ENDOCRINE BOARD REVIEW

18TH EDITION

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ENDOCRINE BOARD REVIEW

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ENDOCRINE SOCIETY

ENDOCRINE SOCIETY
Hormone Science to Health

The Endocrine Society is the world's largest, oldest, and most active organization working to advance the clinical practice of endocrinology and hormone research. Founded in 1916, the Society now has more than 18,000 global members across a range of disciplines. The Society has earned an international reputation for excellence in the quality of its peer-reviewed journals, educational resources, meetings, and programs that improve public health through the practice and science of endocrinology.

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ISBN: 978-1-936704-81-1
eISBN: 978-1-936704-83-5

ISSN: 3070-524X
ISSN Online : 3070-5258

OVERVIEW

The Endocrine Board Review (EBR) is a board examination preparation course designed for endocrine fellows who have completed or are nearing completion of their fellowship and are preparing to sit for the board certification exam, as well as for practicing endocrinologists seeking a comprehensive self-assessment of endocrinology, either to prepare for recertification or to update their practice. EBR consists of 220 case-based, American Board of Internal Medicine (ABIM)-style multiple-choice questions presented in a mock exam format. Each section aligns with the ABIM Endocrinology, Diabetes, and Metabolism Certification Examination blueprint, covering the breadth and depth of the certification and recertification examinations. Each case is discussed comprehensively, with detailed answer explanations and references. A customized score report is provided to participants in the online courses.

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The Endocrine Society is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The Endocrine Society has achieved Accreditation with Commendation.

The Endocrine Society designates this enduring material for a maximum of 55 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with their participation in the activity.

MAINTENANCE OF CERTIFICATION

Successful completion of this CME activity, including participation in the evaluation component, enables the participant to earn up to 55 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. It is the CME activity provider's responsibility to submit participant completion information to the Accreditation Council for Continuing Medical Education for the purpose of granting ABIM MOC credit.

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CME credits and/or MOC points for activities related to this material must be claimed by December 31, 2027.

For questions about content, CME credit, or MOC points, please contact the Endocrine Society at info@endocrine.org.

LEARNING OBJECTIVES

Upon completion of this educational activity, learners will be able to demonstrate enhanced medical knowledge and clinical skills across all major areas of endocrinology; apply this knowledge and these skills to diagnose, manage, and treat a wide spectrum of endocrine disorders; and successfully complete the board examination for certification or recertification in the subspecialty of endocrinology, diabetes, and metabolism.

TARGET AUDIENCE

This CME activity is intended for endocrine fellows preparing for initial certification, practicing endocrinologists preparing for an MOC assessment, or physicians seeking an in-depth review of endocrinology.

STATEMENT OF INDEPENDENCE

As a provider of CME accredited by the ACCME, the Endocrine Society ensures that the content and quality of this educational activity are balanced, independent, objective, and scientifically rigorous. The scientific content of this activity was developed under the supervision of the Endocrine Society's EBR faculty. There are no commercial supporters of this activity, and no commercial entities have influenced the planning of this CME activity.

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The faculty disclosed the following relevant financial relationship(s) during the content development process for this activity:

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Marcelo Correia, MD, MSc, PhD The Obesity Society (*Member*); Novartis, Eli Lilly, Novo Nordisk, Stead Family (Iowa), National Institutes of Health, PCORI (Research Support); Novo Nordisk (*Advisory Board and Consultant*); Genentech/Roche (*Advisory Board*).

Natalie Cusano, MD, MS Ascendis Pharma, Extend Biosciences (*Consultant*); *Endocrine Practice* (*Editor*); Ascendis Pharma, Takeda/Shire (*Research Support*); Alexion (*Speaker*).

Kaniksha Desai, MD *Endocrine Practice* (*Editor*); American Thyroid Association, American Association of Clinical Endocrinologists, Thyroid Disease State Network (*Member*); Medscape Podcast on Thyroid Diseases (*Host*).

Hans K. Ghayee, DO Corcept (*Consultant*); SDHB Pheo Para Coalition (*Funding*); University of Texas Southwestern Medical Center (*Royalties*).

Sangeeta Kashyap, MD GI Dynamics (*Consultant*); Fractyl, Inc (*Research Support*).

E. Michael Lewiecki, MD Ultragenyx, Angitia (*Institutional Research Grants*); Amgen, Radius, Kyowa Kirin, Angitia, Ascendis (*Consultant*); Amgen, Radius, Ascendis, Kyowa Kirin (*Speaker*).

Cecilia C. Low Wang, MD American Association of Clinical Endocrinology, American College of Diabetology, American Heart Association, Clinical Diabetes and Endocrinology Institute (*Advisory Board*); Clinical Diabetes and Endocrinology Institute, Medical Education Resources, Continuing Education Company (*Speaker*); Dexcom Inc, Virta Health (*Research Funding*); American Heart Association (*Guidelines Committee*); FDA Advisory Committee for Endocrinologic Metabolic Drugs (*Committee Member*).

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The medical editor for this activity reported no relevant financial relationships: Abbie L. Young, MS, CGC, ELS(D)

Endocrine Society staff involved in developing content for this activity reported no relevant financial relationships.

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Use of professional judgment:

The educational content in this activity covers basic principles of diagnosis and therapy and does not replace individual patient assessment based on the health care provider's examination of the patient and on consideration of laboratory data and other factors unique to the patient. Medical standards change as new data become available.

Drugs and dosages:

When prescribing medications, the physician is advised to review the prescribing information for each drug to verify the conditions of use and identify any changes to the dosage schedule or contraindications.

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The Endocrine Society has determined that disclosing unlabeled, off-label, or investigational uses of commercial products is informative for audiences and therefore requires that this information be disclosed to learners at the beginning of the presentation. Uses of specific therapeutic agents, devices, and other products discussed in this educational activity may not align with the indications in FDA-approved product labeling. The Endocrine Society requires that any discussions of such "off-label" use be grounded in scientific research that conforms to generally accepted standards of experimental design, data collection, and data analysis. Before recommending or prescribing any therapeutic agent or device, learners should review the complete prescribing information, including indications, contraindications, warnings, precautions, and adverse events.

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ACKNOWLEDGMENT OF COMMERCIAL SUPPORT

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SYSTEM REQUIREMENTS

To complete this activity, participants must have access to a computer or mobile device with an Internet connection and use an up-to-date version of a major Web browser, such as Internet Explorer 10+, Firefox 32+, Safari, or Google Chrome 37+. In addition, cookies and JavaScript must be enabled in the browser's settings.

Last Review: June 2026
Activity Release: July 2026
Activity Expiration Date: December 31, 2027 (the date after which this enduring material is no longer certified for *AMA PRA Category 1 Credits*™ and ABIM Medical Knowledge MOC points)

Contents

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LABORATORY REFERENCE RANGES

Reference ranges vary among laboratories. Conventional units are listed first with SI units in parentheses.

Lipid Values

High-density lipoprotein (HDL) cholesterol
- Optimal ---------- >60 mg/dL (SI: >1.55 mmol/L)
- Normal ---------- 40-60 mg/dL (SI: 1.04-1.55 mmol/L)
- Low ---------- <40 mg/dL (SI: <1.04 mmol/L)

Low-density lipoprotein (LDL) cholesterol
- Optimal ----------
  <100 mg/dL (SI: <2.59 mmol/L) (for primary prevention);
  <70 mg/dL (SI: <1.81 mmol/L) (for secondary prevention)
- Low ----------100-129 mg/dL (SI: 2.59-3.34 mmol/L)
- Borderline-high --------130-159 mg/dL (SI: 3.37-4.12 mmol/L)
- High ----------160-189 mg/dL (SI: 4.14-4.90 mmol/L)
- Very high ----------≥190 mg/dL (SI: ≥4.92 mmol/L)

Non-HDL cholesterol
- Optimal ----------<130 mg/dL (SI: <3.37 mmol/L)
- Borderline-high --------130-159 mg/dL (SI: 3.37-4.12 mmol/L)
- High ----------≥240 mg/dL (SI: ≥6.22 mmol/L)

Total cholesterol
- Optimal ----------<200 mg/dL (SI: <5.18 mmol/L)
- Borderline-high --------200-239 mg/dL (SI: 5.18-6.19 mmol/L)
- High ----------≥240 mg/dL (SI: ≥6.22 mmol/L)

Triglycerides
- Optimal ----------<150 mg/dL (SI: <1.70 mmol/L)
- Borderline-high --------150-199 mg/dL (SI: 1.70-2.25 mmol/L)
- High ----------200-499 mg/dL (SI: 2.26-5.64 mmol/L)
- Very high ----------≥500 mg/dL (SI: ≥5.65 mmol/L)

Lipoprotein (a) ----------≤30 mg/dL (SI: ≤1.07 µmol/L)

Apolipoprotein B ---------- 50-110 mg/dL (SI: 0.5-1.1 g/L)

Hematologic Values

Erythrocyte sedimentation rate ----------0-20 mm/h

Haptoglobin ---------- 30-200 mg/dL (SI: 300-2000 mg/L)

Hematocrit ---------- 41%-51% (SI: 0.41-0.51) (male);
35%-45% (SI: 0.35-0.45) (female)

Hemoglobin A_{1c} ---------- 4.0%-5.6% (20-38 mmol/mol)

Hemoglobin ---------- 13.8-17.2 g/dL (SI: 138-172 g/L) (male);
12.1-15.1 g/dL (SI: 121-151 g/L) (female)

International normalized ratio ----------0.8-1.2

Mean corpuscular volume (MCV) ------80-100 μm^3 (SI: 80-100 fL)

Platelet count ---------- 150-450 × 10^3/µL (SI: 150-450 × 10^9/L)

Protein (total) ----------6.3-7.9 g/dL (SI: 63-79 g/L)

Reticulocyte count -0.5%-1.5% of red blood cells (SI: 0.005-0.015)

White blood cell count ------4500-11,000/µL (SI: 4.5-11.0 × 10^9/L)

Thyroid Values

Thyroglobulin ------ 3-42 ng/mL (SI: 3-42 µg/L) (after surgery and radioactive iodine treatment: <1.0 ng/mL [SI: <1.0 µg/L])

Thyroglobulin antibodies ---------- ≤4.0 IU/mL (SI: ≤4.0 kIU/L)

Thyrotropin (TSH) ---------- 0.5-5.0 mIU/L

Thyrotropin-receptor antibodies (TRAb) ----------≤1.75 IU/L

Thyroid-stimulating immunoglobulin ----- ≤120% of basal activity

Thyroperoxidase (TPO) antibodies ----- <2.0 IU/mL (SI: <2.0 kIU/L)

Thyroxine (T_4) (free) -------0.8-1.8 ng/dL (SI: 10.30-23.17 pmol/L)

Thyroxine (T_4) (total) ---- 5.5-12.5 µg/dL (SI: 94.02-213.68 nmol/L)

Free thyroxine (T_4) index ---------- 4-12

Triiodothyronine (T_3) (free) --- 2.3-4.2 pg/mL (SI: 3.53-6.45 pmol/L)

Triiodothyronine (T_3) (total) -- 70-200 ng/dL (SI: 1.08-3.08 nmol/L)

Triiodothyronine (T_3), reverse -- 10-24 ng/dL (SI: 0.15-0.37 nmol/L)

Triiodothyronine uptake, resin ---------- 25%-38%

Radioactive iodine uptake --- 3%-16% (6 hours); 15%-30% (24 hours)

Endocrine Values

Serum

Aldosterone ---------- 4-21 ng/dL (SI: 111.0-582.5 pmol/L)

Alkaline phosphatase ---------- 50-120 U/L (SI: 0.84-2.00 µkat/L)

Alkaline phosphatase (bone-specific) ------ ≤20 µg/L (adult male);
≤14 µg/L (premenopausal female);
≤22 µg/L (postmenopausal female)

Androstenedione ----------
65-210 ng/dL (SI: 2.27-7.33 nmol/L) (adult male);
30-200 ng/dL (SI: 1.05-6.98 nmol/L) (adult female)

Antimullerian hormone ----------
0.7-19.0 ng/mL (SI: 5.0-135.7 pmol/L) (male, >12 years);
0.9-9.5 ng/mL (SI: 6.4-67.9 pmol/L) (female, 13-45 years);
<1.0 ng/mL (SI: <7.1 pmol/L) (female, >45 years)

Calcitonin ----------<16 pg/mL (SI: <4.67 pmol/L) (basal, male);
<8 pg/mL (SI: <2.34 pmol/L) (basal, female);
≤130 pg/mL (SI: ≤37.96 pmol/L) (peak calcium infusion, male);
≤90 pg/mL (SI: ≤26.28 pmol/L) (peak calcium infusion, female)

Carcinoembryonic antigen ---------- <2.5 ng/mL (SI: <2.5 µg/L)

Chromogranin A ---------- <93 ng/mL (SI: <93 µg/L)

Corticosterone -- 53-1560 ng/dL (SI: 1.53-45.08 nmol/L) (>18 years)

Corticotropin (ACTH) ---------- 10-60 pg/mL (SI: 2.2-13.2 pmol/L)

Cortisol (8 AM) ---------- 5-25 µg/dL (SI: 137.9-689.7 nmol/L)

C-peptide ---------- 0.5-2.0 ng/mL (SI: 0.17-0.66 nmol/L)

C-reactive protein ---------- 0.8-3.1 mg/L (SI: 7.62-29.52 nmol/L)

Cross-linked N-telopeptide of type 1 collagen ----------

5.4-24.2 nmol BCE/mmol creat (male);

6.2-19.0 nmol BCE/mmol creat (female)

Dehydroepiandrosterone sulfate (DHEA-S)

Patient Age	Female	Male
18-29 years	44-332 µg/dL (SI: 1.19-9.00 µmol/L)	89-457 µg/dL (SI: 2.41-12.38 µmol/L)
30-39 years	31-228 µg/dL (SI: 0.84-6.78 µmol/L)	65-334 µg/dL (SI: 1.76-9.05 µmol/L)
40-49 years	18-244 µg/dL (SI: 0.49-6.61 µmol/L)	48-244 µg/dL (SI: 1.30-6.61 µmol/L)
50-59 years	15-200 µg/dL (SI: 0.41-5.42 µmol/L)	35-179 µg/dL (SI: 0.95-4.85 µmol/L)
≥60 years	15-157 µg/dL (SI: 0.41-4.25 µmol/L)	25-131 µg/dL (SI: 0.68-3.55 µmol/L)

Deoxycorticosterone ----<10 ng/dL (SI: <0.30 nmol/L) (>18 years)

1,25-Dihydroxyvitamin D_3 ---16-65 pg/mL (SI: 41.6-169.0 pmol/L)

Estradiol ---------- 10-40 pg/mL (SI: 36.7-146.8 pmol/L) (male);

10-180 pg/mL (SI: 36.7-660.8 pmol/L) (follicular, female);

100-300 pg/mL (SI: 367.1-1101.3 pmol/L) (midcycle, female);

40-200 pg/mL (SI: 146.8-734.2 pmol/L) (luteal, female);

<20 pg/mL (SI: <73.4 pmol/L) (postmenopausal, female)

Estrone ---------- 10-60 pg/mL (SI: 37.0-221.9 pmol/L) (male);

17-200 pg/mL (SI: 62.9-739.6 pmol/L) (premenopausal female);

7-40 pg/mL (SI: 25.9-147.9 pmol/L) (postmenopausal female)

α-Fetoprotein ---------- <6 ng/mL (SI: <6 µg/L)

Follicle-stimulating hormone (FSH) ----------

1.0-7.0 mIU/mL (SI: 1.0-7.0 IU/L) (male);

<3.0 mIU/mL (SI: <3.0 IU/L) (prepuberty, female);

2.0-12.0 mIU/mL (SI: 2.0-12.0 IU/L) (follicular, female);

4.0-36.0 mIU/mL (SI: 4.0-36.0 IU/L) (midcycle, female);

1.0-9.0 mIU/mL (SI: 1.0-9.0 IU/L) (luteal, female);

>30.0 mIU/mL (SI: >30.0 IU/L) (postmenopausal, female)

Free fatty acids ---------- 10.6-18.0 mg/dL (SI: 0.4-0.7 nmol/L)

Gastrin ---------- <100 pg/mL (SI: <100 ng/L)

Growth hormone (GH) 0.01-0.97 ng/mL (SI: 0.01-0.97 µg/L) (male);

0.01-3.61 ng/mL (SI: 0.01-3.61 µg/L) (female)

Homocysteine ---------- ≤1.76 mg/L (SI: ≤13 µmol/L)

β-Human chorionic gonadotropin (β-hCG) ----------

<3.0 mIU/mL (SI: <3.0 IU/L) (nonpregnant female);

>25 mIU/mL (SI: >25 IU/L) indicates a positive pregnancy test

β-Hydroxybutyrate ---------- <3.0 mg/dL (SI: <288.2 µmol/L)

17-Hydroxypregnenolone --- 29-189 ng/dL (SI: 0.87-5.69 nmol/L)

17α-Hydroxyprogesterone ----------

<220 ng/dL (SI: <6.67 nmol/L) (adult male);

<80 ng/dL (SI: <2.42 nmol/L) (follicular, female);

<285 ng/dL (SI: <8.64 nmol/L) (luteal, female);

<51 ng/dL (SI: <1.55 nmol/L) (postmenopausal, female)

25-Hydroxyvitamin D - <20 ng/mL (SI: <49.9 nmol/L) (deficiency);

21-29 ng/mL (SI: 52.4-72.4 nmol/L) (insufficiency);

30-80 ng/mL (SI: 74.9-199.7 nmol/L) (optimal levels);

>80 ng/mL (SI: >199.7 nmol/L) (toxicity possible)

Inhibin B ---------- 15-300 pg/mL (SI: 15-300 ng/L)

Insulinlike growth factor 1 (IGF-1)

Patient Age	Female	Male
18 years	162-541 ng/mL (SI: 21.2-70.9 nmol/L)	170-640 ng/mL (SI: 22.3-83.8 nmol/L)
19 years	138-442 ng/mL (SI: 18.1-57.9 nmol/L)	147-527 ng/mL (SI: 19.3-69.0 nmol/L)
20 years	122-384 ng/mL (SI: 16.0-50.3 nmol/L)	132-457 ng/mL (SI: 17.3-59.9 nmol/L)
21-25 years	116-341 ng/mL (SI: 15.2-44.7 nmol/L)	116-341 ng/mL (SI: 15.2-44.7 nmol/L)
26-30 years	117-321 ng/mL (SI: 15.3-42.1 nmol/L)	117-321 ng/mL (SI: 15.3-42.1 nmol/L)
31-35 years	113-297 ng/mL (SI: 14.8-38.9 nmol/L)	113-297 ng/mL (SI: 14.8-38.9 nmol/L)
36-40 years	106-277 ng/mL (SI: 13.9-36.3 nmol/L)	106-277 ng/mL (SI: 13.9-36.3 nmol/L)
41-45 years	98-261 ng/mL (SI: 12.8-34.2 nmol/L)	98-261 ng/mL (SI: 12.8-34.2 nmol/L)
46-50 years	91-246 ng/mL (SI: 11.9-32.2 nmol/L)	91-246 ng/mL (SI: 11.9-32.2 nmol/L)
51-55 years	84-233 ng/mL (SI: 11.0-30.5 nmol/L)	84-233 ng/mL (SI: 11.0-30.5 nmol/L)
56-60 years	78-220 ng/mL (SI: 10.2-28.8 nmol/L)	78-220 ng/mL (SI: 10.2-28.8 nmol/L)
61-65 years	72-207 ng/mL (SI: 9.4-27.1 nmol/L)	72-207 ng/mL (SI: 9.4-27.1 nmol/L)
66-70 years	67-195 ng/mL (SI: 8.8-25.5 nmol/L)	67-195 ng/mL (SI: 8.8-25.5 nmol/L)
71-75 years	62-184 ng/mL (SI: 8.1-24.1 nmol/L)	62-184 ng/mL (SI: 8.1-24.1 nmol/L)
76-80 years	57-172 ng/mL (SI: 7.5-22.5 nmol/L)	57-172 ng/mL (SI: 7.5-22.5 nmol/L)
>80 years	53-162 ng/mL (SI: 6.9-21.2 nmol/L)	53-162 ng/mL (SI: 6.9-21.2 nmol/L)

Insulinlike growth factor binding protein 3 ---------- 2.5-4.8 mg/L

Insulin---------- 1.4-14.0 µIU/mL (SI: 9.7-97.2 pmol/L)

Islet-cell antibody assay---- 0 Juvenile Diabetes Foundation units

Luteinizing hormone (LH)----------

1.0-9.0 mIU/mL (SI: 1.0-9.0 IU/L) (male);

<1.0 mIU/mL (SI: <1.0 IU/L) (prepuberty, female);

1.0-18.0 mIU/mL (SI: 1.0-18.0 IU/L) (follicular, female);

20.0-80.0 mIU/mL (SI: 20.0-80.0 IU/L) (midcycle, female);

0.5-18.0 mIU/mL (SI: 0.5-18.0 IU/L) (luteal, female);

>30.0 mIU/mL (SI: >30.0 IU/L) (postmenopausal, female)

Metanephrines (plasma fractionated)

Metanephrine----------<99 pg/mL (SI: <0.50 nmol/L)

Normetanephrine---------- <165 pg/mL (SI: <0.90 nmol/L)

75-g oral glucose tolerance test blood glucose values ----------

60-100 mg/dL (SI: 3.3-5.6 mmol/L) (fasting);

<200 mg/dL (SI: <11.1 mmol/L) (1 hour);

<140 mg/dL (SI: <7.8 mmol/L) (2 hour);

between 140-200 mg/dL (SI: 7.8-11.1 mmol/L) is considered impaired glucose tolerance or prediabetes; greater than 200 mg/dL (SI: >11.1 mmol/L) is a sign of diabetes mellitus

50-g oral glucose tolerance test for gestational diabetes --------

<140 mg/dL (SI: <7.8 mmol/L) (1 hour)

100-g oral glucose tolerance test for gestational diabetes -------

<95 mg/dL (SI: <5.3 mmol/L) (fasting);

<180 mg/dL (SI: <10.0 mmol/L) (1 hour);

<155 mg/dL (SI: <8.6 mmol/L) (2 hour);

<140 mg/dL (SI: <7.8 mmol/L) (3 hour)

Osteocalcin ----------9.0-42.0 ng/mL (SI: 9.0-42.0 µg/L)

Parathyroid hormone, intact (PTH)--- 10-65 pg/mL (SI: 10-65 ng/L)

Parathyroid hormone–related protein (PTHrP)--------<2.0 pmol/L

Progesterone ----------≤1.2 ng/mL (SI: ≤3.8 nmol/L) (male);

≤1.0 ng/mL (SI: ≤3.2 nmol/L) (follicular, female);

2.0-20.0 ng/mL (SI: 6.4-63.6 nmol/L) (luteal, female);

≤1.1 ng/mL (SI: ≤3.5 nmol/L) (postmenopausal, female);

>10.0 ng/mL (SI: >31.8 nmol/L) (evidence of ovulatory adequacy)

Proinsulin ---------- 26.5-176.4 pg/mL (SI: 3.0-20.0 pmol/L)

Prolactin ----------4-23 ng/mL (SI: 0.17-1.00 nmol/L) (male);

4-30 ng/mL (SI: 0.17-1.30 nmol/L) (nonlactating female);

10-200 ng/mL (SI: 0.43-8.70 nmol/L) (lactating female)

Prostate-specific antigen (PSA) ----------

<2.0 ng/mL (SI: <2.0 µg/L) (≤40 years);

<2.8 ng/mL (SI: <2.8 µg/L) (≤50 years);

<3.8 ng/mL (SI: <3.8 µg/L) (≤60 years);

<5.3 ng/mL (SI: <5.3 µg/L) (≤70 years);

<7.0 ng/mL (SI: <7.0 µg/L) (≤79 years);

<7.2 ng/mL (SI: <7.2 µg/L) (≥80 years)

Renin activity, plasma, sodium replete, ambulatory ----------

0.6-4.3 ng/mL per h

Renin, direct concentration ------- 4-44 pg/mL (SI: 0.1-1.0 pmol/L)

Sex hormone–binding globulin (SHBG) ----------

1.1-6.7 µg/mL (SI: 10-60 nmol/L) (male);

2.2-14.6 µg/mL (SI: 20-130 nmol/L) (female)

α-Subunit of pituitary glycoprotein hormones ----------

<1.2 ng/mL (SI: <1.2 µg/L)

Testosterone (bioavailable) ----------

0.8-4.0 ng/dL (SI: 0.03-0.14 nmol/L)

(20-50 years, female on oral estrogen);

0.8-10.0 ng/dL (SI: 0.03-0.35 nmol/L)

(20-50 years, female not on oral estrogen);

83.0-257.0 ng/dL (SI: 2.88-8.92 nmol/L) (male 20-29 years);

72.0-235.0 ng/dL (SI: 2.50-8.15 nmol/L) (male 30-39 years);

61.0-213.0 ng/dL (SI: 2.12-7.39 nmol/L) (male 40-49 years);

50.0-190.0 ng/dL (SI: 1.74-6.59 nmol/L) (male 50-59 years);

40.0-168.0 ng/dL (SI: 1.39-5.83 nmol/L) (male 60-69 years)

Testosterone (free) --- 9.0-30.0 ng/dL (SI: 0.31-1.04 nmol/L) (male);

0.3-1.9 ng/dL (SI: 0.01-0.07 nmol/L) (female)

Testosterone (total)- 300-900 ng/dL (SI: 10.4-31.2 nmol/L) (male);

8-60 ng/dL (SI: 0.3-2.1 nmol/L) (female)

Vitamin B_{12} ---------- 180-914 pg/mL (SI: 133-674 pmol/L)

Chemistry Values

Alanine aminotransferase------- 10-40 U/L (SI: 0.17-0.67 µkat/L)

Albumin----------3.5-5.0 g/dL (SI: 35-50 g/L)

Amylase ---------- 26-102 U/L (SI: 0.43-1.70 µkat/L)

Anion gap ----------3-11 mEq/L (SI: 3-11 mmol/L)

Aspartate aminotransferase ---- 20-48 U/L (SI: 0.33-0.80 µkat/L)

Bicarbonate ---------- 21-28 mEq/L (SI: 21-28 mmol/L)

Bilirubin (total)---------- 0.3-1.2 mg/dL (SI: 5.1-20.5 µmol/L)

Blood gases

Po_2, arterial blood ---------80-100 mm Hg (SI: 10.6-13.3 kPa)

Pco_2, arterial blood ----------35-45 mm Hg (SI: 4.7-6.0 kPa)

Blood pH---------- 7.35-7.45

Calcium ----------8.2-10.2 mg/dL (SI: 2.1-2.6 mmol/L)

Calcium (ionized) ---------- 4.60-5.08 mg/dL (SI: 1.2-1.3 mmol/L)

Carbon dioxide ---------- 22-28 mEq/L (SI: 22-28 mmol/L)

CD_4 cell count---------- 500-1400/µL (SI: 0.5-1.4 × 10^9/L)

Chloride---------- 96-106 mEq/L (SI: 96-106 mmol/L)

Creatine kinase ---------- 50-200 U/L (SI: 0.84-3.34 µkat/L)

Creatinine----------0.7-1.3 mg/dL (SI: 61.9-114.9 µmol/L) (male);

0.6-1.1 mg/dL (SI: 53.0-97.2 µmol/L) (female)

Ferritin ---------- 15-200 ng/mL (SI: 33.7-449.4 pmol/L)

Folate ---------- ≥4.0 ng/mL (SI: ≥4.0 µg/L)

Glucose ---------- 70-99 mg/dL (SI: 3.9-5.5 mmol/L)

γ-Glutamyltransferase ---------- 2-30 U/L (SI: 0.03-0.50 µkat/L)

Iron ----------
50-150 µg/dL (SI: 9.0-26.8 µmol/L) (male);
35-145 µg/dL (SI: 6.3-26.0 µmol/L) (female)
Lactate dehydrogenase --------- 100-200 U/L (SI: 1.7-3.3 µkat/L)
Lactic acid ----------5.4-20.7 mg/dL (SI: 0.6-2.3 mmol/L)
Lipase ---------- 10-73 U/L (SI: 0.17-1.22 µkat/L)
Magnesium ---------- 1.5-2.3 mg/dL (SI: 0.6-0.9 mmol/L)
Osmolality ----------275-295 mOsm/kg (SI: 275-295 mmol/kg)
Phosphate ---------- 2.3-4.7 mg/dL (SI: 0.7-1.5 mmol/L)
Potassium ---------- 3.5-5.0 mEq/L (SI: 3.5-5.0 mmol/L)
Prothrombin time ----------8.3-10.8 s
Serum urea nitrogen----------8-23 mg/dL (SI: 2.9-8.2 mmol/L)
Sodium ---------- 136-142 mEq/L (SI: 136-142 mmol/L)
Transferrin saturation ---------- 14%-50%
Troponin I ---------- <0.6 ng/mL (SI: <0.6 µg/L)
Tryptase ---------- <11.5 ng/mL (SI: <11.5 µg/L)
Uric acid ---------- 3.5-7.0 mg/dL (SI: 208.2-416.4 µmol/L)

Urine

Albumin----------30-300 µg/mg creat (SI: 3.4-33.9 µg/mol creat)
Albumin-to-creatinine ratio ---------- <30 mg/g creat
Aldosterone---------- 3-20 µg/24 h (SI: 8.3-55.4 nmol/d)
(should be <12 µg/24 h [SI: <33.2 nmol/d] with oral sodium loading—confirmed with 24-hour urinary sodium >200 mEq)
Calcium ---------- 100-300 mg/24 h (SI: 2.5-7.5 mmol/d)
Catecholamine fractionation
Normotensive normal ranges:
Dopamine ---------- <400 µg/24 h (SI: <2610 nmol/d)
Epinephrine ----------<21 µg/24 h (SI: <115 nmol/d)
Norepinephrine ----------<80 µg/24 h (SI: <473 nmol/d)
Citrate ---------- 320-1240 mg/24 h (SI: 16.7-64.5 mmol/d)
Cortisol ---------- 4-50 µg/24 h (SI: 11-138 nmol/d)
Cortisol following dexamethasone suppression test
(low-dose: 2 day, 2 mg daily) ---<10 µg/24 h (SI: <27.6 nmol/d)
Creatinine---------- 1.0-2.0 g/24 h (SI: 8.8-17.7 mmol/d)
Glomerular filtration rate (estimated) ----->60 mL/min per 1.73 m^2
5-Hydroxyindole acetic acid---2-9 mg/24 h (SI: 10.5-47.1 µmol/d)
Iodine (random)---------- >100 µg/L
17-Ketosteroids -- 6.0-21.0 mg/24 h (SI: 20.8-72.9 µmol/d) (male);
4.0-17.0 mg/24 h (SI: 13.9-59.0 µmol/d) (female)
Metanephrine fractionation
Normotensive normal ranges:
Metanephrine-------- <261 µg/24 h (SI: <1323 nmol/d) (male);
<180 µg/24 h (SI: <913 nmol/d) (female)
Normetanephrine---------- age and sex dependent
Total metanephrine---------- age and sex dependent
Osmolality ---------- 150-1150 mOsm/kg (SI: 150-1150 mmol/kg)
Oxalate ---------- <40 mg/24 h (SI: <456 mmol/d)
Phosphate ---------- 0.9-1.3 g/24 h (SI: 29.1-42.0 mmol/d)
Potassium ----------17-77 mEq/24 h (SI: 17-77 mmol/d)
Sodium ----------40-217 mEq/24 h (SI: 40-217 mmol/d)
Uric acid ----------<800 mg/24 h (SI: <4.7 mmol/d)

Saliva

Cortisol (salivary), midnight --------- <0.13 µg/dL (SI: <3.6 nmol/L)

Semen

Semen analysis----------->20 million sperm/mL; >50% motility

QUESTIONS

ENDOCRINE BOARD REVIEW

Adrenal, Section 1 Board Review

Hans K. Ghayee, DO

1 During a workup for hematuria, a 32-year-old woman is found to have metastatic renal cell carcinoma. Staging CT also shows a pancreatic neuroendocrine tumor and a paraspinous mass with nodal metastasis. The patient is adopted, and her family history is unavailable.

Initial laboratory test results:

Plasma normetanephrine = 900 pg/mL (<165 pg/mL) (SI: 4.9 nmol/L [<0.90 nmol/L])
Sodium = 136 mEq/L (136-142 mEq/L) (SI: 136 mmol/L [136-142 mmol/L])
Potassium = 4.2 mEq/L (3.5-5.0 mEq/L) (SI: 4.2 mmol/L [3.5-5.0 mmol/L])
Calcium = 9.6 mg/dL (8.2-10.2 mg/dL) (SI: 2.4 mmol/L [2.1-2.6 mmol/L])
Creatinine = 2.5 mg/dL (0.6-1.1 mg/dL) (SI: 221 μmol/L [53.0-97.2 μmol/L])
Hematocrit = 38% (35%-45%) (SI: 0.38 [0.35-0.45])

Belzutifan is initiated to treat metastatic renal cell carcinoma. A repeat CT several months later shows shrinkage of the kidney lesions and the paraspinous mass.

On physical examination, her blood pressure is 125/85 mm Hg, and pulse rate is 91 beats/min. Examination findings are normal.

A germline driver variant in which of the following genes is the most likely cause of her tumors?

A. *MEN1* (multiple endocrine neoplasia type 1)
B. *EPAS1* (endothelial PAS domain protein 1)
C. *NF1* (neurofibromin 1)
D. *RET* (RET proto-oncogene)
E. *VHL* (von Hippel-Lindau tumor suppressor)

2 A 21-year-old woman with classic congenital adrenal hyperplasia (21-hydroxylase deficiency) presents for a follow-up visit for hirsutism. She shaves her facial hair several times per week. Her medications include hydrocortisone, 10 mg at 7 AM, 10 mg at 3 PM, and 10 mg at bedtime. She also takes fludrocortisone, 0.05 mg daily.

On physical examination, her BMI is 24 kg/m^2, and blood pressure is 132/70 mm Hg.

Laboratory test results:

Sodium = 141 mEq/L (136-142 mEq/L) (SI: 141 mmol/L [136-142 mmol/L])
Potassium = 3.8 mEq/L (3.5-5.0 mEq/L) (SI: 3.8 mmol/L [3.5-5.0 mmol/L])
Creatinine = 1.0 mg/dL (0.6-1.1 mg/dL) (SI: 88.4 μmol/L [53.0-97.2 μmol/L])
Glucose = 101 mg/dL (<100 mg/dL) (SI: mmol/L [<5.6 mmol/L])
17-hydroxyprogesterone = 8700 ng/dL (<80 ng/dL [follicular]) (SI: 263.6 nmol/L [<2.42 nmol/L])
Androstenedione = 820 ng/dL (30-200 ng/dL) (SI: 28.6 nmol/L [1.05-6.98 nmol/L])
Hemoglobin A_{1c} = 6.1% (4.0%-5.6%) (43 mmol/mol [20-38 mmol/mol])

Which of the following medications should be added to improve this patient's symptoms?

A. Corticotropin-releasing factor type 1 receptor antagonist
B. 11β-Hydroxylase (CYP11β1) inhibitor
C. GLP-1 receptor agonist
D. Mineralocorticoid receptor agonist
E. Selective thyroid hormone receptor-β agonist

3 A 33-year-old man who emigrated from rural Africa presents to the hospital with abdominal pain. CT shows a 6-cm left adrenal mass and a 10-cm right adrenal mass (Hounsfield units are –10 bilaterally). He has been fatigued for several years. The CT also identifies a testicular lesion. In the report, the radiologist notes, "Considering the large size of the adrenal masses, the differential diagnosis includes adrenal cortical carcinoma with metastasis to the testicle." He is referred to the medical oncology clinic for further evaluation.

On physical examination, his blood pressure is 111/80 mm Hg, pulse rate is 91 beats/min, and temperature is 98.6°F (37°C).

Laboratory test results:

Plasma normetanephrine = 161 pg/mL (<165 pg/mL) (SI: 0.88 nmol/L [<0.90 nmol/L])
Sodium = 141 mEq/L (136-142 mEq/L) (SI: 141 mmol/L [136-142 mmol/L])
Potassium = 4.3 mEq/L (3.5-5.0 mEq/L) (SI: 4.3 mmol/L [3.5-5.0 mmol/L])
Calcium = 10.0 mg/dL (8.2-10.2 mg/dL) (SI: 2.5 mmol/L [2.1-2.6 mmol/L])
Creatinine = 1.0 mg/dL (0.7-1.3 mg/dL) (SI: 88.4 μmol/L [61.9-114.9 μmol/L])
Hematocrit = 45% (35%-45%) (SI: 0.45 [0.35-0.45])

A colleague in medical oncology asks whether any studies are recommended before starting mitotane, given the high clinical suspicion of adrenal cortical carcinoma.

Which of the following laboratory assessments should be performed before proceeding with the treatment recommended by medical oncology?

A. ACTH, 17-hydroxyprogesterone, cortisol
B. ACTH, 17-hydroxyprogesterone, testosterone
C. DHEA-S, TSH, prolactin
D. 1-mg dexamethasone-suppression test
E. Repeat metanephrines, renin, DHEA-S

4 A 42-year-old woman is referred to rule out an endocrine cause of secondary hypertension. Several years ago, she had chest pain and noticed an irregular pulse. However, when she presented to the hospital, she was told she had an anxiety attack. A Holter monitor did not show any arrhythmias. A whole-body CT in the emergency department did not show pulmonary embolism or abdominal masses. Morning aldosterone and plasma renin activity have been measured several times in a laboratory that uses liquid chromatography–tandem mass spectrometry. The lab results are all similar. She has never had documented low potassium. She has no history of myocardial infarction, stroke, or vascular disease. Medications include amlodipine, 10 mg daily, and lisinopril, 5 mg daily.

On physical examination, her blood pressure is 141/90 mm Hg. Examination findings are normal.

Laboratory test results:

Sodium = 140 mEq/L (136-142 mEq/L) (SI: 140 mmol/L [136-142 mmol/L])
Potassium = 4.0 mEq/L (3.5-5.0 mEq/L) (SI: 4.0 mmol/L [3.5-5.0 mmol/L])
Aldosterone = 8.5 ng/dL (4-21 ng/dL) (SI: 235.8 pmol/L [111.0-582.5 pmol/L])
Plasma renin activity = <0.6 ng/mL per h (0.6-4.3 ng/mL per h)
Creatinine = 1.0 mg/dL (0.6-1.1 mg/dL) (SI: 88.4 μmol/L [53.0-97.2 μmol/L])

Which of the following is the best next step in this patient's management?

A. Discuss treatment options for hyperaldosteronism
B. Measure plasma metanephrines
C. Perform a dexamethasone-suppression test
D. Repeat measurement of aldosterone and plasma renin activity in 1 year
E. Nothing; the patient does not have primary hyperaldosteronism

ANSWERS

ENDOCRINE BOARD REVIEW

Adrenal, Section 1 Board Review

Hans K. Ghayee, DO

1 ANSWER: E) *VHL* (von Hippel-Lindau tumor suppressor)

This patient has a pathogenic variant in the *VHL* gene (Answer E), which causes von Hippel-Lindau syndrome, characterized by hemangioblastoma, renal cell carcinoma, epididymal cystadenoma, pancreatic neuroendocrine tumors, retinal abnormalities, and pheochromocytoma/paraganglioma. Belzutifan, a hypoxia-inducible factor 2α inhibitor, was initially approved by the US FDA in 2021 for *VHL*-related pancreatic neuroendocrine tumors and renal cell carcinoma. Following the LITESPARK-015 trial of belzutifan in metastatic pheochromocytoma/paraganglioma, it was approved for the treatment of advanced metastatic disease. The *Table* lists the clinical manifestations of germline driver variants in other genes.

EDUCATIONAL OBJECTIVE

Identify key genetic drivers associated with endocrine neoplasias.

REFERENCE(S)

Crona J, Taïeb D, Pacak K. New perspectives on pheochromocytoma and paraganglioma: toward a molecular classification. *Endocr Rev*. 2017;38(6):489-515. PMID: 28938417

Jimenez C, Andreassen M, Durand A, Moog S, Hendifar A, Welin S, et al; LITESPARK-015 Investigators. Belzutifan for advanced pheochromocytoma or paraganglioma. *N Engl J Med*. 2025;393(20):2012-2022. PMID: 41124218

Table. Genetic Drivers Associated With Adrenal or Neuroendocrine Tumors

Gene	Syndrome	Inheritance	Manifestations
MEN1	Multiple endocrine neoplasia type 1	Autosomal dominant	Pancreatic neuroendocrine tumors, primary hyperparathyroidism, pituitary tumors
RET	Multiple endocrine neoplasia type 2	Autosomal dominant	Multiple endocrine neoplasia type 2A: medullary thyroid carcinomas, parathyroid adenomas, pheochromocytomas/paragangliomas Multiple endocrine neoplasia type 2B: medullary thyroid carcinoma, mucosal neuromas, dysmorphic features, pheochromocytomas/paragangliomas
EPAS1	PPGL–somatostatinoma–polycythemia syndrome (Pacak-Zhuang syndrome)	Sporadic/not inherited (postzygotic mosaicism)	Polycythemia, somatostatinomas, retinal abnormalities, organ cysts, pheochromocytomas/paragangliomas
VHL	von Hippel-Lindau syndrome	Autosomal dominant	Hemangioblastoma, renal cell carcinomas, epididymal cystadenomas, pancreatic neuroendocrine tumors, retinal abnormalities, pheochromocytomas/paragangliomas
NF1	Neurofibromatosis type 1	Autosomal dominant	Café-au-lait spots, Lisch nodules in the eye, neurofibromas, learning disabilities, dysmorphic features, skeletal abnormalities, pheochromocytomas/paragangliomas

2 ANSWER: A) Antagonist to corticotropin-releasing factor type 1 receptor

This patient has hyperandrogenism and classic congenital adrenal hyperplasia (CAH). Crinecerfont is a corticotropin-releasing factor type 1 receptor (CRF-1) antagonist (Answer A) developed to reduce androstenedione levels. In a phase 3 clinical trial of patients with classic 21-hydroxylase deficiency treated with a CRF-1 antagonist, daily glucocorticoid doses were reduced by 27% in the crinecerfont-treated group compared with 10% in the placebo group, and androstenedione levels decreased. In 2024, the US FDA approved the use of crinecerfont as adjunctive therapy to glucocorticoids for patients with classic CAH who may have elevated androgens.

Adding a GLP-1 receptor agonist (Answer C) would not address her symptoms associated with elevated androgens.

Selective thyroid hormone receptor-β agonists (Answer E) are used to treat metabolic dysfunction-associated steatotic liver disease (MASLD). There is no indication of MASLD in this patient.

11β-Hydroxylase (CYP11β1) inhibitors (Answer B) are approved for treating hypercortisolism, not CAH. In addition, an adverse effect in some women is elevated testosterone, which can cause hirsutism.

Adding a mineralocorticoid receptor agonist (Answer D) would not help the patient's hirsutism.

EDUCATIONAL OBJECTIVE

Recommend a corticotropin-releasing factor type 1 receptor antagonist as adjunctive therapy to glucocorticoids for patients with classic congenital adrenal hyperplasia and hyperandrogenism.

REFERENCE(S)

Auchus RJ, Hamidi O, Pivonello R, Bancos I, Russo G, Witchel SF, et al; CAHtalyst Adult Trial Investigators. Phase 3 trial of crinecerfont in adult congenital adrenal hyperplasia. *N Engl J Med.* 2024;391(6):504-514. PMID: 38828955

3 ANSWER: A) ACTH, 17-hydroxyprogesterone, cortisol

This patient has undiagnosed congenital adrenal hyperplasia (CAH). Because newborn screening for CAH is unavailable in many resource-limited settings, simple virilizing classic CAH can remain undiagnosed until adulthood, as in this patient. The Hounsfield units on the CT were –10 bilaterally, consistent with adrenal myelolipomas. The medical team was concerned about the bilateral enlargement. The testicular mass is a testicular adrenal rest tumor. The patient should be tested for CAH by measuring early-morning 17-hydroxyprogesterone, ACTH, and cortisol (Answer A).

Although tests assessing thyroid function and the gonadal axis (Answers B and C) are helpful before starting mitotane, this patient does not have adrenal cortical carcinoma.

As the patient has CAH, performing a dexamethasone-suppression test (Answer D) is unnecessary. Instead, he should be checked for adrenal insufficiency.

Repeating metanephrine measurement and measuring renin and DHEA-S (Answer E) would not establish the diagnosis. The normetanephrine value is normal, and the fat-density masses are not pheochromocytomas.

EDUCATIONAL OBJECTIVE

Diagnose congenital adrenal hyperplasia in the workup of an adrenal mass.

REFERENCE(S)

Fassnacht M, Tsagarakis S, Terzolo M, Tabarin A, Sahdev A, Newell-Price J, et al. European Society of Endocrinology clinical practice guidelines on the management of adrenal incidentalomas, in collaboration with the European Network for the Study of Adrenal Tumors. *Eur J Endocrinol.* 2023;189(1):G1-G42. PMID: 37318239

4 ANSWER: A) Discuss treatment options for hyperaldosteronism

This patient has primary hyperaldosteronism. According to the 2025 Endocrine Society guidelines, a positive screen for primary hyperaldosteronism is indicated by an aldosterone concentration ≥10 ng/dL

(≥277 pmol/L) on an immunoassay and a suppressed plasma renin activity, or by an aldosterone concentration ≥7.5 ng/dL (≥208 pmol/L) on liquid chromatography–tandem mass spectrometry (LC-MS/MS) and a suppressed plasma renin activity. In this case, the patient's laboratory used LC-MS/MS rather than an immunoassay. The patient has a positive screen for primary hyperaldosteronism, and the likelihood of lateralization is low, given her aldosterone concentration of 8.5 ng/dL (235.8 pmol/L) on LC-MS/MS and normokalemia. The best next step is to discuss treatment options for hyperaldosteronism (Answer A) with a mineralocorticoid receptor antagonist. Adrenal venous sampling can be discussed, but given that she is unlikely to have lateralization, it was not provided as an answer option.

Because the patient has primary hyperaldosteronism, repeating aldosterone and renin measurements in 1 year (Answer D) or recommending no treatment (Answer E) is incorrect.

There are no chest or abdominal masses to suggest a pheochromocytoma/paraganglioma or a cortisol-secreting tumor, so measuring plasma metanephrines (Answer B) or performing a dexamethasone-suppression test (Answer C) is incorrect.

EDUCATIONAL OBJECTIVE

Apply assay-specific aldosterone thresholds (liquid chromatography–tandem mass spectrometry vs immunoassay) when interpreting primary hyperaldosteronism screening tests.

REFERENCE(S)

Adler GK, Stowasser M, Correa RR, Khan N, Kline G, McGowan MJ, et al. Primary aldosteronism: an Endocrine Society clinical practice guideline [published correction appears in *J Clin Endocrinol Metab.* 2025;110(11):e3933-e3934]. *J Clin Endocrinol Metab.* 2025;110(9):2453-2495. PMID: 40658480

Brown JM, Auchus RJ, Honzel B, Luther JM, Yozamp N, Vaidya A. Recalibrating interpretations of aldosterone assays across the physiologic range: immunoassay and liquid chromatography-tandem mass spectrometry measurements under multiple controlled conditions. *J Endocr Soc.* 2022;6(6):bvac049. PMID: 35475027