	Article
Adrenal Insufficiency: Management	
Quinkler M, Hahner S. What is the best long-term management strategy for patients with primary adrenal insufficiency? <i>Clin Endocrinol (Oxf).</i> 2012;76(1):21-25.	Article
Arlt W. The approach to the adult with newly diagnosed adrenal insufficiency. <i>J Clin Endocrinol Metab.</i> 2009;94(4):1059-1067.	Article
Løvås K, Husebye ES. Replacement therapy for Addison's disease: recent developments. <i>Expert Opin Investig Drugs.</i> 2008;17(4):497-509.	Article
Sprung CL, Annane D, Keh D, et al; CORTICUS Study Group. Hydrocortisone therapy for patients with septic shock. <i>N Engl J Med.</i> 2008;358(2):111-124.	Article
Kleerekoper M, Schiebinger R, Gutai JP. Steroid therapy for adrenal disorders--getting the dose right. <i>J Clin Endocrinol Metab.</i> 1997;82(12):3923-3925.	Article
Glucocorticoid Resistance: Diagnosis and Management	
*Nicolaidis NC, Charmandari E. Crousos syndrome: from molecular pathogenesis to therapeutic management. <i>Eur J Clin Invest.</i> 2015;45(5):504-514.	Article
*Ramamoorthy S, Cidlowski JA. Exploring the molecular mechanisms of glucocorticoid receptor action from sensitivity to resistance. <i>Endocr Dev.</i> 2013;24:41-56.	Article
MINERALOCORTICOIDS	
Hyperaldosteronism: Diagnosis and Management	

*Funder JW, Carey RM, Fardella C, et al; Endocrine Society. Case detection, diagnosis, and treatment of patients with primary aldosteronism: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2008;93(9):3266-3281.	Clinical Practice Guideline
Torre JJ, Bloomgarden ZT, Dickey RA, et al; AACE Hypertension Task Force. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of hypertension [published correction appears in <i>Endocr Pract.</i> 2008;14(6):802-803]. <i>Endocr Pract.</i> 2006;12(2):193-222.	Clinical Practice Guideline
*Moraitis AG, Rainey WE, Auchus RJ. Gene mutations that promote adrenal aldosterone production, sodium retention, and hypertension. <i>Appl Clin Genet.</i> 2013;7:1-13.	Article
*Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. <i>Am J Med.</i> 2013;126(10 Suppl 1):S1-S42.	Article
Halperin F, Dluhy RG. Glucocorticoid-remediable aldosteronism. <i>Endocrinol Metab Clin North Am.</i> 2011;40(2):333-341.	Article
Kempers MJ, Lenders JW, van Outheusden L, et al. Systematic review: diagnostic procedures to differentiate unilateral from bilateral adrenal abnormality in primary aldosteronism. <i>Ann Intern Med.</i> 2009;151(5):329-337.	Article
Young WF Jr. Primary aldosteronism--one picture is not worth a thousand words. <i>Ann Intern Med.</i> 2009;151(5):357-358.	Article
Hew-Butler T, Ayus JC, Kipps C, et al. Statement of the Second International Exercise-Associated Hyponatremia Consensus Development Conference, New Zealand, 2007. <i>Clin J Sport Med.</i> 2008;18(2):111-121.	Article
Young WF. Primary aldosteronism: renaissance of a syndrome. <i>Clin Endocrinol (Oxf).</i> 2007;66(5):607-618.	Article
Khosla N, Hogan D. Mineralocorticoid hypertension and hypokalemia. <i>Semin Nephrol.</i> 2006;26(6):434-440.	Article
Dluhy RG, Lifton RP. Glucocorticoid-remediable aldosteronism. <i>J Clin Endocrinol Metab.</i> 1999;84(12):4341-4344.	Article
Gennari FJ. Hypokalemia. <i>N Engl J Med.</i> 1998;339(7):451-458.	Article
Young WF Jr. Pheochromocytoma and primary aldosteronism: diagnostic approaches. <i>Endocrinol Metab Clin North Am.</i> 1997;26(4):801-827.	Article
White PC. Disorders of aldosterone biosynthesis and action. <i>N Engl J Med.</i> 1994;331(4):250-258.	Article
Hypoaldosteronism: Diagnosis and Management	
Funder JW. Apparent mineralocorticoid excess. <i>J Steroid Biochem Mol Biol.</i> 2016; [Epub ahead of print]	Article
White PC. Aldosterone synthase deficiency and related disorders. <i>Mol Cell Endocrinol.</i> 2004;217(1-2):81-87.	

ADRENAL ANDROGENS

Congenital Adrenal Hyperplasia: Diagnosis and Management

Speiser PW, Azziz R, Baskin LR, et al; Endocrine Society. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice guideline [published correction appears in <i>J Clin Endocrinol Metab</i> . 2010;95(11):5137]. <i>J Clin Endocrinol Metab</i> . 2010;95(9):4133-4160.	Clinical Practice Guideline
Finkelstein GP, Chen W, Mehta SP, et al. Comprehensive genetic analysis of 182 unrelated families with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. <i>J Clin Endocrinol Metab</i> . 2011;96(1):E161-E172.	Article
Merke DP. Approach to the adult with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. <i>J Clin Endocrinol Metab</i> . 2008;93(3):653-660.	Article
Hirvikoski T, Nordenstrom A, Lindholm T, et al. Cognitive functions in children at risk for congenital adrenal hyperplasia treated prenatally with dexamethasone. <i>J Clin Endocrinol Metab</i> . 2007;92(2):542-548.	Article
Speiser PW, White PC. Congenital adrenal hyperplasia. <i>N Engl J Med</i> . 2003;349(8):776-788.	Article
Hughes IA. Congenital adrenal hyperplasia: 21-hydroxylase deficiency in the newborn and during infancy. <i>Semin Reprod Med</i> . 2002;20(3):229-242.	Article
Hughes I. Congenital adrenal hyperplasia: phenotype and genotype. <i>J Pediatr Endocrinol Metab</i> . 2002;15(Suppl 5):1329-1340.	Article
Peter M. Congenital adrenal hyperplasia: 11beta-hydroxylase deficiency. <i>Semin Reprod Med</i> . 2002;20(3):249-254.	Article
Simard J, Moisan AM, Morel Y. Congenital adrenal hyperplasia due to 3beta-hydroxysteroid dehydrogenase/Delta(5)-Delta(4) isomerase deficiency. <i>Semin Reprod Med</i> . 2002;20(3):255-276.	Article
Sultan C, Paris F, Jeandel C, Lumbroso S, Galifer RB. Ambiguous genitalia in the newborn. <i>Semin Reprod Med</i> . 2002;20(3):181-188.	Article
Auchus RJ. The genetics, pathophysiology, and management of human deficiencies of P450c17. <i>Endocrinol Metab Clin North Am</i> . 2001;30(1):101-119.	Article
Pang S. Congenital adrenal hyperplasia. <i>Endocrinol Metab Clin North Am</i> . 1997;26(4):853-891.	Article

ADRENAL INCIDENTALOMA

Adrenal Incidentaloma: Diagnosis and Management

Zeiger MA, Thompson GB, Duh QY, et al; American Association of Clinical Endocrinologists; American Association of Endocrine Surgeons. American Association of Clinical Endocrinologists and American Association of Endocrine Surgeons medical guidelines for the management of adrenal incidentalomas. <i>Endocr Pract.</i> 2009;15(5):450-453.	Clinical Practice Guideline
*Nieman LK. Approach to the patient with an adrenal incidentaloma. <i>J Clin Endocrinol Metab.</i> 2010;95(9):4106-4113	Article
*Young WF Jr. Clinical practice. The incidentally discovered adrenal mass. <i>N Engl J Med.</i> 2007;356(6):601-610.	Article
Bugalho MJ, Domingues R, Sobrinho L. Molecular diagnosis of multiple endocrine neoplasia type 2. <i>Expert Rev Mol Diagn.</i> 2003;3(6):769-779.	Article
Grumbach MM, Biller BM, Braunstein GD, et al. Management of the clinically inapparent adrenal mass ("incidentaloma"). <i>Ann Intern Med.</i> 2003;138(5):424-429.	Article
Sidhu S, Gicquel C, Bambach CP, et al. Clinical and molecular aspects of adrenocortical tumorigenesis. <i>ANZ J Surg.</i> 2003;73(9):727-738.	Article
NIH state-of-the-science statement on management of the clinically inapparent adrenal mass ("incidentaloma"). <i>NIH Consens State Sci Statements.</i> 2002;19(2):1-25.	Article
Angeli A, Osella G, Ali A, Terzolo M. Adrenal incidentaloma: an overview of clinical and epidemiological data from the National Italian Study Group. <i>Horm Res.</i> 1997;47(4-6):279-283.	Article
Cook DM. Adrenal mass. <i>Endocrinol Metab Clin North Am.</i> 1997;26(4):829-852.	Article
Mantero F, Masini AM, Opocher G, Giovagnetti M, Arnaldi G. Adrenal incidentaloma: an overview of hormonal data from the National Italian Study Group. <i>Horm Res.</i> 1997;47(4-6):284-289.	Article
Kloos RT, Gross MD, Francis IR, Korobkin M, Shapiro B. Incidentally discovered adrenal masses. <i>Endocr Rev.</i> 1995;16(4):460-484.	Article
ADRENAL MEDULLA	
Pheochromocytoma and Catecholamine-Secreting Paragangliomas: Diagnosis and Management	
Lenders JW, Duh QY, Eisenhofer G, et al; Endocrine Society. Pheochromocytoma and paraganglioma: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2014;99(6):1915-1942.	Clinical Practice Guideline
Whiting MJ, Doogue MP. Advances in biochemical screening for pheochromocytoma using biogenic amines. <i>Clin Biochem Rev.</i> 2009;30(1):3-17.	Article
Perry CG, Sawka AM, Singh R, Thabane L, Bajnarek J, Young WF Jr. The diagnostic efficacy of urinary fractionated metanephrines measured by tandem mass spectrometry in detection of pheochromocytoma. <i>Clin Endocrinol (Oxf).</i> 2007;66(5):703-708.	Article

Ilias I, Pacak K. Current approaches and recommended algorithm for the diagnostic localization of pheochromocytoma. <i>J Clin Endocrinol Metab.</i> 2004;89(2):479-491.	Article
Bryant J, Farmer J, Kessler LJ, Townsend RR, Nathanson KL. Pheochromocytoma: the expanding genetic differential diagnosis. <i>J Natl Cancer Inst.</i> 2003;95(16):1196-1204.	Article
Herrmann M. Standard and molecular cytogenetics of endocrine tumors. <i>Am J Clin Pathol.</i> 2003;119(Suppl):S17-S38.	Article
Kudva YC, Sawka AM, Young WF Jr. Clinical review 164: the laboratory diagnosis of adrenal pheochromocytoma: the Mayo Clinic experience. <i>J Clin Endocrinol Metab.</i> 2003;88(10):4533-4539.	Article

ADRENAL CANCER

Adrenal Cancer: Diagnosis and Management

Else T, Kim AC, Sabolch A, et al. Adrenocortical carcinoma. <i>Endocr Rev.</i> 2014;35(2):282-326.	Article
Stratakis CA. Adrenal cancer in 2013: time to individualize treatment for adrenocortical cancer? <i>Nat Rev Endocrinol.</i> 2014;10(2):76-78.	Article
Fassnacht M, Terzolo M, Allolio B, et al; FIRM-ACT Study Group. Combination chemotherapy in advanced adrenocortical carcinoma. <i>N Engl J Med.</i> 2012;366(23):2189-2197.	Article
Young WF Jr. Conventional imaging in adrenocortical carcinoma: update and perspectives. <i>Horm Cancer.</i> 2011;2(6):341-347.	Article
Lacroix A. Approach to the patient with adrenocortical carcinoma. <i>J Clin Endocrinol Metab.</i> 2010;95(11):4812-4822.	Article

ADRENAL IMAGING AND PROCEDURES

Imaging

Torpy DJ, Chenn CC, Mullen N, et al. Lack of utility of (111)In-pentetreotide scintigraphy in localizing ectopic ACTH producing tumors: follow-up of 18 patients. <i>J Clin Endocrinol Metab.</i> 1999;84(4):1186-1192.	Article
Dhamija E, Panda A, Das CJ, Gupta AK. Adrenal imaging (part 2): medullary and secondary adrenal lesions. <i>Indian J Endocrinol Metab.</i> 2015;19(1):16-24.	Article
Panda A, Das CJ, Dhamija E, Kumar R, Gupta AK. Adrenal imaging (part 1): imaging techniques and primary cortical lesions. <i>Indian J Endocrinol Metab.</i> 2015;19(1):8-15.	Article
Taffel M, Haji-Momenian S, Nikolaidis P, Miller FH. Adrenal imaging: a comprehensive review. <i>Radiol Clin North Am.</i> 2012;50(2):219-243.	Article

Procedures

Rossi GP, Auchus RJ, Brown M, et al. An expert consensus statement on use of adrenal vein sampling for the subtyping of primary aldosteronism. <i>Hypertension</i> . 2014;63(1):151-160.	Article
Doppman JL, Gill JR Jr. Hyperaldosteronism: sampling the adrenal veins. <i>Radiology</i> . 1996;198(2):309-312.	Article

BONE AND MINERAL METABOLISM

INTRODUCTION

Knowledge and understanding of bone biology, genetics, and disease mechanisms have greatly expanded in the past decade. Osteoporosis is the most common metabolic bone disease in the United States and it has been the subject of intense focus given that it is a major public health problem. Its prevalence will continue to increase as the population ages. Screening, imaging methods, and therapy for osteoporosis should be part of education curriculum and training for fellows. Other disorders of mineral homeostasis such as primary hyperparathyroidism, hypoparathyroidism, vitamin D–related disorders, Paget disease, disorders of phosphate homeostasis, chronic kidney disease, and nephrolithiasis, as well as cancer and bone health issues, are also important areas of learning for fellows. Finally, curriculum should include developmental bone disorders such as osteogenesis imperfecta, fibrous dysplasia, and various chondrodysplasias. Fellows should be competent in the diagnosis and treatment of disorders of bone and mineral metabolism.

MEDICAL KNOWLEDGE

Fellows must demonstrate knowledge about established and evolving biomedical, clinical, and cognate (eg, epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.

Topic	Fundamental	Advanced
BASIC PHYSIOLOGIC PRINCIPLES, BONE BIOLOGY		
Explain the normal mineral homeostasis of calcium, phosphorus, and magnesium and of the calcium-regulating hormones (parathyroid hormone, parathyroid hormone–related protein, calcitonin, 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D, and fibroblast growth factor 23).	√	
Describe normal skeletal homeostasis, including anatomy, structure, bone remodeling unit, and the local and systemic hormones and factors that regulate skeletal homeostasis.	√	
Describe the interrelationships between mineral and skeletal homeostasis, including the role and function of the principal cells involved in bone remodeling (osteoblasts, osteoclasts, and osteocytes).	√	
Explain the signaling pathways within the bone marrow microenvironment such as RANK-L/OPG and the Wnt-signaling pathway and its role in bone formation.	√	

Discuss alterations in mineral homeostasis during physiologic states such as puberty, pregnancy, lactation, and aging.	√	
HYPERCALCEMIA		
Parathyroid Hormone–Mediated Hypercalcemia		
Distinguish between parathyroid hormone–mediated and nonparathyroid hormone–mediated hypercalcemia.	√	
Select parathyroid hormone assays to diagnose primary hyperparathyroidism vs nonparathyroid hormone–mediated hypercalcemia (ie, humoral hypercalcemia of malignancy, hyperabsorptive hypercalcemia due to granulomatous disorders, etc) and interpret results from these assays.		√
<i>Primary Hyperparathyroidism</i>		
<u>Diagnosis</u>		
Diagnose primary hyperparathyroidism, which includes the measurement of serum calcium and parathyroid hormone.	√	
Explain the role of genetic testing in patients with primary hyperparathyroidism and determine when ordering genetic testing is appropriate.	√	
<u>Treatment Guidelines</u>		
Discuss the decision regarding surgical vs medical management and list the current criteria for surgical intervention in asymptomatic primary hyperparathyroidism.	√	
<u>Medical and Surgical Therapy</u>		
Explain surgical approaches (eg, minimally invasive procedure), appropriate preoperative imaging and evaluation, and potential postoperative complications (eg, hungry bone syndrome and postoperative hypoparathyroidism).	√	
Observe, if possible, surgery performed by a competent head and neck or endocrine surgeon.		√
Recommend medical therapy or conservative observation, medications (eg, calcimimetics), and appropriate monitoring (including renal function and bone health) in patients with primary hyperparathyroidism.	√	
Manage the care of patients with hypercalcemia in the setting of suppressed parathyroid hormone (eg, hypercalcemia of malignancy or hyperabsorptive hypercalcemia due to granulomatous disorders).	√	
<u>Natural History</u>	√	

Discuss the gastrointestinal, neuromuscular, renal, and psychological symptoms and signs related to hypercalcemia.	√	
<i>Familial Hypocalciuric Hypercalcemia</i>		
Distinguish sporadic primary hyperparathyroidism from familial hypocalciuric hypercalcemia.	√	
Manage familial hypocalciuric hypercalcemia.	√	
<i>Lithium-Induced</i>		
Diagnose and manage lithium-induced hyperparathyroidism.	√	
Nonparathyroid Hormone–Mediated Hypercalcemia		
<i>Hypercalcemia of Malignancy</i>		
Identify the clinical and biochemical profile of a patient with possible parathyroid cancer.	√	
Diagnose and manage parathyroid hormone–related protein–mediated hypercalcemia of malignancy.	√	
Diagnose and manage hypercalcemia related to destructive bone metastases such as breast cancer and multiple myeloma.		√
Diagnose and manage vitamin D–mediated (25-hydroxyvitamin D or 1,25-dihydroxyvitamin D) hypercalcemia of malignancy.	√	
<i>Milk-Alkali Syndrome</i>		
Diagnose and manage milk-alkali syndrome.	√	
<i>Sarcoidosis, Tuberculosis, and Other Granulomatous Diseases</i>		
Diagnose and manage hypercalcemia related to sarcoidosis, tuberculosis, and other granulomatous diseases.	√	
<i>Vitamin D Intoxication</i>		
Diagnose and manage hypervitaminosis D–associated hypercalcemia.	√	
<i>Post-Rhabdomyolysis</i>		
Diagnose and manage rhabdomyolysis-associated hypercalcemia.	√	
<i>Adynamic Bone Disease</i>		
Diagnose and manage hypocalcemia due to adynamic bone disease such as severe chronic kidney disease and secondary hyperparathyroidism.		√
Recognize tertiary hyperparathyroidism in chronic kidney disease and appropriately evaluate.		√
<i>Myeloma</i>		
Diagnose and manage hypercalcemia due to myeloma.	√	
<i>Acute Adrenal Insufficiency</i>		
Diagnose and manage hypercalcemia due to acute adrenal insufficiency.	√	
<i>Vitamin A Intoxication</i>		

Diagnose and manage hypercalcemia due to vitamin A toxicity.		√
HYPOCALCEMIA		
Hypoparathyroidism		
Diagnose and manage surgical hypoparathyroidism that can occur after thyroid, parathyroid, or radical neck surgery for head and neck cancer.	√	
Diagnose and manage acquired hypoparathyroidism due to autoimmune disease.	√	
Diagnose and manage hypoparathyroidism due to activating mutations in the gene encoding the calcium-sensing receptor (<i>CASR</i>).	√	
Diagnose and manage hypoparathyroidism due to storage or infiltrative disorders of the parathyroid glands (eg, hemochromatosis, Wilson disease, granulomas, or metastatic cancer).	√	
Parathyroid Hormone Resistance		
Diagnose and manage pseudohypoparathyroidism.	√	
Hypomagnesemia		
Diagnose and manage magnesium depletion leading to hypocalcemia.	√	
Hyperphosphatemia		
Diagnose and manage hypocalcemia due to increased phosphate intake in patients with impaired renal excretion or in acute renal failure.	√	
Diagnose and manage acute hypocalcemia due to excess tissue breakdown (eg, rhabdomyolysis, tumor lysis).	√	
Pancreatitis		
Diagnose and manage hypocalcemia in patients with acute pancreatitis in whom it is associated with precipitation of calcium soaps in the abdominal cavity.	√	
Hungry Bone Syndrome		
Diagnose and manage severe and prolonged postoperative hypocalcemia (ie, hungry bone syndrome).	√	
Osteoblastic Metastases		
Diagnose and manage hypocalcemia in the setting of osteoblastic metastases.	√	
Drugs		
Identify drugs that can cause hypocalcemia such as calcium chelators, bisphosphonates, denosumab, cinacalcet, chemotherapy (especially cisplatin), foscarnet, and excess fluoride.	√	

OSTEOPOROSIS

Clinical Presentation

Describe the clinical manifestations of osteoporosis in postmenopausal women.	√	
Describe the clinical manifestations of osteoporosis in men.	√	
Describe the clinical manifestations of glucocorticoid-induced osteoporosis.	√	
Describe the clinical manifestations of posttransplant-associated osteoporosis.		√
Describe the clinical manifestations of osteoporosis due to malabsorption from Celiac disease.	√	

Diagnosis

Define osteoporosis and describe the associated diagnostic criteria.	√	
Evaluate for secondary forms of osteoporosis, including hypogonadism, vitamin D insufficiency or deficiency, genetic or congenital disorders, hyperparathyroidism, glucocorticoid excess, hyperthyroidism, and transplant bone disease.	√	
Identify dual-energy x-ray absorptiometry as the criterion standard for the evaluation of bone mineral density.	√	
Discuss issues of quality control, precision, and interpretation of dual-energy x-ray absorptiometry measurements, in terms of criteria for diagnosis of osteopenia and osteoporosis, as well as in interpretation of longitudinal changes.	√	
Describe alternative sites to measure bone mineral density such as the forearm, as well as indications for lateral vertebral assessment to evaluate for potential vertebral fractures.	√	
Describe the role of quantitative computed tomography in the evaluation of osteoporosis and recommend appropriately.		√
Describe the role of ultrasonography and other peripheral densitometry devices in the evaluation of osteoporosis and recommend appropriately.		√
Describe the role of trabecular bone score in the evaluation of osteoporosis and recommend appropriately.		√
Explain the use and limitations of bone turnover markers in the clinical setting (as well as their relationship to the bone remodeling cycle) and interpret results.	√	

Pathogenesis

Explain the role of estrogen deficiency in the pathogenesis of postmenopausal osteoporosis.	√	
Explain the role of androgen deficiency in the pathogenesis of osteoporosis in men.	√	
Discuss the role of aging in the pathogenesis of osteoporosis.	√	
Explain the role of cytokines and growth factors in the pathogenesis of osteoporosis.		√
Explain the role of genetics, ethnic variation, and environmental factors in the pathogenesis of osteoporosis.	√	
Distinguish nutritional vitamin D deficiency from insufficiency and explain the differences in terms of impact on bone density, fracture risk, and falls.	√	
Discuss the impact of physical activity and nutrition (eg, calcium and vitamin D) on bone mass and fractures, as well as factors such as medications, neuromuscular disorders, impaired vision, and propensity to fall.	√	
Therapy		
Recommend appropriate preventive measures for osteoporosis.	√	
Select appropriate nonpharmacologic treatment modalities such as lifestyle changes, calcium and vitamin D supplementation, and referral to physical therapy.	√	
Manage the care of women going through menopausal transition and incorporate up-to-date guidelines regarding hormone therapy.	√	
Explain the role of the following therapies in the treatment of osteoporosis as well as their short- and long-term adverse effects: hormone therapy, oral and intravenous bisphosphonates, selective estrogen receptor modulators, parathyroid hormone, calcitonin, calcium, vitamin D, and denosumab.	√	
Manage secondary fracture prevention after an initial osteoporotic fracture has been sustained and review measures to reduce the risk of subsequent fractures.	√	
Guide pain management in patients with vertebral or other fractures.	√	
Work with specialists (orthopedists or radiologists) in the management of patients with acute fractures or delayed healing of fractures.		√

PAGET DISEASE

Epidemiology and Pathogenesis

Discuss the pathogenesis and epidemiology of Paget disease of bone.	√	
Biochemical Abnormalities		
Interpret results from laboratory studies used to document the extent and severity of Paget disease activity (biochemical markers of bone turnover).	√	
Radiographic Abnormalities		
Interpret imaging studies used to document the extent and severity of Paget disease activity (scintigraphy and radiographs).		√
Identify the typical radiographic appearance of Paget disease and features that distinguish it from other similar conditions such as fibrous dysplasia or osteoblastic metastases.	√	
Therapy		
Recommend treatment for Paget disease, which may include the use of antiresorptive medications, and describe the biochemical and clinical goals of therapy.	√	
HYPOVITAMINOSIS D		
Discuss the pathogenesis and epidemiology of vitamin D deficiency.	√	
Diagnose and manage vitamin D deficiency.	√	
Differentiate among the causes of vitamin D deficiency, including decreased dietary intake, malabsorption, limited sun exposure, liver failure, renal insufficiency, drug-induced, vitamin D–dependent rickets type 1, and hereditary vitamin D–resistant rickets.	√	
Recognize vitamin D deficiency as a potential sign of celiac disease (in an otherwise minimally symptomatic or asymptomatic patient) and determine appropriate testing to establish a diagnosis.	√	
OSTEOMALACIA AND RICKETS		
Recognize various types of osteomalacic disorders and differentiate them from osteoporosis.	√	
Distinguish osteomalacia from rickets.	√	
Differentiate among various inherited disorders of vitamin D action (eg, vitamin D dependency, hypophosphatemic or vitamin D–resistant rickets, and osteomalacia)		√
Explain how vitamin D deficiency or resistance can result in osteomalacia by impaired availability of vitamin D, impaired 25-hydroxylation of		√

vitamin D in the liver to 1,25-dihydroxyvitamin D, impaired 1 α -hydroxylation of 25-hydroxyvitamin D in the kidney to 1,25-dihydroxyvitamin D, and end-organ insensitivity to vitamin D metabolites.		
Chronic Hypocalcemia		
Describe the clinical manifestations, diagnosis, and management of calcipenic rickets (eg, nutritional rickets, 1 α -hydroxylase deficiency, hereditary resistance to vitamin D, and secondary defects in vitamin D metabolism or absorption of calcium or vitamin D).	√	
Chronic Hypophosphatemia		
Describe the clinical manifestations of phosphopenic rickets (eg, renal tubular disorders, X-linked hypophosphatemic rickets, tumor-induced osteomalacia, hereditary hypophosphatemic rickets with hypercalciuria).		√
Diagnose and manage phosphopenic rickets.		√
Chronic Acidosis		
Diagnose and manage osteomalacia associated with distal renal tubular acidosis.		√
Diagnose and manage osteomalacia associated with proximal renal tubular acidosis.		√
Diagnose and manage osteomalacia associated with acidosis seen after ureterosigmoidostomy.		√
Inhibitors of Mineralization		
Diagnose and manage osteomalacia associated with mineralization inhibitors such as bisphosphonates, aluminum, and sodium fluoride.	√	
RENAL OSTEODYSTROPHY		
Review indications for bone biopsy and evaluation of tetracycline-labeled bone for stratification of bone disease in the setting of chronic kidney disease.	√	
Secondary Hyperparathyroidism		
Discuss the pathogenesis, clinical manifestations, and management of secondary hyperparathyroidism.	√	
Tertiary Hyperparathyroidism		
Discuss the pathogenesis, clinical manifestations, and management of tertiary hyperparathyroidism.		√
NEPHROLITHIASIS		

Evaluate nephrolithiasis.	√	
Perform the differential diagnosis of primary hyperparathyroidism and idiopathic hypercalciuria.	√	
Guide the medical management of nephrolithiasis, which may include thiazide diuretics and/or bisphosphonates and appropriate dietary management.		√

OSTEOGENESIS IMPERFECTA AND BONE DYSPLASIAS

Discuss the pathogenesis and epidemiology of osteogenesis imperfecta.	√	
Diagnose and manage osteogenesis imperfecta.		√

FIBROUS DYSPLASIA AND OTHER DYSPLASTIC SYNDROMES

Discuss the pathogenesis and epidemiology of fibrous dysplasia and other dysplastic syndromes.		√
Guide the diagnosis and medical management of the skeletal aspects of fibrous dysplasia, as well as precocious puberty when present (eg, McCune-Albright syndrome).		√

CALCIPHYLAXIS

Discuss the pathogenesis and epidemiology of calciphylaxis.	√	
Diagnose and manage calciphylaxis.		√

HYPOPHOSPHATEMIA

Renal Losses

Diagnose and manage hypophosphatemia due to increased urinary excretion from primary and secondary hyperparathyroidism, hypercalcemia of malignancy, primary renal phosphate wasting (eg, X-linked hypophosphatemic rickets, tumor-induced osteomalacia), Fanconi syndrome, vitamin D deficiency or resistance, or alcohol and other drugs.	√	
---	---	--

Poor Gastrointestinal Absorption

Diagnose and manage hypophosphatemia due to poor gastrointestinal absorption from malabsorption, vitamin D deficiency, or alcohol and other drugs.	√	
Internal Redistribution		
Diagnose and manage hypophosphatemia due to internal redistribution as a result of intravenous glucose administration, acute respiratory alkalosis, recovery from acidosis, hungry bone syndrome, or osteoblastic metastases.	√	
SKELETAL NEOPLASMS/INFILTRATIVE DISORDERS		
Identify benign and malignant skeletal neoplasms on skeletal radiographs.		√
Institute appropriate referrals to orthopedic surgeons or to radiation and/or medical oncologists.	√	
Diagnose and manage infiltrative disorders of bone, including mast cell disease and histiocytosis X.		√
DISORDERS OF EXTRASKELETAL CALCIFICATION/OSSIFICATION		
Diagnose and manage disorders of extraskeletal calcification/ossification, including tumoral calcinosis, metastatic and dystrophic calcification, dermatomyositis with calcinosis cutis universalis, and various rare ossification disorders.		√
IMAGING TECHNIQUES AND PROCEDURES		
Recognize the typical radiographic appearances of common metabolic bone disorders (eg, vertebral and long bone fractures, stress fractures and reactions, rickets and pseudofractures of osteomalacia, Brown tumors, Paget disease of bone).	√	
Explain the fundamentals of parathyroid imaging (technetium 99m sestamibi scan and ultrasonography), including the appropriate use of this test in the evaluation of patients with primary hyperparathyroidism.	√	
Explain the appropriate use of computed tomography and magnetic resonance imaging in the evaluation of patients with persistent or recurrent hyperparathyroidism to exclude ectopic parathyroid adenoma.		√
Discuss the use of dual-energy x-ray absorptiometry for potential assessment of body composition (see Osteoporosis section for specifics of dual energy x-ray absorptiometry evaluation).		√

Explain the technique and use of bone scintigraphy in various clinical situations.	√	
--	---	--

TEACHING METHODS AND EVALUATION

Much teaching occurs one-on-one with attendings during outpatient clinics and on inpatient hospital rounds. Active learning occurs as fellows participate in patient care under the supervision and guidance of the attending. In addition, a full range of topics are reviewed in didactic sessions at weekly conferences and in the core curriculum/board review weekly sessions. Fellows are also expected to engage in self-directed study guided by the curriculum. Evaluation includes attending review of fellows knowledge base and medical reasoning during clinic and hospital rounds. In addition, the in-training exam taken in February of every year provides a loose benchmark of medical knowledge progression through the fellowship.

SUGGESTED READING

Asterisks denote references that are designated for residents, students, or endocrine fellows early in their training.

GENERAL READING, PHYSIOLOGY, EPIDEMIOLOGY	
*Rosen CJ, Bouillon R, Compston JE, Rosen V, eds. <i>Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism</i> . 8th ed. Washington, DC: Wiley-Blackwell; 2013.	Textbook
*Ross AC, Manson JE, Abrams SA, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. <i>J Clin Endocrinol Metab</i> . 2011; 96(1) :53-58.	Article
*Bilezikian JP, Raisz LG, Martin TJ, eds. <i>Principles of Bone Biology</i> . San Diego, CA: Academic Press; 2008.	Textbook
HYPERCALCEMIA AND HYPERPARATHYROIDISM	
*Silverberg SJ. Primary hyperparathyroidism. In: Rosen CJ, Bouillon R, Compston JE, Rosen V, eds. <i>Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism</i> . 8th ed. Washington, DC: Wiley-Blackwell; 2013.	Textbook
*Arnold A, Marx SJ. Familial hyperparathyroidism. In: Rosen CJ, Bouillon R, Compston JE, Rosen V, eds. <i>Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism</i> . 8th ed. Washington, DC: Wiley-Blackwell; 2013.	Textbook

Rubin MR, Bilezikian JP, McMahon DJ, et al. The natural history of primary hyperparathyroidism with or without parathyroid surgery after 15 years. <i>J Clin Endocrinol Metab.</i> 2008; 93 (9):3462-3470.	Article
Peacock M, Bilezikian JP, Klassen PS, Guo MD, Turner SA, Shoback D. Cinacalcet hydrochloride maintains long-term normocalcemia in patients with primary hyperparathyroidism. <i>J Clin Endocrinol Metab.</i> 2005;90(1):135-141.	Article
Chow CC, Chan WB, Li JK, et al. Oral alendronate increases bone mineral density in postmenopausal women with primary hyperparathyroidism. <i>J Clin Endocrinol Metab.</i> 2003;88(2):581-587.	Article
Rubin MR, Lee KH, McMahon DJ, Silverberg SJ. Raloxifene lowers serum calcium and markers of bone turnover in postmenopausal women with primary hyperparathyroidism. <i>J Clin Endocrinol Metab.</i> 2003;88(3):1174-1178.	Article
Arnold A, Shattuck TM, Mallya SM, et al. Molecular pathogenesis of primary hyperparathyroidism. <i>J Bone Miner Res.</i> 2002;17(Suppl 2):N30-N36.	Article
Carneiro DM, Irvin GL 3rd. New point-of-care intraoperative parathyroid hormone assay for intraoperative guidance in parathyroidectomy. <i>World J Surg.</i> 2002;26(8):1074-1077.	Article
Melton LJ 3rd. The epidemiology of primary hyperparathyroidism in North America. <i>J Bone Miner Res.</i> 2002;17(Suppl 2):N12-N17.	Article
Udelsman R. Surgery in primary hyperparathyroidism: the patient without previous neck surgery. <i>J Bone Miner Res.</i> 2002;17(Suppl 2):N126-N132.	Article
Marx SJ. Hyperparathyroid and hypoparathyroid disorders [published corrections appear in <i>N Engl J Med.</i> 2001;344(9):696 and <i>N Engl J Med.</i> 2001;344(3):240]. <i>N Engl J Med.</i> 2000;343(25):1863-1875.	Article

HYPOCALCEMIA AND HYPOPARATHYROIDISM

Kim ES, Keating GM. Recombinant human parathyroid hormone (1-84): a review in hypoparathyroidism. <i>Drugs.</i> 2015;75(11):1293-1303.	Article
Whitteveen JE, van Thiel S, Romijn JA, Hamdy NA. Hungry bone syndrome: still a challenge in the post-operative management of primary hyperparathyroidism: a systematic review of the literature. <i>Eur J Endocrinol.</i> 2013;169(3):R45-R53.	Article
Marx SJ. Hyperparathyroid and hypoparathyroid disorders [published corrections appear in <i>N Engl J Med.</i> 2001;344(9):696 and <i>N Engl J Med.</i> 2001;344(3):240]. <i>N Engl J Med.</i> 2000;343(25):1863-1875.	Article

OSTEOPOROSIS

General Articles	
Mirza F, Canalis E. Management of endocrine disease: secondary osteoporosis: pathophysiology and management. <i>Eur J Endocrinol.</i> 2015;173(3):R131-R151.	Article
*Cosman F, de Beur SJ, LeBoff MS, et al; National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. <i>Osteoporos Int.</i> 2014;25(10):2359-2381.	Article
*Dawson-Hughes B, Tosteson AN, Melton LJ 3rd, Baim S, Favus MJ, Khosla S, Lindsay RL; National Osteoporosis Foundation Guide Committee. Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA. <i>Osteoporos Int.</i> 2008;19(4):449-458.	Article
*NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. <i>JAMA.</i> 2001;285(6):785-795.	Article
Pathogenesis and Genetics	
Mafi Golchin M, Heidari L, Ghaderian SM, Akhavan-Niaki H. Osteoporosis: a silent disease with complex genetic contribution. <i>J Genet Genomics.</i> 2016;43(2):49-61.	Article
Schett G. Effects of inflammatory and anti-inflammatory cytokines on the bone. <i>Eur J Clin Invest.</i> 2011;41(12):1361-1366.	Article
Syed F, Khosla S. Mechanisms of sex steroid effects on bone. <i>Biochem Biophys Res Commun.</i> 2005;328(3):688-696.	Article
Ralston SH. Genetic control of susceptibility to osteoporosis. <i>J Clin Endocrinol Metab.</i> 2002;87(6):2460-2466.	Article
Seeman E. Pathogenesis of bone fragility in women and men. <i>Lancet.</i> 2002;359(9320):1841-1850.	Article
*Raisz LG. Local and systemic factors in the pathogenesis of osteoporosis. <i>N Engl J Med.</i> 1988;318(13):818-828.	Article
Male Osteoporosis	
*Watts NB, Adler RA, Bilezikian JP, et al Endocrine Society. Osteoporosis in men: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2012;97(6):1802-1822.	Clinical Practice Guideline
LeBlanc ES, Nielson CM, Marshall LM, et al; Osteoporotic Fractures in Men Study Group. The effects of serum testosterone, estradiol, and sex hormone binding globulin levels on fracture risk in older men. <i>J Clin Endocrinol Metab.</i> 2009;94(9):3337-3346.	Article

Fink HA, Ewing SK, Ensrud KE, et al. Association of testosterone and estradiol deficiency with osteoporosis and rapid bone loss in older men. <i>J Clin Endocrinol Metab.</i> 2006;91(10):3908-3915.	Article
Orwoll ES. Men, bone and estrogen: unresolved issues. <i>Osteoporos Int.</i> 2003;14(2):93-98.	Article
Orwoll ES, Scheele WH, Paul S, et al. The effect of teriparatide [human parathyroid hormone (1-34)] therapy on bone density in men with osteoporosis. <i>J Bone Miner Res.</i> 2003;18(1):9-17.	Article
Falahati-Nini A, Riggs BL, Atkinson EJ, O'Fallon WM, Eastell R, Khosla S. Relative contributions of testosterone and estrogen in regulating bone resorption and formation in normal elderly men. <i>J Clin Invest.</i> 2000;106(12):1553-1560.	Article
Orwoll E, Ettinger M, Weiss S, et al. Alendronate for the treatment of osteoporosis in men. <i>N Engl J Med.</i> 2000;343(9):604-610.	Article
Glucocorticoid-Induced Osteoporosis	
*Buehring B, Viswanathan R, Binkley N, Busse W. Glucocorticoid-induced osteoporosis: an update on effects and management. <i>J Allergy Clin Immunol.</i> 2013;132(5):1019-1030.	Article
Van Staa TP, Laan RF, Barton IP, Cohen S, Reid DA, Cooper C. Bone density threshold and other predictors of vertebral fracture in patients receiving oral glucocorticoid therapy. <i>Arthritis Rheum.</i> 2003;48(11):3224-3229.	Article
Rehman Q, Lang TF, Arnaud CD, Modin GW, Lane NE. Daily treatment with parathyroid hormone is associated with an increase in vertebral cross-sectional area in postmenopausal women with glucocorticoid-induced osteoporosis. <i>Osteoporosis Int.</i> 2003;14(1):77-81.	Article
Reid DM, Hughes RA, Laan RF, et al. Efficacy and safety of daily risedronate in the treatment of corticosteroid-induced osteoporosis in men and women: a randomized trial. European Corticosteroid-Induced Osteoporosis Treatment Study. <i>J Bone Miner Res.</i> 2000;15(6):1006-1013.	Article
Fracture Epidemiology and Prediction	
Dufour AB, Roberts B, Broe KE, Kiel DP, Bouxsein ML, Hannan MT. The factor-of-risk biomechanical approach predicts hip fracture in men and women: the Framingham Study [published correction appears in <i>Osteoporos Int.</i> 2014;25(5):1657]. <i>Osteoporos Int.</i> 2012;23(2):513-520.	Article
Cooper C, Cole ZA, Holroyd CR, et al; IOF CSA Working Group on Fracture Epidemiology. Secular trends in the incidence of hip and other osteoporotic fractures. <i>Osteoporos Int.</i> 2011;22(5):1277-1288.	Article
Kanis JA, Johnell O, Oden A, Johansson H, McCloskey EV. FRAX and the assessment of fracture probability in men and women from the UK. <i>Osteoporos Int.</i> 2008;19(4):385-397.	Article

Lindsay R, Silverman SL, Cooper C, et al. Risk of new vertebral fracture in the year following a fracture. <i>JAMA</i> . 2001;285(3):320-323.	Article
Hormonal Therapies	
Eastell R. Role of oestrogen in the regulation of bone turnover at the menarche. <i>J Endocrinol</i> . 2005;185(2):223-234.	Article
Riggs BL, Melton LJ 3rd. Bone turnover matters: the raloxifene treatment paradox of dramatic decreases in vertebral fractures without commensurate increases in bone density. <i>J Bone Miner Res</i> . 2002;17(1):11-14.	Article
Delmas PD, Bjarnason NH, Mitlak BH, et al. Effects of raloxifene on bone mineral density, serum cholesterol concentrations, and uterine endometrium in postmenopausal women. <i>N Engl J Med</i> . 1997;337(23):1641-1647.	Article
Cauley JA, Seeley DG, Ensrud K, Ettinger B, Black D, Cummings SR. Estrogen replacement therapy and fractures in older women. Study of Osteoporotic Fractures Research Group. <i>Ann Intern Med</i> . 1995;122(1):9-16.	Article
Bisphosphonates	
Bone HG, Hosking D, Devogelaer JP, et al; Alendronate Phase III Osteoporosis Treatment Study Group. Ten years' experience with alendronate for osteoporosis in postmenopausal women. <i>N Engl J Med</i> . 2004;350(12):1189-1199.	Article
Reid IR, Brown JP, Burckhardt P, et al. Intravenous zoledronic acid in postmenopausal women with low bone mineral density. <i>N Engl J Med</i> . 2002;346(9):653-661.	Article
McClung MR, Geusens P, Miller PD, et al; Hip Intervention Program Study Group. Effect of risedronate on the risk of hip fracture in elderly women. <i>N Engl J Med</i> . 2001;344(5):333-340.	Article
Parathyroid Hormone Treatment and Combination Therapy	
Cosman F. Anabolic and antiresorptive therapy for osteoporosis: combination and sequential approaches. <i>Curr Osteoporos Rep</i> . 2014;12(4):385-395.	Article
Black DM, Greenspan SL, Ensrud KE, et al; PaTH Study Investigators. The effects of parathyroid hormone and alendronate alone or in combination in postmenopausal osteoporosis. <i>N Engl J Med</i> . 2003;349(13):1207-1215.	Article
Finkelstein JS, Hayes A, Hunzelman JL, Wyland JJ, Lee H, Neer RM. The effects of parathyroid hormone, alendronate, or both in men with osteoporosis. <i>N Engl J Med</i> . 2003;349(13):1216-1226.	Article

Khosla S. Parathyroid hormone plus alendronate--a combination that does not add up. <i>N Engl J Med.</i> 2003;349(13):1277-1279.	Article
Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. <i>N Engl J Med.</i> 2001;344(19):1434-1441.	Article
Recker RR, Heaney RP. The role of combination treatment for osteoporosis. <i>J Clin Endocrinol Metab.</i> 2001;86(5):1888-1889.	Article
Osteonecrosis of the Jaw and Atypical Femoral Fracture	
Khan AA, Morrison A, Hanley DA, et al; International Task Force on Osteonecrosis of the Jaw. Diagnosis and management of osteonecrosis of the jaw: a systematic review and international consensus. <i>J Bone Miner Res.</i> 2015;30(1):3-23.	Article
Bronson WH, Kaye ID, Egol KA. Atypical femur fractures: a review. <i>Curr Osteoporos Rep.</i> 2014;12(4):446-453.	Article
Shane E, Burr D, Abrahamsen B, et al. Atypical subtrochanteric and diaphyseal femoral fractures: second report of the task force of the American Society for Bone and Mineral Research. <i>J Bone Miner Res.</i> 2014;29(1):1-23.	Article
Calcium and Vitamin D for Osteoporosis Prevention	
Gallagher JC, Sai A, Templin T 2nd, Smith L. Dose response to vitamin D supplementation in postmenopausal women: a randomized trial [published correction appears in <i>Ann Intern Med.</i> 2012;156(9):672]. <i>Ann Intern Med.</i> 2012;156(6):425-437.	Article
Bischoff-Ferrari HA, Willett WC, Wong JB, Giovannucci E, Dietrich T, Dawson-Hughes B. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. <i>JAMA.</i> 2005;293(18):2257-2264.	Article
Sakhaee K, Bhuket T, Adams-Huet B, Rao DS. Meta-analysis of calcium bioavailability: a comparison of calcium citrate with calcium carbonate. <i>Am J Ther.</i> 1999;6(6):313-321.	Article
Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age and older. <i>N Engl J Med.</i> 1997;337(10):670-676.	Article
Chapuy MC, Arlot ME, Duboeuf F, et al. Vitamin D3 and calcium to prevent hip fractures in the elderly women. <i>N Engl J Med.</i> 1992;327(23):1637-1642.	Article
Denosumab	

Papapoulos S, Lippuner K, Roux C, et al. The effect of 8 or 5 years of denosumab treatment in postmenopausal women with osteoporosis: results from the FREEDOM Extension Study. <i>Osteoporos Int</i> . 2015;26(12):2773-2783.	Article
Bone HG, Chapurlat R, Brandi ML, et al. The effect of three or six years of denosumab exposure in women with postmenopausal osteoporosis: results from the FREEDOM extension. <i>J Clin Endocrinol Metab</i> . 2013;98(11):4483-4492.	Article
PAGET DISEASE	
*Singer FR, Bone HG 3rd, Hosking DJ, et al. Paget's disease of bone: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab</i> . 2014;99(12):4408-4422.	Clinical Practice Guideline
*Siris ES, Roodman D. Paget's disease of bone. In: Rosen CJ, Bouillon R, Compston JE, Rosen V, eds. <i>Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism</i> . 8th ed. Washington, DC: Wiley-Blackwell; 2013.	Textbook
Seitz S, Priemel M, Zustin J, et al. Paget's disease of bone: histologic analysis of 754 patients. <i>J Bone Miner Res</i> . 2009;24(1):62-69.	Article
Abelson A. A review of Paget's disease of bone with a focus on the efficacy and safety of zoledronic acid 5 mg. <i>Curr Med Res Opin</i> . 2008;24(3):695-705.	Article
Reid IR, Miller P, Lyles K, et al. Comparison of single infusion of zoledronic acid with risedronate for Paget's disease. <i>N Engl J Med</i> . 2005;353(9):898-908.	Article
CALCIUM, VITAMIN D, AND HYPOVITAMINOSIS D	
*Holick MF, Binkley NC, Bischoff-Ferrari HA, et al; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline [published correction appears in <i>J Clin Endocrinol Metab</i> . 2011;96(12):3908]. <i>J Clin Endocrinol Metab</i> . 2011;96(7):1911-1930.	Clinical Practice Guideline
Bischoff-Ferrari HA, Willett WC, Orav EJ, et al. A pooled analysis of vitamin D dose requirements for fracture prevention [published correction appears in <i>N Engl J Med</i> . 2012;367(5):481]. <i>N Engl J Med</i> . 2012;367(1):40-49.	Article
Fleet JC, Schoch RD. Molecular mechanisms for regulation of intestinal calcium absorption by vitamin D and other factors. <i>Crit Rev Clin Lab Sci</i> . 2010;47(4):181-195.	Article
Christakos S, Dhawan P, Benn B, et al. Vitamin D: molecular mechanism of action. <i>Ann N Y Acad Sci</i> . 2007;1116:340-348.	Article
*Holick MF. Vitamin D deficiency. <i>N Engl J Med</i> . 2007; 357(3) :266-281.	Article
OSTEOMALACIA AND RICKETS	

Bianchi ML. Hypophosphatasia: an overview of the disease and its treatment. <i>Osteoporos Int.</i> 2015;26(12):2743-2757.	Article
Hofmann C, Jakob F, Seefried L, et al. Recombinant enzyme replacement therapy in hypophosphatasia. <i>Subcell Biochem.</i> 2015;76:323-341.	Article
Högler W. Complications of vitamin D deficiency from the foetus to the infant: One cause, one prevention, but who's responsibility? <i>Best Pract Res Clin Endocrinol Metab.</i> 2015;29(3):385-398.	Article
Paterson CR, Ayoub D. Congenital rickets due to vitamin D deficiency in the mothers. <i>Clin Nutr.</i> 2015;34(5):793-798.	Article
RENAL OSTEODYSTROPHY	
Miller PD. Bone disease in CKD: a focus on osteoporosis diagnosis and management. <i>Am J Kidney Dis.</i> 2014;64(2):290-304.	Article
Isakova T, Wahl P, Vargas GS, et al. Fibroblast growth factor 23 is elevated before parathyroid hormone and phosphate in chronic kidney disease [published correction appears in <i>Kidney Int.</i> 2012;82(4):498]. <i>Kidney Int.</i> 2011;79(12):1370-1378.	Article
Hruska KA, Teitelbaum SL. Renal osteodystrophy. <i>N Engl J Med.</i> 1995;333(3):166-174.	Article
NEPHROLITHIASIS	
Arrabal-Polo MA, Cano-García MdelC, Canales BK, Arrabal-Martín M. Calcium nephrolithiasis and bone demineralization: pathophysiology, diagnosis, and medical management. <i>Curr Opin Urol.</i> 2014;24(6):633-638.	Article
Coe FL, Parks JH, Asplin JR. The pathogenesis and treatment of kidney stones. <i>N Engl J Med.</i> 1992;327(16):1141-1152.	Article
OSTEOGENESIS IMPERFECTA AND BONE DYSPLASIAS	
Forlino A, Marini JC. Osteogenesis imperfecta. <i>Lancet.</i> 2016;387(10028):1657-1671.	Article
*Joan C, Marini JC. Osteogenesis imperfecta. In: Rosen CJ, Bouillon R, Compston JE, Rosen V, eds. <i>Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism.</i> 8th ed. Washington, DC: Wiley-Blackwell; 2013.	Textbook
FIBROUS DYSPLASIA AND OTHER DYSPLASTIC SYNDROMES	
*Collins MT, Riminucci M, Bianco P. Fibrous dysplasia. In: Rosen CJ, Bouillon R, Compston JE, Rosen V, eds. <i>Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism.</i> 8th ed. Washington, DC: Wiley-Blackwell; 2013.	Textbook

Leet AI, Collins MT. Current approach to fibrous dysplasia of bone and McCune-Albright syndrome. <i>J Child Orthop.</i> 2007;1(1):3-17.	Article
CALCIPHYLAXIS	
Nigwekar SU, Kroshinsky D, Nazarian RM, et al. Calciphylaxis: risk factors, diagnosis, and treatment. <i>Am J Kidney Dis.</i> 2015;66(1):133-146.	Article
Karwowski W, Naumnik B, Szczepanski M, Mysliwiec M. The mechanism of vascular calcification – a systematic review. <i>Med Sci Monit.</i> 2012;18(1):RA1-RA11.	Article
Vedvyas C, Winterfield LS, Vleugels RA. Calciphylaxis: a systematic review of existing and emerging therapies. <i>J Am Acad Dermatol.</i> 2012;67(6):e253-e260.	Article
HYPOPHOSPHATEMIA	
Goldswieg BK, Carpenter TO. Hypophosphatemic rickets: lessons from disrupted FGF23 control of phosphorus homeostasis. <i>Curr Osteoporos Rep.</i> 2015;13(2):88-97.	Article
Manghat P, Sodi R, Swaminathan R. Phosphate homeostasis and disorders. <i>Ann Clin Biochem.</i> 2014;51(Pt 6):631-656.	Article
Wagner CA, Rubio-Aliaga I, Biber J, Hernando N. Genetic diseases of renal phosphate handling. <i>Nephrol Dial Transplant.</i> 2014;29(Suppl 4):iv45-iv54.	Article
SKELETAL NEOPLASMS/INFILTRATIVE DISORDERS	
*Van Poznak C, Taxel P. Skeletal complications of breast and prostate cancer therapies. In: Rosen CJ, Bouillon R, Compston JE, Rosen V, eds. <i>Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism.</i> 8th ed. Washington, DC: Wiley-Blackwell; 2013.	Textbook
Santen RJ. <i>Clinical review: effect of endocrine therapies on bone in breast cancer patients. J Clin Endocrinol Metab.</i> 2011;96(2):308-319.	Article
*Roodman GD. Diagnosis and treatment of myeloma bone disease. In: Rajkumar SV, Kyle RA, eds. <i>Treatment of Multiple Myeloma and Related Disorders.</i> New York, NY: Cambridge University Press; 2009:64-76.	Textbook
Shahinian VB, Kuo YF, Freeman JL, Goodwin JS. Risk of fracture after androgen deprivation for prostate cancer. <i>N Engl J Med.</i> 2005;352(2):154-164.	Article
DISORDERS OF EXTRASKELETAL CALCIFICATION/OSSIFICATION	
Edwards DS, Clasper JC. Heterotopic ossification: a systematic review. <i>J R Army Med Corps.</i> 2015;161(4):315-321.	Article

IMAGING TECHNIQUES AND PROCEDURES

Lee JH, Lee YK, Oh SH, et al. A systematic review of diagnostic accuracy of vertebral fracture assessment (VFA) in postmenopausal women and elderly men. <i>Osteoporos Int</i> . 2016;27(5):1691-1699.	Article
Bonnick SL. Monitoring changes in bone density. <i>Womens Health (Lond Engl)</i> . 2008;4:89-97.	Article
*Bonnick SL, ed. <i>Bone Densitometry in Clinical Practice: Application and Interpretation</i> . 2nd ed. New York, NY: Humana Press; 2004.	Textbook
Cummings SR, Palermo L, Browner W, et al. Monitoring osteoporosis therapy with bone densitometry: misleading changes and regression to the mean. Fracture Intervention Trial Research Group. <i>JAMA</i> . 2000;283(10):1318-1321.	Article

USEFUL WEB SITES

American Society of Bone and Mineral Research www.asbmr.org

National Osteoporosis Foundation www.nof.org

International Society for Clinical Densitometry www.iscd.org

DIABETES

INTRODUCTION

Diabetes mellitus is a common, potentially devastating, expensive, treatable (but incurable) chronic disease. It is the most common endocrine disorder that seriously affects health and limits longevity. In the United States, 30.3 million persons, or 9.4% of the population, have diabetes: 23.1 million diagnosed and 7.2 million undiagnosed (CDC National Diabetes Statistics Report, 2017). The World Health Organization projects the worldwide population of persons with diabetes will grow to 300 million by the year 2025. Many more have impaired glucose tolerance or impaired fasting glucose and are at high risk for atherosclerotic disease and diabetes. Persons with diabetes are at 2- to 4-fold increased risk for myocardial infarction or stroke. Diabetes is the leading cause of blindness and of nontraumatic amputations, and it is the most common single cause of end-stage renal disease requiring dialysis and transplant. In 2012, the estimated economic cost of diabetes was \$245 billion, including \$176 billion in direct medical costs and \$69 billion in reduced productivity. Much of the expenditure went toward caring for long-term microvascular and macrovascular complications of diabetes that are now known to be preventable, in large part. A complete understanding of the metabolic complications of diabetes and the underlying pathology is essential for the endocrinologist and should be part of education curriculum and training for fellows. Fellows should be competent in the diagnosis and treatment of diabetes and its complications.

MEDICAL KNOWLEDGE

Fellows must demonstrate knowledge about established and evolving biomedical, clinical, and cognate (eg, epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.

Topic	Fundamental	Advanced
BASIC PHYSIOLOGIC PRINCIPLES AND METABOLISM		
Review biochemistry and physiology, including cellular and molecular biology as it relates to diabetes and its complications.		√
Describe the epidemiology of diabetes.	√	
Summarize developmental endocrinology, including growth, development, and pubertal maturation as they relate to diabetes.		√
Explain endocrine physiology and its pathophysiology in diabetes and principles of hormone action.		√
Describe signal transduction pathways and biology of hormone receptors.		√
Perform a comprehensive evaluation of patients with diabetes including assessments of glycemic control, blood pressure control, lipid control, the status of microvascular complications, the status of macrovascular	√	

complications, the need for additional self-management education, medical nutrition therapy, and smoking status.		
DEFINITIONS AND DIAGNOSIS		
Prediabetes		
Define impaired fasting glucose.	√	
Define impaired glucose tolerance.	√	
Diabetes Mellitus		
Define the criteria used to diagnose diabetes mellitus, including fasting/random blood glucose, glucose tolerance testing, and hemoglobin A _{1c} measurement.	√	
Summarize the evidence and recommendations related to screening asymptomatic patients for type 2 diabetes.		√
MONITORING GLYCEMIC CONTROL		
Hemoglobin A_{1c}		
Monitor glycemic control by periodic assessment of glycosylated hemoglobin.	√	
List potential sources of error in interpreting glycosylated hemoglobin measurements, including low or high turnover of red blood cells, abnormal hemoglobins, chronic kidney disease, and ethnic variations.		√
Fructosamine and 1,5-Anhydroglucitol		
Determine when assessing glycemic control with fructosamine or 1,5-anhydroglucitol is appropriate and interpret these results.		√
Conventional Glucose Monitoring		
Recommend self-monitoring of blood glucose and instruct the patient on method and frequency.	√	
List common errors in self-monitoring of blood glucose.		√
Differentiate among the methods for self-monitoring of blood glucose, including blood glucose meters and glucose strips.		√
Ketone Testing		
Determine when assessing the urine and/or blood for ketones is appropriate.	√	
Continuous Glucose Monitoring		
Identify candidate patients for whom continuous glucose monitoring would be helpful.	√	

Interpret data collected by continuous glucose monitoring.		√
Summarize the reliability and cost of continuous glucose monitoring.		√
PATHOGENESIS		
Summarize the staging of type 1 diabetes and pathogenesis of type 1 diabetes, including demographics, genetics, environmental factors, insulin resistance, and islet defects.		√
Summarize the pathogenesis of type 2 diabetes, including demographics, genetics, impaired insulin secretion, insulin resistance, diet, obesity, and inflammation.		√
TYPE 1 DIABETES MELLITUS		
Ketoacidosis		
Summarize the signs and symptoms of diabetic ketoacidosis, including neurologic symptoms, abdominal pain, and volume depletion.	√	
List precipitating factors for diabetic ketoacidosis.	√	
Guide the evaluation and diagnosis of diabetic ketoacidosis.	√	
Interpret laboratory findings associated with diabetic ketoacidosis, including hyperglycemia, hyperosmolality, hyponatremia, hypokalemia, elevated serum ketones, anion gap metabolic acidosis, elevated creatinine, and leukocytosis.	√	
Manage diabetic ketoacidosis.	√	
Recent-Onset Type 1 Diabetes Mellitus		
Summarize the presenting signs and symptoms of previously undiagnosed type 1 diabetes, including chronic polydipsia, polyuria, weight loss, hyperglycemia, ketonemia, diabetic ketoacidosis.	√	
Guide the diagnosis of type 1 diabetes and list the diagnostic criteria.	√	
Interpret results from antibody testing (glutamic acid decarboxylase [GAD65], insulin, tyrosine phosphatase IA-2, and zinc transporter 8 [ZnT8]).	√	
Interpret results from measurement of insulin and C-peptide levels.	√	
Latent Autoimmune Diabetes in Adults (LADA)		
Describe the natural history of latent autoimmune diabetes in adults.		√
Distinguish latent autoimmune diabetes in adults from type 1 diabetes, type 2 diabetes and monogenic diabetes		√
Manage latent autoimmune diabetes in adults.		√

Hyperglycemia in Type 1 Diabetes Mellitus		
Recommend intensive diabetes therapy for patients with type 1 diabetes, including setting glycemic targets, recommending insulin replacement, instituting self-monitoring of blood glucose, and providing diabetes education.	√	
Tailor glycated hemoglobin goals to the individual patient.		√
Guide use of continuous glucose monitoring when needed	√	
<i>Insulin</i>		
Determine insulin doses in a variety of inpatient and outpatient settings.	√	
Design multiple daily injection insulin regimens tailored to individual patients using available basal and bolus insulins and guide insulin adjustments.	√	
Determine appropriate candidates for continuous subcutaneous insulin infusion and sensor-augmented insulin pump therapy and guide insulin adjustments.		√
Troubleshoot problems related to insulin pump therapy.		√
<i>Amylin Mimetics</i>		
Determine when use of amylin mimetics is appropriate in patients with type 1 diabetes and summarize their mechanism of action and contraindications.		√
<i>Metformin</i>		
Determine when use of metformin is appropriate in patients with type 1 diabetes and summarize its mechanism of action and contraindications.		√
<i>Nutrition and Carbohydrate Counting</i>		
Provide guidance regarding nutrition and carbohydrate counting to patients with type 1 diabetes.	√	
<i>Role and Effect of Exercise</i>		
Explain the role of exercise in an intensive diabetes treatment program and recommend an appropriate regimen.	√	
Summarize the effect of exercise on blood glucose.	√	
Hypoglycemia Due to Insulin Management		
Define hypoglycemia in the setting of type 1 diabetes.	√	
Identify risk factors for hypoglycemia, including impaired counterregulatory responses, insulin excess, intensive therapy, long duration type 1 diabetes, poor hypoglycemia awareness and cognitive impairment	√	
Recommend strategies to prevent hypoglycemia, including adjusting glycemic targets and insulin regimens, instituting behavioral approaches to improve patients' recognition of hypoglycemia, addressing	√	

hypoglycemia unawareness, eating a bedtime snack, and adjusting management to prevent exercise-induced hypoglycemia.		
Evaluate hypoglycemia in patients with type 1 diabetes.	√	
Guide treatment of hypoglycemia depending on whether it is asymptomatic, symptomatic, or severe.	√	
Recognition and Management of Associated Conditions		
Identify and manage conditions that can be associated with type 1 diabetes, including hypertension, dyslipidemia, thyroid disease, surgery, celiac disease, depression, anxiety and eating disorders.	√	
Pharmacology of Insulins		
Summarize the pharmacology and action of insulins.	√	
Insulin Analogues		
Differentiate among various insulin analogues, including short-acting, rapid-acting, long-acting, and U500 insulins.	√	
TYPE 2 DIABETES MELLITUS		
Hyperosmolar Nonketotic State		
Summarize the signs and symptoms of the hyperosmolar nonketotic state, including an often insidious onset of polyuria, polydipsia, weight loss, neurologic deterioration, and volume depletion.	√	
List precipitating factors for the hyperosmolar nonketotic state.	√	
Guide the evaluation and diagnosis of the hyperosmolar nonketotic state.	√	
Interpret laboratory findings associated with the hyperosmolar nonketotic state, including hyperglycemia, hyperosmolality, hyponatremia, hypokalemia, elevated creatinine, and leukocytosis.	√	
Manage the hyperosmolar nonketotic state.	√	
Hyperglycemia in Type 2 Diabetes Mellitus		
<i>Metformin</i>		
Determine when use of metformin is appropriate in patients with type 2 diabetes and summarize its mechanism of action and contraindications.	√	
<i>Secretagogues</i>		
Determine when use of secretagogues (eg, sulfonylureas and meglitinides) is appropriate in patients with type 2 diabetes and summarize their mechanism of action and contraindications.	√	
<i>Thiazolidinediones</i>		

Determine when use of thiazolidinediones is appropriate in patients with type 2 diabetes and summarize their mechanism of action and contraindications.	√	
<i>Glucosidase inhibitors</i>		
Determine when use of glucosidase inhibitors is appropriate in patients with type 2 diabetes and summarize their mechanism of action and contraindications.	√	
<i>Glucagonlike Peptide 1 Receptor Agonists</i>		
Determine when use of glucagonlike peptide 1 receptor agonists is appropriate in patients with type 2 diabetes and summarize their mechanism of action and contraindications.		√
<i>Insulin</i>		
Determine insulin doses in a variety of inpatient and outpatient settings.	√	
Design a multiple daily injection insulin regimen tailored to the individual patient and guide insulin adjustments.	√	
Determine appropriate candidates for continuous subcutaneous insulin infusion and guide insulin adjustments.		√
Troubleshoot problems related to insulin pump therapy.		√
<i>Amylin Mimetics</i>		
Determine when use of amylin mimetics is appropriate in patients with type 2 diabetes and summarize their mechanism of action and contraindications.		√
<i>Sodium-Glucose Cotransporter 2 Inhibitors</i>		
Determine when the use of sodium-glucose cotransporter 2 inhibitors (SGLT-2 inhibitors) is appropriate in patients with type 2 diabetes and summarize their mechanism of action and contraindications.		√
Summarize the effects of SGLT-2 inhibitors on cardiovascular endpoints.		√
<i>Bromocriptine</i>		
Determine when use of bromocriptine is appropriate in patients with type 2 diabetes and summarize its mechanism of action and contraindications.		√
<i>Nutrition</i>		
Provide guidance regarding nutrition to patients with type 2 diabetes, with emphasis on the importance of weight reduction.	√	
<i>Role and Effect of Exercise</i>		
Explain the role of exercise in the management of type 2 diabetes mellitus and recommend an exercise regimen, with emphasis on the importance of weight reduction.	√	

<i>Bariatric Surgery in the Management of Type 2 Diabetes Mellitus</i>		
Determine which patients with type 2 diabetes are appropriate candidates for bariatric surgery.	√	
Counsel patients on which bariatric surgical procedures are associated with the greatest rates of remission of type 2 diabetes.		√
Hypoglycemia Due to Oral Agents and Insulin Management		
Define hypoglycemia in the setting of type 2 diabetes.	√	
Identify risk factors for hypoglycemia, including impaired counterregulatory responses, insulin excess, and intensive therapy.	√	
Recommend strategies to prevent hypoglycemia, including adjusting glycemic targets and insulin regimens, instituting behavioral approaches to improve patients' recognition of hypoglycemia, addressing hypoglycemia unawareness, eating a bedtime snack, and adjusting management to prevent exercise-induced hypoglycemia.	√	
Evaluate hypoglycemia in patients with type 2 diabetes.	√	
Guide treatment of hypoglycemia depending on whether it is asymptomatic, symptomatic, or severe.	√	
Management of Associated Conditions		
<i>Hypertension</i>		
Assess for and manage hypertension in patients with type 2 diabetes.	√	
<i>Dyslipidemia</i>		
Assess for and manage dyslipidemia in patients with type 2 diabetes.	√	
<i>Obesity</i>		
Assess for and manage obesity in patients with type 2 diabetes.	√	
<i>Sleep Apnea</i>		
Assess for and manage sleep apnea in patients with type 2 diabetes.	√	
<i>Fatty Liver</i>		
Assess for and manage fatty liver in patients with type 2 diabetes.		√
<i>Low Testosterone in Men</i>		
Summarize guidelines concerning the evaluation and treatment of low testosterone in men	√	
ADDITIONAL TYPES OF DIABETES MELLITUS		
Monogenic Diabetes Syndromes		
Summarize the evaluation and management of neonatal diabetes		√

Summarize the signs and symptoms of monogenic diabetes [maturity-onset diabetes of the young (MODY)], including noninsulin-dependent diabetes diagnosed at a young age, autosomal dominant inheritance, and lack of autoantibodies.		√
Determine when genetic testing is appropriate in patients with maturity-onset diabetes of the young and recommend genetic counseling as needed.		√
Manage monogenic diabetes including maturity-onset diabetes of the young.		√
Ketosis-Prone Diabetes		
Summarize the signs and symptoms of ketosis-prone diabetes, including severe β -cell dysfunction manifested as diabetic ketoacidosis or unprovoked ketosis and variable clinical course.	√	
Manage ketosis-prone diabetes—both acute management of diabetic ketoacidosis and long-term management.		√
New-Onset Diabetes After Transplant		
Define the diagnostic criteria for new-onset diabetes after transplant.	√	
List the risk factors for new-onset diabetes after transplant, including older age, obesity, African American or Hispanic ethnicity, family history, and impaired glucose tolerance.		√
Manage new-onset diabetes after transplant.		√
Medication- and Glucocorticoid-Induced Diabetes		
Summarize the pathophysiology of medication-induced diabetes.		√
Manage glucocorticoid-induced diabetes.		√
Cystic Fibrosis-Related Diabetes (CFR-D)		
Describe screening guidelines for CFRD		√
Manage CFRD		√
Pancreatogenic Diabetes		
Explain the pathophysiology of pancreatogenic diabetes.		√
Manage pancreatogenic diabetes.		√
PREGNANCY		
Gestational Diabetes Mellitus		
Define gestational diabetes mellitus.	√	
Recommend an approach to screening and diagnostic testing for identifying pregnant women with gestational diabetes.	√	
Guide antepartum screening for women with gestational diabetes.	√	

Pregestational Diabetes Mellitus		
Counsel women with diabetes mellitus who are planning for pregnancy.	√	
Guide the management of women with pregestational diabetes mellitus during pregnancy, in the peripartum period, and during breastfeeding.	√	
Risks		
List the risks associated with diabetes during pregnancy, including large-for-gestational-age infants and macrosomia, preeclampsia, polyhydramnios, stillbirth, and neonatal morbidity.	√	
Management		
Guide the management of gestational diabetes, which may include glucose monitoring, medical nutrition therapy, exercise, insulin and antihyperglycemic agents, antenatal fetal testing, and assessment of fetal growth.		√
Manage hypertension in pregnant women with gestational diabetes.		√
Manage retinopathy in pregnant women with gestational diabetes.		√
COMPLICATIONS		
Metabolic Control and Other Mechanisms		
Explain how poor glycemic control leads to microvascular and macrovascular disease.		√
Polyneuropathy and Polyradiculoneuropathy		
Summarize the signs and symptoms of diabetic polyneuropathy, including loss of vibratory sensation, altered proprioception, and impairment of pain, light touch, and temperature sensation.	√	
Summarize the signs and symptoms of diabetic thoracic radiculopathy, diabetic amyotrophy, and diabetic cervical radiculoplexus neuropathy.		√
Differentiate among the screening tests for diabetic polyneuropathy and diagnose this condition.	√	
Distinguish diabetic polyneuropathy from other causes of neuropathy.	√	
Manage diabetic polyneuropathy.	√	
Autonomic Dysfunction		
Summarize the signs and symptoms of diabetic autonomic dysfunction, which can affect different organ systems such as the cardiovascular, gastrointestinal, genitourinary, pupillary, sudomotor, and neuroendocrine systems.	√	
Diagnose diabetic autonomic dysfunction.	√	
Manage diabetic autonomic dysfunction.		√

Mononeuropathies and Proximal Motor Neuropathy		
Differentiate among and diagnose cranial mononeuropathy, peripheral mononeuropathy, and mononeuropathy multiplex.		√
Manage mononeuropathies.		√
Nephropathy		
Summarize the signs and symptoms of diabetic nephropathy, including increased albumin excretion.	√	
Diagnose and manage type 4 renal tubular acidosis and nephrotic syndrome.	√	
Recommend treatment to preserve renal function via pharmacotherapy, weight reduction, and lipid lowering.	√	
Counsel patients regarding the importance of good glycemic control and blood pressure control to reduce the incidence and progression of nephropathy.	√	
Cardiovascular and Cerebrovascular Disease		
Identify factors that contribute to increased cardiovascular risk in patients with diabetes, including hypertension, obesity, and dyslipidemia.	√	
Screen for coronary disease in patients with diabetes, which may include computed tomography and stress testing.	√	
Recommend interventions to reduce the risk of cardiovascular disease in patients with diabetes, which may include addressing dyslipidemia and hypertension, instituting lifestyle changes, intensifying glycemic control, and recommending other adjunctive therapies.	√	
Explain the effect of diabetes medications on cardiovascular endpoints in patients with type 2 diabetes.		√
Erectile Dysfunction		
Evaluate for erectile dysfunction in men with diabetes.	√	
Treat erectile dysfunction.	√	
Infections		
Summarize the signs and symptoms of diabetic foot infections, including inflammation, pus in an ulcer, nonpurulent drainage, friable or discolored granulation tissue, and undermining of wound edges.	√	
Evaluate for underlying osteomyelitis.	√	
Manage diabetic foot infections, which may include wound management, antimicrobial therapy, glycemic control, surgery, and fluid and electrolyte balance.		√
Diabetic Foot		

List risk factors for ulcers and amputations, including previous foot ulceration, neuropathy, foot deformity, and vascular disease.	√	
Assess for foot ulceration.	√	
Screen for peripheral neuropathy with vibration sensation, pressure sensation, and superficial pain or temperature sensation.	√	
Counsel patients on preventive foot care.	√	
Diabetic Eye Diseases		
Distinguish between nonproliferative diabetic retinopathy, proliferative diabetic retinopathy and macular edema		√
Recommend appropriate treatment of retinopathy and macular edema		√
Counsel patients regarding the importance of good glycemic control and blood pressure control to reduce the incidence and progression of retinopathy.	√	
Bone Health		
Summarize the effect of diabetes on bone health.	√	
Summarize the effect of diabetes on dual-energy x-ray absorptiometry assessment of bone mineral density.		√
Manage osteoporosis in patients with diabetes.	√	
Psychosocial/Emotional Disorders		
Assess for depression and anxiety and refer to mental health professionals	√	
SKIN DISEASES		
Differentiate among skin diseases associated with diabetes, including lipohypertrophy, lipodystrophy, necrobiosis, and acanthosis nigricans.	√	
Manage the various skin diseases associated with diabetes.		√
ISLET-CELL AND PANCREAS TRANSPLANT		
List indications for transplant.		√
Determine which patients are appropriate candidates for transplant.		√
Summarize effects of transplant on the chronic complications of diabetes.		√
Summarize outcomes data (patient and graft survival) related to pancreas and islet-cell transplant.		√
DIABETES PREVENTION		
Prevention of Type 1 Diabetes Mellitus		

Summarize prevention and reversal strategies that are being investigated for type 1 diabetes, including immunomodulators, anti-inflammatory agents, and supplements.		√
Prevention of Type 2 Diabetes Mellitus		
Recommend measures to prevent type 2 diabetes, including lifestyle modification, pharmacologic therapy, and bariatric surgery.	√	
HYPOGLYCEMIA NOT RELATED TO DIABETES TREATMENT		
Mechanisms		
Explain the pathophysiology of hypoglycemia.	√	
Diagnosis		
Define the Whipple triad.	√	
Determine which patients require further evaluation and management of hypoglycemia on the basis of the Whipple triad.	√	
Guide the clinical evaluation and laboratory testing of patients with hypoglycemia who do not have diabetes, which may include fasting evaluation, postprandial evaluation, and a 72-hour fast.		√
Interpret data obtained from clinical and laboratory testing, including values of plasma insulin, plasma C-peptide, plasma β -hydroxybutyrate, and the glycemic response to glucagon.		√
Recommend localizing studies after endogenous insulin-mediated hypoglycemia has been documented.		√
Causes		
<i>Insulinoma</i>		
Diagnose and manage insulinoma.		√
<i>Liver and Kidney Failure/Sepsis</i>		
Diagnose and manage critical illness that can cause hypoglycemia.	√	
<i>Adrenal Insufficiency</i>		
Diagnose and manage adrenal insufficiency as a possible cause of hypoglycemia.	√	
<i>Factitious</i>		
Identify and manage cases of accidental, surreptitious, or malicious hypoglycemia.	√	
<i>Postprandial</i>		
Diagnose and manage postprandial (reactive) hypoglycemia.		√
<i>Nesidioblastosis</i>		

Diagnose and manage a functional β -cell disorder, nesidioblastosis, as a cause of hypoglycemia.		√
<i>Drug-Induced</i>		
List drugs that can cause hypoglycemia, including insulin, sulfonylureas, and meglitinides.	√	
<i>Type B Insulin Resistance Syndrome/Anti-insulin Receptor Antibodies</i>		
Explain the pathophysiology of hyperglycemia and hypoglycemia associated with insulin receptor antibodies.		√
List conditions associated with type B insulin resistance.		√
Diagnose and manage type B insulin resistance syndrome with hypoglycemia (or hyperglycemia).		√
INPATIENT DIABETES MANAGEMENT		
Recommend glycemic targets in hospitalized patients with diabetes depending on whether they are noncritically ill or critically ill.	√	
Guide the insulin regimen of hospitalized patients with diabetes.	√	
Manage the regimen of hospitalized patients with diabetes who are typically treated with oral agents at home.	√	
Manage the regimen of hospitalized patients with diabetes who are receiving total parenteral nutrition.		√
RARE DISORDERS		
Lipodystrophy		
Diagnose and manage the metabolic abnormalities associated with lipodystrophic disorders.		√
Polyendocrine Failure		
Diagnose and manage the metabolic abnormalities associated with polyendocrine failure.		√

TEACHING METHODS AND EVALUATION

Much teaching occurs one-on-one with attendings during outpatient clinics and on inpatient hospital rounds. Active learning occurs as fellows participate in patient care under the supervision and guidance of the attendings. Attendings review fellows knowledge, skills and medical reasoning during clinic and hospital rounds. In addition, the full range of topics are reviewed in didactic sessions at weekly conferences and in the core curriculum/board review weekly sessions. Fellows are expected to engage in self-directed study guided by the curriculum

and by the faculty. Evaluation includes attending reviews of fellow performance during outpatient and inpatient rotations, as well as the in-training exam taken annually which reflects knowledge progression during fellowship.

SUGGESTED READING

Asterisks denote references that are designated for trainees early in their training.

GENERAL READING: Standards of Medical Care in Diabetes	
*American Diabetes Association. Standards of medical care in diabetes – 2017. <i>Diabetes Care</i> 2017; 40 (Suppl 1):S1-S127. (updated every January and available online at diabetes.org)	Article
*Walsh J, Roberts R. <i>Pumping Insulin: Everything for Success on an Insulin Pump and CGM</i> . 6 th ed. Torrey Pines Press, 2016.	Book
GENERAL READING, PHYSIOLOGY, METABOLISM	
*Melmed S, Polonsky KS, Larsen PR, Kronenberg HM, eds. <i>Williams Textbook of Endocrinology</i> . 13th ed. Philadelphia, PA: Saunders; 2015.	Textbook
DEFINITIONS AND DIAGNOSIS	
*American Diabetes Association. Classification and diagnosis of diabetes mellitus. <i>Diabetes Care</i> . 2017;40 (Suppl 1):S11-S24.	Article
MONITORING GLYCEMIC CONTROL	
*Peters AL, Ahmann AJ, Battelino T et al. Diabetes technology-continuous subcutaneous insulin infusion therapy and continuous glucose monitoring in adults: an Endocrine Society Clinical Practice Guideline. <i>J Clin Endocrinol Metab</i> . 2016; 101:3922-3937.	Article
Bally L, Thabit H, Kojzar H, et al. Day-and-night glycaemic control with closed-loop insulin delivery versus conventional insulin pump therapy in free-living adults with well controlled type 1 diabetes: an open-label, randomised, crossover study. <i>Lancet Diabetes Endocrinol</i> . 2017 [Epub ahead of print]	Article
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Tamborlane WV, Beck RW, et al. Continuous glucose monitoring and intensive treatment of type 1 diabetes. <i>N Engl J Med</i> . 2008; 359(14):1464-1476.	Article

*Bergonstol RM, Gal RL, Conner CG et al. Racial differences in the relationships of glucose concentrations and hemoglobin A1c levels. <i>Ann Intern Med.</i> 2017; 167:95-102.	Article
PATHOGENESIS	
Skyler JS, Bakris GL, Bonifacio E et al. Differentiation of diabetes by pathophysiology, natural history and prognosis. <i>Diabetes.</i> 2017; 66:241-255.	Article
Nolan CJ, Damm P, Prentki M. Type 2 diabetes across generations: from pathophysiology to prevention and management. <i>Lancet.</i> 2011;378(9786):169-181.	Article
TYPE 1 DIABETES MELLITUS	
*Atkinson MA. Type 1 diabetes mellitus. In: Melmed S, Polonsky KS, Larsen PR, Kronenberg HM, eds. <i>Williams Textbook of Endocrinology.</i> 13th ed. Philadelphia, PA: Saunders; 2015:1451-1483.	Textbook
Kakleas K, Soldatou A, Karachaliou F, Karavanaki K. Associated autoimmune diseases in children and adolescents with type 1 diabetes mellitus (T1DM). <i>Autoimmun Rev.</i> 2015;30;14(9):781-797.	Article
Vehik K, Beam CA, Mahon JL, et al; TrialNet Natural History Study Group. Development of Autoantibodies in the TrialNet Natural History Study. <i>Diabetes Care.</i> 2011;34(9):1897-1901.	Article
Kitabchi AE, Umpierrez GE, Murphy MB, et al; American Diabetes Association. Hyperglycemic crises in diabetes. <i>Diabetes Care.</i> 2004;27(Suppl 1):S94-S102.	Article
Umpierrez G, Korytkowski M. Diabetic emergencies: ketoacidosis, hyperglycemic hyperosmolar state and hypoglycemia. <i>Nat Rev Endocrinol.</i> 2016; 12:222-32.	Article
TYPE 2 DIABETES MELLITUS	
*Polonsky KS, Burant CF. Type 2 diabetes mellitus. In: Melmed S, Polonsky KS, Larsen PR, Kronenberg HM, eds. <i>Williams Textbook of Endocrinology.</i> 13th ed. Philadelphia, PA: Saunders; 2015:1386-1450.	Textbook
Ali O. Genetics of type 2 diabetes. <i>World J Diabetes.</i> 2013;4(4):114-123.	Article
DeFronzo RA. Banting Lecture. From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus. <i>Diabetes.</i> 2009;58(4):773-795.	Article
*Duckworth W, Abraira C, Moritz T, et al; VADT Investigators. Glucose control and vascular complications in veterans with type 2 diabetes [published correction appears in <i>N Engl J Med.</i> 2009;361(10):1028]. <i>N Engl J Med.</i> 2009;360(2):129-139.	Article
*Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein HC, Miller ME, et al. Effects of intensive glucose lowering in type 2 diabetes. <i>N Engl J Med.</i> 2008;358(24):2545-2559.	Article

*ADVANCE Collaborative Group, Patel A, MacMahon S, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. <i>N Engl J Med.</i> 2008;358(24):2560-2572.	Article
*Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. <i>N Engl J Med.</i> 2008;359(15):1577-1589.	Article
*Kahn SE, Haffner SM, Heise MA, et al; ADOPT Study Group. Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy [published correction appears in <i>N Engl J Med.</i> 2007;356(13):1387-1388]. <i>N Engl J Med.</i> 2006;355(23):2427-2443.	Article
*Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group [published correction appears in <i>Lancet.</i> 1999;354(9178):602]. <i>Lancet.</i> 1998;352(9131):837-853.	Article
UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33) [<i>Lancet.</i> 1999;354(9178):602]. <i>Lancet.</i> 1998;352(9131):837-853.	Article
UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34) [published correction appears in <i>Lancet.</i> 1998;352(9139):1558]. <i>Lancet.</i> 1998;352(9131):854-865.	Article
UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes [published correction appears in <i>BMJ.</i> 1999;318(7175):29]. <i>BMJ.</i> 1998;317(7160):703-713.	Article
ADDITIONAL TYPES OF DIABETES MELLITUS	
Makuc J. Management of pancreatogenic diabetes: challenges and solutions. <i>Diabetes Metab Syndr Obes.</i> 2016;9:311-315.	Article
Orsi E, Grancini V, Menini S, Aghemo A, Pugliese G. Hepatogenous diabetes: is it time to separate it from type 2 diabetes? <i>Liver Int.</i> 2016 [Epub ahead of print]	Article
Repaske DR. Medication-induced diabetes mellitus. <i>Pediatr Diabetes.</i> 2016;17(6):392-397.	Article
Tamez-Pérez HE, Quintanilla-Flores DL, Rodríguez-Gutiérrez R, González-González JG, Tamez-Peña AL. Steroid hyperglycemia: prevalence, early detection and therapeutic recommendations: a narrative review. <i>World J Diabetes.</i> 2015;6(8):1073-1781.	Article
Hattersley A, Bruining J, Shield J, Njolstad P, Donaghue KC. The diagnosis and management of monogenic diabetes in children and adolescents. <i>Pediatr Diabetes.</i> 2009;10(Suppl 12):33-42.	Article
Balasubramanyam A, Nalini R, Hampe CS, Maldonado M. Syndromes of ketosis-prone diabetes. <i>Endocr Rev.</i> 2008;29(3):292-302.	Article

PREGNANCY

American Diabetes Care. 13. Management of Diabetes in Pregnancy. <i>Diabetes Care</i> . 2017;40(Suppl 1):S114-S119.	Article
Bergel R, Hadar E, Toledano Y, Hod M. Pharmacological management of gestational diabetes mellitus. <i>Curr Diab Rep</i> . 2016;16(11):118.	Article

COMPLICATIONS

*Fayfman M, Pasquel FJ, Umpierrez GE. Management of hyperglycemic crisis: diabetic ketoacidosis and hyperglycemic hyperosmolar state. <i>Med Clin North Am</i> . 2017; 101:587-606.	
Marso SP, Daniels GH, Brown-Frandsen K, et al; LEADER Steering Committee; LEADER Trial Investigators. Liraglutide and cardiovascular outcomes in type 2 diabetes. <i>N Engl J Med</i> . 2016;375(4):311-322.	Article
Schacter GI, Leslie WD. Diabetes and bone disease. <i>Endocrinol Metab Clin North Am</i> . 2016;46(1):63-85.	Article
Zinman B, Wanner C, Lachin JM, et al EMPA-REG OUTCOME Investigators. <i>New Engl J Med</i> . 2015;373(22):2117-2128.	Article
Look AHEAD Research Group, Wing RR, Bolin P, et al. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes [published correction appears in <i>N Engl J Med</i> . 2014;370(19):1866]. <i>N Engl J Med</i> . 2013;369(2):145-154.	Article
*Cholesterol Treatment Trialists' (CTT) Collaborators, Kearney PM, Blackwell, et al. Efficacy of cholesterol-lowering therapy in 18,686 people with diabetes in 14 randomised trials of statins. <i>Lancet</i> . 2008;371(9607):117-125.	Article
Poitout V, Robertson RP. Glucolipototoxicity: fuel excess and beta-cell dysfunction. <i>Endocr Rev</i> . 2008;29(3):351-366.	Article
Nathan DM, Cleary PA, Backlund JY, et al; Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. <i>N Engl J Med</i> . 2005;353(25):2643-2653.	Article
DCCT Research Group. Retinopathy and nephropathy in patients with type 1 diabetes four years after a trial of intensive therapy [published correction appears in <i>N Engl J Med</i> . 2000;342(18):1376]. <i>N Engl J Med</i> . 2000;342(6):381-389.	Article
The DCCT Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. <i>N Engl J Med</i> . 1993;329(14):977-986.	Article

Sellmeyer DE, Civitelli R, Hofbauer LC et al. Skeletal metabolism fracture risk and fracture outcomes in type 1 and type 2 diabetes. <i>Diabetes</i> . 2016; 65:1757-66.	Article
SKIN DISEASES	
de Macedo GM, Nunes S, Barreto T. Skin disorders in diabetes mellitus: an epidemiology and physiopathology review. <i>Diabetol Metab Syndr</i> . 2016;8(1):63.	Article
Makrantonaki E, Jiang D, Hossini AM, et al. Diabetes mellitus and the skin. <i>Rev Endocr Metab Disord</i> . 2016;17(3):269-282.	Article
ISLET-CELL AND PANCREAS TRANSPLANT	
Shapiro AM, Pokrywczynska M, Ricordi C. Clinical pancreatic islet transplantation. <i>Nature Rev Endocrinol</i> . 2017 May; 13:268-277.	Article
Shapiro AJ, Ricordi C, Hering BJ, et al. International trial of the Edmonton protocol for islet transplantation. <i>N Engl J Med</i> . 2006;355(13):1318-1330.	Article
DIABETES PREVENTION	
Orchard TJ, Temprosa M, Goldberg R, et al; Diabetes Prevention Program Research Group. The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: the Diabetes Prevention Program randomized trial. <i>Ann Intern Med</i> . 2005;142(8):611-619.	Article
Lindström J, Eriksson JG, Valle TT, et al. Prevention of diabetes mellitus in subjects with impaired glucose tolerance in the Finnish Diabetes Prevention Study: results from a randomized clinical trial. <i>J Am Soc Nephrol</i> . 2003;14(7 Suppl 2):S108-S113.	Article
Jacobsen L, Schatz D. Current and future efforts toward the prevention of type 1 diabetes. <i>Pediatric Diabetes</i> . 2016; 17 (Suppl 22):78-86.	
HYPOGLYCEMIA NOT RELATED TO DIABETES TREATMENT	
Davi MV, Pia A, Guarnotta V, Pizza G, Colao A, Faggiano A; NIKE Group. The treatment of hyperinsulinemic hypoglycaemia in adults: an update. <i>J Endocrinol Invest</i> . 2017;40(1):9-20.	Article
*Cryer PE. Hypoglycemia. In: Melmed S, Polonsky KS, Larsen PR, Kronenberg HM, eds. <i>Williams Textbook of Endocrinology</i> . 13th ed. Philadelphia, PA: Saunders; 2015:1582-1607.	Textbook
Arioglu E, Andewelt A, Diabo C, Bell M, Taylor SI, Gorden P. Clinical course of the syndrome of autoantibodies to the insulin receptor (type B insulin resistance): a 28-year perspective. <i>Medicine (Baltimore)</i> . 2002;81(2):87-100.	Article
INPATIENT DIABETES MANAGEMENT	

Umpierrez GE, Hellman R, Korytkowski MT, et al; Endocrine Society. Management of hyperglycemia in hospitalized patients in non-critical care setting: an endocrine society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2012;97(1):16-38.	Clinical Practice Guideline
*NICE-SUGAR Study Investigators, Finfer S, Chittock DR, et al. Intensive versus conventional glucose control in critically ill patients. <i>N Engl J Med.</i> 2009;360(13):1283-1297.	Article
RARE DISORDERS	
Gupta N, Asi N, Farah W, et al. Clinical features and management of non-HIV related lipodystrophy in children: a systematic review. <i>J Clin Endocrinol Metab.</i> 2016 [Epub ahead of print]	Article
Vantyghem MC, Balavoine AS, Douillard C, et al. How to diagnose a lipodystrophy syndrome. <i>Ann Endocrinol (Paris).</i> 2012;30:73(3):170-189.	Article
Cutolo M. Autoimmune polyendocrine syndromes. <i>Autoimmun Rev.</i> 2014;13(2):85-89.	Article
Eisenbarth GS, Gottlieb PA. Autoimmune polyendocrine syndromes. <i>N Engl J Med.</i> 2004;350(20):2068-2079.	Article

GONADAL DISORDERS

INTRODUCTION

Endocrinology of the reproductive system (male and female) encompasses normal pubertal development; normal adult reproductive function; myriad disorders of reproductive development and reproductive function; the effects of reproductive hormone excess or deficiency on other body systems; and the physiologic decline of reproductive function with aging. Issues related to reproductive endocrinology are highly prevalent, highlighting the importance of this area in an endocrine fellowship training program. Disorders of this system may arise at various functional levels (eg, hypothalamus, pituitary, gonad, end organ), and dysfunction may constitute a primary abnormality and/or occur secondarily in response to nonreproductive abnormalities. Reproductive issues commonly encountered in a general endocrine practice include male and female hypogonadism, ovulatory dysfunction, polycystic ovary syndrome, subfertility or infertility, and menopause. In addition, this area of study includes abnormalities affecting sex steroid-responsive organs such as skin (eg, hirsutism), penis (eg, erectile dysfunction), prostate (an androgen-sensitive organ), uterus (eg, dysfunctional uterine bleeding), and breast (eg, gynecomastia, hormone-responsive breast cancer). Primary abnormalities of the reproductive system may also have a profound impact on other endocrine and nonendocrine systems (eg, musculoskeletal, metabolic, cardiovascular, etc). Fellows should be competent in the diagnosis and management of gonadal disorders.

MEDICAL KNOWLEDGE

Fellows must demonstrate knowledge about established and evolving biomedical, clinical, and cognate (eg, epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.

Topic	Fundamental	Advanced
FEMALE REPRODUCTION: BASIC PHYSIOLOGIC PRINCIPLES AND ASSESSMENT TOOLS		
Summarize the synthesis/secretion, cyclic patterns (eg, serum concentrations), and cellular/tissue actions of gonadotropin-releasing hormone, gonadotropins (luteinizing hormone and follicle-stimulating hormone), and sex steroids (estradiol, progesterone, testosterone—in addition to their precursors and metabolites).	√	
Summarize the synthesis/secretion and cellular/tissue actions of other proteins important to the regulation of reproductive function such as the inhibin/activin/follistatin family of proteins and antimüllerian hormone.		√
Describe the normal menstrual cycle, including oogenesis, follicular development, ovulation, luteal function, cycle phase-dependent	√	

regulation of sex steroid production, and the end-organ effects of sex steroids as they relate to preparation for pregnancy.		
Explain the endocrine physiology of pregnancy, parturition, and lactation.	√	
Explain the myriad physiologic alterations that occur in other nonreproductive endocrine systems during pregnancy.		√
Explain the physiology of reproductive aging in women and the effects of reproductive aging on other body systems.		√
Summarize the effects of acute and chronic disease on the reproductive system in women.		√
Provide basic interpretation of ovarian ultrasonography, computed tomography, and magnetic resonance imaging.		√
Interpret results from hormone assays (peptide and steroid) and dynamic hormone testing (eg, gonadotropin-releasing hormone stimulation test).	√	

FEMALE REPRODUCTION: SEXUAL DIFFERENTIATION AND PUBERTY

Summarize the normal growth and differentiation of the female gonads (including germ-cell development), internal genitalia, and accessory sex organs.		√
Develop a basic understanding of disorders of sex development.		√
Describe normal female puberty, including both adrenarche and gonadarche.	√	
Evaluate precocious pubarche/adrenarche in female patients.		√
Evaluate precocious thelarche.		√
Evaluate delayed thelarche.		√
Evaluate primary amenorrhea.		√

FEMALE REPRODUCTION: OVULATORY DYSFUNCTION

Primary Amenorrhea

Explain the diagnostic approach to primary amenorrhea, including important components of the history and physical examination (eg, presence or absence of breast development, presence or absence of the uterus) and measurement of follicle-stimulating hormone.	√	
Diagnose the most common causes of primary amenorrhea such as gonadal dysgenesis (eg, Turner syndrome), mullerian agenesis/dysgenesis, physiologic delay of puberty, and polycystic ovary syndrome.	√	

Diagnose less common causes of primary amenorrhea such as structural abnormalities (transverse vaginal septum, imperforate hymen), hypogonadotropic hypogonadism (eg, hyperprolactinemia, congenital gonadotropin-releasing hormone deficiency [eg, Kallman syndrome], hypopituitarism, functional hypothalamic amenorrhea, systemic illness), complete androgen insensitivity syndrome, steroidogenic enzyme and sex steroid receptor defects (eg, 5 α -reductase deficiency, 17 α -hydroxylase deficiency), and other endocrine disease (hypothyroidism, Cushing syndrome).		√
Explain general management principles for primary amenorrhea, including appropriate psychological counseling, surgical consultation (when appropriate), induction of puberty (when appropriate), and sex steroid replacement therapy.		√
<i>Turner Syndrome</i>		
Diagnose and manage the reproductive manifestations of Turner syndrome (eg, hypogonadism).	√	
Perform appropriate screening for nonreproductive disease in Turner syndrome.		√
<i>Congenital Gonadotropin-Releasing Hormone Deficiency</i>		
Diagnose and manage congenital gonadotropin-releasing hormone deficiency, including induction of puberty, sex steroid replacement therapy, and infertility treatment options.		√
<i>Complete and Partial Androgen Insensitivity Syndromes</i>		
Diagnose and manage androgen insensitivity syndrome, including psychological support, gender assignment/determination, and surgical considerations (eg, indications for gonadectomy).		√
Secondary Amenorrhea/Oligomenorrhea		
Explain the diagnostic approach to secondary amenorrhea/oligomenorrhea, including important components of history and physical examination and initial laboratory testing (ie, pregnancy testing; measurement of follicle-stimulating hormone, prolactin, thyrotropin).	√	
Diagnose the most common causes of secondary amenorrhea/oligomenorrhea such as pregnancy, functional hypothalamic amenorrhea, polycystic ovary syndrome, hyperprolactinemia, and primary ovarian insufficiency.	√	
Diagnose less common causes of secondary amenorrhea/oligomenorrhea such as intrauterine adhesions (Asherman syndrome), structural		√

pituitary/hypothalamic disease, Cushing syndrome, hypothyroidism, and nonclassic congenital adrenal hyperplasia.		
Explain management principles for secondary amenorrhea/oligomenorrhea, including methods, benefits, and risks of sex steroid replacement therapy; treatment options; and fertility counseling.	√	
<i>Primary Ovarian Insufficiency</i>		
Diagnose and manage primary ovarian insufficiency due to autoimmune etiologies (eg, autoimmune oophoritis, syndromes of polyglandular autoimmune failure [types I and II]), genetic etiologies (eg, Turner syndrome, Fragile X premutations), and ovarian toxins (eg, chemotherapy, radiation therapy).	√	
Explain general management principles for primary ovarian insufficiency, including methods, benefits, and risks of sex steroid replacement therapy; treatment options; and fertility counseling.	√	
<i>Hypogonadotropic Hypogonadism</i>		
Diagnose and manage hypogonadotropic hypogonadism related to structural pituitary/hypothalamic disease.	√	
Diagnose and manage hypogonadotropic hypogonadism related to reduced energy availability (ie, functional hypothalamic amenorrhea).		√
<i>Hyperprolactinemia</i>		
Diagnose and manage ovulatory dysfunction and galactorrhea due to hyperprolactinemia.	√	
Evaluate and manage normoprolactinemic galactorrhea.		√
FEMALE REPRODUCTION: HYPERANDROGENISM		
Explain the diagnostic approach to hyperandrogenism, including clinical assessment of hirsutism, appropriate biochemical testing, and relevant limitations of current androgen assays.	√	
Differentiate among the following potential causes of hyperandrogenism: polycystic ovary syndrome, idiopathic hirsutism, congenital adrenal hyperplasia (eg, 21-hydroxylase deficiency), androgen-secreting ovarian or adrenal tumors, ovarian hyperthecosis, exogenous androgen exposure, and other endocrine disease (severe insulin resistance syndromes, Cushing syndrome, acromegaly).	√	
Polycystic Ovary Syndrome		
<i>Diagnosis</i>		

Describe the potential strengths and weaknesses of different diagnostic criteria for polycystic ovary syndrome: Rotterdam criteria, National Institutes of Health criteria, and Androgen Excess-PCOS Society criteria.	√	
Define the presence and degree of clinical and biochemical hyperandrogenism and assess ovulatory function via history (and laboratory testing as needed).	√	
Explain the diagnostic limitations of current androgen assays and of polycystic ovarian morphology assessments.	√	
Exclude other causes of hyperandrogenism and/or oligo-ovulation or anovulation such as nonclassic congenital adrenal hyperplasia, androgen-secreting ovarian or adrenal tumors, primary ovarian insufficiency, hyperprolactinemia, thyroid disease, Cushing syndrome, acromegaly, and exogenous androgen exposure.	√	
<i>Comorbidities</i>		
Identify and address potential comorbidities associated with polycystic ovary syndrome, including obesity, impaired glucose tolerance, type 2 diabetes mellitus, dyslipidemia, metabolic syndrome, obstructive sleep apnea, and depression/anxiety.	√	
<i>Management</i>		
Recommend management strategies for hyperandrogenic symptoms, oligo-ovulation or anovulation, risk for endometrial hyperplasia, metabolic abnormalities, contraception (as needed), and infertility (as needed).	√	
Ovarian Hyperthecosis		
Diagnose and manage ovarian hyperthecosis.		√
Androgen-Secreting Ovarian Tumors		
Diagnose and manage hyperandrogenism due to ovarian sex cord-stromal tumors (eg, Sertoli-Leydig cell tumors, Sertoli-cell tumors, Leydig-cell tumors).		√
Androgen-Secreting Adrenal Tumors		
Diagnose and manage hyperandrogenism due to adrenal tumors, including adenomas and carcinomas.		√
Nonclassic Congenital Adrenal Hyperplasia		
<i>Diagnosis</i>		
In the setting of suggestive clinical findings, screen for nonclassic 21-hydroxylase deficiency and perform appropriate confirmatory testing as needed.	√	
<i>Management</i>		

Recommend treatment for nonclassic congenital adrenal hyperplasia, which can include oral contraceptives, glucocorticoids, and spironolactone.	√	
Recommend genetic counseling as appropriate.		√
Other Hyperandrogenism		
Diagnose and manage gestational (pregnancy-associated) hyperandrogenism.		√
Diagnose and manage postmenopausal hyperandrogenism.		√
FEMALE REPRODUCTION: INFERTILITY		
Define infertility and describe the indications for evaluation and treatment.		√
Perform a basic evaluation of infertility, including assessments of ovulatory function and possibly ovarian reserve, patency of the female reproductive tract, and semen analysis for the male partner.		√
Explain the role of hysterosalpingogram in the evaluation of female infertility.		√
Anovulation		
Explain the various ways to assess ovulatory function (eg, by menstrual history, midluteal serum progesterone measurement, ovulation prediction kits, ultrasonographic surveillance).	√	
Differentiate among causes of anovulatory infertility according to gonadotropin and estrogen concentrations, including hypogonadotropic hypogonadal anovulation, normogonadotropic normoestrogenic anovulation, or hypergonadotropic hypoestrogenic anovulation.	√	
Recommend infertility treatment options as they relate to the above categories: hypogonadotropic hypogonadal anovulation (eg, gonadotropin therapy, pulsatile GnRH therapy), normogonadotropic normoestrogenic anovulation (eg, clomiphene, aromatase inhibitors, gonadotropin therapy), or hypergonadotropic hypoestrogenic anovulation.	√	
Provide basic counseling regarding more advanced infertility treatments (eg, in vitro fertilization).		√
Age-Associated Infertility (Diminished Ovarian Reserve)		
Perform basic assessments of ovarian reserve.	√	
Counsel patients about age-associated infertility.		√
Fertility Preservation		

Perform basic counseling regarding options for fertility preservation in patients at high risk for developing infertility (eg, patients with certain cancers, female-to-male transgender patients).		√
FEMALE REPRODUCTION: HORMONAL CONTRACEPTION		
Provide basic counseling regarding available forms of contraception, including the various forms of hormonal contraception, intrauterine contraceptive devices, and barrier methods.	√	
Explain noncontraceptive indications for hormonal contraceptive preparations.		√
Combined Estrogen-Progestin Contraceptives		
Identify appropriate candidates for—and those with contraindications to—combined estrogen-progestin contraceptives.	√	
Counsel patients regarding the risks and benefits of—and alternatives to—combined estrogen-progestin contraceptives.	√	
Prescribe and monitor the safety of combined estrogen-progestin contraceptives.	√	
Progestin-Only Contraceptives		
Identify appropriate and inappropriate candidates for progestin-only contraceptives.		√
Counsel patients regarding the risks and benefits of—and alternatives to—progestin-only contraceptives.		√
Prescribe and monitor the safety of progestin-only contraceptives.		√
FEMALE REPRODUCTION: PREMENSTRUAL SYNDROME/PREMENSTRUAL DYSPHORIC DISORDER		
Diagnose and manage premenstrual syndrome/premenstrual dysphoric disorder.		√
FEMALE REPRODUCTION: PERIMENOPAUSE AND MENOPAUSE		
Perimenopause and Menopause		
Identify clinical manifestations and consequences of perimenopause and menopause, including estrogen deficiency.	√	
Use the STRAW staging system (Stages of Reproductive Aging Workshop) to characterize the stages of reproductive aging in women.		√

When appropriate, distinguish menopause from pregnancy and other endocrine abnormalities.	√	
Address special diagnostic considerations in the setting of premature primary ovarian insufficiency (premature menopause).		√
Menopausal Hormone Therapy		
Counsel patients regarding the risks and benefits of—and alternatives to—menopausal hormone therapy.	√	
Devise a personalized approach to hormone therapy, taking into consideration a woman's baseline cardiovascular and breast cancer risk.	√	
List the indications for combined estrogen-progestin therapy and estrogen-alone therapy.	√	
Develop a thorough working knowledge of nonhormonal strategies for menopausal symptoms.		√

MALE REPRODUCTION: BASIC PHYSIOLOGIC PRINCIPLES AND ASSESSMENT TOOLS

Summarize the synthesis/secretion, daily patterns (eg, serum concentrations), and cellular/tissue actions of gonadotropin-releasing hormone, gonadotropins (luteinizing hormone and follicle-stimulating hormone), and sex steroids (testosterone and estradiol—in addition to their precursors and metabolites).	√	
Summarize the synthesis/secretion and cellular/tissue actions of other proteins important to the regulation of reproductive function such as the inhibin family of proteins.		√
Describe normal male reproductive physiology, including regulation of androgen production and spermatogenesis.	√	
Explain the physiology of reproductive aging in men and the effects of reproductive aging on other body systems.		√
Summarize the effects of acute and chronic disease on the reproductive system in men.		√
Interpret results from hormone assays (peptide and steroid) and dynamic hormone testing (eg, gonadotropin-releasing hormone stimulation test).	√	

MALE REPRODUCTION: SEXUAL DIFFERENTIATION AND PUBERTY

Summarize the normal growth and differentiation of the male gonads (including germ-cell development), internal genitalia, and accessory sex organs.		√
Develop a basic understanding of disorders of sex development.		√

Describe normal male puberty.	√	
Evaluate precocious puberty in male patients.		√
Evaluate delayed puberty in male patients.		√
List the indications for induction of male puberty.		√
Guide the appropriate use of testosterone to induce male secondary sexual characteristics.		√
Genetic Disorders of Androgen Action		
<i>5α-Reductase Deficiency</i>		
Diagnose and manage 5 α -reductase deficiency.		√
<i>Androgen Insensitivity Syndromes Due to Androgen Receptor Mutations</i>		
Diagnose and manage androgen insensitivity syndromes.		√
MALE REPRODUCTION: HYPOGONADISM		
Clinical Presentation		
Describe the clinical features of male hypogonadism.	√	
Explain the ways that clinical features may differ between primary and secondary (hypogonadotropic) hypogonadism.	√	
Diagnosis		
<i>Appropriate Use of Diagnostic Tests</i>		
Determine when evaluation for male hypogonadism is appropriate.	√	
Recommend appropriate testing for hypogonadism (eg, morning serum testosterone measurements, confirmation of abnormal values, indications for measurement of sex hormone-binding globulin and free testosterone).	√	
In patients with confirmed hypogonadism, perform and appropriately interpret gonadotropin testing (luteinizing hormone, follicle-stimulating hormone) to distinguish between primary and secondary (hypogonadotropic or central) hypogonadism.	√	
Perform appropriate testing to determine the cause of hypogonadism, guided by gonadotropin results (eg, prolactin and other pituitary hormones, iron studies, and possible pituitary magnetic resonance imaging for patients with secondary hypogonadism, and karyotype for patients with primary hypogonadism).	√	
List the indications for semen analysis and what constitutes abnormal results.	√	
<i>Potential Pitfalls of Diagnostic Tests</i>		

List potential pitfalls of current methods of serum total testosterone and free testosterone measurement.	√	
Primary Hypogonadism		
<i>Cryptorchidism</i>		
Explain the causes, diagnosis, management, and potential long-term sequelae of cryptorchidism.	√	
<i>Klinefelter Syndrome and Other Genetic Etiologies</i>		
Diagnose and manage Klinefelter syndrome.	√	
Describe extragonadal manifestations of Klinefelter syndrome.	√	
Identify rare genetic disorders associated with primary hypogonadism (eg, Y-chromosome microdeletions, gonadotropin receptor mutations, defects of androgen biosynthesis, myotonic dystrophy).		√
<i>Acquired Primary Hypogonadism</i>		
Identify potential causes of acquired primary hypogonadism, including mumps infection (mumps orchitis), direct radiation exposure, alkylating agents, other medications (eg, ketoconazole, suramin), trauma, and testicular torsion.	√	
Secondary Hypogonadism		
<i>Hypothalamic/Pituitary Disease</i>		
Diagnose and manage benign and malignant tumors that can interfere with secretion of luteinizing hormone and follicle-stimulating hormone.	√	
Diagnose and manage infiltrative diseases that can cause hypothalamic hypogonadism (eg, sarcoidosis, Langerhans cell histiocytosis).	√	
Diagnose and manage hyperprolactinemia as a cause of male hypogonadism.	√	
Diagnose and manage hemochromatosis as a cause of male hypogonadism.	√	
<i>Kallmann Syndrome and Normosmic Congenital Gonadotropin-Releasing Hormone Deficiency</i>		
Diagnose and manage congenital gonadotropin-releasing hormone deficiency.		√
<i>Constitutional Delay of Puberty</i>		
Distinguish constitutional delay of puberty from congenital or organic hypogonadotropic hypogonadism.		√
Recommend appropriate treatment depending on the underlying cause (if one is identified).		√
<i>Chronic Conditions and Illness</i>		

List chronic illnesses associated with male hypogonadism, including obesity, obstructive sleep apnea, cirrhosis, renal failure, acquired immune deficiency syndrome, anorexia nervosa, and lung disease.	√	
<i>Drug-Induced</i>		
List drugs that can be associated with secondary hypogonadism, including gonadotropin-releasing hormone analogues, opioids, glucocorticoids, and exogenous sex steroids.	√	
<i>Uncommon Causes of Secondary Hypogonadism</i>		
Diagnose and manage uncommon causes of secondary hypogonadism, including head trauma, Prader-Willi syndrome, gonadotropin subunit mutations, and leptin (or receptor) mutations.		√
Treatment		
<i>Testosterone Replacement</i>		
Discuss the appropriate therapeutic use of testosterone.	√	
Identify contraindications to testosterone therapy.	√	
Counsel patients regarding expected benefits of testosterone treatment (eg, virilization, libido/sexual function, body composition, bone density), including the likelihood, degree, and time course of expected benefits.	√	
Counsel patients regarding the potential adverse effects of testosterone therapy, including prostate hypertrophy, impact on sleep apnea, erythrocytosis, venous thromboembolism, and cardiovascular risks.	√	
Describe the relative advantages and disadvantages of various forms of testosterone delivery (eg, intramuscular injection, transdermal administration via patch or gel, subcutaneous implants).	√	
Monitor and adjust testosterone therapy in hypogonadal men to determine when the dosage is therapeutic.	√	
<i>Gonadotropin Therapy</i>		
List the indications for gonadotropin therapy in patients with hypogonadotropic hypogonadism (eg, to induce spermatogenesis and, thus, enhance fertility).		√
Guide the appropriate use of gonadotropins in the treatment of hypogonadotropic hypogonadism.		√
<i>Other Potential Therapies for Hypogonadism</i>		
Explain the rationale behind selective estrogen receptor modulators or aromatase inhibitors potential (eg, to induce spermatogenesis and, thus, enhance fertility).		√

MALE REPRODUCTION: INFERTILITY

List indications for semen analysis.	√	
Interpret results of semen analysis.	√	
Explain the role of additional tests (eg, testosterone and gonadotropin measurements, genetic testing, assessment of antisperm antibodies, semen fructose) in the evaluation of male infertility.		√
Causes		
<i>Environmental Factors</i>		
Describe the effects of environmental toxins, cigarette smoking, and hyperthermia on male fertility.	√	
<i>Primary and Secondary Hypogonadism</i>		
Identify causes of primary and secondary hypogonadism (above) as etiologies of male infertility.	√	
<i>Varicocele</i>		
Identify varicocele as a potential cause of male infertility.	√	
<i>Cryptorchidism</i>		
Identify cryptorchidism as a cause of lower sperm counts, poor-quality sperm, and lower fertility rates.	√	
<i>Sertoli Cell-Only Syndrome</i>		
Diagnose Sertoli cell-only syndrome as a cause of male infertility.		√
<i>Drug-Induced</i>		
List drugs associated with impaired spermatogenesis or Leydig-cell function, including alkylating drugs, antiandrogens, ketoconazole, and cimetidine.	√	
<i>Ductal System Obstruction or Dysfunction</i>		
Identify obstruction as a cause of male infertility.		√
Diagnose congenital bilateral absence of the vas deferens in men with cystic fibrosis as a cause of infertility.		√
Explain how to diagnose ejaculatory duct obstruction as a cause of male infertility.		√
Explain how to diagnose retrograde ejaculation as a cause of male infertility.		√
<i>Y-Chromosome Microdeletions</i>		
Diagnose Y-chromosome microdeletions as a cause of male infertility.		√
<i>Idiopathic Oligospermia and Azoospermia</i>		
Counsel patients regarding idiopathic male infertility after excluding all possible causal mechanisms.		√

Treatment		
<i>Gonadotropins</i>		
Recommend and manage exogenous gonadotropins (eg, human chorionic gonadotropin, human menopausal gonadotropin, recombinant follicle-stimulating hormone pulsatile gonadotropin-releasing hormone) for the induction of spermatogenesis in patients with hypogonadotropic hypogonadism.		√
<i>Other Treatment Options</i>		
Describe the use of pulsatile gonadotropin-releasing hormone in patients with hypogonadotropic hypogonadism.		√
Describe the indications for and general procedures for intracytoplasmic sperm injection.		√
MALE REPRODUCTION: ERECTILE AND EJACULATORY DYSFUNCTION		
Erectile Dysfunction		
<i>Causes</i>		
Identify factors associated with erectile dysfunction, including drugs, hypogonadism, cigarette smoking, diabetes mellitus, hypertension, Peyronie disease, pelvic/prostate surgery, and obesity.	√	
<i>Diagnostic Tests</i>		
Evaluate erectile dysfunction via physical examination, sexual history, validated instruments (eg, the International Index of Erectile Dysfunction), and laboratory tests (eg, fasting glucose or hemoglobin A _{1c} , complete blood cell count, thyrotropin, lipid panel, total testosterone).	√	
List indications for additional testing such as nocturnal penile tumescence testing and duplex Doppler imaging.		√
<i>Treatment</i>		
Initiate first-line therapy for erectile dysfunction with phosphodiesterase-5 Inhibitors.	√	
Counsel patients regarding other treatment options for erectile dysfunction such as vacuum devices, penile self-injectable drugs, intraurethral alprostadil, or penile implant and initiate urologic consultation as indicated.		√
Ejaculatory Dysfunction		
<i>Premature Ejaculation</i>		
Summarize the diagnosis and management of premature ejaculation.		√

<i>Delayed Ejaculation</i>		
Summarize the diagnosis and management of delayed ejaculation.		√
MALE REPRODUCTION: GYNECOMASTIA		
Causes		
<i>Drugs</i>		
List drugs associated with gynecomastia.	√	
<i>Testicular and Extratesticular Tumors</i>		
Understand how to identify germ-cell tumors, Leydig-cell tumors, and Sertoli-cell tumors as causes of gynecomastia.	√	
Understand how to identify rare feminizing adrenal tumors and ectopic human chorionic gonadotropin as causes of gynecomastia.	√	
<i>Systemic Illness</i>		
Explain the association of gynecomastia with systemic illness such as chronic kidney disease and cirrhosis.		√
<i>Hyperthyroidism</i>		
Explain the association of gynecomastia with hyperthyroidism.	√	
<i>Refeeding</i>		
Explain the association of gynecomastia with starvation and refeeding.		√
<i>Pubertal</i>		
Distinguish pubertal gynecomastia from gynecomastia due to other underlying causes and discuss the natural history.		√
<i>Congenital/Familial Excess Aromatase Activity</i>		
Describe familial prepubertal gynecomastia due to increased aromatase activity.		√
<i>Idiopathic</i>		
Determine when gynecomastia is idiopathic.		√
Evaluation		
Perform appropriate hormone testing as needed to evaluate potential causes of gynecomastia (eg, testosterone, estradiol, β -hCG, TSH).	√	
Distinguish benign gynecomastia from breast cancer.	√	
Treatment		
<i>Pharmacologic Therapy</i>		
Describe the mechanisms of action, indications, likely benefits, and potential risks of various pharmacologic therapies for gynecomastia (eg,	√	

selective estrogen receptor modulators, aromatase inhibitors, or androgens).		
<i>Mastectomy and Mammoplasty</i>		
Recommend surgical therapy for gynecomastia when appropriate.	√	
MALE REPRODUCTION: TESTOSTERONE IN AGING MEN		
Describe (a) changes that occur with normal aging in serum total testosterone, serum sex hormone-binding globulin, serum free testosterone, and gonadotropins; and (b) potential consequences of age-related reductions in testosterone concentrations.	√	
Guide the appropriate diagnostic evaluation of low testosterone in aging men, especially how to distinguish age-related changes from other causes of hypogonadism.	√	
List the indications for, potential benefits of, and potential risks of testosterone administration in aging men with evidence of testosterone deficiency.	√	
MALE REPRODUCTION: ABUSE OF ANDROGENS AND ANABOLIC STEROIDS		
Health Consequences of Androgenic/Anabolic Steroid Abuse		
Describe the putative rationale underlying the use of supraphysiologic doses of anabolic steroids, human chorionic gonadotropin, selective androgen receptor modulators, selective estrogen receptor modulators, and aromatase inhibitors.		√
List potential adverse effects of androgens, including increased cardiovascular risk, psychological abnormalities, hypogonadism, and gynecomastia.		√
Detection of Banned Substances		
Explain the methods used to detect exogenous androgen use.		√
Management		
Guide patients through the process of ceasing exogenous androgen use.		√
MALE AND FEMALE GENDER DYSPHORIA		
Identify the clinical presentation of and diagnostic criteria for gender dysphoria in men and women.		√
Collaborate with a mental health professional for initial assessment, diagnosis, and treatment planning for gender dysphoria.		√

Explain the therapeutic goals of male-to-female transgender treatment, including reduction of sexual hair growth, induction of breast growth, and induction of a female-pattern of fat distribution.		√
Explain the therapeutic goals of female-to-male transgender treatment, including induction of sexual hair growth, virilization/masculinization, and amenorrhea.		√
Identify appropriate targets for (a) serum estradiol and testosterone concentrations in male-to-female transgender patients; and (b) serum testosterone concentrations in female-to-male transgender patients.		√
Explain preparations, routes of administration, and potential adverse effects of estrogen delivery in male-to-female transgender patients.		√
Explain preparations, routes of administration, and potential adverse effects of agents available for suppression of androgen secretion or action in male-to-female transgender patients (eg, antiandrogens, progestins, and long-acting gonadotropin-releasing hormone agonists).		√
Explain preparations, routes of administration, and potential adverse effects of androgen therapy in the treatment of female-to-male transgender patients.		√
Explain supplementary methods of inducing amenorrhea in female-to-male transgender patients (eg, progestins).		√
Monitor pharmacologic treatment of male-to-female and female-to-male transgender patients regarding dosage adequacy, effectiveness, and adverse events.		√
Counsel male-to-female and female-to-male transgender patients regarding fertility preservation and surgical sex reassignment.		√

TEACHING METHODS AND EVALUATION

Much teaching occurs one-on-one with attendings during outpatient clinics and on inpatient hospital rounds. Active learning occurs as fellows participate in patient care under the supervision and guidance of the attending. In addition, a full range of topics are reviewed in didactic sessions at weekly conferences and in the core curriculum/board review weekly sessions. Fellows are also expected to engage in self-directed study guided by the curriculum. Evaluation includes attending review of fellows knowledge base and medical reasoning during clinic and hospital rounds. In addition, the in-training exam taken in February of every year provides a loose benchmark of medical knowledge progression through the fellowship.

SUGGESTED READING

Asterisks denote references that are designated for residents, students, or endocrine fellows early in their training.

GENERAL READING, BASIC PHYSIOLOGIC PRINCIPLES	
*Sperling MA, ed. <i>Pediatric Endocrinology</i> . 4th ed. Philadelphia, PA: Elsevier Saunders; 2014. (chapters on Ambiguous Genitalia, Puberty and Its Disorders in the Female, Turner Syndrome, and Puberty and Its Disorders in the Male)	Textbook
*Strauss JF, Barbieri RL, eds. <i>Yen & Jaffe's Reproductive Endocrinology: Physiology, Pathophysiology, and Clinical Management</i> . 7th ed. Philadelphia, PA: Elsevier Saunders; 2014.	Textbook
*Jameson JL, De Groot LJ, de Kretser D, et al, eds. <i>Endocrinology: Adult and Pediatric</i> . 7th ed. Philadelphia, PA: Elsevier Saunders; 2016. (Chapters in Part 11 [Reproductive Endocrinology and Sexual Function], Part 12 [Female Reproduction], Part 13 [Male Reproduction], and Part 14 [Endocrinology of Pregnancy])	Textbook
FEMALE REPRODUCTION: SEXUAL DIFFERENTIATION AND PUBERTY	
Dwyer AA, Phan-Hug F, Hauschild M, Elowe-Gruau E, Pitteloud N. Transition in Endocrinology: hypogonadism in adolescence. <i>Eur J Endocrinol</i> . 2015;173(1):R15-R24.	Article
Dunkel L, Quinton R. Transition in endocrinology: induction of puberty. <i>Eur J Endocrinol</i> . 2014;170(6):R229-R239.	Article
Hiort O, Birnbaum W, Marshall L, et al. Management of disorders of sex development. <i>Nat Rev Endocrinol</i> . 2014;10(9):520-529.	Article
Brown DB, Loomba-Albrecht LA, Bremer AA. Sexual precocity and its treatment. <i>World J Pediatr</i> . 2013;9(2):103-111.	Article
Fuqua JS. Treatment and outcomes of precocious puberty: an update. <i>J Clin Endocrinol Metab</i> . 2013;98(6):2198-2207.	Article
Harrington J, Palmert MR. Clinical review: distinguishing constitutional delay of growth and puberty from isolated hypogonadotropic hypogonadism: critical appraisal of available diagnostic tests. <i>J Clin Endocrinol Metab</i> . 2012;97(9):3056-3067.	Article
Palmert MR, Dunkel L. Clinical practice. Delayed puberty. <i>N Engl J Med</i> . 2012;366(5):443-453.	Article
Williams RM, Ward CE, Hughes IA. Premature adrenarche. <i>Arch Dis Child</i> . 2012;97(3):250-254.	Article

FEMALE REPRODUCTION: OVULATORY DYSFUNCTION

Gordon CM, Ackerman KE, Berga SL, et al. Functional hypothalamic amenorrhea: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2017 [Epub ahead of print]	Clinical Practice Guideline
Boehm U, Bouloux PM, Dattani MT, et al. Expert consensus document: European Consensus Statement on congenital hypogonadotropic hypogonadism--pathogenesis, diagnosis and treatment. <i>Nat Rev Endocrinol.</i> 2015;11(9):547-564.	Article
Gordon CM, Kanaoka T, Nelson LM. Update on primary ovarian insufficiency in adolescents. <i>Curr Opin Pediatr.</i> 2015;27(4):511-519.	Article
Torre S, Pal L. Premature menopause. <i>Endocrinol Metab Clin North Am.</i> 2015;44(3):543-557.	Article
Della Torre S, Benedusi V, Fontana R, Maggi A. Energy metabolism and fertility: a balance preserved for female health. <i>Nat Rev Endocrinol.</i> 2014;10(1):13-23.	Article
Committee on Practice Bulletins—Gynecology. Practice bulletin no. 136: management of abnormal uterine bleeding associated with ovulatory dysfunction. <i>Obstet Gynecol.</i> 2013;122(1):176-185.	Article
Silveira LF, Latronico AC. Approach to the patient with hypogonadotropic hypogonadism. <i>J Clin Endocrinol Metab.</i> 2013;98(5):1781-1788.	Article
Gonzalez L, Witchel SF. The patient with Turner syndrome: puberty and medical management concerns. <i>Fertil Steril.</i> 2012;98(4):780-786.	Article
Huang W, Molitch ME. Evaluation and management of galactorrhea. <i>Am Fam Physician.</i> 2012;85(11):1073-1080	Article
Hughes IA, Werner R, Bunch T, Hiort O. Androgen insensitivity syndrome. <i>Semin Reprod Med.</i> 2012;30(5):432-442.	Article
Pinsker JE. Clinical review: Turner syndrome: updating the paradigm of clinical care. <i>J Clin Endocrinol Metab.</i> 2012;97(6):E994-E1003.	Article
*Melmed S, Casanueva FF, Hoffman AR, et al; Endocrine Society. Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2011;96(2):273-288.	Clinical Practice Guideline
*Gordon CM. Clinical practice. Functional hypothalamic amenorrhea. <i>N Engl J Med.</i> 2010;363(4):365-371.	Article
Nelson LM. Clinical practice. Primary ovarian insufficiency. <i>N Engl J Med.</i> 2009;360(6):606-614.	Article

FEMALE REPRODUCTION: HYPERANDROGENISM

*McCartney CR, Marshall JC. Clinical practice. Polycystic ovary syndrome. <i>N Engl J Med.</i> 2016;375(1):54-64.	Article
---	---------

Turcu AF, Auchus RJ. Adrenal steroidogenesis and congenital adrenal hyperplasia. <i>Endocrinol Metab Clin North Am.</i> 2015;44(2):275-296.	Article
Conway G, Dewailly D, Diamanti-Kandarakis E, et al; ESE PCOS Special Interest Group. The polycystic ovary syndrome: a position statement from the European Society of Endocrinology. <i>Eur J Endocrinol.</i> 2014;171(4):P1-P29.	Clinical Practice Guideline
*Legro RS, Arslanian SA, Ehrmann DA, et al; Endocrine Society. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2013;98(12):4565-4592.	Clinical Practice Guideline
Fausser BC, Tarlatzis BC, Rebar RW, et al. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. <i>Fertil Steril.</i> 2012;97(1):28-38.	Clinical Practice Guideline
Rothman MS, Wierman ME. How should postmenopausal androgen excess be evaluated? <i>Clin Endocrinol (Oxf).</i> 2011;75(2):160-164.	Article
*Speiser PW, Azziz R, Baskin LS, et al; Endocrine Society. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice guideline [published correction appears in <i>J Clin Endocrinol Metab.</i> 201;95(11)5137]. <i>J Clin Endocrinol Metab.</i> 2010;95(9):4133-4160.	Clinical Practice Guideline
Martin KA, Chang RJ, Ehrmann DA, et al. Evaluation and treatment of hirsutism in premenopausal women: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2008;93(4):1105-1120.	Clinical Practice Guideline
Azziz R, Carmina E, Dewailly D, et al; Androgen Excess Society. Positions statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an Androgen Excess Society guideline. <i>J Clin Endocrinol Metab.</i> 2006;91(11):4237-4245.	Clinical Practice Guideline
FEMALE REPRODUCTION: INFERTILITY	
Practice Committee of the American Society for Reproductive Medicine. Diagnostic evaluation of the infertile female: a committee opinion. <i>Fertil Steril.</i> 2015;103(6):e44-e50.	Article
FEMALE REPRODUCTION: HORMONAL CONTRACEPTION	
Curtis KM, Tepper NK, Jatlaoui TC, et al. U.S. Medical Eligibility Criteria for Contraceptive Use, 2016. <i>MMWR Recomm Rep.</i> 2016;65(3):1-103.	Article
Burke AE. The state of hormonal contraception today: benefits and risks of hormonal contraceptives: progestin-only contraceptives. <i>Am J Obstet Gynecol.</i> 2011;205(4 Suppl):S14-S17.	Article
ACOG Practice Bulletin No. 110: noncontraceptive uses of hormonal contraceptives. <i>Obstet Gynecol.</i> 2010;115(1):206-218.	Article

Kiley J, Hammond C. Combined oral contraceptives: a comprehensive review. <i>Clin Obstet Gynecol.</i> 2007;50(4):868-877.	Article
FEMALE REPRODUCTION: PREMENSTRUAL SYNDROME/PREMENSTRUAL DYSPHORIC DISORDER	
Ismaili E, Walsh S, O'Brien PM, et al; Consensus Group of the International Society for Premenstrual Disorders. Fourth consensus of the International Society for Premenstrual Disorders (ISPMDD): auditable standards for diagnosis and management of premenstrual disorder. <i>Arch Womens Ment Health.</i> 2016;19(6):953-958.	Article
Yonkers KA, O'Brien PM, Eriksson E. Premenstrual syndrome. <i>Lancet.</i> 2008;371(9619):1200-1210.	Article
FEMALE REPRODUCTION: PERIMENOPAUSE AND MENOPAUSE	
Manson JE, Ames JM, Shapiro M, et al. Algorithm and mobile app for menopausal symptom management and hormonal/non-hormonal therapy decision making: a clinical decision-support tool from The North American Menopause Society. <i>Menopause.</i> 2015;22(3):247-253.	Article
*Stuenkel CA, Davis SR, Gompel A, et al. Treatment of symptoms of the menopause: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2015;100(11):3975-4011.	Clinical Practice Guideline
Torrealday S, Pal L. Premature menopause. <i>Endocrinol Metab Clin North Am.</i> 2015;44(3):543-557.	Article
Santen RJ, Kagan R, Altomare CJ, Komm B, Mirkin S, Taylor HS. Current and evolving approaches to individualizing estrogen receptor-based therapy for menopausal women. <i>J Clin Endocrinol Metab.</i> 2014;99(3):733-747.	Article
Harlow SD, Gass M, Hall JE, et al; STRAW + 10 Collaborative Group. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. <i>J Clin Endocrinol Metab.</i> 2012;97(4):1159-1168.	Article
Santen RJ, Allred DC, Ardoin SP, et al; Endocrine Society. Postmenopausal hormone therapy: an Endocrine Society scientific statement. <i>J Clin Endocrinol Metab.</i> 2010;95(7 Suppl 1):S1-S66.	Article
Nelson LM. Clinical practice. Primary ovarian insufficiency. <i>N Engl J Med.</i> 2009;360(6):606-614.	Article
MALE REPRODUCTION: SEXUAL DIFFERENTIATION AND PUBERTY	
Hiort O, Birnbaum W, Marshall L, et al. Management of disorders of sex development. <i>Nat Rev Endocrinol.</i> 2014;10(9):520-529.	Article

Brown DB, Loomba-Albrecht LA, Bremer AA. Sexual precocity and its treatment. <i>World J Pediatr.</i> 2013;9(2):103-111.	Article
Dwyer AA, Phan-Hug F, Hauschild M, Elowe-Gruau E, Pitteloud N. Transition in endocrinology: hypogonadism in adolescence. <i>Eur J Endocrinol.</i> 2015;173(1):R15-R24.	Article
Dunkel L, Quinton R. Transition in endocrinology: induction of puberty. <i>Eur J Endocrinol.</i> 2014;170(6):R229-R239.	Article
Harrington J, Palmert MR. Clinical review: distinguishing constitutional delay of growth and puberty from isolated hypogonadotropic hypogonadism: critical appraisal of available diagnostic tests. <i>J Clin Endocrinol Metab.</i> 2012;97(9):3056-3067.	Article
Palmert MR, Dunkel L. Clinical practice. Delayed puberty. <i>N Engl J Med.</i> 2012;366(5):443-453.	Article
Hughes IA, Werner R, Bunch T, Hiort O. Androgen insensitivity syndrome. <i>Semin Reprod Med.</i> 2012;30(5):432-442.	Article
MALE REPRODUCTION: HYPOGONADISM	
Boehm U, Bouloux PM, Dattani MT, et al. Expert consensus document: European Consensus Statement on congenital hypogonadotropic hypogonadism--pathogenesis, diagnosis and treatment. <i>Nat Rev Endocrinol.</i> 2015;11(9):547-564.	Article
Dwyer AA, Phan-Hug F, Hauschild M, Elowe-Gruau E, Pitteloud N. Transition in endocrinology: hypogonadism in adolescence. <i>Eur J Endocrinol.</i> 2015;173(1):R15-R24.	Article
Dwyer AA, Raivio T, Pitteloud N. Gonadotrophin replacement for induction of fertility in hypogonadal men. <i>Best Pract Res Clin Endocrinol Metab.</i> 2015;29(1):91-103.	Article
*Basaria S. Male hypogonadism. <i>Lancet.</i> 2014;383(9924):1250-1263.	Article
Dunkel L, Quinton R. Transition in endocrinology: induction of puberty. <i>Eur J Endocrinol.</i> 2014;170(6):R229-R239.	Article
Groth KA, Skakkebaek A, Host C, Gavholt CH, Bojesen A. Clinical review: Klinefelter syndrome--a clinical update. <i>J Clin Endocrinol Metab.</i> 2013;98(1):20-30.	Article
Matsumoto AM. Testosterone administration in older men. <i>Endocrinol Metab Clin North Am.</i> 2013;42(2):271-286.	Article
Saboor Aftab SA, Kumar S, Barber TM. The role of obesity and type 2 diabetes mellitus in the development of male obesity-associated secondary hypogonadism. <i>Clin Endocrinol (Oxf).</i> 2013;78(3):330-337.	Article
Silveira LF, Latronico AC. Approach to the patient with hypogonadotropic hypogonadism. <i>J Clin Endocrinol Metab.</i> 2013;98(5):1781-1788.	Article
Harrington J, Palmert MR. Clinical review: Distinguishing constitutional delay of growth and puberty from isolated hypogonadotropic hypogonadism: critical appraisal of available diagnostic tests. <i>J Clin Endocrinol Metab.</i> 2012;97(9):3056-3067.	Article

Palmert MR, Dunkel L. Clinical practice. Delayed puberty. <i>N Engl J Med.</i> 2012;366(5):443-453.	Article
Balasubramanian R, Crowley WF Jr. Isolated GnRH deficiency: a disease model serving as a unique prism into the systems biology of the GnRH neuronal network. <i>Mol Cell Endocrinol.</i> 2011;346(1-2):4-12.	Article
*Bhasin S, Cunningham GR, Hayes FJ, et al; Endocrine Society. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2010;95(6):2536-2559.	Clinical Practice Guideline

MALE REPRODUCTION: INFERTILITY

Kathrins M, Niederberger C. Diagnosis and treatment of infertility-related male hormonal dysfunction. <i>Nat Rev Urol.</i> 2016;13(6):309-323.	Article
Dwyer AA, Raivio T, Pitteloud N. Gonadotrophin replacement for induction of fertility in hypogonadal men. <i>Best Pract Res Clin Endocrinol Metab.</i> 2015;29(1):91-103.	Article
Practice Committee of the American Society for Reproductive Medicine. Diagnostic evaluation of the infertile male: a committee opinion. <i>Fertil Steril.</i> 2015;103(3):e18-e25.	Article
Jarow J, Sigman M, Kolettis PN, et al. The optimal evaluation of the infertile male: AUA Best Practice Statement. (2010) https://www.auanet.org/common/pdf/education/clinical-guidance/Male-Infertility-d.pdf . Accessed February 25, 2016.	Web site

MALE REPRODUCTION: ERECTILE DYSFUNCTION AND EJACULATORY DISORDERS

Yafi FA, Jenkins L, Albersen M, et al. Erectile dysfunction. <i>Nat Rev Dis Primers.</i> 2016;2:16003.	Article
Jenkins LC, Mulhall JP. Delayed orgasm and anorgasmia. <i>Fertil Steril.</i> 2015;104(5):1082-1088.	Article
Althof SE, McMahon CG, Waldinger MD, et al. An update of the International Society of Sexual Medicine's guidelines for the diagnosis and treatment of premature ejaculation (PE). <i>Sex Med.</i> 2014;2(2):60-90.	Article
Montague DK, Jarow JP, Broderick GA, et al. The management of erectile dysfunction: an update. (2005) https://www.auanet.org/common/pdf/education/clinical-guidance/Erectile-Dysfunction.pdf . Accessed February 25, 2016.	Web site

MALE REPRODUCTION: GYNecomastia

Nuttall FQ, Warriar RS, Gannon MC. Gynecomastia and drugs: a critical evaluation of the literature. <i>Eur J Clin Pharmacol.</i> 2015;71(5):569-578.	Article
--	---------

Narula HS, Carlson HE. Gynaecomastia--pathophysiology, diagnosis and treatment. <i>Nat Rev Endocrinol.</i> 2014;10(11):684-698.	Article
*Braunstein GD. Clinical practice. Gynecomastia. <i>N Engl J Med.</i> 2007;357(12):1229-1237.	Article
MALE REPRODUCTION: TESTOSTERONE IN AGING MEN	
Nguyen CP, Hirsch MS, Moeny D, Kaul S, Mohamoud M, Joffe HV. Testosterone and "age-related hypogonadism"--FDA concerns. <i>N Engl J Med.</i> 2015;373(8):689-691.	Article
Basaria S. Reproductive aging in men. <i>Endocrinol Metab Clin North Am.</i> 2013;42(2):255-270.	Article
Matsumoto AM. Testosterone administration in older men. <i>Endocrinol Metab Clin North Am.</i> 2013;42(2):271-286.	Article
*Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM. Testosterone therapy in adult men with androgen deficiency syndromes: an endocrine society clinical practice guideline [published correction appears in <i>J Clin Endocrinol Metab.</i> 2006;91(7):2688]. <i>J Clin Endocrinol Metab.</i> 2006;91(6):1995-2010.	Article
MALE REPRODUCTION: ABUSE OF ANDROGENS AND ANABOLIC STEROIDS	
Alquraini H, Auchus RJ. Strategies that athletes use to avoid detection of androgenic-anabolic steroid doping and sanctions. <i>Mol Cell Endocrinol.</i> 2017. [Epub ahead of print]	Article
Pope HG Jr, Wood RI, Rogol A, Nyberg F, Bowers L, Bhasin S. Adverse health consequences of performance-enhancing drugs: an Endocrine Society scientific statement. <i>Endocr Rev.</i> 2014;35(3):341-375.	Article
Rahnema CD, Lipshultz LI, Crosnoe LE, Kovac JR, Kim ED. Anabolic steroid-induced hypogonadism: diagnosis and treatment. <i>Fertil Steril.</i> 2014;101(5):1271-1279.	Article
Kanayama G, Brower KJ, Wood RI, Hudson JI, Pope HG Jr. Treatment of anabolic-androgenic steroid dependence: emerging evidence and its implications. <i>Drug Alcohol Depend.</i> 2010;109(1-3):6-13.	Article
MALE AND FEMALE GENDER DYSPHORIA	
Colebunders B, Brondeel S, D'Arpa S, Hoebeke P, Monstrey S. An update on the surgical treatment for transgender patients. <i>Sex Med Rev.</i> 2017;5(1):103-109.	Article
Shumer DE, Nokoff NJ, Spack NP. Advances in the care of transgender children and adolescents. <i>Adv Pediatr.</i> 2016;63(1):79-102.	Article
Saraswat A, Weinand JD, Safer JD. Evidence supporting the biologic nature of gender identity. <i>Endocr Pract.</i> 2015;21(2):199-204.	Article

<p>Weinand JD, Safer JD. Hormone therapy in transgender adults is safe with provider supervision; a review of hormone therapy sequelae for transgender individuals. <i>J Clin Transl Endocrinol</i>. 2015;2(2):55-60.</p>	<p>Article</p>
<p>Coleman E, Bockting W, Botzer M, et al; World Professional Association for Transgender Health. <i>Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People</i>. 7th version. 2012. http://www.wpath.org/uploaded_files/140/files/Standards%20of%20Care,%20V7%20Full%20Book.pdf. Accessed February 25, 2016.</p>	<p>Web site</p>
<p>Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, et al; Endocrine Society. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab</i>. 2009;94(9):3132-3154.</p>	<p>Clinical Practice Guideline</p>

HYPOTHALAMIC-PITUITARY

INTRODUCTION

Growth, development, and reproduction are regulated by the interactions of the endocrine and nervous systems. Under the influence of the hypothalamus, the pituitary gland regulates endocrine target glands. Disorders of the pituitary and hypothalamus may therefore cause isolated or multisystem endocrine hypofunction and hyperfunction. Furthermore, expanding lesions of the pituitary/hypothalamic area may cause neurologic dysfunction. A complete understanding of normal physiology and the pathologic disease affecting the pituitary gland is essential for the endocrinologist and should be part of education curriculum and training for fellows. Fellows should be competent in the diagnosis and treatment of pituitary disorders.

MEDICAL KNOWLEDGE

Fellows must demonstrate knowledge about established and evolving biomedical, clinical, and cognate (eg, epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.

Topic	Fundamental	Advanced
BASIC PHYSIOLOGIC PRINCIPLES, PITUITARY BIOLOGY		
Describe basal hormone levels of prolactin, insulinlike growth factor 1, growth hormone, free T ₄ , thyrotropin, cortisol, corticotropin, luteinizing hormone, follicle-stimulating hormone, testosterone, and estradiol, as well as normal serum and urine osmolality.	√	
Explain regulation of the hypothalamic-pituitary-adrenal axis, including normal patterns of corticotropin and cortisol secretion.		√
Explain pituitary gland embryology and anatomy.		√
Interpret growth charts.		√
Interpret radiologic bone age.		√
List indications for and interpret findings from formal visual field assessment.		√
PROLACTIN		
Hyperprolactinemia		
<i>Clinical Manifestations</i>		

Summarize the symptoms and signs of hyperprolactinemia, including hypogonadism (infertility, oligomenorrhea, or amenorrhea in women; decreased libido, erectile dysfunction, infertility, gynecomastia in men), galactorrhea, osteopenia, and neurologic mass effects (in the setting of prolactinoma).	√	
Describe the appearance of prolactinomas on radiographic imaging.	√	
<i>Diagnosis</i>		
Perform the differential diagnosis of hyperprolactinemia and differentiate among macroprolactinemia, the "hook effect," and prolactinomas.		√
Guide diagnostic testing, including basal prolactin measurement, assessment for hypopituitarism when indicated, and radiographic imaging.	√	
<i>Treatment</i>		
Determine when treatment for a prolactinoma is appropriate depending on existing or impending neurologic symptoms, hypogonadism, or other symptoms related to hyperprolactinemia.	√	
Determine when dopamine agonist therapy is appropriate to treat a prolactinoma and manage this therapeutic regimen.	√	
Determine when surgery is indicated to treat a prolactinoma.	√	
Manage prolactinoma during pregnancy.		√
Manage prolactinoma after menopause.		√
Normoprolactinemic Galactorrhea		
Diagnose galactorrhea without hyperprolactinemia.		√
Manage galactorrhea.		√
GROWTH HORMONE		
Acromegaly		
<i>Clinical Manifestations</i>		
Summarize the symptoms and signs of growth hormone excess, including enlargement of the jaw, hands, and feet; coarse facial features; cardiovascular disease; sleep apnea; type 2 diabetes mellitus; arthropathy; carpal tunnel syndrome; headache; and tumor mass effects such as cranial nerve palsies and vision loss.	√	
Describe the appearance of growth hormone–secreting adenomas on radiographic imaging.	√	
<i>Diagnosis</i>		

Guide the diagnostic evaluation for acromegaly, which includes biochemical testing (measurement of insulinlike growth factor 1, as well as assessment of growth hormone suppression with oral glucose tolerance testing), followed by radiographic imaging.	√	
Assess for ectopic growth hormone–releasing hormone secretion in patients with acromegaly who do not have a pituitary adenoma.		√
Assess for cosecretion of prolactin, thyrotropin, and corticotropin when appropriate.		√
<i>Treatment</i>		
Recommend treatment strategies for acromegaly, which may include transsphenoidal surgery; radiation therapy; and medical therapy with somatostatin analogues, dopamine agonists, or a growth hormone receptor antagonist (ie, pegvisomant).	√	
Manage acromegaly in the context of pregnancy.		√
Guide the long-term monitoring and management of acromegaly.		√
Growth Hormone Deficiency		
<i>Clinical Manifestations</i>		
Summarize the symptoms and signs of growth hormone deficiency in childhood (including short stature) and distinguish between congenital and acquired growth hormone deficiency.	√	
Summarize the symptoms and signs of growth hormone deficiency in adulthood, including decreased lean body mass, decreased bone mineral density, decreased quality of life, increased fat mass, increased fracture rate, increased rates of cardiovascular disease, and increased mortality.		√
<i>Diagnosis</i>		
Recommend appropriate diagnostic testing, including measurement of insulinlike growth factor 1 and provocative growth hormone tests with use of arginine, levodopa, growth hormone–releasing hormone, glucagon, or insulin-induced hypoglycemia.	√	
<i>Treatment</i>		
List indications for therapy in adults with growth hormone deficiency.	√	
Monitor the effectiveness of growth hormone therapy and adjust the growth hormone dosage on the basis of insulinlike growth factor 1 levels.		√

THYROTROPIN

Thyrotropin-Secreting Pituitary Adenoma		
<i>Clinical Manifestations</i>		
Summarize the symptoms and signs of thyrotropin-secreting adenomas, which are typical of hyperthyroidism, such as palpitations, tremor, and heat intolerance.		√
<i>Diagnosis</i>		
Differentiate thyrotropin-secreting adenomas from thyroid hormone resistance and conditions that cause assay interference (eg, elevated serum T ₄ -binding globulin concentrations, familial dysalbuminemic hyperthyroxinemia, and anti-T ₄ antibodies).		√
Guide the diagnostic assessment of thyrotropin-secreting adenomas, which may include repeating thyroid function tests in another laboratory, measuring α -subunit, measuring sex hormone-binding globulin, measuring other pituitary hormones, and performing radiographic imaging.		√
<i>Treatment</i>		
Recommend treatment strategies for thyrotropin-secreting adenomas, including restoration of euthyroidism before surgery and definitive treatment with transsphenoidal surgery.		√
Discuss other treatment modalities, including radiation, somatostatin analogues, and thyroidectomy.		√
Guide the long-term monitoring and management of thyrotropin-secreting adenomas.		√
Hyperplasia Secondary to Longstanding Primary Hypothyroidism		
Distinguish thyrotropin-secreting pituitary adenomas from hyperplasia of the thyrotroph cells secondary to longstanding primary hypothyroidism with measurement of thyrotropin and free T ₄ and imaging appearance on pituitary-directed magnetic resonance imaging.		√
Thyrotropin Deficiency		
<i>Clinical Manifestations</i>		
Summarize the symptoms and signs of thyrotropin deficiency, which are typical of hypothyroidism, such as lethargy, cold intolerance, constipation, bradycardia, and dry and brittle hair.	√	
<i>Diagnosis</i>		
Distinguish primary hypothyroidism from secondary hypothyroidism with measurement of thyrotropin and serum free T ₄ .	√	
<i>Treatment</i>		

Adjust the levothyroxine replacement dosage clinically and on the basis of serum free T ₄ levels.	√	
GONADOTROPINS		
Gonadotroph Pituitary Tumors		
<i>Clinical Manifestations</i>		
Summarize the symptoms and signs of luteinizing hormone– or follicle-stimulating hormone–secreting pituitary tumors, which can include ovarian hyperstimulation and amenorrhea or oligomenorrhea in premenopausal women, precocious puberty, and tumor mass effects.		√
Describe the appearance of gonadotroph pituitary tumors on radiographic imaging.		√
<i>Diagnosis</i>		
Guide the diagnostic assessment of gonadotroph pituitary tumors, including confirmation of the presence of a sellar mass with radiographic imaging, visual field testing, and biochemical testing for excess secretion of gonadotropins and glycoprotein α -subunit.		√
<i>Treatment</i>		
Recommend treatment strategies for gonadotroph pituitary tumors, including surgery and radiation.		√
Guide the long-term monitoring and management of gonadotroph pituitary tumors.		√
Hypogonadotropic Hypogonadism		
<i>Clinical Manifestations</i>		
Describe the clinical manifestations of congenital gonadotropin-releasing hormone deficiency.	√	
Differentiate among the genetic etiologies of congenital gonadotropin-releasing hormone deficiency.		√
Differentiate among the etiologies of acquired hypogonadotropic hypogonadism such as diseases that affect the hypothalamic-pituitary axis and drugs that cause hypogonadism.	√	
<i>Diagnosis</i>		
Confirm the diagnosis biochemically with measurement of sex steroid hormones, measurement of gonadotropins, confirmation of otherwise normal anterior pituitary function, and a normal appearance of the pituitary on radiographic imaging.	√	

Distinguish congenital gonadotropin-releasing hormone deficiency from primary gonadal failure.	√	
<i>Treatment</i>		
Recommend appropriate treatment for hypogonadotropic hypogonadism, which may include pulsatile gonadotropin-releasing hormone therapy, gonadotropins, and gonadal steroid hormones.		√
Determine when genetic testing is appropriate in the setting of congenital hypogonadotropic hypogonadism.		√
NONSECRETING PITUITARY TUMORS		
<i>Clinical Manifestations</i>		
Summarize the symptoms and signs of nonsecreting pituitary tumors, which can include tumor mass effects and hypopituitarism.	√	
Describe the appearance of nonsecreting pituitary tumors on radiographic imaging.	√	
<i>Diagnosis</i>		
Guide the diagnostic assessment of nonsecreting pituitary tumors, including confirmation of the presence of a sellar mass with radiographic imaging, visual field testing, and assessment for hypopituitarism when indicated.	√	
<i>Treatment</i>		
Recommend treatment strategies for nonsecreting pituitary tumors, which may include surgery and radiation.	√	
CORTICOTROPIN		
Cushing Disease		
<i>Clinical Manifestations</i>		
Summarize the symptoms and signs of Cushing disease resulting from chronic exposure to excess glucocorticoid, including progressive obesity, dermatologic manifestations, menstrual irregularities, proximal muscle wasting and weakness, bone loss, glucose intolerance, cardiovascular disease, thromboembolic events, neuropsychological changes and impaired cognition, and infection and impaired immune function.	√	
Describe the appearance of pituitary corticotropin-secreting tumors on radiographic imaging.	√	
<i>Diagnosis</i>		

Select and interpret results from appropriate case-detection (screening) tests, which may include measurement of 24-hour urinary cortisol excretion, late-night salivary or serum cortisol measurement, diurnal serum cortisol measurement, or 1-mg overnight dexamethasone suppression.	√	
Select and interpret results from appropriate diagnostic tests to determine the source of glucocorticoid excess, which may include corticotropin measurement, inferior petrosal sinus sampling, corticotropin-releasing hormone stimulation testing, vasopressin stimulation testing, and/or dexamethasone suppression testing (with or without corticotropin-releasing hormone).		√
Differentiate a corticotropin-secreting pituitary adenoma from ectopic corticotropin syndrome and ectopic corticotropin-releasing hormone syndrome.	√	
Assess for hypopituitarism when indicated.	√	
Discuss the diagnostic challenge of glucocorticoid excess in the setting of pregnancy.		√
<i>Treatment</i>		
Recommend transsphenoidal surgery or pituitary irradiation as the initial therapy of choice, depending on clinical circumstances.	√	
Recommend medical therapy with ketoconazole, mitotane, metyrapone, pasireotide, mifepristone, and other agents when appropriate.		√
Recommend appropriate long-term management depending on the initial treatment strategy and resolution of signs and symptoms.		√
Corticotropin Deficiency		
<i>Clinical Manifestations</i>		
Summarize the symptoms and signs of acute adrenal crisis, including shock, abdominal tenderness, fever, weight loss, and electrolyte abnormalities.	√	
Summarize the symptoms and signs of secondary adrenal insufficiency, including signs of glucocorticoid and androgen deficiencies; chronic malaise; lassitude; fatigue; generalized weakness; anorexia; weight loss; gastrointestinal complaints; psychiatric manifestations; hypotension; vitiligo; hypoglycemia; and sometimes severe headache and/or vision disturbances and/or cranial nerve abnormalities.	√	
List causes of secondary adrenal insufficiency, including panhypopituitarism, isolated corticotropin deficiency, lymphocytic hypophysitis, traumatic brain injury, and drugs.	√	
<i>Diagnosis</i>		

Guide the diagnosis of adrenal insufficiency, which may include measurement of cortisol, corticotropin, renin, and aldosterone; corticotropin stimulation test; metyrapone test; insulin-induced hypoglycemia test, and corticotropin-releasing hormone test.	√	√
Evaluate for other pituitary hormone deficiencies in patients with secondary adrenal insufficiency.	√	
<i>Treatment</i>		
Recommend treatment approaches for secondary adrenal insufficiency depending on etiology.	√	
Adjust the glucocorticoid dosage clinically.	√	
HYPOPITUITARISM		
<i>Clinical Manifestations</i>		
Describe how the clinical presentation of hypopituitarism varies depending on the deficiency of each anterior pituitary hormone, the rapidity with which a disease affects the anterior pituitary cells, the severity of the hormone deficiency, and the number of different anterior pituitary cells that are affected.		√
Describe the clinical manifestations of panhypopituitarism, including growth failure, fatigue, decreased strength, body hair loss, fine facial skin wrinkling, infertility, amenorrhea, erectile dysfunction, constipation, cold intolerance, bradycardia, and orthostatic hypotension.	√	
Differentiate among the congenital causes of hypopituitarism, including inherited disorders (eg, <i>PROPI</i> , <i>POU1F1</i> , <i>TBX19</i> gene mutations) and pituitary stalk interruption syndrome.		√
Differentiate among the acquired causes of hypopituitarism, including tumors, apoplexy, Sheehan syndrome, hemochromatosis, lymphocytic hypophysitis, sarcoidosis, metabolic causes, traumatic brain injury, and iatrogenic causes (eg, drugs, radiation, surgery).	√	
<i>Diagnosis</i>		
Guide the diagnosis of hypopituitarism, which may include corticotropin measurement, the metyrapone test, the insulin-induced hypoglycemia test, the low-dose cosyntropin stimulation test, thyroid function testing, gonadotropin measurement, testosterone measurement, growth hormone measurement, insulinlike growth factor 1 measurement, provocative tests of growth hormone secretion, and prolactin measurement.	√	√
<i>Treatment</i>		

Recommend treatment on the basis of individual pituitary hormone deficiencies.	√	
Adjust the growth hormone dosage on the basis of insulinlike growth factor 1 levels.		√
Adjust the levothyroxine dosage clinically and on the basis of serum free T ₄ levels.	√	
Adjust the glucocorticoid dosage clinically.	√	
Determine when genetic testing is appropriate in the setting of congenital hypopituitarism.		√

EMPTY SELLA

Define empty sella.	√	
Describe the radiographic appearance of empty sella.	√	
Describe the typical findings on pituitary function testing in patients with empty sella (ie, usually normal).	√	

ANTIDIURETIC HORMONE

Diabetes Insipidus

Clinical Manifestations

Summarize the symptoms and signs of diabetes insipidus, including polyuria, polydipsia, thirst, and dehydration.	√	
--	---	--

Diagnosis

Perform the differential diagnosis to distinguish between central vs nephrogenic, partial vs complete, and congenital vs acquired diabetes insipidus.		√
Guide the diagnosis of diabetes insipidus, which may include a water deprivation test, vasopressin measurement, diagnostic trial of desmopressin, radiographic imaging, and assessment of anterior pituitary function.		√
Assess for psychogenic polydipsia.		√
Exclude other causes of polyuria.	√	

Treatment

Recommend treatment of diabetes insipidus, which may include desmopressin, other drugs (eg, chlorpropamide, carbamazepine, thiazide diuretics, and nonsteroidal anti-inflammatory drugs), and a low-solute diet.	√	
--	---	--

Syndrome of Inappropriate Antidiuretic Hormone Secretion		
<i>Clinical Manifestations</i>		
Summarize the symptoms and signs of the syndrome of inappropriate antidiuretic hormone secretion, including hyponatremia, serum hypoosmolality with simultaneous inappropriately high urine osmolality, nausea, vomiting, headache, confusion, seizure, and coma.	√	
Differentiate among the causes of the syndrome of inappropriate antidiuretic hormone secretion, including central nervous system disturbances, malignancies, drugs, surgery, pulmonary disease, hormone deficiency (hypopituitarism and hypothyroidism), hormone administration, HIV infection, and hereditary disorders.	√	
<i>Diagnosis</i>		
Guide the evaluation of a patient with hyponatremia, which may include a detailed medical history, measurement of glucose and creatinine, assessment of serum and urine osmolality, measurement of electrolytes, and assessment of thyroid and adrenal function.	√	
<i>Treatment</i>		
Recommend treatment (eg, water restriction, salt tablets, saline, hypertonic saline, furosemide, vasopressin receptor antagonists, demeclocycline) of the syndrome of inappropriate antidiuretic hormone secretion depending on the degree of hyponatremia, the presence or absence of symptoms, and urine osmolality.	√	
CRANIOPHARYNGIOMA, OTHER SPACE-OCCUPYING LESIONS, AND INFILTRATIVE OR INFLAMMATORY DISORDERS OF THE PITUITARY		
Craniopharyngioma and Other Space-Occupying Lesions		
<i>Clinical Manifestations</i>		
Summarize the symptoms and signs of craniopharyngioma, Rathke cleft cysts, meningiomas, arachnoid cysts, chordomas, and hamartomas, which may include vision symptoms, endocrine abnormalities, and headache.		√
Describe the appearance of these space-occupying pituitary and parasellar lesions on radiographic imaging.		√
<i>Treatment</i>		
Recommend treatment strategies for craniopharyngioma and other space-occupying pituitary lesions, which may include surgery and radiation.		√
Guide the long-term monitoring and management of craniopharyngioma and other space-occupying pituitary lesions after initial treatment, which		√

may include addressing endocrine complications (eg, panhypopituitarism and hypothalamic dysfunction), neurologic complications, vision deficits, vascular abnormalities, secondary malignancies, and recurrent disease.		
Infiltrative or Inflammatory Disorders		
Differentiate among sarcoidosis, tuberculosis, Langerhans cell histiocytosis, lymphoma, lymphocytic hypophysitis, and hemochromatosis in their capacity to affect the pituitary gland.		√
PITUITARY INCIDENTALOMA		
Recall the prevalence of pituitary masses identified incidentally on imaging performed for other reasons.	√	
Radiographic Appearance		
Identify the imaging phenotype of various pituitary lesions.	√	
Diagnostic Studies		
Guide the appropriate evaluation for a pituitary incidentaloma (depending on the size of the lesion), which may include assessment of visual fields and visual acuity and clinical and biochemical evaluation for hormone hypersecretion and hypopituitarism.	√	
PITUITARY IMAGING AND PROCEDURES		
Imaging		
Describe the typical imaging phenotypes on magnetic resonance imaging for primary pituitary tumors, pituitary cysts, pituitary hyperplasia, metastatic lesions to the pituitary, pituitary stalk lesions, and hypothalamic masses.	√	
Procedures		
List indications for inferior petrosal sinus sampling for corticotropin.		√
Interpret results from inferior petrosal sinus sampling.		√
DYNAMIC HORMONE TESTING		
List indications for and interpret results from tests to diagnose growth hormone deficiency (growth hormone stimulation tests: insulin tolerance, levodopa, arginine, clonidine, glucagon, growth hormone–releasing hormone stimulation tests) or growth hormone excess (growth hormone suppressive tests: oral glucose tolerance test).		√

List indications for and interpret results from tests to diagnose corticotropin and cortisol deficiency (insulin tolerance test, cosyntropin stimulation test, metyrapone test, corticotropin-releasing hormone stimulation test) or corticotropin and cortisol excess (baseline cortisol measurements in the blood, saliva, and urine; dexamethasone suppression tests; corticotropin-releasing hormone stimulation test).		√
List indications for and interpret results from tests to assess the gonadal axis (baseline gonadal steroid measurements, trophic hormone measurements, and gonadotropin-releasing hormone stimulation test).		√
List indications for and interpret results from tests to assess posterior pituitary function and evaluate for diabetes insipidus (overnight fast with measurement of simultaneous serum and urine osmolality and the formal water deprivation test).		√

TEACHING METHODS AND EVALUATION

Much teaching occurs one-on-one with attendings during outpatient clinics and on inpatient hospital rounds. Active learning occurs as fellows participate in patient care under the supervision and guidance of the attending. In addition, a full range of topics are reviewed in didactic sessions at weekly conferences and in the core curriculum/board review weekly sessions. Fellows are also expected to engage in self-directed study guided by the curriculum. Evaluation includes attending review of fellows knowledge base and medical reasoning during clinic and hospital rounds. In addition, the in-training exam taken in February of every year provides a loose benchmark of medical knowledge progression through the fellowship.

SUGGESTED READING

Asterisks denote references that are designated for residents, students, or endocrine fellows early in their training. While some of the references are organized under “Diagnosis” and “Management” subheadings, please note there may be overlapping content.

GENERAL READING, BASIC PHYSIOLOGIC PRINCIPLES, PITUITARY BIOLOGY

*Melmed S, Polonsky KS, Larsen PR, Kronenberg HM, eds. <i>Williams Textbook of Endocrinology</i> . 13th ed. Philadelphia, PA: Saunders; 2015.	Textbook
*Gardner D, Shoback D. <i>Greenspan's Basic and Clinical Endocrinology (LANGE Clinical Medicine)</i> . 9th ed. China: The McGraw-Hill Companies; 2011.	Textbook

*Jameson JL, De Groot LJ, de Kretser DM, Giudice LC, Grossman AB, Melmed S, Potts JT Jr, Weir GC, eds. <i>Endocrinology: Adult and Pediatric</i> . 7th ed. Philadelphia, PA: Elsevier Saunders; 2010.	Textbook
*Becke KL, Bilezikian JP, Bremner WJ, et al, eds. <i>Principles and Practice of Endocrinology and Metabolism</i> . 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2002.	Textbook
PROLACTIN	
Hyperprolactinemia: Diagnosis and Management	
*Melmed S, Casanueva FF, Hoffman AR, et al; Endocrine Society. Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guidelines. <i>J Clin Endocrinol Metab</i> . 2011;96(2):273-288.	Clinical Practice Guideline
*Casanueva FF, Molitch ME, Schlechte JA, et al. Guidelines of the Pituitary Society for the diagnosis and management of prolactinomas. <i>Clin Endocrinol (Oxf)</i> . 2006;65(2):265-273.	Clinical Practice Guideline
*Klibanski A. Clinical practice. Prolactinomas [published correction appears in <i>N Engl J Med</i> . 2010;362(22):2142]. <i>N Engl J Med</i> . 2010;362(13):1219-1226.	Article
*Molitch ME. Diagnosis and treatment of prolactinomas. <i>Adv Intern Med</i> . 1999;44:117-153	Article
Molitch ME. Management of prolactinomas during pregnancy. <i>J Reprod Med</i> . 1999;44(Suppl):1121-1126.	Article
Normoprolactinemic Galactorrhea	
Huang W, Molitch ME. Evaluation and management of galactorrhea. <i>Am Fam Physician</i> . 2012;85(11):1073-1080.	Article
Xue T, Li SW, Wang Y. Effectiveness of bromocriptine monotherapy or combination treatment with clomiphene for infertility in women with galactorrhea and normal prolactin: a systematic review and meta-analysis. <i>Curr Ther Clin Exp</i> . 2010;71(4):199-210.	Article
GROWTH HORMONE	
Acromegaly: Diagnosis and Management	
*Katznelson L, Laws ER Jr, Melmed S. Acromegaly: an Endocrine Society Clinical Practice Guideline. <i>J Clin Endocrinol Metab</i> . 2014;99(11):3933-3951.	Clinical Practice Guideline

*Katznelson L, Atkinson JL, Cook DM, et al; AACE Acromegaly Task Force. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Acromegaly--2011 update: executive summary. <i>Endocr Pract.</i> 2011;17(4):1-44.	Clinical Practice Guideline
Giustina A, Chanson P, Kleinberg D, et al. Acromegaly Consensus Group. A consensus on the medical treatment of acromegaly. <i>Nat Rev Endocrinol.</i> 2014;10(4):243-248.	Article
Melmed S. Acromegaly pathogenesis and treatment. <i>J Clin Invest.</i> 2009;119(11):3189-3202.	Article
Melmed S. Medical progress: acromegaly [published correction appears in <i>N Engl J Med.</i> 2007;356(8):879]. <i>N Engl J Med.</i> 2006;355(24):2558-2573.	Article
Powell JS, Wardlaw SL, Post KD, Freda PU. Outcome of radiotherapy for acromegaly using normalization of insulin-like growth factor I to define cure. <i>J Clin Endocrinol Metab.</i> 2000;85(5):2068-2071.	Article
Newman CB. Medical therapy for acromegaly. <i>Endocrinol Metab Clin North Am.</i> 1999;28(1):171-190.	Article
Abosch A, Tyrrell JB, Lamborn KR, et al. Transsphenoidal microsurgery for growth hormone-secreting pituitary adenomas: initial outcome and long-term results. <i>J Clin Endocrinol Metab.</i> 1998;83(10):3411-3416.	Article
Abs R, Verhelst J, Maiter D, et al. Cabergoline in the treatment of acromegaly: a study in 64 patients. <i>J Clin Endocrinol Metab.</i> 1998;83(2):374-378	Article
Landolt AM, Haller D, Lomax N, et al. Stereotactic radiosurgery for recurrent surgically treated acromegaly: comparison with fractionated radiotherapy. <i>J Neurosurg.</i> 1998;88(6):1002-1008.	Article
Swearingen B, Barker FG 2nd, Katznelson L, et al. Long-term mortality after transsphenoidal surgery and adjunctive therapy for acromegaly. <i>J Clin Endocrinol Metab.</i> 1998;83(10):3419-3426.	Article
Flogstad AK, Halse J, Barke S, et al. Sandostatin LAR in acromegalic patients: long-term treatment. <i>J Clin Endocrinol Metab.</i> 1997;81(1):23-28.	Article
Newman CB, Melmed S, Snyder PJ, et al. Safety and efficacy of long-term octreotide therapy of acromegaly: results of a multicenter trial in 103 patients--a clinical research center study [published correction appears in <i>J Clin Endocrinol Metab.</i> 1995;80(11):3238]. <i>J Clin Endocrinol Metab.</i> 1995;80(9):2768-2775.	Article
Growth Hormone Deficiency: Diagnosis and Management	
*Molitch ME, Clemmons DR, Malozowski S, Merriam GR, Vance ML; Endocrine Society. Evaluation and treatment of adult growth hormone deficiency: an Endocrine Society Clinical Practice Guideline. <i>J Clin Endocrinol Metab.</i> 2011;96(6):1587-1609	Clinical Practice Guideline
*Cook DM, Yuen KC, Biller BM, Kemp SF, Vance ML; American Association of Clinical Endocrinologists. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in growth hormone-deficient adults and transition patients – 2009 update. <i>Endocr Pract.</i> 2009;15(Suppl 2):1-29.	Clinical Practice Guideline

*Growth Hormone Research Society. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. <i>J Clin Endocrinol Metab.</i> 2000;85(11):3990-3993.	Clinical Practice Guideline
Consensus guidelines for the diagnosis and treatment of adults with growth hormone deficiency: summary statement of the Growth Hormone Research Society Workshop on Adult Growth Hormone Deficiency. <i>J Clin Endocrinol Metab.</i> 1998;83(2):379-381.	Clinical Practice Guideline
Carroll PV, Christ ER, Bengtsson BA, et al. Growth hormone deficiency in adulthood and the effects of growth hormone replacement: a review. Growth Hormone Research Society Scientific Committee. <i>J Clin Endocrinol Metab.</i> 1998;83(2):382-395.	Article
Tritos NA, Mantzoros CS. Recombinant human growth hormone: old and novel uses. <i>Am J Med.</i> 1998;105(1):44-57.	Article
Vance ML, Mauras N. Growth hormone therapy in adults and children. <i>N Engl J Med.</i> 1999;341(16):1206-1216.	Article
Tritos NA, Mantzoros CS. Recombinant human growth hormone: old and novel uses. <i>Am J Med.</i> 1998;105(1):44-57.	Article
Hoffman DM, O'Sullivan AJ, Baxter RC, Ho KK. Diagnosis of growth hormone deficiency in adults [published correction appears in <i>Lancet.</i> 1994;344(8916):206]. <i>Lancet.</i> 1994;343(8905):1064-1068.	Article

THYROTROPIN

Thyrotropin-Secreting Pituitary Adenoma

*Beck-Peccoz P, Brucker-Davis F, Persani L, Smallridge RC, Weintraub BD. Thyrotropin-secreting pituitary tumors. <i>Endocr Rev.</i> 1996;17(6):610-638.	Article
*Shomali ME, Katznelson L. Medical therapy for gonadotroph and thyrotroph tumors. <i>Endocrinol Metab Clin North Am.</i> 1999;28(1):223-240.	Article
Malchiodi E, Profka E, Ferrante E, et al. Thyrotropin-secreting pituitary adenomas: outcome of pituitary surgery and irradiation. <i>J Clin Endocrinol Metab.</i> 2014;99(6):2069-2076.	Article
Brucker-Davis F, Oldfield EH, Skarulis MC, Doppman JL, Weintraub BD. Thyrotropin-secreting pituitary tumors: diagnostic criteria, thyroid hormone sensitivity, and treatment outcome in 25 patients followed at the National Institutes of Health. <i>J Clin Endocrinol Metab.</i> 1999;84(2):476-486.	Article
Shomali ME, Katznelson L. Medical therapy for gonadotroph and thyrotroph tumors. <i>Endocrinol Metab Clin North Am.</i> 1999;28(1):223-240.	Article

Hyperplasia Secondary to Longstanding Primary Hypothyroidism

Joshi AS, Woolf PD. Pituitary hyperplasia secondary to primary hypothyroidism: a case report and review of the literature. <i>Pituitary</i> . 2005;8(2):99-103.	Article
GONADOTROPINS	
Gonadotropin Pituitary Tumors	
Shomali ME, Katznelson L. Medical therapy for gonadotroph and thyrotroph tumors. <i>Endocrinol Metab Clin North Am</i> . 1999;28(1):223-240.	Article
Young WF Jr, Scheithauer BW, Kovacs KT, Horvath E, Davis DH, Randall RV. Gonadotroph adenoma of the pituitary gland: a clinicopathologic analysis of 100 cases. <i>Mayo Clin Proc</i> . 1996;71(7):649-656.	Article
Daneshdoost L, Gennarelli TA, Bashey HM, et al. Recognition of gonadotroph adenomas in women. <i>N Engl J Med</i> . 1991;324(9):589-594.	Article
Hypogonadotropic Hypogonadism	
Boehm U, Bouloux PM, Dattani MT, et al. Expert consensus document: European Consensus Statement on congenital hypogonadotropic hypogonadism—pathogenesis, diagnosis and treatment. <i>Nat Rev Endocrinol</i> . 2015;11(9):547-564.	Article
Silveira LF, Latronico AC. Approach to the patient with hypogonadotropic hypogonadism. <i>J Clin Endocrinol Metab</i> . 2013;98(5):1781-1788.	Article
NONSECRETING PITUITARY TUMORS	
Fernández-Balsells MM, Murad MH, Barwise A, et al. Natural history of nonfunctioning pituitary adenomas and incidentalomas: a systematic review and metaanalysis. <i>J Clin Endocrinol Metab</i> . 2011;96(4):905-912.	Article
Jaffe CA. Clinically non-functioning pituitary adenoma. <i>Pituitary</i> . 2006;9(4):317-321.	Article
CORTICOTROPIN	
Cushing Disease: Diagnosis and Management	
*Nieman LK, Biller BM, Findling JW, et al. The diagnosis of Cushing's syndrome: an Endocrine Society Clinical Practice Guideline. <i>J Clin Endocrinol Metab</i> . 2008;93(5):1526-1540.	Clinical Practice Guideline

*Prevedello DM, Challinor SM, Tomycz ND, et al. Diagnosing, managing Cushing's disease: a multidisciplinary overview. <i>Review of Endocrinology</i> . 2009;19-24.	Article
*Findling JW, Raff H. Cushing's syndrome: important issues in diagnosis and management. <i>J Clin Endocrinol Metab</i> . 2006;91(10):3746-3753.	Article
*Findling JW, Raff H. Newer diagnostic techniques and problems in Cushing's disease. <i>Endocrinol Metab Clin North Am</i> . 1999;28(1):191-210.	Article
*Sonino N, Boscaro M. Medical therapy for Cushing's disease. <i>Endocrinol Metab Clin North Am</i> . 1999;28(1):211-222.	Article
*Newell-Price J, Trainer P, Besser M, Grossman A. The diagnosis and differential diagnosis of Cushing's syndrome and pseudo-Cushing's states. <i>Endocr Rev</i> . 1998;19(5):647-672.	Article
Pivonello R, Petersenn S, Newell-Price J, et al; Pasireotide B2305 Study Group. Pasireotide treatment significantly improves clinical signs and symptoms in patients with Cushing's disease: results from a Phase III study. <i>Clin Endocrinol (Oxf)</i> . 2014;81(3):408-417.	Article
Colao A, Petersenn S, Newell-Price J, et al; Pasireotide B2305 Study Group. A 12-month phase 3 study of pasireotide in Cushing's disease [published correction appears in <i>N Engl J Med</i> . 2012;367(8):780]. <i>N Engl J Med</i> . 2012;366(10):914-924.	Article
Fleseriu M, Biller BM, Findling JW, Molitch ME, Scheingart DE, Gross C; SEISMIC Study Investigators. Mifepristone, a glucocorticoid receptor antagonist, produces clinical and metabolic benefits in patients with Cushing's syndrome. <i>J Clin Endocrinol Metab</i> . 2012;97(6):2039-2049.	Article
Elamin MB, Murad MH, Mullan R, et al. Accuracy of diagnostic tests for Cushing's syndrome: a systematic review and metaanalyses. <i>J Clin Endocrinol Metab</i> . 2008;93(5):1553-1562.	Article
Viardot A, Huber P, Puder JJ, Zulewski H, Keller U, Müller B. Reproducibility of nighttime salivary cortisol and its use in the diagnosis of hypercortisolism compared with urinary free cortisol and overnight dexamethasone suppression test. <i>J Clin Endocrinol Metab</i> . 2005;90(10):5730-5736.	Article
Yaneva M, Mosnier-Pudar H, Dugué MA, Grabar S, Fulla Y, Bertagna X. Midnight salivary cortisol for the initial diagnosis of Cushing's syndrome of various causes. <i>J Clin Endocrinol Metab</i> . 2004;89(7):3345-3351.	Article
Oldfield EH, Doppman JL, Nieman LK, et al. Petrosal sinus sampling with and without corticotropin-releasing hormone for the differential diagnosis of Cushing's syndrome [published correction appears in <i>N Engl J Med</i> . 1992;326(17):1172]. <i>N Engl J Med</i> . 1991;325(13):896-905.	Article
HYPOPITUITARISM	
*Prabhakar VK, Shalet SM. Aetiology, diagnosis, and management of hypopituitarism in adult life. <i>Postgrad Med J</i> . 2006;82(966):259-266.	Article

Benvenega S, Campenni A, Ruggeri RM, Trimarchi F. Clinical review 113: Hypopituitarism secondary to head trauma. <i>J Clin Endocrinol Metab.</i> 2000;85(4):1353-1361.	Article
Chrousos GP, Torpy DJ, Gold PW. Interactions between the hypothalamic-pituitary-adrenal axis and the female reproductive system: clinical implications. <i>Ann Intern Med.</i> 1998;129(3):229-240.	Article
*Lamberts SW, de Herder WW, van der Lely AJ. Pituitary insufficiency. <i>Lancet.</i> 1998;352(9122):127-134.	Article
Seminara SB, Hayes FJ, Crowley WF Jr. Gonadotropin-releasing hormone deficiency in the human (idiopathic hypogonadotropic hypogonadism and Kallmann's syndrome): pathophysiological and genetic considerations. <i>Endocr Rev.</i> 1998;19(5):521-539.	Article
Gama R, Smith MJ, Wright J, Marks V. Hypopituitarism in primary haemochromatosis; recovery after iron depletion. <i>Postgrad Med J.</i> 1995;71(835):297-298.	Article
*Vance ML. Hypopituitarism [published correction appears in <i>N Engl J Med.</i> 1994;331(7):487]. <i>N Engl J Med.</i> 1994;330(23):1651-1662.	Article
Constine LS, Woolf PD, Cann D, et al. Hypothalamic-pituitary dysfunction after radiation for brain tumors [published correction appears in <i>N Engl J Med.</i> 1993;328(16):1208]. <i>N Engl J Med.</i> 1993;328(2):87-94.	Article
Littley MD, Shalet SM, Beardwell CG, Ahmed SR, Applegate G, Sutton ML. Hypopituitarism following external radiotherapy for pituitary tumours in adults. <i>Q J Med.</i> 1989;70(262):145-160.	Article
EMPTY SELLA	
Guitelman M, Garcia Basavilbaso N, Vitale M, et al. Primary empty sella (PES): a review of 175 cases. <i>Pituitary.</i> 2013;16(2):270-274.	Article
De Marinis L, Bonadonna S, Bianchi A, Maira G, Guistina A. Primary empty sella. <i>J Clin Endocrinol Metab.</i> 2005;90(9):5471-5477.	Article
ANTIDIURETIC HORMONE	
Diabetes Insipidus	
*Oiso Y, Robertson GL, Norgaard JP, Juul KV. Clinical review: treatment of neurohypophyseal diabetes insipidus. <i>J Clin Endocrinol Metab.</i> 2013;98(10):3958-3967.	Article
*Fenske W, Allolio B. Clinical review: current state and future perspectives in the diagnosis of diabetes insipidus: a clinical review. <i>J Clin Endocrinol Metab.</i> 2012;97(10):3426-3437.	Article
*Makaryus AN, McFarlane SI. Diabetes insipidus: diagnosis and treatment of a complex disease. <i>Cleveland Clin J Med.</i> 2006;93:65-71.	Article

*Verbalis JG. Diabetes insipidus. <i>Rev Endocr Metab Disord.</i> 2003;4(2):177-185.	Article
*Robertson GL. Diabetes insipidus. <i>Endocrinol Metab Clin North Am.</i> 1995;24(3):549-572.	Article
Syndrome of Inappropriate Antidiuretic Hormone Secretion	
*Adrogué HJ, Madias NE. Hyponatremia. <i>N Engl J Med.</i> 2000;342(21):1581-1589.	Article
*Harrigan MR. Cerebral salt wasting syndrome: a review. <i>Neurosurgery.</i> 1996;38(1):152-160.	Article
*Verbalis JG. Hyponatremia: epidemiology, pathophysiology, and therapy. <i>Curr Opin Nephrol Hypertens.</i> 1993;2(4):636-652.	Article
Greenberg A, Verbalis JG. Vasopressin receptor antagonists. <i>Kidney Int.</i> 2006;69(12):2124-2130.	Article
Schrier RW, Gross P, Gheorghide M, et al; SALT Investigators. Tolvaptan, a selective oral vasopressin V2-receptor antagonist, for hyponatremia. <i>N Engl J Med.</i> 2006;355(20):2099-2112.	Article
CRANIOPHARYNGIOMA, OTHER SPACE-OCCUPYING LESIONS, AND INFILTRATIVE OR INFLAMMATORY DISORDERS OF THE PITUITARY	
*Shin JL, Asa SL, Woodhouse LJ, Smyth HS, Ezzat S. Cystic lesions of the pituitary: clinicopathological features distinguishing craniopharyngioma, Rathke's cleft cyst, and arachnoid cyst. <i>J Clin Endocrinol Metab.</i> 1999;84(11):3972-3982.	Article
Mukerjee JJ, Islam N, Kaltsas G, et al. Clinical, radiological and pathological features of patients with Rathke's cleft cysts: tumors that may recur. <i>J Clin Endocrinol Metab.</i> 1997;82(7):2357-2362.	Article
DeVile CJ, Grant DB, Hayward RD, Stanhope R. Growth and endocrine sequelae of craniopharyngioma. <i>Arch Dis Child.</i> 1996;75(2):108-114.	Article
Chapelon C, Ziza JM, Piette JC, et al. Neurosarcoïdosis: signs, course and treatment in 35 confirmed cases. <i>Medicine (Baltimore).</i> 1990;69(5):261-276.	Article
PITUITARY INCIDENTALOMA	
*Freda PU, Beckers AM, Katznelson L, et al; Endocrine Society. Pituitary incidentaloma: an endocrine society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2011;96(4):894-904.	Clinical Practice Guideline
Fernández-Balsells MM, Murad MH, Barwise A, et al. Natural history of nonfunctioning pituitary adenomas and incidentalomas: a systematic review and metaanalysis. <i>J Clin Endocrinol Metab.</i> 2011;96(4):905-912.	Article
*Molitch ME. Pituitary incidentalomas. <i>Best Pract Res Clin Endocrinol Metab.</i> 2009;23:667-675.	Article
Laws ER Jr, Thapar K. Pituitary surgery. <i>Endocrinol Metab Clin North Am.</i> 1999;28(1):119-131.	Article
Melmed S. Pathogenesis of pituitary tumors. <i>Endocrinol Metab Clin North Am.</i> 1999;28(1):1-12.	Article

PITUITARY IMAGING AND PROCEDURES

Imaging

Pantalone KM, Jones SE, Weil RJ, Hamrahian AH. <i>MRI Atlas of Pituitary Pathology</i> . New York, NY: Elsevier; 2015.	Textbook
Ouyang T, Rothfus WE, Ng JM, Challinor SM. Imaging of the pituitary. <i>Radiol Clin North Am</i> . 2011;49(3):549-571.	Article
Naidich MJ, Russell EJ. Current approaches to imaging of the sellar region and pituitary. <i>Endocrinol Metab Clin North Am</i> . 1999;28(1):45-79.	Article

Procedures

Deipolyi A, Karaosmanoglu A, Habito C, et al. The role of bilateral inferior petrosal sinus sampling in the diagnostic evaluation of Cushing syndrome. <i>Diagn Interv Radiol</i> . 2012;18(1):132-138.	Article
Colao A, Faggiano A, Pivonello R, Pecori Giraldi F, Gavagnini F, Lombardi G; Study Group of the Italian Endocrinology Society on the Pathophysiology of the Hypothalamic-Pituitary-Adrenal Axis. Inferior petrosal sinus sampling in the differential diagnosis of Cushing's syndrome: results of an Italian multicenter study. <i>Eur J Endocrinol</i> . 2001;144(5):499-507.	Article
Miller DL, Doppman JL. Petrosal sinus sampling: technique and rationale. <i>Radiology</i> . 1991;178(1):37-47.	Article

DYNAMIC HORMONE TESTING

Ergin AB, Kennedy AL, Gupta MK, Hamrahian AH. <i>The Cleveland Clinic Manual of Dynamic Endocrine Testing</i> . New York, NY: Springer; 2015.	Textbook
---	----------

Lipid Metabolism

INTRODUCTION

Disorders of lipid metabolism result from genetic and/or acquired defects in the synthesis and catabolism of lipoproteins. Lipoproteins have a hydrophobic core that contains cholesterol and triglycerides. They are classified on the basis of their density as chylomicron, very low-density lipoprotein, intermediate-density lipoprotein, low-density lipoprotein, and high-density lipoprotein. Hyperlipidemia refers to elevations in plasma cholesterol, triglycerides, or both. Dyslipidemia is a term used to describe abnormalities in plasma lipids or lipoproteins. Understanding the physiology and pathophysiology of lipoprotein metabolism is the starting point of the curriculum. Genetic and acquired defects in the metabolic pathway result in dyslipidemia. Clinical manifestations, laboratory findings, and therapeutic options should be covered. Fellows should be competent in the diagnosis and treatment of lipid disorders. Goals of therapy and potential adverse effects must be addressed.

MEDICAL KNOWLEDGE

Fellows must demonstrate knowledge about established and evolving biomedical, clinical, and cognate (eg, epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.

Topic	Fundamental	Advanced
BASIC PHYSIOLOGIC PRINCIPLES		
Classify lipoproteins as chylomicrons, very low-density lipoproteins, intermediate-density lipoproteins, low-density lipoproteins, high-density lipoproteins, or apolipoproteins.	√	
Summarize pathways of lipid metabolism.	√	
Explain the role of lipoproteins in atherosclerosis.	√	
Determine which patients should undergo screening for lipid abnormalities on the basis of cardiovascular risk independent of lipid levels.	√	
List the risk factors for cardiovascular disease, including age, sex, hypertension, cigarette smoking, and family history of premature coronary artery disease.	√	
Use risk calculators to determine a patient's cardiovascular disease risk.	√	
PRIMARY DISORDERS OF HYPERLIPIDEMIA		
Familial Hypercholesterolemia		

Summarize the symptoms and signs of familial hypercholesterolemia, including a high low-density lipoprotein cholesterol level (from birth), tendon xanthomas, and early-onset coronary heart disease.	√	
Diagnose familial hypercholesterolemia.	√	
Describe the underlying genetic etiology of familial hypercholesterolemia, including mutations in the gene encoding the low-density lipoprotein receptor and mutations in the <i>PCSK9</i> gene.	√	
Explain the inheritance of familial hypercholesterolemia and the “gene dosing” effect with regard to the phenotype of homozygotes vs heterozygotes with mutations in the gene encoding the low-density lipoprotein receptor.		√
Explain the role of genetic testing in patients with familial hypercholesterolemia and determine when ordering genetic testing is appropriate.		√
Recommend initial treatment for familial hypercholesterolemia.	√	
Familial Defective Apolipoprotein B₁₀₀		
Summarize the symptoms and signs of familial defective apolipoprotein B ₁₀₀ .	√	
Describe the underlying genetic etiology of familial defective apolipoprotein B ₁₀₀ .	√	
Diagnose familial defective apolipoprotein B ₁₀₀ .	√	
Recommend lipid-lowering therapy for patients with familial defective apolipoprotein B ₁₀₀ .	√	
Familial Combined Hyperlipidemia		
Summarize the heterogeneous symptoms and signs of familial combined hyperlipidemia, including both hypertriglyceridemia and hypercholesterolemia or isolated hypercholesterolemia or isolated hypertriglyceridemia.	√	
Diagnose familial combined hyperlipidemia.	√	
Describe the underlying genetic etiology of familial combined hyperlipidemia.	√	
Recommend treatment for familial combined hyperlipidemia depending on the relative concentrations of low-density lipoprotein cholesterol and triglycerides.	√	
Familial Dysbetalipoproteinemia (Type III)		
Summarize the symptoms and signs of familial dysbetalipoproteinemia including premature coronary heart disease, peripheral vascular disease, tuberoeruptive xanthomas, and xanthomas of the palmar creases.	√	

Diagnose familial dysbetalipoproteinemia.	√	
Describe the underlying genetic etiology of familial dysbetalipoproteinemia.	√	
Manage familial dysbetalipoproteinemia.	√	
Chylomicronemia Syndrome		
Summarize the symptoms and signs of chylomicronemia, including triglyceride levels above the 99th percentile, creamy plasma supernatant and cloudy infranatant, hepatosplenomegaly, eruptive xanthomas, memory loss, abdominal pain, pancreatitis, dyspnea, and lipemia retinalis.	√	
Diagnose fasting chylomicronemia by confirming the presence of chylomicrons and excess very low-density lipoprotein.	√	
Manage chylomicronemia.	√	
Apolipoprotein C-II Deficiency		
Summarize clinical and biochemical findings of apolipoprotein C-II deficiency.	√	
Diagnose apolipoprotein C-II deficiency.	√	
Manage apolipoprotein C-II deficiency.	√	
Familial Hypertriglyceridemia		
Summarize the symptoms and signs of familial hypertriglyceridemia and screen for associated abnormalities.	√	
Describe the underlying genetic etiology of familial hypertriglyceridemia, including mutations in the gene encoding lipoprotein lipase.	√	
Diagnose and manage secondary causes of hypertriglyceridemia, including obesity, diabetes mellitus, hypothyroidism, nephrotic syndrome, pregnancy, and drug-induced causes, etc.	√	
Manage hypertriglyceridemia.	√	
Elevated Lipoprotein (a)		
Summarize the symptoms and signs of lipoprotein (a) excess.	√	
Determine when screening for lipoprotein (a) is appropriate.	√	
Recommend lipid-lowering therapy for patients with elevated lipoprotein (a).	√	
PRIMARY DISORDERS OF HIGH-DENSITY LIPOPROTEIN METABOLISM		
Describe disorders associated with low high-density lipoprotein cholesterol levels, including familial hypoalphalipoproteinemia, familial high-density		√

lipoprotein deficiency, Tangier disease, and familial combined hypolipidemia.		
Counsel patients regarding elevated high-density lipoprotein cholesterol levels.		√
Explain the pathogenesis of low high-density lipoprotein cholesterol levels.		√
Manage disorders resulting in low high-density lipoprotein cholesterol levels.		√

PRIMARY GENETIC HYPOLIPEMIAS

Familial Hypobetalipoproteinemia

Summarize the symptoms and signs of familial hypobetalipoproteinemia, including intestinal fat malabsorption, hepatic steatosis, and fat-soluble vitamin deficiencies.		√
Diagnose familial hypobetalipoproteinemia.		√
Describe the underlying genetic etiology of familial hypobetalipoproteinemia.		√
Manage familial hypobetalipoproteinemia.		√

Abetalipoproteinemia

Summarize the symptoms and signs of abetalipoproteinemia, including presentation in infancy, impaired transport of fat-soluble vitamins, mental retardation, growth abnormalities, and peripheral neuropathies.		√
Diagnose abetalipoproteinemia.		√
Describe the underlying genetic etiology of abetalipoproteinemia.		√
Manage abetalipoproteinemia.		√

SECONDARY DISORDERS OF LIPID METABOLISM

Obesity/Insulin Resistance

Explain the relationship between obesity and insulin resistance and lipid disorders.	√	
Guide the management of lipid disorders in obese and/or insulin-resistant patients.	√	

Diabetes Mellitus

Explain the relationship between diabetes mellitus and lipid disorders.	√	
Guide the management of lipid disorders in patients with diabetes mellitus.	√	

Hypothyroidism

Explain the relationship between hypothyroidism and lipid disorders.		√
Guide the management of lipid disorders in patients with hypothyroidism.		√
Renal		
Explain the relationship between kidney disease (ie, nephrotic syndrome and chronic renal insufficiency) and lipid disorders.		√
Guide the management of lipid disorders in patients with kidney disease.		√
Lipodystrophic Disorders		
Explain the relationship between lipodystrophic disorders and lipid disorders.		√
Guide the management of lipid disorders in patients with lipodystrophic disorders.		√
Drug-Induced Disorders		
Explain the relationship between some drugs (eg, thiazide diuretics, adrenergic blockers, oral estrogens, alcohol, and protease inhibitors) and lipid disorders.		√
Guide the management of lipid disorders in patients with drug-induced changes in lipid concentrations.		√
TREATMENT		
Dietary		
<i>Nutritional Supplements</i>		
Summarize the evidence base for lipid lowering with dietary supplements such as fish oil and omega-3 fatty acids, soy, and red yeast rice.		√
Recommend appropriate nutritional supplements in the management of patients with dyslipidemia.		√
<i>Weight Reduction</i>		
Summarize the evidence base for weight loss for lipid lowering and cardiovascular risk reduction.	√	
Recommend weight-loss strategies in the management of patients with dyslipidemia.	√	
<i>Diet Composition</i>		
Summarize the evidence base regarding various diet compositions, such as the Mediterranean diet and DASH diet, for lipid lowering.		√
Make dietary recommendations in the management of patients with dyslipidemia.		√
Drug Therapy/Clinical Trials		
<i>HMG-CoA Reductase Inhibitors</i>		

Summarize the evidence base for use of statins in treating hyperlipidemia.	√	
Explain the mechanism of action by which statins work.	√	
Determine which patients are appropriate candidates for statin therapy.	√	
Recommend an appropriate statin dosage.	√	
Monitor the effectiveness of statin therapy.	√	
Manage statin intolerance.	√	
<i>Niacin</i>		
Summarize the evidence base for use of niacin in treating hyperlipidemia.	√	
Explain the mechanism of action by which niacin works.	√	
Determine which patients are appropriate candidates for niacin.	√	
Manage the adverse effects of therapy with niacin.	√	
<i>Fibrates</i>		
Summarize the evidence base for use of fibrates in treating dyslipidemia.	√	
Explain the mechanism of action by which fibrates work.	√	
Determine which patients are appropriate candidates for fibrates.	√	
Manage the adverse effects of therapy with fibrates.	√	
<i>Bile Acid Sequestrants</i>		
Summarize the evidence base for use of bile acid sequestrants in treating hyperlipidemia.	√	
Explain the mechanism of action by which bile acid sequestrants work.	√	
Determine which patients are appropriate candidates for bile acid sequestrants.	√	
Manage the adverse effects of therapy with bile acid sequestrants.	√	
<i>Ezetimibe</i>		
Summarize the evidence base for use of ezetimibe in treating hyperlipidemia.	√	
Explain the mechanism of action by which ezetimibe works.	√	
Determine which patients are appropriate candidates for ezetimibe.	√	
Manage the adverse effects of therapy with ezetimibe.	√	
<i>Combination Therapy</i>		
Determine which patients are appropriate candidates for combination therapy to treat dyslipidemia.	√	
Guide combination therapy in patients with dyslipidemia.	√	
<i>Other Drugs</i>		
Summarize new and emerging therapy with other drugs such as proprotein convertase subtilisin kexin 9 inhibitors.		√

Drug Interactions		
Identify drug-drug interactions when treating patients with hyperlipidemia.	√	
Pregnancy		
Manage dyslipidemia in the setting of pregnancy.		√

TEACHING METHODS AND EVALUATION

Much teaching occurs one-on-one with attendings during outpatient clinics and on inpatient hospital rounds. Active learning occurs as fellows participate in patient care under the supervision and guidance of the attending. In addition, a full range of topics are reviewed in didactic sessions at weekly conferences and in the core curriculum/board review weekly sessions. Fellows are also expected to engage in self-directed study guided by the curriculum. Evaluation includes attending review of fellows knowledge base and medical reasoning during clinic and hospital rounds. In addition, the in-training exam taken in February of every year provides a loose benchmark of medical knowledge progression through the fellowship.

SUGGESTED READING

Asterisks denote references that are designated for residents, students, or endocrine fellows early in their training.

BASIC PHYSIOLOGIC PRINCIPLES		
*Benjamin IJ, Griggs RC, Wing EJ, Fitz JG, eds. <i>Andreoli and Carpenter's Cecil Essentials of Medicine</i> . 9th ed. Philadelphia, PA: WB Saunders; 2015.		Textbook
*Gardner D, Shoback D. <i>Greenspan's Basic and Clinical Endocrinology (LANGE Clinical Medicine)</i> . 9th ed. Philadelphia, PA: Saunders; 2015.		Textbook
*Goff DC Jr, Lloyd-Jones DM, Bennett G, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines.. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. <i>Circulation</i> . 2014;129(25 Suppl 2):S49-S73.		Clinical Practice Guideline
Melmed M, Polonsky KS, Larsen RP, Kronenberg HM, eds. <i>Williams Textbook of Endocrinology</i> . 12th ed. Philadelphia, PA: WB Saunders; 2011:1633-1674.		Textbook
D'Agostino RB Sr, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. <i>Circulation</i> . 2008;117(6):743-753.		Article
PRIMARY DISORDERS OF HYPERLIPIDEMIA		

Lewis GF, Xiao C, Hegele RA. Hypertriglyceridemia in the genomic era: a new paradigm. <i>Endocr Rev.</i> 2015;36(1):131-147.	Article
Gidding SS, Champagne MA, de Ferranti SD, et al. The agenda for familial hypercholesterolemia: a scientific statement from the American Heart Association. <i>Circulation.</i> 2015;132(22):2167-2192.	Article
Hegele RA, Ginsberg HN, Chapman MJ, et al; European Atherosclerosis Society Consensus Panel. The polygenic nature of hypertriglyceridaemia: implications for definition, diagnosis, and management. <i>Lancet Diabetes Endocrinol.</i> 2014;2(8):655-666.	Article
Sniderman AD, Tsimikas S, Fazio S. The severe hypercholesterolemia phenotype: clinical diagnosis, management, and emerging therapies. <i>J Am Coll Cardiol.</i> 2014;63(19):1935-1947.	Article
Jacobson TA. Lipoprotein(a), cardiovascular disease, and contemporary management. <i>Mayo Clin Proc.</i> 2013;88(11):1294-1311.	Article
Leaf DA. Chylomicronemia and the chylomicronemia syndrome: a practical approach to management. <i>Am J Med.</i> 2008;121(1):10-12.	Article
Santamarina-Fojo S. The familial chylomicronemia syndrome. <i>Endocrinol Metab Clin North Am.</i> 1998;27(3):551-567.	Article
PRIMARY DISORDERS OF HIGH-DENSITY LIPOPROTEIN METABOLISM	
Feig JE, Hewing B, Smith JD, Hazen SL, Fisher EA. High-density lipoprotein and atherosclerosis regression: evidence from preclinical and clinical studies. <i>Circ Res.</i> 2014;114(1):205-213.	Article
Rosenson RS, Brewer HB Jr, Ansell B, et al. Translation of high-density lipoprotein function into clinical practice: current prospects and future challenges. <i>Circulation.</i> 2013;128(11):1256-1257.	Article
PRIMARY GENETIC HYPOLIPEMIAS	
Welty FK. Hypobetalipoproteinemia and abetalipoproteinemia. <i>Curr Opin Lipidol.</i> 2014;25(3):161-168.	Article
SECONDARY DISORDERS OF LIPID METABOLISM	
Reiss AB, Voloshyna I, De Leon J, Miyawaki N, Mattana J. Cholesterol metabolism in in CKD. <i>Am J Kidney Dis.</i> 2015;66(6):1071-1082.	Article
Wild R, Weedon EA, Wilson D. Dyslipidemia in pregnancy. <i>Cardiol Clin.</i> 2015;33(2):209-215.	Article
Wu L, Parhofer KG. Diabetic dyslipidemia. <i>Metabolism.</i> 2014;63(12):1469-1479.	Article
Franssen R, Monajemi H, Stroes ES, Kastelein JJ. Obesity and dyslipidemia. <i>Med Clin North Am.</i> 2011;95(5):893-902.	Article
Stone NJ. Secondary causes of hyperlipidemia. <i>Med Clin North Am.</i> 1994;78(1):117-141.	Article

TREATMENT	
Chait A, Eckel RH. Lipids, lipoproteins, and cardiovascular disease: clinical pharmacology now and in the future. <i>J Clin Endocrinol Metab.</i> 2016;101(3):804-814.	Article
*American Diabetes Association. (8) Cardiovascular disease and risk management. <i>Diabetes Care.</i> 2015;38(Suppl):S49-S57.	Article
Fox CS, Golden SH, Anderson C, et al. Update on prevention of cardiovascular disease in adults with type 2 diabetes mellitus in light of recent evidence: a scientific statement from the American Heart Association and the American Diabetes Association. <i>Circulation.</i> 2015;132(8):691-718.	Article
Gryn SE, Hegele RA. Novel therapeutics in hypertriglyceridemia. <i>Curr Opin Lipidol.</i> 2015;26(6):484-491.	Article
Hegele RA, Gidding SS, Ginsberg HN, et al. Nonstatin low-density lipoprotein-lowering therapy and cardiovascular risk reduction-statement from ATVB council. <i>Arterioscler Thromb Vasc Biol.</i> 2015;35(11):2269-2280.	Article
Martin SS, Abd TT, Jones SR, Michos ED, Blumenthal RS, Blaha MJ. 2013 ACC/AHA cholesterol treatment guideline: what was done well and what could be done better. <i>J Am Coll Cardiol.</i> 2014;63(24):2674-2678.	Article
Rader DJ, Kastelein JJ. Lomitapide and mipomersen: two first-in-class drugs for reducing low-density lipoprotein cholesterol in patients with homozygous familial hypercholesterolemia. <i>Circulation.</i> 2014;129(9):1022-1032.	Article
*Stone NJ, Robinson JG, Lichtenstein AH, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines [published correction appears in <i>Circulation.</i> 2014;129(25 Suppl 2):S46-S48.	Guideline
Subedi BH, Joshi PH, Jones SR, Martin SS, Blaha MJ, Michos ED. Current guidelines for high-density lipoprotein cholesterol in therapy and future direction. <i>Vasc Health Risk Manag.</i> 2014;10:205-216.	Article
*Berglund L, Brunzell JD, Goldberg AC, et al; Endocrine Society. Evaluation and treatment of hypertriglyceridemia: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2012;97(9):2969-2989.	Clinical Practice Guideline
Katcher HI, Hill AM, Lanford JL, Yoo JS, Kris-Etherton PM. Lifestyle approaches and dietary strategies to lower LDL-cholesterol and triglycerides and raise HDL-cholesterol. <i>Endocrinol Metab Clin North Am.</i> 2009;38(1):45-78.	Article

USEFUL WEB SITES

RISK Calculator: <https://www.framinghamheartstudy.org/risk-functions/cardiovascular-disease/10-year-risk.php#>

RISK Calculator: <http://my.americanheart.org/cvriskscalculator>

RISK Calculator: <http://www.cardiosource.org/en/Science-And-Quality/Practice-Guidelines-and-Quality-Standards/2013-Prevention-Guideline-Tools.aspx>.

Obesity and Nutrition

INTRODUCTION

Endocrinology is concerned with the actions of hormones and the organs and tissues in which the hormones are formed. Many hormones are involved with fuel, vitamin, and mineral metabolism. They are profoundly involved in substrate flux and the use of food for energy production and storage. As such, many hormones are important in nutrition. Education curriculum and training for fellows should cover basic knowledge of nutrition to understand the endocrine interactions that occur. Fellows should be competent in core knowledge about nutrition, including nutritional support, and in the diagnosis and treatment of obesity and eating disorders.

MEDICAL KNOWLEDGE

Fellows must demonstrate knowledge about established and evolving biomedical, clinical, and cognate (eg, epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.

Topic	Fundamental	Advanced
PATHOPHYSIOLOGY AND BASIC PRINCIPLES		
Neurophysiology of Weight Regulation		
Explain the roles of leptin, ghrelin, insulin, glucagonlike peptide 1, cholecystokinin, pancreatic polypeptide, peptide YY, and pro-opiomelanocortin in weight regulation.		√
Summarize the function of "central controller" brain regions, including the hypothalamus, brainstem, and ventral striatum, in weight regulation.	√	
Energy Balance and Energy Expenditure		
Determine the percentage of energy expenditure used for basal/resting metabolic processes, thermic response to food, and activity or exercise.	√	
Explain the relationship between brown adipose tissue and energy balance/energy expenditure.		√
Describe methods for measuring total daily energy expenditure such as questionnaires, electronic monitoring devices, and the doubly-labeled water technique.	√	
OBESITY		
Definition		

Define overweight and obesity according to the standard criteria for categorization using body mass index.	√	
List the body mass index criteria that are used for persons from Asia.	√	
Prevalence		
Summarize the prevalence and trends in overweight and obesity among adults, children, and adolescents in the United States and worldwide.	√	
Pathogenesis		
Describe the role of diet, physical activity, sleep, and drugs in the pathogenesis of obesity.	√	
List endocrine disorders associated with obesity.	√	
Differentiate among single-gene disorders known to cause obesity, including <i>FTO</i> variants, <i>MC4R</i> mutations, leptin deficiency, and leptin receptor deficiency.		√
Describe the clinical features associated with genetic disorders that cause obesity such as Prader-Willi syndrome and Bardet-Biedl syndrome.		√
Body Fat Distribution		
Describe the role of gonadal steroids in the distribution of body fat.	√	
Explain the association of metabolic and cardiovascular disorders with visceral central adiposity.	√	
Evaluation		
Screen for obesity with body mass index, waist circumference, and risk factor assessment.	√	
Take a complete medical history, including the age at onset of weight gain, events associated with weight gain, weight-loss attempts, change in dietary patterns, history of exercise, history of smoking cessation, and medication history (eg, insulin, sulfonylureas, thiazolidinediones, psychiatric medications, glucocorticoids).	√	
Guide a complete diet assessment using tools such as estimating portion sizes, 24-hour dietary recall, food diary, food frequency questionnaire, etc.	√	
Comorbidities		
Diagnose and manage type 2 diabetes mellitus in obese patients.	√	
Diagnose and manage cardiovascular disease in obese patients.	√	
Diagnose and manage hypertension in obese patients.	√	
Diagnose and manage obstructive sleep apnea in obese patients.	√	

OBESITY MANAGEMENT

Lifestyle Intervention		
<i>Diet</i>		
Differentiate among diet types (eg, low-calorie, low-carbohydrate, high-protein, Mediterranean) in terms of composition and outcomes data.	√	
Describe the use of meal replacements in diet management.		√
Explain how the techniques of self-monitoring and electronic self-help tools can assist in diet management.	√	
Provide patients with nutritional education and assist with meal planning skills.	√	
<i>Exercise</i>		
Prescribe an appropriate program for physical activity tailored to the needs of individual patients with respect to exercise frequency, intensity, duration, and exercise type for general health and weight-loss maintenance.	√	
Determine which patients require a medical evaluation before initiation of an exercise program.	√	
<i>Behavioral Treatment</i>		
Assist patients with setting realistic goals for weight loss.	√	
Encourage social support as a means to improve long-term weight loss.	√	
Demonstrate an understanding of the Stages of Change approach as a technique to improve outcomes in the management of obesity.	√	
Demonstrate effective cognitive-behavioral strategies as a technique to improve outcomes in the management of obesity.		√
Demonstrate effective motivational interviewing as a technique to improve outcomes in the management of obesity.		√
Pharmacotherapy		
Define the goals of pharmacologic therapy for obesity.	√	
Define criteria for selecting obese patients for whom pharmacologic therapy would be appropriate.	√	
Counsel patients on the risks and benefits of pharmacologic therapy for obesity.	√	
Monitor for weight loss, blood pressure, heart rate, and potential adverse effects after initiation of pharmacologic therapy.	√	
Describe drugs that alter fat digestion such as orlistat, as well as data on effectiveness, safety, and adverse effects.		√
Describe serotonin agonists such as lorcaserin, as well as data on effectiveness, safety, and adverse effects.		√

Describe sympathomimetic drugs such as phentermine, as well as data on effectiveness, safety, and adverse effects.		√
Describe the use of bupropion/naltrexone in the treatment of obese patients, as well as data on effectiveness, safety, and adverse effects.		√
Describe the use of phentermine/topiramate extended release in the treatment of obese patients, as well as data on effectiveness, safety, and adverse effects.		√
Describe the use of liraglutide, 3 mg daily, in the treatment of obese patients, as well as data on effectiveness, safety, and adverse effects.		√

Bariatric Surgery

Differentiate among the following procedures: Roux-en-Y gastric bypass, sleeve gastrectomy, laparoscopic adjustable gastric banding, and biliopancreatic diversion with duodenal switch.	√	
Describe mechanisms by which bariatric surgery induces weight loss.		√
Define indications for bariatric surgery with regard to body mass index and comorbid conditions.	√	
List contraindications to bariatric surgery.	√	
Describe the potential health benefits of bariatric surgery, including remission of type 2 diabetes, hypertension, and sleep apnea.	√	
Describe the risks of bariatric surgery, including short-term postoperative morbidity and complications, common nutritional deficiencies, mechanical complications, and mortality.	√	
Recommend appropriate preoperative assessment, including presurgical psychologic assessment, medical assessment, and anesthetic risk assessment.		√
Guide postoperative follow-up and monitoring for patients who have undergone bariatric surgery.		√

NUTRITION IN HOSPITALIZED PATIENTS

Assessment of Nutritional Status in Hospitalized Patients

Assess nutritional status of hospitalized patients.		√
List indications for nutritional support such as preexisting nutritional deprivation, multiorgan system disease, and inadequate oral intake.		√

Nutrition Therapy

Define goals of nutrition therapy in hospitalized patients.	√	
Guide enteral feedings (oral supplementation or tube feeding) and determine appropriate nutritional composition.	√	

Appropriately prescribe and monitor total parenteral nutrition.		√
Guide nutrition therapy in patients with liver or renal failure.		√
Manage malnutrition in hospitalized patients.	√	
Describe an approach to dietary management of hospitalized patients with diabetes mellitus.	√	

NUTRITION IN OUTPATIENTS

Diet Assessment

Guide a complete diet assessment using tools such as estimating portion sizes, 24-hour dietary recall, food diary, food frequency questionnaire, etc.	√	
---	---	--

Vitamin Deficiencies

Diagnose and manage deficiency of water-soluble vitamins (vitamin B ₁ , vitamin B ₂ , vitamin B ₃ , vitamin B ₅ , vitamin B ₆ , biotin, vitamin C, vitamin B ₁₂ , folic acid).		√
Diagnose and manage deficiency of fat-soluble vitamins (vitamin A, vitamin D, vitamin E, vitamin K).		√

Dietary Guidelines

Describe the core principles of the dietary guidelines for Americans.	√	
Describe evidence-based healthful diet strategies, including the Mediterranean diet, the DASH diet, and the American Heart Association diet.	√	
Describe the principles of dietary management in patients with diabetes mellitus.	√	

EATING DISORDERS

Screen patients to identify those who need further evaluation for possible eating disorders.		√
Differentiate among eating disorders, including anorexia nervosa, avoidant/restrictive food intake disorder, binge eating disorder, and bulimia nervosa.		√
Describe metabolic abnormalities and other clinical sequelae associated with eating disorders such as gonadotropin abnormalities, hypometabolic manifestations, osteoporosis, amenorrhea, dentition problems, and cardiovascular disease.		√

Make appropriate referrals to ensure an interdisciplinary team approach to managing eating disorders.

√

TEACHING METHODS AND EVALUATION

Much teaching occurs one-on-one with attendings during outpatient clinics and on inpatient hospital rounds. Active learning occurs as fellows participate in patient care under the supervision and guidance of the attending. In addition, a full range of topics are reviewed in didactic sessions at weekly conferences and in the core curriculum/board review weekly sessions. Fellows are also expected to engage in self-directed study guided by the curriculum. Evaluation includes attending review of fellows knowledge base and medical reasoning during clinic and hospital rounds. In addition, the in-training exam taken in February of every year provides a loose benchmark of medical knowledge progression through the fellowship.

SUGGESTED READING

Asterisks denote references that are designated for residents, students, or endocrine fellows early in their training.

PATHOPHYSIOLOGY AND BASIC PRINCIPLES

Lam YY, Redman LM, Smith SR, et al. Determinants of sedentary 24-h energy expenditure: equations for energy prescription and adjustment in a respiratory chamber. <i>Am J Clin Nutr.</i> 2014;99(4):834-842.	Article
Morton GJ, Meek TH, Schwartz MW. Neurobiology of food intake in health and disease. <i>Nat Rev Neurosci.</i> 2014;15(6):367-378.	Article
Shah M, Vella A. Effects of GLP-1 on appetite and weight. <i>Rev Endocr Metab Disord.</i> 2014;15(3):181-187.	Article
Sohn JW, Elmquist JK, Williams KW. Neuronal circuits that regulate feeding behavior and metabolism. <i>Trends Neurosci.</i> 2013;36(9):504-512.	Article
Goldsmith R, Joanisse DR, Gallagher D, et al. Effects of experimental weight perturbation on skeletal muscle work efficiency, fuel utilization, and biochemistry in human subjects. <i>Am J Physiol Regul Integr Comp Physiol.</i> 2010;298(1):R79-R88.	Article
Cone RD. Studies on the physiological functions of the melanocortin system. <i>Endocr Rev.</i> 2006;27(7):736-749.	Article

Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight [published correction appears in <i>N Engl J Med</i> . 1995;333(6):399]. <i>N Engl J Med</i> . 1995;332(10):621-628.	Article
Lichtman SW, Pisarska K, Berman ER, et al. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. <i>N Engl J Med</i> . 1992;327(27):1893-1898.	Article
OBESITY	
Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD, Ogden CL. Trends in obesity among adults in the United States, 2005 to 2014. <i>JAMA</i> . 2016;315(21):2284-2291.	Article
Kyle TK, Dhurandhar EJ, Allison DB. Regarding obesity as a disease: evolving policies and their implications. <i>Endocrinol Metab Clin North Am</i> . 2016;45(3):511-520.	Article
Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. <i>Nature</i> . 2015;518(7538):197-206.	Article
Shook RP, Hand GA, Drenowatz C, et al. Low levels of physical activity are associated with dysregulation of energy intake and fat mass gain over 1 year. <i>Am J Clin Nutr</i> . 2015;102(6):1332-1338.	Article
Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: A systematic review and meta-analysis. <i>Ann Intern Med</i> . 2013;159(11):758-769.	Article
Killick R, Banks S, Liu PY. Implications of sleep restriction and recovery on metabolic outcomes. <i>J Clin Endocrinol Metab</i> . 2012;97(11):3876-3890.	Article
Kushner RF. Clinical assessment and management of adult obesity. <i>Circulation</i> . 2012;126(24):2870-2877.	Article
Ranadive SA, Vaisse C. Lessons from extreme human obesity: monogenic disorders. <i>Endocrinol Metab Clin North Am</i> . 2008;37(3):733-751.	Article
Farooqi S. Insights from the genetics of severe childhood obesity. <i>Horm Res</i> . 2007;68(Suppl 5):5-7.	Article
Farooqi S, O'Rahilly S. Genetics of obesity in humans. <i>Endocr Rev</i> . 2006;27(7):710-718.	Article
Collop NA. Obstructive sleep apnea syndromes. <i>Semin Respir Crit Care Med</i> . 2005;26(1):13-24.	Article
Bray GA. Medical consequences of obesity. <i>J Clin Endocrinol Metab</i> . 2004;89(6):2583-2589.	Article
Allison DB, Casey DE. Antipsychotic-induced weight gain: a review of the literature. <i>J Clin Psychiatry</i> . 2001;62(Suppl 7):22-31.	Article
OBESITY MANAGEMENT	
Khera R, Murad MH, Chandar AK, et al. Association of pharmacological treatments for obesity with weight loss and adverse events: a systematic review and meta-analysis. <i>JAMA</i> . 2016;315(22):2424-2434.	Article

Rariy CM, Rometo D, Korytkowski M. Post-gastric bypass hypoglycemia. <i>Curr Diab Rep.</i> 2016;16(2):19.	Article
Apovian CM, Aronne LJ, Bessesen DH, et al; Endocrine Society. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2015;100(2):342-362.	Article
Arterburn DE, Olsen MK, Smith VA, et al. Association between bariatric surgery and long-term survival. <i>JAMA.</i> 2015;313(1):62-70.	Article
Chang SH, Stoll CR, Song J, Varela JE, Eagon CJ, Colditz GA. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003-2012. <i>JAMA Surg.</i> 2014;149(3):275-287.	Article
Jensen MD, Ryan DH, Apovian CM, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; Obesity Society. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society [published correction appears in <i>Circulation.</i> 2014;129(25 Suppl 2):S139-S140]. <i>Circulation.</i> 2014;129(25 Suppl 2):S102-S138.	Article
Kushner RF, Ryan DH. Assessment and lifestyle management of patients with obesity: clinical recommendations from systematic reviews. <i>JAMA.</i> 2014;312(9):943-952.	Article
Li G, Zhang P, Wang J, et al. Cardiovascular mortality, all-cause mortality, and diabetes incidence after lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study: a 23-year follow-up study. <i>Lancet Diabetes Endocrinol.</i> 2014;2(6):474-480.	Article
Look AHEAD Research Group, Wing RR, Bolin P, et al. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes [published correction appears in <i>N Engl J Med.</i> 2014;370(19):1866]. <i>N Engl J Med.</i> 2013;369(2):145-154.	Article
Schauer PR, Bhatt DL, Kirwan JP, et al; STAMPEDE Investigators. Bariatric surgery versus intensive medical therapy for diabetes--3-year outcomes. <i>N Engl J Med.</i> 2014;370(21):2002-2013.	Article
Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. <i>JAMA.</i> 2014;311(1):74-86.	Article
Miller WR, Rollnick S, eds. <i>Motivational Interviewing: Helping People for Change.</i> 3rd ed. New York, New York: The Guilford Press; 2013.	Textbook
Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. <i>N Engl J Med.</i> 2012;366(17):1567-1576.	Article
Kushner RF, Sarwer DB. Medical and behavioral evaluation of patients with obesity. <i>Psychiatr Clin North Am.</i> 2011;34(4):797-812.	Article
Powell KE, Paluch AE, Blair SN. Physical activity for health: What kind? How much? How intense? On top of what? <i>Annu Rev Public Health.</i> 2011;32:349-365.	Article

Wing RR, Lang W, Wadden TA, et al; Look AHEAD Research Group. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. <i>Diabetes Care</i> . 2011;34(7):1481-1486.	Article
Mechanick JI, Kushner RF, Sugerman HJ, et al; American Association of Clinical Endocrinologists; Obesity Society; American Society for Metabolic & Bariatric Surgery. American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery medical guidelines for clinical practice for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient [published correction appears in <i>Obesity (Silver Spring)</i> . 2010;18(3):649]. <i>Obesity (Silver Spring)</i> . 2009;17(Suppl 1):S1-S70.	Article
Aasheim ET. Wernicke encephalopathy after bariatric surgery, a systematic review. <i>Ann Surg</i> . 2008;248(5):714-720.	Article
ArticleTsai AG, Wadden TA. The evolution of very-low-calorie diets: an update and meta-analysis. <i>Obesity (Silver Spring)</i> . 2006;14(8):1283-1293.	Article
Wadden TA, Foster GD. Behavioral treatment of obesity. <i>Med Clin North Am</i> . 2000;84(2):441-461.	Article
NUTRITION IN HOSPITALIZED PATIENTS	
McClave SA, DiBaise JK, Mullin GE, Martindale RG. ACG clinical guideline: nutrition therapy in the adult hospitalized patient. <i>Am J Gastroenterol</i> . 2016;111(3):315-334.	Article
Boullata JI, Gilbert K, Sacks G, et al; American Society for Parenteral and Enteral Nutrition. A.S.P.E.N. clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing. <i>JPEN J Parenter Enteral Nutr</i> . 2014;38(3):334-377.	Article
Mueller C, Compher C, Ellen DM; American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors. A.S.P.E.N. clinical guidelines: nutrition screening, assessment, and intervention in adults. <i>JPEN J Parenter Enteral Nutr</i> . 2011;35(1):16-24.	Article
NUTRITION IN OUTPATIENTS	
Kushner RF. Providing nutritional care in the office practice: teams, tools, and techniques. <i>Med Clin North Am</i> . 2016;100(6):1157-1168.	Article
Eckel RH, Jakicic JM, Ard JD, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. <i>J Am Coll Cardiol</i> . 2014;63(25 Pt B):2960-2984.	Article
Estruch R, Ros E, Salas-Salvadó J, et al; PREDIMED Study Investigators. Primary prevention of cardiovascular disease with a Mediterranean diet [published correction appears in <i>N Engl J Med</i> . 2014;370(9):886]. <i>N Engl J Med</i> . 2013;368(14):1279-1290.	Article

Rejeski WJ, Ip EH, Bertoni AG, et al; Look AHEAD Research Group. Lifestyle change and mobility in obese adults with type 2 diabetes. <i>N Engl J Med.</i> 2012;366(13):1209-1217.	Article
Shai I, Schwarzfuchs D, Henkin Y, et al; Dietary Intervention Randomized Controlled Trial (DIRECT) Group. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet [published correction appears in <i>N Engl J Med.</i> 2009;361(27):2681]. <i>N Engl J Med.</i> 2008;359(3):229-241.	Article
Knowler WC, Barrett-Connor E, Fowler SE, et al; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. <i>N Engl J Med.</i> 2002;346(6):393-403.	Article
Sacks FM, Svetkey LP, Vollmer WM, et al; DASH-Sodium Collaborative Research Group. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. <i>N Engl J Med.</i> 2001;344(1):3-10.	Article
American Diabetes Association. Nutrition recommendations and principles for people with diabetes mellitus. <i>Diabetes Care.</i> 2000;23(Suppl 1):S43-S46.	Article
de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. <i>Circulation.</i> 1999;99(6):779-785.	Article
EATING DISORDERS	
Misra M, Klibanski A. Endocrine consequences of anorexia nervosa. <i>Lancet Diabetes Endocrinol.</i> 2014;2(7):581-592.	Article
Sim LA, McAlpine DE, Grothe KB, Himes SM, Cockerill RG, Clark MM. Identification and treatment of eating disorders in the primary care setting. <i>Mayo Clin Proc.</i> 2010;85(8):746-751.	Article
Treasure J, Claudino AM, Zucker N. Eating disorders. <i>Lancet.</i> 2010;375(9714):583-593.	Article

USEFUL WEB SITES

Dietary Guidelines for Americans: <https://health.gov/dietaryguidelines/2015/2>. Physical Activity Guidelines for Americans: <https://health.gov/PAGuidelines/>

Motivational Interviewing: <http://www.motivationalinterviewing.org/>

American Society of Metabolic and Bariatric Surgery: <https://asmbs.org/>

Tool to find a Bariatric Surgeon: <https://asmbs.org/patients/find-a-provider>

My Plate tool for dietary intake: <https://www.choosemyplate.gov/>

United States Department of Agriculture National Agricultural Library: <https://www.nal.usda.gov/food-and-human-nutrition>

Bariatric Surgery Care Guideline: <https://www.aace.com/files/publish-ahead-of-print-final-version.pdf>

American Society of Enteral and Parenteral Nutrition guidelines:

http://www.nutritioncare.org/Guidelines_and_Clinical_Resources/Clinical_Guidelines/

THYROID

INTRODUCTION

Thyroid-specific disorders include thyroid hyperfunction, hypofunction, benign nodularity, and cancers. Thyroid disorders are among the most common conditions encountered by endocrinologists; they occur at a prevalence of greater than 10% in some studies. Furthermore, the incidence of thyroid disorders is rising, in part because diagnostic tools are becoming more sensitive and sophisticated. Thyroid disorders account for a significant amount of morbidity in the population, and fellows should be competent in the diagnosis and treatment of these conditions.

MEDICAL KNOWLEDGE

Fellows must demonstrate knowledge about established and evolving biomedical, clinical, and cognate (eg, epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.

Topic	Fundamental	Advanced
BASIC PHYSIOLOGIC PRINCIPLES, THYROID FUNCTION TESTING		
Explain normal thyroid physiology, including synthesis and secretion of thyroid hormone, cellular and tissue actions of thyroid hormone, and the hypothalamic-pituitary-thyroid axis.	√	
Summarize the pathophysiology of thyroid diseases such as hypothyroidism and hyperthyroidism.	√	
Summarize the pathophysiology of thyroid diseases such as thyroid hormone receptor abnormalities and iodine deficiency and excess.		√
Explain biochemistry, including cellular and molecular biology and immunology, as it relates to thyroid disease.	√	
Summarize signal transduction pathways and biology of thyroid hormone receptors and their interaction with other hormone receptor pathways.		√
Interpret clinical laboratory test results in the evaluation of thyroid disease.	√	
Identify the limitations of specific assays in the evaluation and interpretation of thyroid disease (eg, antibody interference, macrothyrotropin, and binding proteins).		√
Explain radiation safety issues associated with radionuclide use for evaluation and treatment of thyroid disorders.		√
HYPERTHYROIDISM		

Clinical Manifestations		
Summarize the symptoms and signs of hyperthyroidism, including enlarged thyroid, warm skin, sweating, heat intolerance, tremor, stare and lid lag, fatigue, palpitations, weight loss, frequent bowel movements, sleep disturbance, and weakness.	√	
Laboratory Diagnosis		
Describe the differential diagnosis of hyperthyroidism, the laboratory findings of low thyrotropin and high free T ₄ and/or T ₃ in patients with primary hyperthyroidism, and the algorithm for thyroid function testing.	√	
Graves Disease		
<i>Clinical Manifestations</i>		
Summarize the symptoms and signs of Graves disease, which include those of hyperthyroidism, as well as potential for exophthalmos, periorbital and conjunctival edema, limitation of eye movement, and pretibial myxedema.	√	
Describe the ophthalmopathy, dermopathy, and acropachy associated with Graves disease.		√
<i>Diagnostic Tests</i>		
Describe the diagnostic tests used to confirm the diagnosis of Graves disease, including radioactive iodine uptake, assessment of thyrotropin receptor antibodies, and determination of the T ₃ to T ₄ ratio.	√	
<i>Treatment</i>		
Guide treatment of Graves disease, including the use of β-adrenergic blockers, thionamides, radioactive iodine, and surgery.	√	
Guide treatment of Graves ophthalmopathy.		√
Diagnose and manage agranulocytosis secondary to antithyroid drug therapy.		√
Diagnose and manage drug-induced thyroid dysfunction (including amiodarone, interferon, tyrosine kinase inhibitors, and lithium).		√
Toxic Adenoma and Toxic Multinodular Goiter		
Diagnose and manage toxic adenoma and toxic multinodular goiter.	√	
Differentiate among the tests used to diagnose toxic multinodular goiter such as ultrasonography and radionuclide scans and determine when biopsy may be indicated.		√
Inappropriate Thyrotropin Syndromes		

Differentiate among inappropriate thyrotropin syndromes, including thyrotropin-secreting tumors, thyroid hormone resistance syndromes, and artifactual thyrotropin derangements.		√
Recommend management of inappropriate thyrotropin syndromes depending on the etiology.		√
Low Radioactive Iodine Uptake Forms of Thyrotoxicosis		
<i>Thyroiditis</i>		
Differentiate among the various types of thyroiditis such as de Quervain, painless/silent thyroiditis, postpartum thyroiditis, amiodarone-induced thyroiditis, Riedel thyroiditis, and acute thyroiditis.		√
Order diagnostic studies to confirm thyroiditis.	√	
Recommend management approaches for thyroiditis.	√	
<i>Other Forms of Thyrotoxicosis</i>		
Diagnose and manage factitious and iatrogenic thyrotoxicosis, struma ovarii, and iodine-induced thyroiditis.		√
Complicated Thyrotoxicosis		
Diagnose and manage thyroid storm.	√	
Diagnose and manage periodic paralysis.		√
Subclinical Hyperthyroidism		
Diagnose and manage subclinical hyperthyroidism.	√	
HYPOTHYROIDISM		
Clinical Manifestations		
Summarize the symptoms and signs of hypothyroidism, including fatigue, anemia, cold intolerance, weight gain, coarse or thin hair, delayed relaxation of deep tendon reflexes, bradycardia, goiter, and constipation.	√	
Laboratory Diagnosis		
Describe laboratory diagnosis of hypothyroidism, including high thyrotropin and low free T ₄ levels and measurement of thyroid peroxidase antibodies.	√	
Differentiate among the causes of an elevated serum thyrotropin level, including resistance to thyrotropin or thyroid hormone, recovery from nonthyroidal illness, and thyrotropin-secreting pituitary adenomas.		√
Primary Hypothyroidism		
Distinguish between congenital and acquired primary hypothyroidism.		√

Differentiate among the etiologies of acquired hypothyroidism such as autoimmune causes, postirradiation and postsurgical, goitrogens (eg, lithium, iodine), and consumptive hypothyroidism due to hemangiomas.	√	
Secondary (Central) Hypothyroidism		
Diagnose hypothyroidism resulting from pituitary/hypothalamic disease.	√	
Subclinical Hypothyroidism		
Diagnose and manage subclinical hypothyroidism.	√	
Complicated Hypothyroidism		
Diagnose and manage myxedema coma.		√
Thyrotropin Resistance in Pseudohypoparathyroidism		
Diagnose and manage thyrotropin resistance in pseudohypoparathyroidism.		√
Therapy		
Guide treatment of hypothyroidism, which involves managing replacement therapy.	√	
Monitor effectiveness of levothyroxine therapy and adjustment the dosage as necessary.	√	
SOLITARY THYROID NODULES AND NONTOXIC MULTINODULAR GOITER		
Prevalence and Modes of Presentation		
Discuss the prevalence of and modes of presentation of solitary nodules and nontoxic multinodular goiter.	√	
Clinical Assessment		
Perform the clinical assessment of solitary nodules and nontoxic multinodular goiter and explain the significance of radiation exposure, family history of thyroid cancer, and other risk factors for nodules and malignancy.	√	
List the genetic syndromes associated with thyroid cancer and thyroid disorders, including Cowden syndrome, familial adenomatous polyposis, Birt-Hogg-Dube syndrome, multiple endocrine neoplasia type 2, familial medullary thyroid cancer, polyglandular autoimmune syndrome, and thyroid hormone transporter defects.		√
Appropriately recommend genetic testing for specific thyroid disorders.		√
Fine-Needle Aspiration/Cytology Interpretation		
List indications for thyroid fine-needle aspiration biopsy and interpret results.		√
Explain the Bethesda System for reporting thyroid cytopathology.		√

Explain the use of molecular markers in the evaluation of indeterminate results from fine-needle aspiration biopsy of thyroid nodules.		√
Role of Ultrasonography and Radionuclide Scanning (<i>see also Procedures</i>)		
List the indications for thyroid ultrasonography.	√	
Interpret thyroid ultrasonography by viewing images.		√
Identify the imaging characteristics for benign vs suspicious thyroid nodules.		√
Identify the imaging characteristics of benign vs suspicious cervical lymph nodes.		√
List the indications for radionuclide testing (ie, ^{123}I or ^{131}I uptake and scan) in the evaluation of thyroid disease.	√	
Discuss radiation safety issues associated with radionuclide usage for evaluation and treatment of thyroid disorders.	√	
Treatment		
Recommend treatment approaches to solitary nodules and nontoxic multinodular goiter, which may include biopsy, surgery, or observation.		√
THYROID CANCER		
Well-Differentiated Epithelial: Papillary and Follicular Carcinoma (Including All Variants and Hurthle-Cell Carcinoma)		
Explain the staging and risk stratification of thyroid carcinoma.		√
<i>Initial Therapeutic Approach</i>		
Recommend the initial therapeutic approach to thyroid carcinoma, which may include thyroidectomy, whole-body radioactive iodine scanning and remnant ablation, and levothyroxine for replacement and thyrotropin suppression.	√	
Guide the evaluation and risk stratification on the basis of pathology.		√
Determine the appropriate extent of surgery for an individual patient.		√
Recommend appropriate adjuvant therapies, such as radiotherapy, ^{131}I , and other systemic treatments.		√
Determine the appropriate preparation and dosing for radioiodine therapy and counsel patients regarding the adverse effects and radiation precautions.		√
<i>Monitoring or Follow-Up</i>		
Monitor and follow-up patients who have been treated for thyroid carcinoma, including measurement of serum thyroglobulin (and thyroglobulin antibody interference), thyroid function tests (with		√

appropriate level of thyrotropin suppression), and imaging with thyroid ultrasonography.		
Recommend an approach for scan-negative/thyroglobulin-positive patients.		√
Evaluate and manage metastatic and non-radioiodine-avid thyroid carcinoma, including use of systemic therapies such as tyrosine kinase inhibitors and high-dose radioactive iodine therapy with the use of dosimetry.		√
Discuss recombinant thyrotropin applications.		√
Explain the role of imaging modalities such as computed tomography and positron emission tomography in the setting of thyroid carcinoma.		√
Explain the role of levothyroxine treatment in the setting of thyroid carcinoma and describe different thyrotropin goals based on response to therapy.	√	
Anaplastic/Undifferentiated Cancer		
Distinguish anaplastic/undifferentiated thyroid cancer from well-differentiated thyroid cancer and describe the aggressiveness of the tumor.		√
Recommend appropriate imaging needed to evaluate for disease outside of the neck.		√
Recommend available treatment options.		√
Lymphoma		
List risk factors for thyroid lymphoma, including Hashimoto thyroiditis.		√
Diagnose thyroid lymphoma.		√
Recommend a treatment approach to lymphoma and explain how it differs from the approach to well-differentiated thyroid carcinoma.		√
Medullary Cancer		
List risk factors for medullary thyroid carcinoma, including genetic syndromes such as multiple endocrine neoplasia type 2 and familial medullary thyroid carcinoma (germline <i>RET</i> proto-oncogene mutations).		√
Recommend appropriate surgery for medullary thyroid carcinoma.		√
List indications for adjuvant radiotherapy or systemic therapy such as tyrosine kinase inhibitors.		√
Monitor and follow-up patients who have been treated for medullary thyroid carcinoma with methods including serum calcitonin measurement, carcinoembryonic antigen measurement, and imaging.		√

Refer patients for genetic counseling and genetic testing and screen for other endocrine disorders that can be associated with medullary thyroid carcinoma (eg, pheochromocytoma, hyperparathyroidism).		√
---	--	---

DIAGNOSTIC THYROID TESTING/THYROID TEST ABNORMALITIES WITHOUT THYROID DISEASE

Euthyroid Hypothyroxinemia

Diagnose and manage causes of euthyroid hypothyroxinemia such as thyroxine-binding globulin abnormalities and pregnancy and the effects on thyroid function tests.		√
--	--	---

Euthyroid Hyperthyroxinemia

Diagnose and manage causes of euthyroid hyperthyroxinemia such as thyroxine-binding globulin abnormalities, familial dysalbuminemic hyperthyroxinemia, and drugs (eg, amiodarone).		√
--	--	---

Effect of Drugs on Thyroid Function Tests

Identify the effects of various drugs such as amiodarone, salsalate, anticonvulsant medications, estrogen, and androgens on thyroid function tests.	√	
---	---	--

Euthyroid Sick Syndrome

Explain the effects of euthyroid sick syndrome on thyroid function tests.	√	
---	---	--

Antithyroid Hormone Antibodies

Explain the effects of antithyroid hormone antibodies on thyroid function tests.	√	
--	---	--

Heterophilic Antibody Interference With Thyrotropin Measurements

Explain how heterophilic antibodies can interfere with thyrotropin measurements.		√
--	--	---

PREGNANCY

Hypothyroidism

Diagnose hypothyroidism during pregnancy.	√	
Recommend appropriate treatment of overt and subclinical hypothyroidism during pregnancy and list trimester-specific thyrotropin goals.	√	
Monitor therapy effectiveness during pregnancy.	√	

Hyperthyroidism

Diagnose hyperthyroidism during pregnancy, taking into account physiologic thyrotropin suppression.	√	
---	---	--

Recommend appropriate treatment of hyperthyroidism during pregnancy, including checking for thyroid-stimulating antibodies in the second trimester.	√	
Thyroid Nodules and Cancer		
Diagnose and manage thyroid nodules and thyroid cancer during pregnancy.		√
PROCEDURES		
Physical Examination		
Perform a comprehensive thyroid and neck examination and estimate thyroid volume.	√	
Thyroid Ultrasonography		
List indications for neck ultrasonography in the evaluation and surveillance of thyroid nodules and for postoperative thyroid cancer surveillance.	√	
Interpret thyroid imaging (done by others) with respect to:		
-The quality of imaging.		√
-Thyroid parenchyma echotexture and size of the thyroid lobes.		√
-The location and size of nodules in 3 dimensions.		√
-The sonographic features of nodules (margins, microcalcifications and macrocalcifications, vascular flow, taller-than-wide shape, and elasticity if indicated).		√
Perform ultrasonography of the lateral neck, visualize the cervical lymph nodes, and interpret worrisome vs benign characteristics (eg, shape, size, calcifications, blood flow, presence of fatty hilum).		√
Perform a sufficient number of ultrasound-guided fine-needle aspiration biopsies of thyroid nodules to be deemed competent (minimum of 5 studies) with documentation of images and reporting to include:		
-Measurement of each thyroid lobe in 3 dimensions with description of thyroid parenchyma echotexture.		√
-Measurement of the isthmus in transverse view.		√
-Measurement of each nodule of interest in 3 dimensions with description of location and sonographic features (echogenicity, composition, presence of calcifications, margins, vascularity).		√
Other Procedures and Studies		
Interpret computed tomography or magnetic resonance imaging of the neck.		√
Interpret results from radioactive iodine uptake and scan.		√

TEACHING METHODS AND EVALUATION

Much teaching occurs one-on-one with attendings during outpatient clinics and on inpatient hospital rounds. Active learning occurs as fellows participate in patient care under the supervision and guidance of the attending. In addition, a full range of topics are reviewed in didactic sessions at weekly conferences and in the core curriculum/board review weekly sessions. Fellows are also expected to engage in self-directed study guided by the curriculum. Evaluation includes attending review of fellows knowledge base and medical reasoning during clinic and hospital rounds. In addition, the in-training exam taken in February of every year provides a loose benchmark of medical knowledge progression through the fellowship.

SUGGESTED READING

Asterisks denote references that are designated for residents, students, or endocrine fellows early in their training.

GENERAL READING, THYROID PHYSIOLOGY, THYROID EPIDEMIOLOGY	
*Melmed S, Polonsky KS, Larsen PR, Kronenberg HM, eds. <i>Williams Textbook of Endocrinology</i> . 13th ed. Philadelphia, PA: Saunders; 2015.	Textbook
Davies L, Welch HG. Current thyroid cancer trends in the United States. <i>JAMA Otolaryngol Head Neck Surg</i> . 2014;140(4):317-322.	Article
*Fekete C, Lechan RM. Central regulation of hypothalamic-pituitary-thyroid axis under physiological and pathophysiological conditions. <i>Endocr Rev</i> . 2014;35(2):159-194.	Article
McLeod DS, Caturegli P, Cooper DS, Matos PG, Hutfless S. Variation in rates of autoimmune thyroid disease by race/ethnicity in US military personnel. <i>JAMA</i> . 2014;311(15):1563-1565.	Article
*Braverman LE, Cooper D, eds. <i>Werner & Ingbar's The Thyroid: A Fundamental and Clinical Text</i> . 10th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2013.	Textbook
Brito JP, Yarur AJ, Prokop LJ, McIver B, Murad MH, Montori VM. Prevalence of thyroid cancer in multinodular goiter versus single nodule: a systematic review and meta-analysis. <i>Thyroid</i> . 2013;23(4):449-455.	Article
Brent GA. Mechanisms of thyroid hormone action. <i>J Clin Invest</i> . 2012;122(9):3035-3043.	Article
*Hayter SM, Cook MC. Updated assessment of the prevalence, spectrum and case definition of autoimmune disease. <i>Autoimmun Rev</i> . 2012;11(10):754-765.	Article
McLeod DS, Cooper DS. The incidence and prevalence of thyroid autoimmunity. <i>Endocrine</i> . 2012;42(2):252-265.	Article

Waring AC, Arnold AM, Newman AB, Buzkova P, Hirsch C, Cappola AR. Longitudinal changes in thyroid function in the oldest old and survival: the cardiovascular health study all-stars study. <i>J Clin Endocrinol Metab.</i> 2012;97(11):3944-3950.	Article
*Gardner DG, Shoback D, eds. <i>Greenspan's Basic & Clinical Endocrinology</i> . 9th ed. New York, NY: McGraw-Hill Education; 2011.	Textbook
Surks MI, Hollowell JG. Age-specific distribution of serum thyrotropin and antithyroid antibodies in the US population: implications for the prevalence of subclinical hypothyroidism. <i>J Clin Endocrinol Metab.</i> 2007;92(12):4575-4582.	Article
Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). <i>J Clin Endocrinol Metab.</i> 2002;87(2):489-499.	Article
Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. <i>Arch Intern Med.</i> 2000;160(4):526-534.	Article
Surks MI, Schadow AR, Stock JM, Oppenheimer JH. Determination of iodothyronine absorption and conversion of L-thyroxine (T4) to L-triiodothyronine (T3) using turnover rate techniques. <i>J Clin Invest.</i> 1973;52(4):805-811.	Article
HYPERTHYROIDISM	
Rokni H, Sadeghi R, Moossavi Z, Treglia G, Zakavi SR. Efficacy of different protocols of radioiodine therapy for treatment of toxic nodular goiter: systematic review and meta-analysis of the literature. <i>Int J Endocrinol Metab.</i> 2014;12(2):e14424.	Article
Selmer C, Olesen JB, Hansen ML, et al. Subclinical and overt thyroid dysfunction and risk of all-cause mortality and cardiovascular events: a large population study. <i>J Clin Endocrinol Metabolism.</i> 2014;99(7):2372-2382.	Article
Bakos B, Takacs I, Nagy Z, et al. Long term efficacy of radioiodine treatment in hyperthyroidism. <i>Exp Clin Endocrinol Diabetes.</i> 2013;121(8):494-497.	Article
*Sundaresh V, Brito JP, Wang Z, et al. Comparative effectiveness of therapies for Graves' hyperthyroidism: a systematic review and network meta-analysis. <i>J Clin Endocrinol Metab.</i> 2013;98(9):3671-3677.	Article
Mai VQ, Burch HB. A stepwise approach to the evaluation and treatment of subclinical hyperthyroidism. <i>Endocr Pract.</i> 2012;18(5):772-780.	Article
*Bahn Chair RS, Burch HB, Cooper DS, et al; American Thyroid Association; American Association of Clinical Endocrinologists. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists [published corrections appear in <i>Thyroid.</i> 2011;21(10):1169 and <i>Thyroid.</i> 2012;22(11):1195]. <i>Thyroid.</i> 2011;21(6):593-646.	Clinical Practice Guideline
Matthews DC, Syed AA. The role of TSH receptor antibodies in the management of Graves' disease. <i>Eur J Intern Med.</i> 2011;22(3):213-216.	Article

*The American Thyroid Association Taskforce on Radioiodine Safety, Sisson JC, Freitas J, McDougall IR, Dauer LT, Hurley JR, et al. Radiation safety in the treatment of patients with thyroid diseases by radioiodine 131I: practice recommendations of the American Thyroid Association [published correction appears in <i>Thyroid</i> . 2011;21(6):689]. <i>Thyroid</i> . 2011;21(4):335-346.	Clinical Practice Guideline
Emiliano AB, Governale L, Parks M, Cooper DS. Shifts in propylthiouracil and methimazole prescribing practices: antithyroid drug use in the United States from 1991 to 2008. <i>J Clin Endocrinol Metab</i> . 2010;95(5):2227-2233.	Article
Schussler-Fiorenza CM, Bruns CM, Chen H. The surgical management of Graves' disease. <i>J Surg Res</i> . 2006;133(2):207-214.	Article
Holm IA, Manson JE, Michels KB, Alexander EK, Willett WC, Utiger RD. Smoking and other lifestyle factors and the risk of Graves' hyperthyroidism. <i>Arch Intern Med</i> . 2005;165(14):1606-1611.	Article
HYPOTHYROIDISM	
Wassner AJ, Brown RS. Congenital hypothyroidism: recent advances. <i>Curr Opin Endocrinol Diabetes Obes</i> . 2015;22(5):407-412.	Article
*Biondi B, Wartofsky L. Treatment with thyroid hormone. <i>Endocr Rev</i> . 2014;35(3):433-512.	Article
*Caturegli P, De Remigis A, Rose NR. Hashimoto thyroiditis: clinical and diagnostic criteria. <i>Autoimmun Rev</i> . 2014;13(4-5):391-397.	Article
*Jonklaas J, Bianco AC, Bauer AJ, et al; American Thyroid Association Task Force on Thyroid Hormone Replacement. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association Task Force on Thyroid Hormone Replacement. <i>Thyroid</i> . 2014;24(12):1670-1751.	Clinical Practice Guideline
*Taylor PN, Okosieme OE, Dayan CM, Lazarus JH. Therapy of endocrine disease: impact of iodine supplementation in mild-to-moderate iodine deficiency: systematic review and meta-analysis. <i>Eur J Endocrinol</i> . 2014;170(1):R1-R15.	Article
Zimmermann MB. Iodine deficiency and excess in children: worldwide status in 2013. <i>Endocr Pract</i> . 2013;19(5):839-846.	Article
Biondi B, Wartofsky L. Combination treatment with T4 and T3: toward personalized replacement therapy in hypothyroidism? <i>J Clin Endocrinol Metab</i> . 2012;97(7):2256-2271.	Article
*Garber JR, Cobin RH, Gharib H, et al; American Association of Clinical Endocrinologists and American Thyroid Association Taskforce on Hypothyroidism in Adults. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. <i>Endocr Pract</i> . 2012;18(6):988-1028.	Clinical Practice Guideline
Khandelwal D, Tandon N. Overt and subclinical hypothyroidism: who to treat and how. <i>Drugs</i> . 2012;72(1):17-33.	Article

Somwaru LL, Rariy CM, Arnold AM, Cappola AR. The natural history of subclinical hypothyroidism in the elderly: the Cardiovascular Health Study. <i>J Clin Endocrinol Metab.</i> 2012;97(6):1962-1969.	Article
*Thvilum M, Brandt F, Brix TH, Hegedus L. A review of the evidence for and against increased mortality in hypothyroidism. <i>Nat Rev Endocrinol.</i> 2012;8(7):417-424.	Article
SOLITARY NODULES AND NONTOXIC MULTINODULAR GOITER	
Nikiforov YE, Carty SE, Chiosea SI, et al. Impact of the multi-gene ThyroSeq Next-Generation sequencing assay on cancer diagnosis in thyroid nodules with atypia of undetermined significance/follicular lesion of undetermined significance cytology. <i>Thyroid.</i> 2015;25(11):1217-1223.	Article
Rossi M, Buratto M, Tagliati F, et al. Relevance of BRAF(V600E) mutation testing versus RAS point mutations and RET/PTC rearrangements evaluation in the diagnosis of thyroid cancer. <i>Thyroid.</i> 2015;25(2):221-228.	Article
Campanella P, Ianni F, Rota CA, Corsello SM, Pontecorvi A. Quantification of cancer risk of each clinical and ultrasonographic suspicious feature of thyroid nodules: a systematic review and meta-analysis. <i>Eur J Endocrinol.</i> 2014;170(5):R203-R211.	Article
McIver B, Castro MR, Morris JC, et al. An independent study of a gene expression classifier (Afirma) in the evaluation of cytologically indeterminate thyroid nodules. <i>J Clin Endocrinol Metab.</i> 2014;99(11):4069-4077.	Article
Nou E, Kwong N, Alexander LK, Cibas ES, Marqusee E, Alexander EK. Determination of the optimal time interval for repeat evaluation after a benign thyroid nodule aspiration. <i>J Clin Endocrinol Metab.</i> 2014;99(2):510-516.	Article
Alexander EK, Kennedy GC, Baloch ZW, et al. Preoperative diagnosis of benign thyroid nodules with indeterminate cytology. <i>N Engl J Med.</i> 2012;367(8):705-715.	Article
Nikiforov YE, Ohori NP, Hodak SP, et al. Impact of mutational testing on the diagnosis and management of patients with cytologically indeterminate thyroid nodules: a prospective analysis of 1056 FNA Samples. <i>J Clin Endocrinol Metab.</i> 2011;96(11):3390-3397.	Article
Cibas ES, Ali SZ. The Bethesda System for reporting thyroid cytopathology. <i>Thyroid.</i> 2009;19(11):1159-1165.	Article
Mazzaferri EL. Management of a solitary thyroid nodule. <i>N Engl J Med.</i> 1993;328(8):553-559.	Article
THYROID CANCER	
*Francis GL, Waguespack SG, Bauer AJ, et al; American Thyroid Association Guidelines Task Force. Management guidelines for children with thyroid nodules and differentiated thyroid cancer. <i>Thyroid.</i> 2015;25(7):716-759.	Clinical Practice Guideline

*Wells SA Jr, Asa SL, Dralle H, et al; American Thyroid Association Guidelines Task Force on Medullary Thyroid Carcinoma. Revised American Thyroid Association guidelines for the management of medullary thyroid carcinoma. <i>Thyroid</i> . 2015;25(6):567-610.	Clinical Practice Guideline
Hauch A, Al-Qurayshi Z, Randolph G, Kandil E. Total thyroidectomy is associated with increased risk of complications for low- and high-volume surgeons. <i>Ann Surg Oncol</i> . 2014;21(12):3844-3852.	Article
Ito Y, Miyauchi A, Kihara M, Higashiyama T, Kobayashi, Miya A. Patient age is significantly related to the progression of papillary microcarcinoma of the thyroid under observation. <i>Thyroid</i> . 2014;24(1):27-34	Article
Pitolo F, Bueno F, Urciuoli C, Abelleira E, Cross G, Tuttle RM. Outcomes of patients with differentiated thyroid cancer risk-stratified according to the American Thyroid Association and Latin American Thyroid Society risk of recurrence classification systems. <i>Thyroid</i> . 2013;23(11):1401-1407.	Article
Sosa JA, Hanna JW, Robinson KA, Lanman RB. Increases in thyroid nodule fine-needle aspirations, operations, and diagnoses of thyroid cancer in the United States. <i>Surgery</i> . 2013;154(6):1420-1426.	Article
Randolph GW, Duh QY, Heller KS, et al; American Thyroid Association Surgical Affairs Committee's Taskforce on Thyroid Cancer Nodal Surgery. The prognostic significance of nodal metastases from papillary thyroid carcinoma can be stratified based on the size and number of metastatic lymph nodes, as well as the presence of extranodal extension. <i>Thyroid</i> . 2012;22(11):1144-1152.	Clinical Practice Guideline
*Smallridge RC, Ain KB, Bible KC, et al; American Thyroid Association Anaplastic Thyroid Cancer Guidelines Taskforce. American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. <i>Thyroid</i> . 2012;22(11):1104-1139.	Clinical Practice Guideline

DIAGNOSTIC THYROID TESTING/THYROID TEST ABNORMALITIES WITHOUT THYROID DISEASE

Durfee SM, Benson CB, Arthaud DM, Alexander EK, Frates MC. Sonographic appearance of thyroid cancer in patients with Hashimoto thyroiditis. <i>J Ultrasound Med</i> . 2015;34(4):697-704.	Article
Remonti LR, Kramer CK, Leitao CB, Pinto LC, Gross JL. Thyroid ultrasound features and risk of carcinoma: a systematic review and meta-analysis of observational studies. <i>Thyroid</i> . 2015;25(5):538-550.	Article
Yeh MW, Bauer AJ, Bernet VA, et al; American Thyroid Association Surgical Affairs Committee Writing Task Force. American Thyroid Association statement on preoperative imaging for thyroid cancer surgery. <i>Thyroid</i> . 2015;25(1):3-14.	Article
Adler SM, Wartofsky L. The nonthyroidal illness syndrome. <i>Endocrinol Metab Clin North Am</i> . 2007;36(3):657-672.	Article

PREGNANCY

Nathan N, Sullivan SD. Thyroid disorders during pregnancy. <i>Endocrinol Metab Clin North Am.</i> 2014;43(2):573-597.	Article
Caldwell KL, Pan Y, Mortensen ME, Makhmudov A, Merrill L, Moye J. Iodine status in pregnant women in the National Children's Study and in U.S. women (15-44 years), National Health and Nutrition Examination Survey 2005-2010. <i>Thyroid.</i> 2013;23(8):927-937.	Article
*Chang DL, Pearce EN. Screening for maternal thyroid dysfunction in pregnancy: a review of the clinical evidence and current guidelines. <i>J Thyroid Res.</i> 2013;2013:851326.	Article
Zhou SJ, Anderson AJ, Gibson RA, Makrides M. Effect of iodine supplementation in pregnancy on child development and other clinical outcomes: a systematic review of randomized controlled trials. <i>Am J Clin Nutr.</i> 2013;98(5):1241-1254.	Article
*De Groot L, Abalovich M, Alexander EK, et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2012;97(8):2543-2565.	Clinical Practice Guideline
Lazarus JH, Bestwick JP, Channon S, et al. Antenatal thyroid screening and childhood cognitive function [published correction appears in <i>N Engl J Med.</i> 2012;366(17):1650]. <i>N Engl J Med.</i> 2012;366(6):493-501.	Article
Stagnaro-Green A. Approach to the patient with postpartum thyroiditis. <i>J Clin Endocrinol Metab.</i> 2012;97(2):334-342.	Article
*Stagnaro-Green A, Abalovich M, Alexander E, et al; American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. <i>Thyroid.</i> 2011;21(10):1081-1125.	Clinical Practice Guideline
PROCEDURES	
<i>See above under Diagnostic Thyroid Testing</i>	