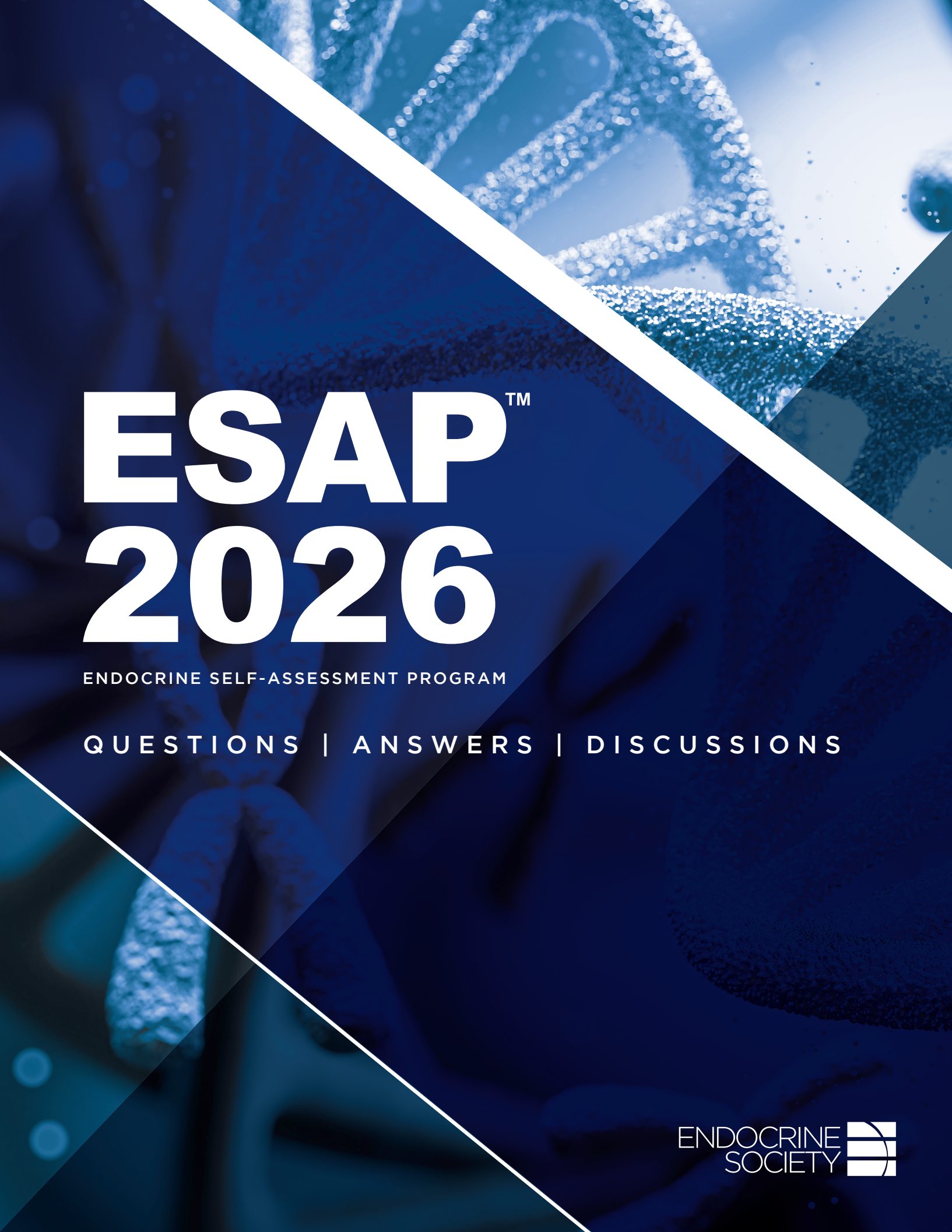

ESAP™ 2026

ENDOCRINE SELF-ASSESSMENT PROGRAM

QUESTIONS | ANSWERS | DISCUSSIONS

ENDOCRINE SOCIETY

ESAP™ 2026

Endocrine Society's Endocrine Self-Assessment Program Questions, Answers, and Discussions

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ENDOCRINE SOCIETY
Hormone Science to Health

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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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OVERVIEW

The *Endocrine Self-Assessment Program* (ESAP™) is a self-study curriculum designed for physicians looking to reinforce existing knowledge, identify knowledge gaps, and stay current with the latest advances in endocrinology. ESAP 2026 is available in both book and online formats. It consists of 120 brand-new multiple-choice questions in all areas of endocrinology, diabetes, and metabolism. There is extensive discussion of each correct answer, a comprehensive syllabus, and references. ESAP is updated annually with new questions and new syllabus materials. ESAP is composed of two key components: the online interactive module and the book. Upon purchase, learners initially receive access to the online module. To use ESAP as a true self-assessment tool, learners are strongly encouraged to complete the online interactive self-assessment module first before continuing self-study with the book; the online module may be accessed at education.endocrine.org.

ACCREDITATION STATEMENT

The Endocrine Society is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The Endocrine Society has received Accreditation with Commendation. The Endocrine Society designates this enduring material for a maximum of 40.0 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

MAINTENANCE OF CERTIFICATION

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 40 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.

LEARNING OBJECTIVES

ESAP 2026 allows learners to assess their knowledge of all aspects of endocrinology, diabetes, and metabolism.

Upon completion of this educational activity, learners will be able to:

- Recognize clinical manifestations of endocrine and metabolic disorders and select among current options for diagnosis, management, and therapy.
- Identify risk factors for endocrine and metabolic disorders and develop strategies for prevention.
- Evaluate endocrine and metabolic manifestations of systemic disorders.
- Use existing resources pertaining to clinical guidelines and treatment recommendations for endocrine and related metabolic disorders to guide diagnosis and treatment.

TARGET AUDIENCE

ESAP is a self-study curriculum designed for physicians looking to reinforce existing knowledge, identify knowledge gaps, and stay current with the latest advances in endocrinology.

STATEMENT OF INDEPENDENCE

As a provider of CME accredited by the Accreditation Council for Continuing Medical Education, the Endocrine Society has a policy of ensuring 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 ESAP Faculty Working Group.

DISCLOSURE POLICY

The faculty, committee members, and staff who are in position to control the content of this activity are required to disclose to the Endocrine Society and to learners any relevant financial relationship(s) of the individual or spouse/partner that have occurred within the last 12 months with any commercial interest(s) whose products or services are related to the CME content. Financial relationships are defined by remuneration in any amount from the commercial interest(s) in the form of grants; research support; consulting fees; salary; ownership interest (eg, stocks, stock options, or ownership interest excluding diversified mutual funds); honoraria or other payments for participation in speakers' bureaus, advisory boards, or boards of directors; or other financial benefits. The intent of this disclosure is not to prevent CME planners with relevant financial relationships from planning or delivering content, but rather to provide learners with information that allows them to make their own judgments of whether these financial relationships may have influenced the educational activity with regard to exposition or conclusion. The Endocrine Society has reviewed all disclosures and resolved or managed all identified conflicts of interest, as applicable.

The following faculty reported relevant financial relationship(s): **Bradley D. Anawalt, MD,** is a consultant for Biozen and the United States Anti-Doping Agency. **Erik A. Imel, MD,** is a clinical trial investigator for Ultragenyx, Alexion, Amgen, Amolyt, Kyowa Kirin, Calciolytix, Spruce, Neurocrine, and Sanofi. He serves

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The following faculty reported no relevant financial relationships: **Danit Ariel, MD, MS; Palak Choksi, MD; David Cooper, MD; Aoife Egan, MD; Angela M. Leung, MD, MSc; Deepika Reddy, MD; Meera Shah, MB ChB; Anu Sharma, MBBS;** and **Vinaya Simha, MBBS, MD**.

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

The Endocrine Society staff associated with the development of content for this activity reported no relevant financial relationships.

DISCLAIMERS

The information presented in this activity represents the opinion of the faculty and is not necessarily the official position of the Endocrine Society.

USE OF PROFESSIONAL JUDGMENT:

The educational content in this self-assessment test relates to basic principles of diagnosis and therapy and does not substitute for individual patient assessment based on the health care provider's examination of the patient and consideration of laboratory data and other factors unique to the patient. Standards in medicine change as new data become available.

DRUGS AND DOSAGES:

When prescribing medications, the physician is advised to check the product information sheet accompanying each drug to verify conditions of use and to identify any changes in drug dosage schedule or contraindications.

POLICY ON UNLABELED/OFF-LABEL USE

The Endocrine Society has determined that disclosure of unlabeled/off-label or investigational use of commercial product(s) is informative for audiences and therefore requires this information to be disclosed to the learners at the beginning of the presentation. Uses of specific therapeutic agents, devices, and other products discussed in this educational activity may not be the same as those indicated in product labeling approved by the Food and Drug Administration (FDA). The Endocrine Society requires that any discussions of such "off-label" use be based on 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.

PRIVACY AND CONFIDENTIALITY STATEMENT

The Endocrine Society will record learners' personal information as provided on CME evaluations to allow for issuance and tracking of CME certificates. The Endocrine Society may also track aggregate responses to questions in activities and evaluations and use these data to inform the ongoing evaluation and improvement of its CME program. No individual performance data or any other personal information collected from evaluations will be shared with third parties.

ACKNOWLEDGMENT OF COMMERCIAL SUPPORT

This activity is not supported by educational grant(s) or other funds from any commercial supporter.

AMA PRA CATEGORY 1 CREDIT (CME) INFORMATION

To receive a maximum of 40.0 *AMA PRA Category 1 Credits*, participants must complete the learning mode of the online interactive module and activity evaluation located at education.endocrine.org. Participants must achieve a minimum score of 70% to claim CME credit within three attempts. After initially completing the module, if participants do not achieve a minimum score of 70%, they have the option to re-take questions that were marked incorrect to achieve a passing score.

METHOD OF PARTICIPATION

This enduring material is presented online and in book format. The estimated time to complete this activity, including review of material, is 40 hours. Participants must achieve a minimum score of 70% to claim CME credit and MOC points. After initially completing the module(s), if participants do not achieve a minimum score of 70%, they have the option to re-take questions that were marked incorrect to achieve a passing score.

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 Web browser. In addition, cookies and Javascript must be enabled in the browser's options.

LAST REVIEW DATE: December 2025

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For questions about content or obtaining CME credit or MOC points, please contact the Endocrine Society by visiting: endocrine.org/education-and-training.

Laboratory Reference Ranges

Reference ranges vary among laboratories. The listed reference ranges should be used when interpreting laboratory values presented in ESAP™. 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: <0.1 ng/mL [SI: <0.1 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: 70.79-160.88 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)

Cortisol (4 PM)----2-14 µg/dL (SI: 55.2-386.2 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) ----------
1.0-13.0 mIU/mL (SI: 1.0-13.0 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 ---------- <6.3 mg/dL (SI: <0.6 mmol/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: 1.1-6.9 pmol/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

Abbreviations

ACTH ---------- corticotropin
ACE inhibitor---------- angiotensin-converting enzyme inhibitor
ALT ---------- alanine aminotransferase
AST ---------- aspartate aminotransferase
BMI ---------- body mass index
CDC ---------- Centers for Disease Control and Prevention
CNS ---------- central nervous system
CT ---------- computed tomography
DHEA ---------- dehydroepiandrosterone
DHEA-S---------- dehydroepiandrosterone sulfate
DNA ---------- deoxyribonucleic acid
DPP-4 inhibitor ---------- dipeptidyl-peptidase 4 inhibitor
DXA---------- dual-energy x-ray absorptiometry
FDA ---------- Food and Drug Administration
FGF-23 ---------- fibroblast growth factor 23
FNA ---------- fine-needle aspiration
FSH ---------- follicle-stimulating hormone
GH ---------- growth hormone
GHRH---------- growth hormone–releasing hormone
GLP-1 receptor agonist----- glucagonlike peptide 1 receptor agonist
GnRH ---------- gonadotropin-releasing hormone
hCG ---------- human chorionic gonadotropin
HDL ---------- high-density lipoprotein
HIV---------- human immunodeficiency virus
HMG-CoA reductase inhibitor ---------- 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor
IGF-1---------- insulinlike growth factor 1
LDL ---------- low-density lipoprotein
LH ---------- luteinizing hormone
MCV ---------- mean corpuscular volume
MIBG---------- *meta*-iodobenzylguanidine
MRI ---------- magnetic resonance imaging
NPH insulin ---------- neutral protamine Hagedorn insulin
PCSK9 inhibitor---- proprotein convertase subtilisin/kexin 9 inhibitor
PET ---------- positron emission tomography
PSA ---------- prostate-specific antigen
PTH ---------- parathyroid hormone
PTHrP---------- parathyroid hormone–related protein
SGLT-2 inhibitor ---------- sodium-glucose cotransporter 2 inhibitor
SHBG ---------- sex hormone–binding globulin
T_3 ---------- triiodothyronine
T_4 ---------- thyroxine
TPO antibodies ---------- thyroperoxidase antibodies
TRH ---------- thyrotropin-releasing hormone
TRAb ---------- TSH-receptor antibodies
TSH ---------- thyrotropin
VLDL---------- very low-density lipoprotein

QUESTIONS

ENDOCRINE SELF-ASSESSMENT PROGRAM 2026

Part I

1 A 34-year-old woman presents for review of postpartum glucose testing completed earlier this week. In her recent pregnancy, she had gestational diabetes that was managed with medical nutritional therapy, exercise, and once-daily basal insulin. She had a normal vaginal delivery 12 weeks ago and is breastfeeding her baby. Her BMI is currently 27 kg/m^2. Her 75-g oral glucose tolerance test documented a fasting glucose concentration of 112 mg/dL (6.2 mmol/L) and a 2-hour glucose concentration of 132 mg/dL (7.3 mmol/L). Her hemoglobin A_{1c} value is 5.9% (41 mmol/mol). Her mother and maternal aunt have type 2 diabetes.

In addition to lifestyle recommendations, which of the following medications would be best to prescribe?

A. Empagliflozin
B. Metformin
C. Pioglitazone
D. Semaglutide
E. Tirzepatide

2 A 48-year-old woman presents with a 3-month history of absent menses and recent breast tenderness. Her last menstrual period was 2 months ago. She had 2 spontaneous and uncomplicated pregnancies at age 22 and 24 years. She has no galactorrhea, headaches, or hot flashes. She reports progressive weight gain over the past year (15 lb [6.8 kg]), which seems to have accelerated in the last 2 months. She takes no medications.

Her medical history is remarkable for a 6-mm pituitary adenoma diagnosed at age 38 years when she experienced oligomenorrhea. At that time, her prolactin concentration was 120 ng/mL (5.22 nmol/L). Bromocriptine, 5 mg daily, subsequently normalized menses and prolactin levels. She took bromocriptine until 3 months ago when she relocated and could not obtain a refill.

On physical examination, her blood pressure is 122/80 mm Hg and pulse rate is 89 beats/min. Her height is 64.6 in (164 cm), and weight is 163.1 lb (74 kg) (BMI = 27.5 kg/m^2). She has generalized fat distribution without supraclavicular or dorsocervical fat accumulation. There is no acral enlargement, acne, hirsutism, or striae. Visual fields are normal to confrontation.

Laboratory tests from 6 months ago indicate normal results on a chemistry panel, complete blood cell count, and hemoglobin A_{1c} measurement.

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

A. Measure FSH
B. Measure IGF-1
C. Measure prolactin
D. Measure urine hCG
E. Obtain pituitary gland imaging

3 A 63-year-old man is seen for evaluation of hypercalcemia. He was first noted to have mild hypercalcemia (10.5 mg/dL [2.63 mmol/L]) 6 months ago. On recent measurement, his calcium concentration is still elevated at 10.7 mg/dL (2.68 mmol/L). He has no fatigue, difficulty concentrating, flank pain, fragility fractures, recurrent falls, or kidney stones. He often goes hours without drinking any fluids. His mother has a history of osteoporosis and fractured her right hip after a fall at age 72 years. His father is healthy and has no notable medical history. There is no family history of nephrolithiasis. The patient does not smoke cigarettes, and he drinks 7 to 8 units of alcohol per week. His medical history is relevant for hypertension, hyperlipidemia, and lactose intolerance.

Medications are carvedilol, 25 mg twice daily; simvastatin, 40 mg daily at bedtime; and a daily multivitamin containing calcium, 600 mg, and vitamin D, 25 mcg (1000 international units).

On physical examination, his blood pressure is 126/74 mm Hg and pulse rate is 73 beats/min. His height is 68 in (172.7 cm) (similar to his peak adult height), and weight is 220 lb (99.8 kg) (BMI = 33.4 kg/m^2). The thyroid gland is normal with no palpable nodules. His abdomen is soft with no tenderness or organomegaly. His skin has normal turgor and no hyperpigmentation. On musculoskeletal exam, he has normal spinal curvature and no spinal or paraspinal tenderness. The rest of the physical examination findings are unremarkable.

Laboratory test results:

Calcium = 10.6 mg/dL (8.2-10.2 mg/dL) (SI: 2.64 mmol/L [2.1-2.6 mmol/L])
Intact PTH = 82 pg/mL (10-65 pg/mL) (SI: 8.7 pmol/L [1.1-6.9 pmol/L])
Creatinine = 1.1 mg/dL (0.7-1.3 mg/dL) (SI: μmol/L [61.9-114.9 μmol/L])
Phosphate = 2.5 mg/dL (2.3-4.7 mg/dL) (SI: 0.8 mmol/L [0.7-1.5 mmol/L])
Complete blood cell count, normal
AST = 45 U/L (20-48 U/L) (SI: 0.75 μkat/L [0.33-0.80 μkat/L])
ALT = 52 U/L (10-40 U/L) (SI: 0.87 μkat/L [0.17-0.67 μkat/L])
Bilirubin, normal
25-Hydroxyvitamin D = 32 ng/mL (30-80 ng/mL [optimal]) (SI: 79.9 nmol/L [74.9-199.7 nmol/L])
Albumin = 3.9 mg/dL (3.5-5.0 g/dL) (SI: 39 g/L [35-50 g/L])
Urinary calcium = 220 mg/24 h (100-300 mg/24 h) (SI: 5.5 mmol/d [2.5-7.5 mmol/d])
Urinary creatinine = 1.4 g/24 h (1.0-2.0 g/24 h) (SI: 12.4 mmol/d [8.8-17.7 mmol/d])
Urine volume = 2400 mL/24 h

X-ray findings of the kidneys, ureters, and bladder are normal. On DXA, the lowest T-score is –0.9 at the lumbar spine, –0.9 at the left total hip, 0.8 at the left femoral neck, and –1.4 at the distal one-third of the nondominant forearm. His FRAX score is 10% for major osteoporotic fracture and 0.5% for hip fracture.

Which of the following is the best management option for this patient?

A. Monitor serum calcium every 6 to 12 months
B. Monitor 24-hour urinary calcium every 12 months
C. Refer to surgery for parathyroidectomy
D. Start alendronate
E. Start cinacalcet

4 A 52-year-old woman with a 10-year history of type 2 diabetes presents for a follow-up appointment. Her medical history is notable for coronary artery disease, atrial fibrillation, hypertension, dyslipidemia, and diabetic neuropathy. Her medication regimen consists of insulin glargine, 34 units subcutaneous daily; short-acting insulin, 10 units with meals; semaglutide, 1 mg weekly; and metformin, 500 mg twice daily.

Her current hemoglobin A_{1c} value is 8.2% (66 mmol/mol). She describes night sweats for the last 3 months that occur 2 to 3 times per week. Her current BMI is 29.5 kg/m^2. The patient brings her glucose meter to her appointment, and review of the glucose values shows that the patient usually checks in the morning and before meals. Her average point-of-care glucose value in the morning is 161 mg/dL (8.9 mmol/L). Her average point-of-care glucose value before meals is 182 mg/dL (10.1 mmol/L).

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

A. Continue current management
B. Discontinue insulin glargine
C. Increase the insulin glargine dosage
D. Increase the short-acting insulin aspart dosage
E. Recommend a continuous glucose monitoring device

5 A 28-year-old woman is seen in urgent care after twisting her ankle while dancing. Besides a swollen right ankle, the physician also notes slight bilateral thickening of the Achilles tendons. She has no history of lower-extremity pain or injury, and her only significant medical history is a prolonged episode of epistaxis as a teenager. Her brother has a diagnosis of idiopathic thrombocytopenic purpura, but he has never received treatment.

On physical examination, her blood pressure is 116/74 mm Hg and pulse rate is 70 beats/min. Her height is 64 in (162.6 cm), and weight is 135 lb (61.2 kg) (BMI = 23.2 kg/m^2). The rest of the examination findings are normal. There is no corneal arcus or thickening of the extensor tendons on the hands, but bilateral Achilles tendon thickening is noted.

Laboratory test results:

White blood cell count = 9800/μL (4500-11,000/μL) (SI: 9.8×10^9/L [4.5-11.0 × 10^9/L])
Hemoglobin = 14 g/dL (12.1-15.1 g/dL) (SI: 140 g/L [121-151 g/L])
Platelet count = 96×10^3/μL ($150-450 \times 10^3$/μL) (SI: 96×10^9/L [$150-450 \times 10^9$/L])
Plasma glucose = 88 mg/dL (70-99 mg/dL) (SI: 4.9 mmol/L [3.9-5.5 mmol/L])
Total bilirubin = 0.9 mg/dL (0.3-1.2 mg/dL) (SI: 15.4 μmol/L [5.1-20.5 μmol/L])
ALT = 34 U/L (10-40 U/L) (SI: 0.57 μkat/L [0.17-0.67 μkat/L])
AST = 36 U/L (20-48 U/L) (SI: 0.60 μkat/L [0.33-0.80 μkat/L])
Total cholesterol = 160 mg/dL (<200 mg/dL [optimal]) (SI: 4.14 mmol/L [<5.18 mmol/L])
Triglycerides = 135 mg/dL (<150 mg/dL [optimal]) (SI: 1.53 mmol/L [<1.70 mmol/L])
HDL cholesterol = 60 mg/dL (>60 mg/dL [optimal]) (SI: 1.55 mmol/L [>1.55 mmol/L])

No fractures are evident on foot x-ray.

She is prescribed an ankle boot, ice packs, and analgesics with instructions to follow-up if there is worsening pain or swelling.

Which of the following should also be advised?

A. Carotid ultrasonography
B. Hematology consultation for low platelet count
C. Measurement of lipoprotein (a)
D. Measurement of plasma sitosterol
E. Testing for *CYP27A1* pathogenic variants

ANSWERS

ENDOCRINE SELF-ASSESSMENT PROGRAM 2026

Part II

1 ANSWER: B) Metformin

This patient's results from the postpartum 75-g oral glucose tolerance test are consistent with a diagnosis of prediabetes because the fasting value is in the range of 100 to 125 mg/dL (5.6-6.9 mmol/L). Her hemoglobin A_{1c} value is also consistent with prediabetes, as it is in the range of 5.7% to 6.4% (39-47 mmol/mol). The presence of prediabetes, combined with a BMI in the overweight range and a first-degree relative with type 2 diabetes, significantly increases her risk of developing type 2 diabetes. The prior diagnosis of gestational diabetes is an additional, strong risk factor for type 2 diabetes. Following the diagnosis of gestational diabetes, the risk of developing type 2 diabetes increases throughout an individual's lifetime—approximately 20% 10 years after diagnosis and a total lifetime risk of approximately 60%. For individuals who have prediabetes in the context of overweight/obesity and a history of gestational diabetes, the American Diabetes Association recommends intensive lifestyle interventions and/or metformin to prevent progression to type 2 diabetes. This recommendation is based on findings from the Diabetes Prevention Program, which found that intensive lifestyle intervention and metformin reduced the progression to diabetes over 10 years by 35% and 40%, respectively, compared with placebo. Because long-term adherence to behavior changes can be difficult, pharmacotherapy is generally considered for patients at highest risk of type 2 diabetes, such as the individual described in this vignette. Metformin (Answer B) is the best medication to prescribe in this scenario. Metformin is weight neutral and safe to take while breastfeeding, as data from well-conducted studies demonstrate that metformin concentrations are low in human milk. Furthermore, this medication is considered safe during pregnancy, which may be a future consideration for this patient.

Alternative glucose-lowering agents, including SGLT-2 inhibitors (eg, empagliflozin [Answer A]), thiazolidinediones (eg, pioglitazone [Answer C]), and GLP-1 receptor agonists (eg, semaglutide [Answer D]) or combined glucose-dependent insulinotropic polypeptide (GIP) receptor and GLP-1 receptor agonists (eg, tirzepatide [Answer E]), have also shown efficacy in reducing progression from prediabetes to type 2 diabetes. However, metformin has the strongest evidence base and safety profile, particularly among those with a history of gestational diabetes. While semaglutide and tirzepatide are indicated for the treatment of obesity, this patient does not meet typical treatment criteria. Criteria include a BMI of 30 kg/m^2 or higher or a BMI of 27 kg/m^2 or higher with a weight-related comorbid condition, such as hypertension, dyslipidemia, type 2 diabetes, obstructive sleep apnea, or cardiovascular disease. None of these alternative agents is considered safe during pregnancy, and data on their use during lactation are limited.

Educational Objective

Explain the benefit of metformin in preventing type 2 diabetes in women with a history of gestational diabetes.

Reference(s)

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2 ANSWER: D) Measure urine hCG

Evaluation for pregnancy (Answer D) is essential in premenopausal and perimenopausal women with oligomenorrhea or amenorrhea. The differential diagnosis of oligomenorrhea in this 48-year-old woman also includes perimenopause and hyperprolactinemia after stopping bromocriptine. Since pregnancy is still possible in the early stages of perimenopause, this should be ruled out first. Breast tenderness and abrupt cessation of menses are highly suspicious for pregnancy.

Once pregnancy is excluded, prolactin measurement (Answer C) is indicated to determine the biochemical status of the prolactin-secreting tumor after stopping the dopamine agonist. Menopause is associated with a decrease in prolactin secretion. Therefore, reducing the dosage or stopping the dopamine agonist should be considered in perimenopausal or postmenopausal women with prolactin-secreting adenomas measuring 10 mm or less in largest diameter (microprolactinomas). Studies have shown that almost 50% of patients maintain a normal prolactin concentration despite stopping the medication. Studies in menopausal patients have been small, making it difficult to identify predictors of normoprolactinemia after dopamine agonist withdrawal in this patient population. The Pituitary Society guidelines recommend a trial of medication cessation in menopausal women with microprolactinomas, with subsequent monitoring of prolactin. Conversely, women with macroprolactinomas usually require continuation of medical therapy for tumor control.

Acromegaly is unlikely in this case. Although the vignette does not include the patient's IGF-1 concentration before starting bromocriptine, she has no clinical signs or comorbidities of acromegaly, and her clinical course on bromocriptine has been favorable. Baseline IGF-1 measurement is recommended for all patients diagnosed with pituitary adenomas because the primary treatment is surgical removal. Repeating IGF-1 measurement (Answer B) in medically treated patients with prolactinomas should be individualized depending on clinical course.

FSH concentrations fluctuate during the years preceding menopause and its measurement (Answer A) is not required for diagnosis. Also, hyperprolactinemia has an inhibitory effect on the hypothalamic-pituitary-gonadal axis, which confounds FSH interpretation.

Pituitary imaging (Answer E) may not be necessary. Studies have shown that women with microprolactinomas are unlikely to experience tumor enlargement, especially when prolactin levels normalize during treatment with dopamine agonist therapy. In some patients, adenomas involute and are no longer visible on imaging. The likelihood of normoprolactinemia after dopamine agonist cessation is higher when a discrete pituitary abnormality is no longer detected by imaging. In meta-analyses, normoprolactinemia after stopping the dopamine agonist was maintained in 87.7% patients with microprolactinomas and in 58.4% of patients with macroprolactinomas. Other favorable predictors of maintained biochemical remission were treatment with cabergoline at a low maintenance dosage, cabergoline treatment duration longer than 2 years, and older age. If prolactin is elevated in this perimenopausal patient, pituitary imaging could be considered. Notably, recurrent hyperprolactinemia does not require resumption of dopamine agonist therapy in the absence of galactorrhea or tumor growth; instead, patients require clinical monitoring and serial prolactin measurement.

Educational Objective

Guide management of disordered menses in perimenopausal women previously treated with a dopamine agonist for a microprolactinoma.

Reference(s)

Andersen IB, Sorensen MGR, Dogansen SC, et al. Withdrawal of dopamine agonist treatment in patients with hyperprolactinemia: a systematic review and meta-analysis. *Clin Endocrinol (Oxf).* 2022;97(5):519-531. PMID: 35261059

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3 ANSWER: A) Monitor serum calcium every 6 to 12 months

This patient has mild, asymptomatic hyperparathyroidism. In a 10-year prospective follow-up study of individuals with primary hyperparathyroidism, most patients who were asymptomatic did well and had no disease progression. Age was the predictor of progression, and those younger than 50 years were 3 times more likely to experience disease progression. Since this man is 63 years old, he does not meet the age criteria for surgical intervention and thus close follow-up with calcium measurement every 6 to 12 months (Answer A) initially followed by annual measurement is appropriate. Surgery can be recommended if, during follow-up, the calcium

concentration remains greater than 1 mg/dL above the upper normal limit, bone mineral density worsens with T-scores less than –2.5, creatinine clearance decreases, or fragility fractures or kidney stones occur.

Referral to a surgeon (Answer C) is not needed now, especially since he is asymptomatic and does not meet criteria for surgery. If surgery were planned, a sestamibi scan could be considered to help localize the abnormal parathyroid gland, but it is not required for diagnosis. Improvement in urinary calcium levels following parathyroidectomy can occur after a few years, while the low estimated glomerular filtration rate does not generally improve.

Cinacalcet (Answer E) can be used to lower serum calcium levels in individuals who have high calcium levels and/or are symptomatic but are not good candidates for surgery or in those with recurrent or tertiary hyperparathyroidism. With this patient's mild asymptomatic hypercalcemia, cinacalcet is not necessary now.

He has no history of fragility fracture or balance issues. DXA shows normal bone mineral density at the spine and hip with slightly low T-scores (within the osteopenia range) at the forearm.

Hyperparathyroidism preferentially affects the distal one-third of the forearm, which is mainly cortical bone, and it should therefore be included in DXA evaluations for primary hyperparathyroidism. Bisphosphonates can be considered for individuals with primary hyperparathyroidism and osteoporosis, especially if they are not good surgical candidates for fracture prevention. Parathyroidectomy has been shown to improve bone mineral density at the lumbar spine and hip sites but not at the more cortical one-third distal radius site. However, studies have shown that total, ionized, and urinary calcium levels do not change with oral alendronate therapy (Answer D).

In the 1990s, annual urinary calcium measurement (Answer B) was recommended for individuals with asymptomatic primary hyperparathyroidism. However, annual monitoring of 24-hour urinary calcium excretion is no longer recommended.

Educational Objective

In an asymptomatic patient with primary hyperparathyroidism, recommend close monitoring of serum calcium every 6 to 12 months.

Reference(s)

Bilezikian JP, Khan AA, Silverberg SJ, et al; International Workshop on Primary Hyperparathyroidism. Evaluation and management of primary hyperparathyroidism: summary statement and guidelines from the Fifth International Workshop. *J Bone Miner Res.* 2022;37(11):2293-2314. PMID: 36245251

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4 ANSWER: E) Recommend a continuous glucose monitoring device

Achieving better glycemic control with no or minimal hypoglycemia should be the goal in diabetes management. Hypoglycemia is associated with adverse cardiovascular events and increased mortality, especially among individuals who have underlying cardiovascular disease.

When interviewing patients, physicians should always be on alert for symptoms of hypoglycemia. Hypoglycemia symptoms are usually characterized as autonomic or neuroglycopenic. Autonomic symptoms include tremors, palpitations, anxiety, sweating, and hunger. Neuroglycopenic symptoms include dizziness, weakness, and confusion or altered mental status. Given that some of these symptoms are nonspecific, they must be correlated with the presence of low glucose values to diagnose hypoglycemia.

This patient is experiencing night sweats, which have a broad differential diagnosis, including malignancy, infections, and endocrine conditions. Rather than assuming that her night sweats are secondary to hypoglycemia, low glucose values must be confirmed and correlated with the timing of her symptoms. Confirming hypoglycemia overnight with point-of-care fingerstick glucose testing can be difficult because it negatively affects quality of sleep and quality of life. Many patients decide to treat the presumed hypoglycemic episode rather than wake up during the night to actually measure their blood glucose concentration. Continuous glucose monitoring devices (Answer E) that automatically check glucose values every 1 to 5 minutes can easily identify hypoglycemia that occurs overnight. Point-of-care fingersticks should also be done to confirm hypoglycemia, especially if the patient does not experience accompanying symptoms.

After documenting hypoglycemia, the next appropriate step is to decrease the insulin glargine dosage, as higher-than-needed insulin doses are the cause of hypoglycemia in this patient. Discontinuing insulin glargine (Answer B) would not be appropriate because this would significantly raise her glucose values.

Continuing current management (Answer A) or increasing basal or short-acting insulin dosages (Answers C and D) would not be appropriate strategies.

Educational Objective

Recommend continuous glucose monitoring devices to identify hypoglycemia.

Reference(s)

Klonoff DC, Ahn D, Drincic A. Continuous glucose monitoring: a review of the technology and clinical use. *Diabetes Res Clin Pract.* 2017;133:178-192. PMID: 28965029

Lee AK, Warren B, Lee CJ, et al. The association of severe hypoglycemia with incident cardiovascular events and mortality in adults with type 2 diabetes. *Diabetes Care.* 2018;41(1):104-111. PMID: 29127240

5 ANSWER: D) Measurement of plasma sitosterol

This patient has incidentally discovered tendon xanthomas and a longstanding history of thrombocytopenia. The differential diagnosis of tendon xanthomas includes familial hypercholesterolemia, sitosterolemia, and cerebrotendinous xanthomatosis (CTX). Patients with familial hypercholesterolemia typically have marked elevations in total and LDL-cholesterol levels, which this patient does not have. Cholesterol levels may be low to normal in both sitosterolemia and CTX. Individuals with CTX have early onset of neurological manifestations, including infantile spasms, cognitive decline, and motor function abnormalities. Thrombocytopenia is not associated with either familial hypercholesterolemia or CTX, but it is commonly seen in individuals with sitosterolemia. Therefore, measurement of plasma sitosterol levels (Answer D) is the most appropriate first step to help identify the cause of this patient's xanthomas and thrombocytopenia.

Testing for *CYP27A1* pathogenic variants (Answer E) would have been appropriate if there were a strong suspicion for CTX. CTX is a rare autosomal recessive condition in which deficiency of the mitochondrial enzyme sterol 27-hydroxylase interferes with bile acid synthesis, leading to accumulation of the cholesterol-derived precursor of bile acid, cholestanol, in nerve cells and membranes. This results in progressive neurological problems, including seizures, ataxia, and cognitive impairment in addition to tendon xanthomas and early cataract formation.

Sitosterolemia is an autosomal recessive disorder due to biallelic pathogenic variants in the *ABCG5* or *ABCG8* genes, which encode proteins involved in cellular sterol excretion. These 2 proteins form obligate heterodimers and are mainly expressed in the intestine, liver, and gallbladder. They help in the extrusion of absorbed sterols, including cholesterol and plant sterols, into the gut and bile. Plant sterols are preferred over cholesterol, and thus defective functioning of these proteins results in accumulation of plant sterols, predominantly sitosterol. Other xenosterols that are atherogenic and predispose to premature atherosclerotic cardiovascular disease may also accumulate. While tendon xanthomas and atherosclerotic cardiovascular disease are the main clinical features, hematological abnormalities, such as anemia and thrombocytopenia, are also noted in many patients with sitosterolemia. Accumulation of abnormal sterols in the membrane of platelets and red blood cells predisposes them to accelerated destruction causing hemolytic anemia and macrothrombocytopenia. In some patients, the only manifestation of this disorder is thrombocytopenia, while in others it is coexistent with cardiovascular manifestations.

Screening for subclinical atherosclerosis by carotid ultrasonography (Answer A) is a reasonable option after establishing the diagnosis, but it is not the initial approach. In this patient, plasma sitosterol measured by gas chromatography–mass spectrometry was markedly elevated (272 mg/L [normal <15 mg/L]), while the concentrations of precursors of endogenous cholesterol synthesis, such as 7-dehydrocholesterol, were low. Genetic testing also showed a homozygous null variant in the *ABCG5* gene, confirming the diagnosis of sitosterolemia. The same pathogenic variant was noted in the patient's brother whose platelet count has ranged from 80 to 100 × $10^3/\mu L$. The treatment of choice is ezetimibe, which blocks the NPC1L1 receptor involved in absorption of both cholesterol and xenosterols. Limited evidence has shown that this therapy not only reduces sitosterol levels but also decreases the size of xanthomas and improves platelet count and function.

Measurement of lipoprotein (a) (Answer C) would have been appropriate if there were suspicion for familial hypercholesterolemia, which is unlikely in this patient.

Referral to hematology (Answer B) would have been reasonable if sitosterolemia were ruled out and other causes of thrombocytopenia were investigated.

Educational Objective

Identify clinical features of sitosterolemia and recommend appropriate management strategies.

Reference(s)

Patel SB, Graf GA, Temel RE. ABCG5 and ABCG8: more than a defense against xenosterols. *J Lipid Res.* 2018;59(7):1103-1113. PMID: 29728459

Tada H, Nomura A, Ogura M, et al. Diagnosis and management of sitosterolemia 2021. *J Atheroscler Thromb.* 2021;28(8):791-801. PMID: 33907061

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