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.		√
Adrenal Neoplasm		
Evaluate for adrenal adenoma, carcinoma, and micronodular and macronodular hyperplasia.	√	
Ectopic Corticotropin/Corticotropin-Releasing Hormone		
Evaluate for tumors associated with the ectopic ACTH (corticotropin) syndrome or the ectopic CRH (corticotropin-releasing hormone) syndrome.	√	
Treatment		
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		
Primary Adrenal Insufficiency		
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.	√	
Secondary/Tertiary Adrenal Insufficiency		
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.	√	
Diagnosis		
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.		√
Stress Doses		
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		
Primary Hyperaldosteronism		
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.	√	
Pseudohyperaldosteronism		
Differentiate among other causes of hypertension and hypokalemia such as Liddle syndrome, licorice ingestion, 17α-hydroxylase deficiency/17,20-lyase deficiency, and 11β-hydroxylase deficiency.		√
Diagnostic Tests		
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.		√
Treatment		
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 *CYP21A* 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		
Clinical Presentation		
Summarize the signs and symptoms of catecholamine-secreting tumors, which include sustained or paroxysmal hypertension, episodic headaches, sweating, and tachycardia.	√	
Diagnostic Tests		
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.		
Treatment		
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.		√
Familial Disorders Associated With Pheochromocytoma		

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 (*SDH* 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.	√	
Benign Adenomas		
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.	√	
Pheochromocytomas		
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.	√	
Adrenocortical carcinoma		
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.	√	
Adrenal metastases		
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. *Williams Textbook of Endocrinology*. 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. *Endocrinology: Adult and Pediatric*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2010.	Textbook
*Snyder PM. Minireview: regulation of epithelial Na+ channel trafficking. *Endocrinology*. 2005;146(12):5079-5085.	Article
*Herrmann M. Standard and molecular cytogenetics of endocrine tumors. *Am J Clin Pathol.* 2003;119(Suppl):S17-S38	Article
*The adrenal cortex and the adrenal medulla. In: Grossman A, ed. *Clinical Endocrinology*. 2nd ed. London: Blackwell Science Ltd; 1998.	Textbook
*Disturbances in control of body fluid volume and composition. In: BM Brenner, ed. *Brenner and Rector's The Kidney*. 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, Rubenstien AH, eds. *Endocrinology*. 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, Nylen ES, Rebar RW, Robertson GL, Wartofsky L, eds. *Principles and Practice of Endocrinology and Metabolism*. 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. *J Clin Endocrinol Metab*. 2008;93(5):1526-1540.	Clinical Practice Guideline
*Lacroix A, Feelders RA, Stratakis CA, Nieman LK. Cushing's syndrome. *Lancet*. 2015:386(9996):913-927.	Article
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Kirschner LS. Medicine. A unified cause for adrenal Cushing's syndrome. *Science*. 2014;344(6186):804-805.	Article
Assié G, Libé R, Espiard S, et al. *ARMC5* mutations in macronodular adrenal hyperplasia with Cushing's syndrome. *N Engl J Med*. 2013;369(22):2105-2114.	Article
Lacroix A. Heredity and cortisol regulation in bilateral macronodular adrenal hyperplasia. *N Engl J Med*. 2013;369(22):2147-2149.	Article
Louiset E, Duparc C, Young J, et al. Intraadrenal corticotropin in bilateral macronodular adrenal hyperplasia. *N Engl J Med*. 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. *J Clin Endocrinol Metab*. 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. *J Clin Endocrinol Metab*. 2011;96(4):E728-E738.	Article
Chiodini I. Clinical review: diagnosis and treatment of subclinical hypercortisolism. *J Clin Endocrinol Metab*. 2011;96(5):1223-1236.	Article
Sharma ST, Nieman LK. Cushing's syndrome: all variants, detection, and treatment. *Endocrinol Metab Clin North Am*. 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. *Eur J Endocrinol*. 2010;163(1):129-138.	Article

Morelli V, Masserini B, Salcuni AS, et al. Subclinical hypercortisolism: correlation between biochemical diagnostic criteria and clinical aspects. *Clin Endocrinol (Oxf)*. 2010;73(2):161-166.	Article
Lacroix A. ACTH-independent macronodular adrenal hyperplasia. *Best Pract Res Clin Endocrinol Metab*. 2009;23(2):245-259.	Article
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Findling JW, Raff H. Cushing's Syndrome: important issues in diagnosis and management. *J Clin Endocrinol Metab*. 2006;91(10):3746-3753.	Article
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Findling JW, Raff H. Newer diagnostic techniques and problems in Cushing's disease. *Endocrinol Metab Clin North Am*. 1999;28(1):191-210.	Article
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Newell-Price J, Trainer P, Besser M, Grossman A. The diagnosis and differential diagnosis of Cushing's syndrome and pseudo-Cushing's states. *Endocr Rev*. 1998;19(5):647-672.	Article
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Fleseriu M. Medical treatment of Cushing disease: new targets, new hope. *Endocrinol Metab Clin North Am*. 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. *J Clin Endocrinol Metab*. 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 *Surgery*. 2008;143(2):302]. *Surgery*. 2007;142:900-905.	Article
Adrenal Insufficiency: Diagnosis	

*Bancos I, Hahner S, Tomlinson J, Arlt W. Diagnosis and management of adrenal insufficiency. *Lancet Diabetes Endocrinol*. 2015;3(3):216-226.	Article
Betterle C, Morlin L. Autoimmune Addison's disease. *Endocr Dev*. 2011;20:161-172.	Article
*Grossman AB. Clinical Review#: the diagnosis and management of central hypoadrenalism. *J Clin Endocrinol Metab*. 2010;95(11):4855-4863.	Article
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*Salvatori R. Adrenal insufficiency. *JAMA*. 2005;294(19):2481-2488.	Article
Betterle C, Greggio NA, Volpato M. Clinical review 93: autoimmune polyglandular syndrome type 1. *J Clin Endocrinol Metab*. 1998;83(4):1049-1055.	Article
Adrenal Insufficiency: Management	
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Glucocorticoid Resistance: Diagnosis and Management	
*Nicolaides NC, Charmandari E. Chrousos syndrome: from molecular pathogenesis to therapeutic management. *Eur J Clin Invest*. 2015;45(5):504-514.	Article
*Ramamoorthy S, Cidlowski JA. Exploring the molecular mechanisms of glucocorticoid receptor action from sensitivity to resistance. *Endocr Dev*. 2013;24:41-56.	Article
MINERALOCORTICOIDS	
Hyperaldosteronism: Diagnosis and Management	

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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.		√
Primary Hyperparathyroidism		
Diagnosis		
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.	√	
Treatment Guidelines		
Discuss the decision regarding surgical vs medical management and list the current criteria for surgical intervention in asymptomatic primary hyperparathyroidism.	√	
Medical and Surgical Therapy		
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).	√	
Natural History	√	

Discuss the gastrointestinal, neuromuscular, renal, and psychological symptoms and signs related to hypercalcemia.	√	
Familial Hypocalciuric Hypercalcemia		
Distinguish sporadic primary hyperparathyroidism from familial hypocalciuric hypercalcemia.	√	
Manage familial hypocalciuric hypercalcemia.	√	
Lithium-Induced		
Diagnose and manage lithium-induced hyperparathyroidism.	√	
Nonparathyroid Hormone–Mediated Hypercalcemia		
Hypercalcemia of Malignancy		
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.	√	
Milk-Alkali Syndrome		
Diagnose and manage milk-alkali syndrome.	√	
Sarcoidosis, Tuberculosis, and Other Granulomatous Diseases		
Diagnose and manage hypercalcemia related to sarcoidosis, tuberculosis, and other granulomatous diseases.	√	
Vitamin D Intoxication		
Diagnose and manage hypervitaminosis D–associated hypercalcemia.	√	
Post-Rhabdomyolysis		
Diagnose and manage rhabdomyolysis-associated hypercalcemia.	√	
Adynamic Bone Disease		
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.		√
Myeloma		
Diagnose and manage hypercalcemia due to myeloma.	√	
Acute Adrenal Insufficiency		
Diagnose and manage hypercalcemia due to acute adrenal insufficiency.	√	
Vitamin A Intoxication		

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 (*CASR*).	√	
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 1α-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, 1α-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. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism*. 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. *J Clin Endocrinol Metab. 2011*,**96(1)**.53-58.	Article
*Bilezikian JP, Raisz LG, Martin TJ, eds. *Principles of Bone Biology*. San Diego, CA: Academic Press; 2008.	Textbook
HYPERCALCEMIA AND HYPERPARATHYROIDISM	
*Silverberg SJ. Primary hyperparathyroidism. In: Rosen CJ, Bouillon R, Compston JE, Rosen V, eds. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism*. 8th ed. Washington, DC: Wiley-Blackwell; 2013.	Textbook
*Arnold A, Marx SJ. Familial hyperparathyroidism. In: Rosen CJ, Bouillon R, Compston JE, Rosen V, eds. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism*. 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. *J Clin Endocrinol Metab. 2008;***93***(9):*3462-3470*.*	Article
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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 glycated hemoglobin.	√	
List potential sources of error in interpreting glycated 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	√	
Insulin		
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.		√
Amylin Mimetics		
Determine when use of amylin mimetics is appropriate in patients with type 1 diabetes and summarize their mechanism of action and contraindications.		√
Metformin		
Determine when use of metformin is appropriate in patients with type 1 diabetes and summarize its mechanism of action and contraindications.		√
Nutrition and Carbohydrate Counting		
Provide guidance regarding nutrition and carbohydrate counting to patients with type 1 diabetes.	√	
Role and Effect of Exercise		
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		
Metformin		
Determine when use of metformin is appropriate in patients with type 2 diabetes and summarize its mechanism of action and contraindications.	√	
Secretagogues		
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.	√	
Thiazolidinediones		

Determine when use of thiazolidinediones is appropriate in patients with type 2 diabetes and summarize their mechanism of action and contraindications.	√	
Glucosidase inhibitors		
Determine when use of glucosidase inhibitors is appropriate in patients with type 2 diabetes and summarize their mechanism of action and contraindications.	√	
Glucagonlike Peptide 1 Receptor Agonists		
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.		√
Insulin		
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.		√
Amylin Mimetics		
Determine when use of amylin mimetics is appropriate in patients with type 2 diabetes and summarize their mechanism of action and contraindications.		√
Sodium-Glucose Cotransporter 2 Inhibitors		
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.		√
Bromocriptine		
Determine when use of bromocriptine is appropriate in patients with type 2 diabetes and summarize its mechanism of action and contraindications.		√
Nutrition		
Provide guidance regarding nutrition to patients with type 2 diabetes, with emphasis on the importance of weight reduction.	√	
Role and Effect of Exercise		
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.	√	

Bariatric Surgery in the Management of Type 2 Diabetes Mellitus		
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		
Hypertension		
Assess for and manage hypertension in patients with type 2 diabetes.	√	
Dyslipidemia		
Assess for and manage dyslipidemia in patients with type 2 diabetes.	√	
Obesity		
Assess for and manage obesity in patients with type 2 diabetes.	√	
Sleep Apnea		
Assess for and manage sleep apnea in patients with type 2 diabetes.	√	
Fatty Liver		
Assess for and manage fatty liver in patients with type 2 diabetes.		√
Low Testosterone in Men		
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, lipoatrophy, 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		
Insulinoma		
Diagnose and manage insulinoma.		√
Liver and Kidney Failure/Sepsis		
Diagnose and manage critical illness that can cause hypoglycemia.	√	
Adrenal Insufficiency		
Diagnose and manage adrenal insufficiency as a possible cause of hypoglycemia.	√	
Factitious		
Identify and manage cases of accidental, surreptitious, or malicious hypoglycemia.	√	
Postprandial		
Diagnose and manage postprandial (reactive) hypoglycemia.		√
Nesidioblastosis		

Diagnose and manage a functional β-cell disorder, nesidioblastosis, as a cause of hypoglycemia.		√
Drug-Induced		
List drugs that can cause hypoglycemia, including insulin, sulfonylureas, and meglitinides.	√	
Type B Insulin Resistance Syndrome/Anti-insulin Receptor Antibodies		
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. *Diabetes Care* 2017; 40 (Suppl 1):S1-S127. (updated every January and available online at diabetes.org)	Article
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GENERAL READING, PHYSIOLOGY, METABOLISM	
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DEFINITIONS AND DIAGNOSIS	
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MONITORING GLYCEMIC CONTROL	
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TYPE 2 DIABETES MELLITUS	
*Polonsky KS, Burant CF. Type 2 diabetes mellitus. In: Melmed S, Polonsky KS, Larsen PR, Kronenberg HM, eds. *Williams Textbook of Endocrinology*. 13th ed. Philadelphia, PA: Saunders; 2015:1386-1450.	Textbook
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*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 *N Engl J Med*. 2009;361(10):1028]. *N Engl J Med*. 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. *N Engl J Med*. 2008;358(24):2545-2559.	Article

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*Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med*. 2008;359(15):1577-1589.	Article
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PREGNANCY	
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SKIN DISEASES	
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HYPOGLYCEMIA NOT RELATED TO DIABETES TREATMENT	
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INPATIENT DIABETES MANAGEMENT	

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*NICE-SUGAR Study Investigators, Finfer S, Chittock DR, et al. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med*. 2009;360(13):1283-1297.	Article
RARE DISORDERS	
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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 antimullerian 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, 5α-reductase deficiency, 17α-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.		√
Turner Syndrome		
Diagnose and manage the reproductive manifestations of Turner syndrome (eg, hypogonadism).	√	
Perform appropriate screening for nonreproductive disease in Turner syndrome.		√
Congenital Gonadotropin-Releasing Hormone Deficiency		
Diagnose and manage congenital gonadotropin-releasing hormone deficiency, including induction of puberty, sex steroid replacement therapy, and infertility treatment options.		√
Complete and Partial Androgen Insensitivity Syndromes		
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.	√	
Primary Ovarian Insufficiency		
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.	√	
Hypogonadotropic Hypogonadism		
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).		√
Hyperprolactinemia		
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		
Diagnosis		

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.	√	
Comorbidities		
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.	√	
Management		
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		
Diagnosis		
In the setting of suggestive clinical findings, screen for nonclassic 21-hydroxylase deficiency and perform appropriate confirmatory testing as needed.	√	
Management		

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		
5α-Reductase Deficiency		
Diagnose and manage 5α-reductase deficiency.		√
Androgen Insensitivity Syndromes Due to Androgen Receptor Mutations		
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		
Appropriate Use of Diagnostic Tests		
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.	√	
Potential Pitfalls of Diagnostic Tests		

List potential pitfalls of current methods of serum total testosterone and free testosterone measurement.	√	
Primary Hypogonadism		
Cryptorchidism		
Explain the causes, diagnosis, management, and potential long-term sequelae of cryptorchidism.	√	
Klinefelter Syndrome and Other Genetic Etiologies		
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).		√
Acquired Primary Hypogonadism		
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		
Hypothalamic/Pituitary Disease		
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.	√	
Kallmann Syndrome and Normosmic Congenital Gonadotropin-Releasing Hormone Deficiency		
Diagnose and manage congenital gonadotropin-releasing hormone deficiency.		√
Constitutional Delay of Puberty		
Distinguish constitutional delay of puberty from congenital or organic hypogonadotropic hypogonadism.		√
Recommend appropriate treatment depending on the underlying cause (if one is identified).		√
Chronic Conditions and Illness		

List chronic illnesses associated with male hypogonadism, including obesity, obstructive sleep apnea, cirrhosis, renal failure, acquired immune deficiency syndrome, anorexia nervosa, and lung disease.	√	
Drug-Induced		
List drugs that can be associated with secondary hypogonadism, including gonadotropin-releasing hormone analogues, opioids, glucocorticoids, and exogenous sex steroids.	√	
Uncommon Causes of Secondary Hypogonadism		
Diagnose and manage uncommon causes of secondary hypogonadism, including head trauma, Prader-Willi syndrome, gonadotropin subunit mutations, and leptin (or receptor) mutations.		√
Treatment		
Testosterone Replacement		
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.	√	
Gonadotropin Therapy		
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.		√
Other Potential Therapies for Hypogonadism		
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		
Environmental Factors		
Describe the effects of environmental toxins, cigarette smoking, and hyperthermia on male fertility.	√	
Primary and Secondary Hypogonadism		
Identify causes of primary and secondary hypogonadism (above) as etiologies of male infertility.	√	
Varicocele		
Identify varicocele as a potential cause of male infertility.	√	
Cryptorchidism		
Identify cryptorchidism as a cause of lower sperm counts, poor-quality sperm, and lower fertility rates.	√	
Sertoli Cell–Only Syndrome		
Diagnose Sertoli cell–only syndrome as a cause of male infertility.		√
Drug-Induced		
List drugs associated with impaired spermatogenesis or Leydig-cell function, including alkylating drugs, antiandrogens, ketoconazole, and cimetidine.	√	
Ductal System Obstruction or Dysfunction		
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.		√
Y-Chromosome Microdeletions		
Diagnose Y-chromosome microdeletions as a cause of male infertility.		√
Idiopathic Oligospermia and Azoospermia		
Counsel patients regarding idiopathic male infertility after excluding all possible causal mechanisms.		√

Treatment		
Gonadotropins		
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.		√
Other Treatment Options		
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		
Causes		
Identify factors associated with erectile dysfunction, including drugs, hypogonadism, cigarette smoking, diabetes mellitus, hypertension, Peyronie disease, pelvic/prostate surgery, and obesity.	√	
Diagnostic Tests		
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.		√
Treatment		
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		
Premature Ejaculation		
Summarize the diagnosis and management of premature ejaculation.		√

Delayed Ejaculation		
Summarize the diagnosis and management of delayed ejaculation.		√
MALE REPRODUCTION: GYNECOMASTIA		
Causes		
Drugs		
List drugs associated with gynecomastia.	√	
Testicular and Extratesticular Tumors		
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.	√	
Systemic Illness		
Explain the association of gynecomastia with systemic illness such as chronic kidney disease and cirrhosis.		√
Hyperthyroidism		
Explain the association of gynecomastia with hyperthyroidism.	√	
Refeeding		
Explain the association of gynecomastia with starvation and refeeding.		√
Pubertal		
Distinguish pubertal gynecomastia from gynecomastia due to other underlying causes and discuss the natural history.		√
Congenital/Familial Excess Aromatase Activity		
Describe familial prepubertal gynecomastia due to increased aromatase activity.		√
Idiopathic		
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		
Pharmacologic Therapy		
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).		
Mastectomy and Mammoplasty		
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. *Pediatric Endocrinology*. 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. *Yen & Jaffe's Reproductive Endocrinology: Physiology, Pathophysiology, and Clinical Management*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2014.	Textbook
*Jameson JL, De Groot LJ, de Kretser D, et al, eds. *Endocrinology: Adult and Pediatric*. 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	
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Hiort O, Birnbaum W, Marshall L, et al. Management of disorders of sex development. *Nat Rev Endocrinol*. 2014;10(9):520-529.	Article
Brown DB, Loomba-Albrecht LA, Bremer AA. Sexual precocity and its treatment. *World J Pediatr*. 2013;9(2):103-111.	Article
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Boehm U, Bouloux PM, Dattani MT, et al. Expert consensus document: European Consensus Statement on congenital hypogonadotropic hypogonadism--pathogenesis, diagnosis and treatment. *Nat Rev Endocrinol*. 2015;11(9):547-564.	Article
Gordon CM, Kanaoka T, Nelson LM. Update on primary ovarian insufficiency in adolescents. *Curr Opin Pediatr*. 2015;27(4):511-519.	Article
Torrealday S, Pal L. Premature menopause. *Endocrinol Metab Clin North Am*. 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. *Nat Rev Endocrinol*. 2014;10(1):13-23.	Article
Committee on Practice Bulletins—Gynecology. Practice bulletin no. 136: management of abnormal uterine bleeding associated with ovulatory dysfunction. *Obstet Gynecol*. 2013;122(1):176-185.	Article
Silveira LF, Latronico AC. Approach to the patient with hypogonadotropic hypogonadism. *J Clin Endocrinol Metab*. 2013;98(5):1781-1788.	Article
Gonzalez L, Witchel SF. The patient with Turner syndrome: puberty and medical management concerns. *Fertil Steril*. 2012;98(4):780-786.	Article
Huang W, Molitch ME. Evaluation and management of galactorrhea. *Am Fam Physician*. 2012;85(11):1073-1080	Article
Hughes IA, Werner R, Bunch T, Hiort O. Androgen insensitivity syndrome. *Semin Reprod Med*. 2012;30(5):432-442.	Article
Pinsker JE. Clinical review: Turner syndrome: updating the paradigm of clinical care. *J Clin Endocrinol Metab*. 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. *J Clin Endocrinol Metab*. 2011;96(2):273-288.	Clinical Practice Guideline
*Gordon CM. Clinical practice. Functional hypothalamic amenorrhea. *N Engl J Med*. 2010;363(4):365-371.	Article
Nelson LM. Clinical practice. Primary ovarian insufficiency. *N Engl J Med*. 2009;360(6):606-614.	Article
FEMALE REPRODUCTION: HYPERANDROGENISM	
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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		
Clinical Manifestations		

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.	√	
Diagnosis		
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.	√	
Treatment		
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		
Clinical Manifestations		
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.	√	
Diagnosis		

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.		√
Treatment		
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		
Clinical Manifestations		
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.		√
Diagnosis		
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.	√	
Treatment		
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		
Clinical Manifestations		
Summarize the symptoms and signs of thyrotropin-secreting adenomas, which are typical of hyperthyroidism, such as palpitations, tremor, and heat intolerance.		√
Diagnosis		
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.		√
Treatment		
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		
Clinical Manifestations		
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.	√	
Diagnosis		
Distinguish primary hypothyroidism from secondary hypothyroidism with measurement of thyrotropin and serum free T_4.	√	
Treatment		

Adjust the levothyroxine replacement dosage clinically and on the basis of serum free T_4 levels.	√	
GONADOTROPINS		
Gonadotroph Pituitary Tumors		
Clinical Manifestations		
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.		√
Diagnosis		
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.		√
Treatment		
Recommend treatment strategies for gonadotroph pituitary tumors, including surgery and radiation.		√
Guide the long-term monitoring and management of gonadotroph pituitary tumors.		√
Hypogonadotropic Hypogonadism		
Clinical Manifestations		
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.	√	
Diagnosis		
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.	√	
Treatment		
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		
Clinical Manifestations		
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.	√	
Diagnosis		
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.	√	
Treatment		
Recommend treatment strategies for nonsecreting pituitary tumors, which may include surgery and radiation.	√	
CORTICOTROPIN		
Cushing Disease		
Clinical Manifestations		
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.	√	
Diagnosis		

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.		√
Treatment		
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		
Clinical Manifestations		
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.	√	
Diagnosis		

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.	√	
Treatment		
Recommend treatment approaches for secondary adrenal insufficiency depending on etiology.	√	
Adjust the glucocorticoid dosage clinically.	√	
HYPOPITUITARISM		
Clinical Manifestations		
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, *PROP1*, *POU1F1*, *TBX19* 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).	√	
Diagnosis		
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.	√	√
Treatment		

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		
Clinical Manifestations		
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.	√	
Diagnosis		
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.	√	
Treatment		
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		
Clinical Manifestations		
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.		√
Treatment		
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	
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Acromegaly: Diagnosis and Management	
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PITUITARY IMAGING AND PROCEDURES	
Imaging	
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Naidich MJ, Russell EJ. Current approaches to imaging of the sellar region and pituitary. *Endocrinol Metab Clin North Am*. 1999;28(1):45-79.	Article
Procedures	
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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 *PCSK9* 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 B_{100}		
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 HYPOLIPIDEMIAS		
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		
Nutritional Supplements		
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.		√
Weight Reduction		
Summarize the evidence base for weight loss for lipid lowering and cardiovascular risk reduction.	√	
Recommend weight-loss strategies in the management of patients with dysplipidemia.	√	
Diet Composition		
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		
HMG-CoA Reductase Inhibitors		

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.	√	
Niacin		
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.	√	
Fibrates		
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.	√	
Bile Acid Sequestrants		
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.	√	
Ezetimibe		
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.	√	
Combination Therapy		
Determine which patients are appropriate candidates for combination therapy to treat dyslipidemia.	√	
Guide combination therapy in patients with dyslipidemia.	√	
Other Drugs		
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. *Andreoli and Carpenter's Cecil Essentials of Medicine.* 9th ed. Philadelphia, PA: WB Saunders; 2015.	Textbook
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USEFUL WEB SITES

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

RISK Calculator: http://my.americanheart.org/cvriskcalculator

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 *FTO* variants, *MC4R* 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		
Diet		
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.	√	
Exercise		
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.	√	
Behavioral Treatment		
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 nervose, 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.

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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. *Am J Clin Nutr*. 2014;99(4):834-842.	Article
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NUTRITION IN OUTPATIENTS	
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Treasure J, Claudino AM, Zucker N. Eating disorders. *Lancet*. 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		
Clinical Manifestations		
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.		√
Diagnostic Tests		
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.	√	
Treatment		
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		
Thyroiditis		
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.	√	
Other Forms of Thyrotoxicosis		
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 (*see also Procedures*)		
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.		√
Initial Therapeutic Approach		
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.		√
Monitoring or Follow-Up		
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 *RET* 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	
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Davies L, Welch HG. Current thyroid cancer trends in the United States. *JAMA Otolaryngol Head Neck Surg*. 2014;140(4):317-322.	Article
*Fekete C, Lechan RM. Central regulation of hypothalamic-pituitary-thyroid axis under physiological and pathophysiological conditions. *Endocr Rev*. 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. *JAMA*. 2014;311(15):1563-1565.	Article
*Braverman LE, Cooper D, eds. *Werner & Ingbar's The Thyroid: A Fundamental and Clinical Text*. 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. *Thyroid*. 2013;23(4):449-455.	Article
Brent GA. Mechanisms of thyroid hormone action. *J Clin Invest*. 2012;122(9):3035-3043.	Article
*Hayter SM, Cook MC. Updated assessment of the prevalence, spectrum and case definition of autoimmune disease. *Autoimmun Rev*. 2012;11(10):754-765.	Article
McLeod DS, Cooper DS. The incidence and prevalence of thyroid autoimmunity. *Endocrine*. 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. *J Clin Endocrinol Metab*. 2012;97(11):3944-3950.	Article
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Surks MI, Hollowell JG. Age-specific distribution of serum thyrotropin and antithyroid antibodies in the US population: implications for the prevalence of subclinical hypothyroidism. *J Clin Endocrinol Metab*. 2007;92(12):4575-4582.	Article
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Surks MI, Schadlow AR, Stock JM, Oppenheimer JH. Determination of iodothyronine absorption and conversion of L-thyroxine (T4) to L-triiodothyronine (T3) using turnover rate techniques. *J Clin Invest*. 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. *Int J Endocrinol Metab*. 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. *J Clin Endocrinol Metabolism*. 2014;99(7):2372-2382.	Article
Bakos B, Takacs I, Nagy Z, et al. Long term efficacy of radioiodine treatment in hyperthyroidism. *Exp Clin Endocrinol Diabetes*. 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. *J Clin Endocrinol Metab*. 2013;98(9):3671-3677.	Article
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*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 *Thyroid*. 2011;21(10):1169 and *Thyroid*. 2012;22(11):1195]. *Thyroid*. 2011;21(6):593-646.	Clinical Practice Guideline
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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. *J Clin Endocrinol Metab*. 2010;95(5):2227-2233.	Article
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*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. *Thyroid*. 2014;24(12):1670-1751.	Clinical Practice Guideline
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Biondi B, Wartofsky L. Combination treatment with T4 and T3: toward personalized replacement therapy in hypothyroidism? *J Clin Endocrinol Metab*. 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. *Endocr Pract*. 2012;18(6):988-1028.	Clinical Practice Guideline
Khandelwal D, Tandon N. Overt and subclinical hypothyroidism: who to treat and how. *Drugs*. 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. *J Clin Endocrinol Metab*. 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. *Nat Rev Endocrinol*. 2012;8(7):417-424.	Article
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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. *J Clin Endocrinol Metab*. 2014;99(11):4069-4077.	Article
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PROCEDURES	
See above under Diagnostic Thyroid Testing	

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