Coding Implications
Revision log

CONCERT ENDOCRINOLOGY NON-GENETIC TESTING

See Important Reminder at the end of this policy for important regulatory and legal information.

OVERVIEW

The endocrine system is the body system that controls hormones. Hormones are responsible for regulating many bodily functions, including sexual development, reproduction, growth, breathing and metabolism. Imbalances in hormones can lead to several conditions, depending on the particular imbalance.

Laboratory testing can sometimes be used to identify whether an underlying hormonal imbalance is the cause of health problems such as thyroid disease, infertility, abnormal growth of bones and other tissues (overgrowth or short stature), Cushing's syndrome, polycystic ovary disease, erectile dysfunction, and more. Endocrine testing can also be indicated in the treatment of symptoms that arise from normal changes in hormone production with age, such as with menopause or low testosterone.

Identifying an underlying hormone imbalance can allow providers to select the most appropriate treatment, such as surgery, medication, or hormone replacement therapies.

The terms male and female are used, where necessary, based on published guidelines, to reference sex assigned at birth.

Note: Please see *Concert Genetic Testing: Endocrinology* for genetic and molecular endocrinology testing.

POLICY REFERENCE TABLE

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Criteria Sections	Example Tests (Labs)	Support
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CRITERIA

It is the policy of health plans affiliated with Centene Corporation® that the specific tests noted below are **medically necessary** when meeting the related criteria:

THYROID FUNCTION TESTING

Thyroid Stimulating Hormone (TSH) Tests

I. TSH testing is considered **medically necessary** when:

A. The member/enrollee has signs or symptoms of thyroid dysfunction, **OR**

B. The member/enrollee has one or more increased risk factors associated with thyroid dysfunction, **OR**

C. The member/enrollee is being monitored during treatment for thyroid dysfunction, **OR**

D. The member/enrollee is being monitored during treatment of thyroid carcinoma including post thyroidectomy, radiation, and suppression.

II. Current evidence does not support the use of TSH testing for all other indications, including screening of asymptomatic adults without increased risk factors for thyroid dysfunction.

Free Thyroxine (T4) Tests OR Total Thyroxine (T4) Tests OR Free Thyroxine Index (Total T4 and T3 Uptake)

I. Free thyroxine (T4) tests OR total thyroxine (T4) OR free thyroxine index (Total T4 and T3 Uptake) testing is considered **medically necessary** when:

A. The member/enrollee has an abnormal TSH result[1], **OR**

B. The member/enrollee has signs or symptoms of thyroid dysfunction, **OR**

C. The member/enrollee is being monitored during treatment for thyroid dysfunction.

II. Current evidence does not support the use of measurement of T3 uptake when performed without total T4.

III. Current evidence does not support the use of free thyroxine index (total T4 and T3 uptake) when performed simultaneously with free T4.

IV. Current evidence does not support the use of free thyroxine (T4) tests OR total thyroxine (T4) OR free thyroxine index (Total T4 and T3 Uptake) testing for all other indications, including screening of asymptomatic adults without increased risk factors for thyroid dysfunction.

[1]This includes free T4 testing performed as an automatic reflex from initial TSH testing; this approach is considered appropriate for initial thyroid dysfunction testing.

Total Triiodothyronine (T3) Tests

I. Total triiodothyronine (T3) testing is considered **medically necessary** when:

A. The member/enrollee has an abnormal TSH result[1], **OR**

B. The member/enrollee has signs or symptoms of hyperthyroidism, **OR**

C. The member/enrollee is being monitored during treatment for hyperthyroidism.

II. Current evidence does not support the use of total triiodothyronine (T3) testing for all other indications, including but not limited to, screening of asymptomatic adults without increased risk factors for thyroid dysfunction.

[1]This includes total T3 testing performed as an automatic reflex from initial TSH testing; this approach is considered appropriate for initial thyroid dysfunction testing.

Free Triiodothyronine (T3) Tests

I. Free triiodothyronine (T3) testing is considered **medically necessary** when:

A. The member/enrollee is receiving combined T3/T4 (liothyronine/levothyroxine) therapy, **AND**

B. The member/enrollee has a low or suppressed TSH level suggestive of possible over-replacement.

II. Current evidence does not support the use of free triiodothyronine (T3) testing for all other indications, including, but not limited to, screening of asymptomatic member/enrollees without increased risk factors for thyroid dysfunction.

Reverse Triiodothyronine (T3) Tests

I. Current evidence does not support the use of reverse triiodothyronine T3 testing for all indications, including but not limited to, screening of asymptomatic member/enrollees without increased risk factors for thyroid dysfunction.

SEXUAL DEVELOPMENT/FUNCTION AND REPRODUCTIVE HORMONE TESTING

Testosterone Tests

I. Testosterone testing (total and/or free/bioavailable measurements) is considered **medically necessary** when:

A. The member/enrollee is being monitored during testosterone therapy, anti-androgen/androgen deprivation therapy, or treatment with a gonadotropin-releasing hormone (GnRH) agonist, **OR**

B. The member/enrollee has irregular menstrual cycles, **OR**

C. The member/enrollee has clinical signs of hyperandrogenism (e.g., hirsutism, severe acne, and female pattern hair loss), **OR**

D. The member/enrollee is male, **AND**

1. Has one or more of the following:

a) Sexual/erectile dysfunction, **OR**

b) Infertility due to oligo- or azoospermia, **OR**

c) Signs or symptoms of male hypogonadism, **OR**

d) Personal history of conditions associated with increased risk for testosterone deficiency, **OR**

e) Signs of precocious puberty (e.g., premature testicular and penile enlargement), **OR**

f) Signs of delayed puberty (e.g., lack of expected development of secondary sex characteristics).

II. Measuring both total and free testosterone simultaneously may be considered **medically necessary for one of the following:**

A. The member/enrollee is being evaluated for irregular menstrual cycles and/or hyperandrogenism for PCOS, **OR**

B. The member/enrollee has signs/symptoms of hypogonadism, **AND**

1. The member/enrollee has a factor known to alter sex hormone binding globulin (SHBG) levels.

III. Current evidence does not support the use of measuring both total and free testosterone simultaneously for all other indications.

IV. Current evidence does not support the use of testosterone testing for all other indications, including for routine evaluation of age-related low testosterone in adult men.

Anti Mullerian Hormone (AMH) Tests

I. Anti mullerian hormone (AMH) testing is considered **medically necessary** when:

A. The member/enrollee is an adult[1] being evaluated for ovarian stimulation/in vitro fertilization (IVF), **OR**

B. The member/enrollee is an adult[1] being evaluated for for polycystic ovarian syndrome (PCOS), **AND**

1. AMH is being used as an alternative to ultrasound to confirm polycystic ovary morphology (PCOM)

C. The member/enrollee has signs of a disorder of sexual development (e.g., ambiguous genitalia, cryptorchidism, hypospadias).

II. Current evidence does not support the use of Anti mullerian hormone (AMH) testing for all other indications.

[1]AMH testing is not recommended for evaluation of adolescents for PCOS due to poor specificity.

Estradiol Tests

I. Estradiol testing is considered **medically necessary** when:

A. The member/enrollee has irregular menstruation prior to 40 years of age, **OR**

B. Testing is required to make a definitive clinical diagnosis of menopause due to inadequate menstrual history or hysterectomy without bilateral oophorectomy, **OR**

C. The member/enrollee is being monitored during estrogen therapy and/or anti-androgen/androgen deprivation therapy, **OR**

D. The member/enrollee is being monitored during endocrine therapy for a history of premenopausal hormone receptor positive breast cancer (i.e., ovarian function suppression), **OR**

E. The member/enrollee has gynecomastia that cannot be attributed to hepatic, renal or thyroid dysfunction, **OR**

F. The member/enrollee has female factor infertility, **AND**

1. Irregular menstruation (oligomenorrhea or amenorrhea) and/or anovulation, **OR**

G. The member/enrollee has a female reproductive system, **AND**

1. Has signs or symptoms of female hypogonadism, delayed puberty, and/or primary amenorrhea, **OR**

2. Has signs of precocious puberty (e.g., premature thelarche/breast development).

II. Current evidence does not support the use of estradiol testing for all other indications.

Follicle Stimulating Hormone (FSH) Tests

I. Follicle Stimulating Hormone testing is considered **medically necessary** when:

A. Testing is required to make a definitive clinical diagnosis of menopause due to inadequate menstrual history or hysterectomy without bilateral oophorectomy, **OR**

B. The member/enrollee is being monitored during endocrine therapy for a history of premenopausal hormone receptor positive breast cancer (i.e., ovarian function suppression), **OR**

C. The member/enrollee is being monitored during treatment with a gonadotropin-releasing hormone (GnRH) agonist, **OR**

D. The member/enrollee has gynecomastia that is not explained by hepatic, renal or thyroid dysfunction, **OR**

E. The member/enrollee has one or more of the following:

1. Signs/symptoms of polycystic ovarian syndrome (PCOS) (e.g. irregular menstrual cycles, clinical or biochemical hyperandrogenism), **OR**

2. Irregular menstruation prior to 40 years of age, **OR**

3. Signs or symptoms of male hypogonadism, **OR**

F. The member/enrollee has male factor infertility, **AND**

1. Sexual/erectile dysfunction, **OR**

2. Oligo/azoospermia, **OR**

3. Atrophic testes, **OR**

4. Evidence of hormonal abnormality upon exam (e.g., gynecomastia, abnormally sized testes), **OR**

G. The member/enrollee has female factor infertility, **AND**

1. Irregular menstruation (oligomenorrhea or amenorrhea) and/or anovulation, **OR**

H. The member/enrollee has a pituitary neoplasm detected on brain imaging.

II. Current evidence does not support the use of follicle stimulating hormone (FSH) testing for all other indications.

Luteinizing Hormone (LH) Tests

I. Luteinizing hormone (LH) testing is considered **medically necessary** when:

A. The member/enrollee has signs or symptoms of male or female hypogonadism, **OR**

B. The member/enrollee has gynecomastia that is not explained by hepatic, renal or thyroid dysfunction, **OR**

C. The member/enrollee has signs of precocious puberty (e.g., premature thelarche/breast development or premature testicular and penile enlargement), **OR**

D. The member/enrollee is being monitored during endocrine therapy for a history of premenopausal hormone receptor positive breast cancer (i.e., ovarian function suppression), **OR**

E. The member/enrollee is being monitored during treatment with a gonadotropin-releasing hormone (GnRH) agonist, **OR**

F. The member/enrollee has a pituitary neoplasm detected on brain imaging.

II. Current evidence does not support the use of luteinizing hormone (LH) testing for all other indications.

Prolactin Tests

I. Prolactin testing is considered **medically necessary** when:

A. The member/enrollee has one or more of the following:

1. Signs/symptoms of polycystic ovarian syndrome (PCOS) (e.g., irregular menstrual cycles, clinical or biochemical hyperandrogenism), **OR**

2. Signs/symptoms of male or female hypogonadism, **OR**

3. Gynecomastia that is not explained by hepatic, renal or thyroid dysfunction, **OR**

4. Galactorrhea, **OR**

5. Low bone mass, **OR**
6. Symptoms of a pituitary mass (e.g., double vision and/or decreased peripheral vision, or frequent, severe, and prolonged headaches), **OR**
7. A pituitary neoplasm detected on brain imaging, **OR**

B. The member/enrollee has female factor infertility, **AND**

1. Irregular menstruation (oligomenorrhea or amenorrhea) and/or anovulation, **OR**

C. The member/enrollee has male factor infertility, **AND**

1. A fasting morning total testosterone level below <300 ng/dL**, OR**

D. The member/enrollee is being evaluated for or monitored during treatment of a prolactinoma/hyperprolactinemia or for hypopituitarism, **OR**

E. The member/enrollee is being monitored during estrogen therapy and/or anti-androgen/androgen deprivation therapy.

II. Current evidence does not support the use of prolactin testing for all other indications.

Progesterone Tests

I. Progesterone testing is considered **medically necessary** when:

A. The member/enrollee has first-trimester bleeding, **AND**

1. Ultrasound-confirmed intrauterine pregnancy, **AND**
2. Inconclusive pregnancy viability, **OR**

B. The member/enrollee is being evaluated for embryo transfer, **OR**

C. The member/enrollee has regular menstruation, **AND**

1. Clinical signs of hyperandrogenism (e.g., hirsutism, severe acne, and female pattern hair loss), **OR**
2. Female factor infertility.

II. Current evidence does not support the use of progesterone testing for all other indications.

MONOGENIC DIABETES PANEL TESTS

Monogenic Diabetes (Including Maturity Onset Diabetes of the Young (MODY)) Panels

I. Multigene panel analysis to establish or confirm a diagnosis of monogenic diabetes (including maturity-onset diabetes of the young (MODY)) is considered **medically necessary** when:

A. The member/enrollee has a diagnosis of diabetes within the first 12 months of life, **OR**

B. The member/enrollee has a diagnosis of diabetes before 30 years of age, **AND**

1. The member/enrollee has at least one of the following:

a) Autoantibody negative, **OR**

b) Retained C-peptide levels, **OR**

C. The member/enrollee has a diagnosis of diabetes not characteristic of type 1 or type 2 diabetes, **AND**

1. The member/enrollee has a family history of diabetes consistent with an autosomal dominant pattern of inheritance.

II. Current evidence does not support the use of multigene panel analysis to establish or confirm a diagnosis of monogenic diabetes (maturity-onset diabetes of the young (MODY)) for all other indications.

GENERAL HEALTH TESTS

General Health Panel (Comprehensive Metabolic Panel (CMP), Thyroid Stimulating Hormone (TSH), and Complete Blood Count (CBC))

I. General Health Panel[1] testing is considered **medically necessary** when:

A. The member/enrollee meets criteria for Thyroid Stimulating Hormone (TSH) Testing.

II. Current evidence does not support the use of general Health Panel testing for all other indications.

[1]A "General Health Panel" is an order set, billed with a single procedure code, that includes all of the following test components: CMP, TSH, and CBC.

HEMOGLOBIN A1C (HBA1C) TESTS

Hemoglobin A1C (HbA1c)

I. Hemoglobin A1C (HbA1c) testing is considered **medically necessary** when:

A. The member/enrollee is pregnant, **AND**

1. Has diabetes mellitus or gestational diabetes mellitus (GDM), **AND**

2. It has been at least 30 days since the member/enrollee's last test, **OR**

B. The member/enrollee meets **BOTH** of the following:

1. One of the following:

a) Diabetes mellitus, **OR**

b) Prediabetes, **OR**

c) Use of high-risk medications (e.g., statins, second-generation antipsychotic, glucocorticoids), **AND**

2. It has been at least 90 days since the member/enrollee's last test, **OR**

C. The member/enrollee meets **BOTH** of the following:

1. One of the following:

a) The member/enrollee has signs/symptoms of insulin resistance or diabetes mellitus (e.g., elevated A1C, elevated glucose level, acanthosis nigra, erectile dysfunction, polycystic ovary syndrome, excessive thirst), **OR**

b) The member/enrollee has overweight or obesity, **AND**

(1) One or more additional risk factors for diabetes mellitus (e.g., cardiovascular disease, family history of diabetes mellitus, hypertension, high-risk race or ethnicity), **OR**

c) The member/enrollee has a personal history of gestational diabetes, **OR**

d) The member/enrollee has a personal history of pancreatitis, **AND**

2. It has been at least one year since the member/enrollee's last test.

II. Current evidence does not support the use of Hemoglobin A1C (HbA1c) testing for all other indications.

PARATHYROID HORMONE TESTS

Parathyroid Hormone (PTH) Tests

I. Parathyroid hormone (PTH) testing is considered **medically necessary** when:

A. The member/enrollee has signs or symptoms of parathyroid dysfunction, **OR**

B. The member/enrollee has risk factors for parathyroid dysfunction, **OR**

C. The member/enrollee is being monitored during and/or after treatment for parathyroid dysfunction/cancer (e.g., medication, dietary control, surgery), **OR**

D. There is clinical suspicion or diagnosis of cancer known to affect the parathyroid or known to cause signs of parathyroid dysfunction (e.g., MEN2A/Familial medullary thyroid carcinoma, multiple endocrine neoplasia types 1 and 2, brown tumor of hyperparathyroidism).

II. Current evidence does not support the use of Parathyroid hormone (PTH) testing for all other indications, including:

A. For screening of asymptomatic individuals with no additional risk factors or clinical findings.

RATIONALE AND REFERENCES

Thyroid Stimulating Hormone (TSH) Tests

US Preventive Services Task Force (USPSTF)

There is currently insufficient evidence to support screening nonpregnant, asymptomatic adults according to USPSTF. In "Thyroid Dysfunction: Screening" (2015), the authors note that early detection can be beneficial but population-wide screening and treatment of asymptomatic individuals has a likelihood of important and frequent harms such as psychological effects from labeling, false positives, overdiagnosis and overtreatment (p. 1-4).

US Preventive Services Task Force. Thyroid Dysfunction: Screening: US Preventive Services Task Force Recommendation Statement. 2015. Accessed April 29 2024. https://www.uspreventiveservicestaskforce.org/uspstf/document/literature-surveillance-report-/thyroid-dysfunction-screening

American College of Obstetrics and Gynecology (ACOG)

ACOG Practice Bulletin Number 194, "Polycystic Ovary Syndrome" (2009; 2018 interim update to treatment sections only, as highlighted), contains a suggested clinical workup to include laboratory assessment of Thyroid-stimulating hormone (TSH) levels, total testosterone and sex hormone-binding globulin, or bioavailable and free testosterone, and prolactin (Box 1, p. e159).

American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin No. 194: Polycystic ovary syndrome. Obstet Gynecol. 2018;131(6):e157-e171. doi:10.1097/AOG.0000000000002656. Published correction appears in Obstet Gynecol. 2020;136(3):638. doi:10.1097/AOG.0000000000004069

American Academy of Family Physicians (AAFP)

In "Thyroid Disease in Pregnancy" (2014), the AAFP notes that current guidelines recommend targeted screening of women at high risk which can include personal history of thyroid disease, current or personal history of thyroid therapy, personal history of autoimmune disease (such as type I diabetes mellitus), or a family history of autoimmune thyroid disease (p. 273).

Carney LA, Quinlan JD, West JM. Thyroid disease in pregnancy. Am Fam Physician. 2014;89(4):273-278.

In "Hypothyroidism: Diagnosis and Treatment" (2021), the authors state that the signs and symptoms of hypothyroidism are numerous, nonspecific, and vary in presentation (Table 2 and Table 3).

AAFP recommends thyroid stimulating hormone (TSH) for initial evaluation of suspected hypothyroidism (p. 606-607).

Risk factors for hypothyroidism can include individuals aged 65 years and older, females carry a higher risk than males, diagnosis of an autoimmune disease (e.g., type 1 diabetes mellitus, celiac disease, autoimmune gastric atrophy, multiple autoimmune endocrinopathies), Down syndrome, and Turner syndrome (p. 606).

It is also noted that TSH should be monitored, at varying frequencies, in individuals receiving therapy for hypothyroidism. Specifically, once the TSH level is normalized (amount of time to normalization varies from person to person), it should be checked again after one year or if symptoms change prompt more frequent testing (p. 607-609).

Wilson SA, Stem LA, Bruehlman RD. Hypothyroidism: Diagnosis and Treatment: Am Fam Physician. 2021;103(10):605-613. Accessed May 1 2024.
https://www.aafp.org/pubs/afp/issues/2021/0515/p605.html#screening

In "Hyperthyroidism: Diagnosis and Treatment" (2016), the diagnostic workup for hyperthyroidism includes analysis of TSH, Free T4, and Total T3 to help establish presence of hyperthyroidism and severity (p. 365-368).

Risk factors for hyperthyroidism can include personal or family history of autoimmune disease (such as in Grave's disease) (p. 363-364).

The frequency of monitoring of TSH during and/or post therapy is variable, depending on patient response, treatment and cause of hyperthyroidism (p. 367-369).

Kravetz I. Hyperthyroidism: Diagnosis and Treatment: Am Fam Physician. 2016;93(5):363-370. Accessed May 2 2024. https://www.aafp.org/pubs/afp/issues/2016/0301/p363.html#:~:text=The%20diagnostic%20workup%20for%20hyperthyroidism,gland%20to%20determine%20the%20cause.

In "Thyroiditis: Evaluation and Treatment" (2021), the authors recommend TSH as part of the initial workup for all forms of thyroiditis (p. 609-616).

Martinez Quintero B, Yazbeck C, Sweeney LB. Thyroiditis: Evaluation and Treatment: Am Fam Physician. 2021;104(6):609-617. Accessed May 7 2024. https://www.aafp.org/pubs/afp/issues/2021/1200/p609.html

National Comprehensive Cancer Network (NCCN): Thyroid Carcinoma (1.2025)

This guideline recommends TSH testing for multiple indications and treatment surveillance including post surgery for radiation, suppression and both lobectomy and total thyroidectomy (p. PAP-3, PAP-7- PAP-8, FOLL-2, FOLL-6 - FOLL-7, ONC-2, ONC-6 - ONC-7, MEDU-1, ANAP-1, MS-24 - MS-25, MS-38).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Thyroid Carcinoma 1.2025 https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf

Free Thyroxine (T4) Tests OR Total Thyroxine (T4) Tests OR Free Thyroxine Index (Total T4 and T3 Uptake)

American Academy of Family Physicians (AAFP)

In "Hypothyroidism: Diagnosis and Treatment" (2021), Free T4 (FT4) testing is recommended for hypothyroidism when the TSH result is abnormal (p. 608, Figure 1).

Wilson SA, Stem LA, Bruehlman RD. Hypothyroidism: Diagnosis and Treatment: Am Fam Physician. 2021;103(10):605-613. Accessed May 1 2024. https://www.aafp.org/pubs/afp/issues/2021/0515/p605.html#screening

In "Hyperthyroidism: Diagnosis and Treatment" (2016), the diagnostic workup for hyperthyroidism includes analysis of TSH, Free T4, and Total T3 to help establish presence of hyperthyroidism and severity. Total T4 may help determine the type of hyperthyroidism for certain clinical scenarios as seen in Table 3 (p. 365-368).

Monitoring of thyroid function during and/or post therapy is widely varied due to patient response, treatment and cause of hyperthyroidism (p. 367-369).

Kravetz I. Hyperthyroidism: Diagnosis and Treatment: Am Fam Physician. 2016;93(5):363-370. Accessed May 2 2024.
https://www.aafp.org/pubs/afp/issues/2016/0301/p363.html#:~:text=The%20diagnostic%20workup%20for%20hyperthyroidism,gland%20to%20determine%20the%20cause

British Thyroid Association/British Society for Endocrinology

In their 2023 consensus statement, "Use of liothyronine (T3) in hypothyroidism," the joint societies discuss the controversiality of T3 therapy in hypothyroidism. In the case that T3 therapy is implemented, it is recommended to monitor for adequate replacement via serum TSH only, with additional free T4 measurements if TSH is outside the reference range. Free T4 may also be monitored if assessment of over-replacement is required in patients with a low or suppressed serum TSH (Table 1, p. 211).

Ahluwalia R, Baldeweg SE, Boelaert K, et al. Use of liothyronine (T3) in hypothyroidism: Joint British Thyroid Association/Society for endocrinology consensus statement. Clin Endocrinol (Oxf). 2023;99(2):206-216. doi: 10.1111/cen.14935

Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd ed.

T3 Resin Uptake is a poor estimator of thyroid function on its own, but when used in conjunction with total T4 it offers insight into deviations of T4 concentrations (p. 667).

Dunlap DB. Thyroid function tests. In: Walker HK, Hall WD, Hurst JW, eds. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd ed. Boston: Butterworths; 1990:667.
https://www.ncbi.nlm.nih.gov/books/NBK249/

American Thyroid Association (ATA)

In "Thyroid Function Tests" (2019) the ATA states that total T4 is variable in response to the amount bound versus available to enter the system and affect body tissues. Therefore, using a test that measures unbound/free T4, either a free T4 or a free T4 index, more accurately reflects thyroid function.

American Thyroid Association. Thyroid function tests. Published 2019. https://www.thyroid.org/thyroid-function-tests/

Total Triiodothyronine (T3) Tests

American Academy of Family Physicians (AAFP)

In "Hyperthyroidism: Diagnosis and Treatment" (2016), the diagnostic workup for hyperthyroidism includes analysis of TSH (which can be either elevated OR low depending on the cause of hyperthyroidism, see Figure 1), Free T4, and Total T3 to help establish presence of hyperthyroidism and severity (p. 365-368).

Monitoring of thyroid function during and/or post therapy may include measuring TT3, FT4, and TSH, with frequency and specific tests determined by patient response, treatment and cause of hyperthyroidism (p. 367-369).

Kravetz I. Hyperthyroidism: Diagnosis and Treatment: Am Fam Physician. 2016;93(5):363-370. Accessed May 2 2024.
https://www.aafp.org/pubs/afp/issues/2016/0301/p363.html#:~:text=The%20diagnostic%20workup%20for%20hyperthyroidism,gland%20to%20determine%20the%20cause

American Thyroid Association (ATA)

In "Thyroid Function Tests" (2019) the ATA states T3 levels are useful in diagnosis of hyperthyroidism as some individuals with a low TSH have only an elevation of T3 with a normal FT4 or FTI.

For hypothyroidism, T3 testing is typically not recommended. It is rarely helpful in the hypothyroid setting as it is the last test to become abnormal. A severely hypothyroid individual could have a normal T3 level.

American Thyroid Association. Thyroid function tests. Published 2019. https://www.thyroid.org/thyroid-function-tests/

Free Triiodothyronine (T3) Tests

The Endocrine Society

In the "American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis" (2016) the authors state that assays for estimating free T3 are less widely-validated and less reliable, measurement of total T3 rather than free T3 is generally preferred in clinical practice (p. 1384).

Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, Rivkees SA, Samuels M, Sosa JA, Stan MN, Walter MA. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid. 2016 Oct;26(10):1343-1421. Erratum in: Thyroid. 2017 Nov;27(11):1462. PMID: 27521067. doi:10.1089/thy.2016.0229.

British Thyroid Association/British Society for Endocrinology

In their 2023 consensus statement "Use of liothyronine (T3) in hypothyroidism", the joint societies discuss the controversiality of T3 therapy in hypothyroidism. In the rare case that T3 therapy is implemented, it is recommended to monitor for adequate replacement via serum TSH only, with additional free T4 measurements if TSH is outside the reference range. If assessment of over-replacement is required in patients with a low or suppressed serum TSH, free T3 or free T4 should be measured (Table 1, p. 211).

Ahluwalia R, Baldeweg SE, Boelaert K, et al. Use of liothyronine (T3) in hypothyroidism: Joint British Thyroid Association/Society for endocrinology consensus statement. Clin Endocrinol (Oxf). 2023;99(2):206-216. doi: 10.1111/cen.14935

Reverse Triiodothyronine (T3) Tests

American Thyroid Association (ATA)

The ATA makes a statement in "Thyroid Function Tests" (2019) describing reverse T3 testing as not clinically useful and does not help diagnose hypothyroidism in the healthy, non-hospitalized population (p. 2).

American Thyroid Association. Thyroid function tests. Published 2019. https://www.thyroid.org/thyroid-function-tests/

Neither the "American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis" (2016), nor the joint American Association of Clinical Endocrinologists and the American Thyroid Association's "Clinical practice guidelines for hypothyroidism in adults" (2012), recommend measurement of reverse T3.

Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, Rivkees SA, Samuels M, Sosa JA, Stan MN, Walter MA. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid. 2016 Oct;26(10):1343-1421. Erratum in: Thyroid. 2017 Nov;27(11):1462. PMID: 27521067. doi:10.1089/thy.2016.0229.

Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract. 2012;18(6):988-1028. doi:10.4158/EP12280.GL. Published correction appears in Endocr Pract. 2013;19(1):175.

Testosterone Tests

National Comprehensive Cancer Network (NCCN): Prostate Cancer (2.2025)

This guideline states that diligent monitoring for disease progression via measurement of PSA and testosterone levels, and sometimes imaging, is required during intermittent androgen deprivation therapy (ADT), particularly during off-treatment periods. Frequency of testing is not addressed (PROS-G, p. 3).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf

American Urological Society (AUA)

The AUA guideline "Erectile Dysfunction" (2018) recommends measurement of morning serum total testosterone in men with erectile dysfunction (p. 634).

Burnett AL, Nehra A, Breau RH, et al. Erectile dysfunction: AUA guideline. J Urol. 2018;200(3):633-641. doi: 10.1016/j.juro.2018.05.004. Published correction appears in J Urol. 2022;207(3):743.

The AUA guideline "Evaluation and Management of Testosterone Deficiency" (2018) recommends that clinicians consider serum testosterone testing in patients with clinical signs/symptoms of hypogonadism, or, even in absence of signs/symptoms in patients with a history of unexplained anemia, bone density loss, diabetes, exposure to chemotherapy, exposure to testicular radiation, HIV/AIDS, chronic narcotic use, male infertility, pituitary dysfunction, and chronic corticosteroid use (p. 424).

Mulhall JP, Trost LW, Brannigan RE, et al. Evaluation and Management of Testosterone Deficiency: AUA Guideline. J Urol. 2018;200(2):423-432. doi:10.1016/j.juro.2018.03.115

American College of Physicians (ACP)

In "Testosterone Treatment in Adult Men With Age-Related Low Testosterone: A Clinical Guideline From the American College of Physicians" (2020), endorsed by the American Academy of Family Physicians, the ACP discusses the current evidence and recommendations for age-related low testosterone. Chiefly, they recommend against initiating testosterone treatment in men with age-related low testosterone to improve energy, vitality, physical function, or cognition, and only to initiate treatment in men with age-related low testosterone with sexual dysfunction who want to improve sexual function. They point to several unknowns from the research regarding whether nonspecific signs and symptoms associated with age-related low testosterone, such as decreases in energy and muscle mass, mood disturbances, weakness, and mortality, are truly due to age-related low testosterone or whether they are a consequence of other factors, such as chronic illnesses. They also point out that testosterone therapy for age-related low testosterone is a controversial issue (p. 126-133).

Qaseem A, Horwitch CA, Vijan S, Etxeandia-Ikobaltzeta I, Kansagara D; Clinical Guidelines Committee of the American College of Physicians; Forciea MA, Crandall C, Fitterman N, Hicks LA, Lin JS, Maroto M, McLean RM, Mustafa RA, Tufte J. Testosterone Treatment in Adult Men With Age-Related Low Testosterone: A Clinical Guideline From the American College of Physicians. Ann Intern Med. 2020 Jan 21;172(2):126-133. Epub 2020 Jan 7. Erratum in: Ann Intern Med. 2023 Apr;176(4):584. PMID: 31905405. doi:10.7326/M19-0882.

UpToDate

The indications for testing of adult males for hypogonadism are poorly defined and conflicting among guidelines. In "Clinical features and diagnosis of male hypogonadism," UpToDate advocates for evaluation of adult males with common, albeit nonspecific symptoms of testosterone deficiency, including decreased libido and "vigor", and depressed mood. They argue for early evaluation on the basis that the more definitive signs of hypogonadism, such as decreased muscle mass and hair and gynecomastia, are only present in advanced stages of testosterone deficiency. However, this conflicts somewhat with other guidelines, such as the American College of Physicians guideline on age related testosterone deficiency, as studies have not shown definitive benefit to testosterone therapy in men with reduced energy and mood changes due to age-related low testosterone.

Snyder PJ. Clinical features and diagnosis of male hypogonadism. UpToDate. Last update May 5, 2022. https://www.uptodate.com/contents/clinical-features-and-diagnosis-of-male-hypogonadism

The Endocrine Society

The Endocrine Society guideline "Testosterone Therapy in Men With Hypogonadism" (2018) recommends measurement of morning total testosterone levels in men with symptoms and signs of testosterone deficiency for the diagnosis of hypogonadism, along with measurement of free testosterone in those with conditions that alter levels of sex hormone binding globulin (SHBG) or in those with borderline low testosterone measurements. Conditions associated with altered levels of SHBG include aging, obesity, diabetes mellitus, use of glucocorticoids, progestins, and androgenic steroids, use of estrogens, nephrotic syndrome, cirrhosis/hepatitis, hypo/hyperthyroidism, acromegaly, HIV disease, certain anticonvulsants, and polymorphisms in the *SHBG* gene (Figure 1 and Table 2, p. 1720-1721).

The guideline recommends against routine, general population screening of men for hypogonadism (p. 1716).

Bhasin S, Brito JP, Cunningham GR, et al. Testosterone therapy in men with hypogonadism: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2018;103(5):1715-1744. doi: 10.1210/jc.2018-00229.

The Endocrine Society clinical practice guideline "Evaluation and Treatment of Hirsutism in Premenopausal Women" (2018), co-sponsored by the Androgen Excess and Polycystic Ovary Syndrome Society and European Society of Endocrinology, recommends serum total, and sometimes free, testosterone measurements for all women presenting with hirsutism (as defined

by an abnormal hirsutism score, and not for those with only unwanted excess hair). The authors note that their suggestion to test for hyperandrogenemia in all women with hirsutism places a relatively high value on the identification of rare treatable underlying hyperandrogenic diseases, such as non-classical congenital adrenal hyperplasia or a virilizing tumor (p. 1234).

Martin KA, Anderson RR, Chang RJ, Ehrmann DA, Lobo RA, Murad MH, Pugeat MM, Rosenfield RL. Evaluation and Treatment of Hirsutism in Premenopausal Women: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2018 Apr 1;103(4):1233-1257. PMID: 29522147. doi:10.1210/jc.2018-00241.

The Endocrine Society clinical practice guideline "Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons" (2017) recommends the following for monitoring of testosterone levels:

- Once every 6-12 months for adolescents undergoing puberty suppression (table 7, p. 3883)
- Once every 6-12 months for adolescent transgender males undergoing induction of puberty (Table 9, p. 3884)
- Once every 3 months for the first year, then 1-2 times per year thereafter for adults receiving gender-affirming hormone therapy (Tables 14 and 15, p. 3890).

Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, Rosenthal SM, Safer JD, Tangpricha V, T'Sjoen GG. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017 Nov 1;102(11):3869-3903. Erratum in: J Clin Endocrinol Metab. 2018 Feb 1;103(2):699. Erratum in: J Clin Endocrinol Metab. 2018 Jul 1;103(7):2758-2759. PMID: 28945902. doi:10.1210/jc.2017-01658.

International PCOS Network

The "Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome," supported by a partnership with American Society for Reproductive Medicine and the Endocrine Society, recommends total and free testosterone testing to confirm biochemical hyperandrogenism in individuals with irregular menstrual cycles and no or minimal clinical signs of hyperandrogenism, noting that hirsutism alone should be considered predictive of biochemical hyperandrogenism and PCOS in adults (Figure 1, p. G60).

Irregular menstrual cycles are defined as follows:

- Normal in the first year post menarche as part of the pubertal transition.
- 1 to <3 years post menarche: <21 or >45 days.
- 3 years post menarche to perimenopause: <21 or >35 days or <8 cycles per year.
- 1 year post menarche >90 days for any 1 cycle.
- Primary amenorrhoea by age 15 or >3 years post thelarche (breast development). (Table 4, p. G46)

Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, Costello MF, Boivin J, Redman LM, Boyle JA, Norman RJ, Mousa A, Joham AE; International PCOS Network. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Eur J Endocrinol. 2023 Aug 2;189(2):G43-G64. PMID: 37580861. doi:10.1093/ejendo/lvad096.

American College of Obstetrics and Gynecology (ACOG)

ACOG Practice Bulletin Number 194, "Polycystic Ovary Syndrome" (2009; 2018 interim update to treatment sections only, as highlighted) contains a suggested clinical workup to include laboratory assessment of total testosterone and sex hormone-binding globulin, or bioavailable and free testosterone levels (Box 1, p. e159).

American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin No. 194: Polycystic ovary syndrome. Obstet Gynecol. 2018;131(6):e157-e171. doi:10.1097/AOG.0000000000002656. Published correction appears in Obstet Gynecol. 2020;136(3):638. doi:10.1097/AOG.0000000000004069

American Urological Society (AUA) and American Society for Reproductive Medicine (ASRM)

The AUA/ASRM guideline "Diagnosis and Treatment of Infertility in Men" (2021) recommends evaluation of follicle-stimulating hormone (FSH) and testosterone for infertile men with impaired libido, erectile dysfunction, oligozoospermia or azoospermia, atrophic testes, or evidence of hormonal abnormality on physical evaluation (p. 37-39).

Schlegel PN, Sigman M, Collura B, et al. Diagnosis and treatment of infertility in men: AUA/ASRM guideline part I. J Urol. 2021;205(1):36-43. doi:10.1097/JU.0000000000001521.

American Academy of Pediatrics (AAP)

In "Evaluation and Referral of Children With Signs of Early Puberty" (2016), the AAP defines central precocious puberty (CPP) as the full activation of the HPG axis before 8 years of age in girls and before 9 years of age in boys. They suggest considering a CPP diagnosis in girls who display progressive breast development and who cross percentiles upward on the linear growth chart. They state that CPP is much less common in boys but suggest considering a diagnosis of CPP in boys who display both testicular and penile enlargement before 9 years of age. The baseline workup suggested for CPP in a child includes FSH, LH, and either estradiol (for girls) or testosterone (for boys) (p. 4).

Kaplowitz P, Bloch C; Section on Endocrinology, American Academy of Pediatrics. Evaluation and Referral of Children With Signs of Early Puberty. Pediatrics. 2016 Jan;137(1). Epub 2015 Dec 14. PMID: 26668298. doi:10.1542/peds.2015-3732.

Anti Mullerian Hormone (AMH) Tests

International PCOS Network

The "International evidence-based guideline for the assessment and management of polycystic ovary syndrome" (2023), supported by a partnership with American Society for Reproductive Medicine and the Endocrine Society, recommends that PCOS be diagnosed based on the presence of two of the following: clinical/biochemical hyperandrogenism; ovulatory dysfunction; and polycystic ovaries on ultrasound. Serum AMH can be used in place of ultrasound for adults to fulfill diagnostic criteria. Serum AMH is not necessary for PCOS diagnosis in patients with irregular menstrual cycles and hyperandrogenism. The guidelines state that serum AMH should not yet be used in adolescents; in adolescents, both hyperandrogenism and ovulatory dysfunction are required, with ultrasound and AMH not recommended due to poor specificity. Additionally, providers should not perform both ultrasound and AMH (TABLE 4).

Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, Costello MF, Boivin J, Redman LM, Boyle JA, Norman RJ, Mousa A, Joham AE; International PCOS Network. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Eur J Endocrinol. 2023 Aug 2;189(2):G43-G64. PMID: 37580861. doi:10.1093/ejendo/lvad096.

American Society for Reproductive Medicine (ASRM)

In "Fertility evaluation of infertile women: a committee opinion" (2021), the ASRM explains that ovarian reserve testing can include ultrasound imaging of the ovaries and biochemical testing via estradiol and follicle stimulating hormone (FSH) or antimullerian hormone (AMH). ASRM asserts that ovarian reserve testing is not a reliable measure of fertility in women without infertility or as a random biomarker, but can be used to tailor fertility treatments/identify women who may have a poor response to ovarian stimulation (p. 1258-1259).

Practice Committee of the American Society for Reproductive Medicine. Fertility evaluation of infertile women: a committee opinion. Fertil Steril. 2021 Nov;116(5):1255-1265. Epub 2021 Oct 2. PMID: 34607703. doi:10.1016/j.fertnstert.2021.08.038.

Global DSD Update Consortium

In the consensus statement, "Global Disorders of Sex Development Update since 2006: Perceptions, Approach and Care," the consortium states that extensive biochemical investigation is required in newborns/infants when external genitalia are ambiguous enough to impede sex assignment or if they are inconsistent with the results of prenatal tests. First-line testing includes measurement of anti-Müllerian hormone (AMH), in addition to measurement of 17-hydroxyprogesterone (17-OHP) and serum electrolyte, androgen, and gonadotropin levels, in tandem with evaluation of the sex chromosomes (p. 165).

Lee PA, Nordenström A, Houk CP, et al. Global DSD Update Consortium. Global disorders of sex development update since 2006: perceptions, approach and care. Horm Res Paediatr. 2016;85(3):158-180. doi:10.1159/000442975. Erratum in: Horm Res Paediatr. 2016;86(1):71. doi:10.1159/000447367

Estradiol Tests

National Comprehensive Cancer Network (NCCN): Breast Cancer (4.2025)

This guideline recommends monitoring of estradiol and follicle stimulating hormone (FSH) levels for individuals in whom menopausal status must be assessed to guide selection of endocrine therapy for breast cancer (p. BINV-O). Frequency of testing should be personalized to the patient (p. BINV-k 1 of 2).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer 4.2025 https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

American Society for Reproductive Medicine (ASRM)

In "Fertility evaluation of infertile women: a committee opinion" (2021), the ASRM lists estradiol as a test that should not be routinely ordered for infertility unless specifically indicated. They recommend estradiol testing for women with infertility who have oligomenorrhea or anovulation (p. 1258).

Practice Committee of the American Society for Reproductive Medicine. Fertility evaluation of infertile women: a committee opinion. Fertil Steril. 2021 Nov;116(5):1255-1265. Epub 2021 Oct 2. PMID: 34607703. doi:10.1016/j.fertnstert.2021.08.038.

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In "Evaluation and Referral of Children With Signs of Early Puberty" (2016), the AAP defines central precocious puberty (CPP) as the full activation of the HPG axis before 8 years of age in girls and before 9 years of age in boys. They suggest considering a CPP diagnosis in girls who display progressive breast development and who cross percentiles upward on the linear growth chart. They state that CPP is much less common in boys but suggest considering a diagnosis of CPP in boys who display both testicular and penile enlargement before 9 years of age. The baseline workup suggested for CPP in a child includes FSH, LH, and either estradiol (for girls) or testosterone (for boys) (p. 4).

Kaplowitz P, Bloch C; Section on Endocrinology, American Academy of Pediatrics. Evaluation and Referral of Children With Signs of Early Puberty. Pediatrics. 2016 Jan;137(1). Epub 2015 Dec 14. PMID: 26668298. doi:10.1542/peds.2015-3732.

The Endocrine Society

In the clinical practice guideline "Treatment of Symptoms of the Menopause" (2015), The Endocrine Society recommends that menopause be diagnosed based on the clinical criteria of the menstrual cycle. If the menstrual history is inadequate, they suggest making a presumptive diagnosis of menopause based on the presence of vasomotor symptoms (e.g., hot flashes, night sweats), and when indicated, FSH and serum estradiol, such as in women who have undergone hysterectomy without bilateral oophorectomy (p. 3976).

Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Murad MH, Pinkerton JV, Santen RJ. Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015 Nov;100(11):3975-4011. Epub 2015 Oct 7. PMID: 26444994. doi:10.1210/jc.2015-2236.

In the clinical practice guideline "Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons" (2017), The Endocrine Society recommends the following for monitoring of estradiol:

- Once every 6-12 months for adolescents undergoing puberty suppression (table 7, p. 3883)
- Once every 6-12 months for adolescent transgender females undergoing induction of puberty (table 9, p. 3884)
- Once every 3 months for the first year, then 1-2 times per year thereafter for adult transgender females receiving gender-affirming hormone therapy (Table 15, p. 3890)

Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, Rosenthal SM, Safer JD, Tangpricha V, T'Sjoen GG. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017 Nov 1;102(11):3869-3903. Erratum in: J Clin Endocrinol Metab. 2018 Feb 1;103(2):699. Erratum in: J Clin Endocrinol Metab. 2018 Jul 1;103(7):2758-2759. PMID: 28945902. doi:10.1210/jc.2017-01658.

American College of Obstetricians and Gynecologists (ACOG)

ACOG Committee Opinion Number 605, "Primary Ovarian Insufficiency in Adolescents and Young Women" (published 2014; reaffirmed 2020) recommends using the following in evaluation/diagnosis of primary ovarian insufficiency (Box 1, p. 2):

- History of irregular menses for at least three consecutive months
- Results of two random FSH and estradiol tests performed at least one month apart
- Prolactin and thyroid function testing

Committee opinion no. 605: primary ovarian insufficiency in adolescents and young women. Obstet Gynecol. 2014 Jul;124(1):193-197. PMID: 24945456. doi:10.1097/01.AOG.0000451757.51964.98.

American Academy of Family Physicians (AAFP)

In their practice resource, "Gynecomastia" (2012), the AAFP recommends a diagnostic algorithm of first testing hepatic function and measuring creatinine and thyroid stimulating hormone levels to determine whether a chronic disease underlies the gynecomastia. Then, if there is no evidence of

chronic disease, performing serum hCG, DHEAS, LH, FSH, estradiol, testosterone, and prolactin levels (p. 720).

Dickson G. Gynecomastia. Am Fam Physician. 2012 Apr 1;85(7):716-22. PMID: 22534349.

European Society of Human Reproduction and Embryology (ESHRE)

In the guideline "Ovarian Stimulation for IVF/ICSI" (2019), the ESHRE states that estradiol measurements are probably not recommended in addition to ultrasound during ovarian stimulation, as estradiol does not appear to benefit patients (i.e., has not been shown to increase probability of pregnancy or number of oocytes retrieved or decrease probability of ovarian hyperstimulation syndrome) (p. 88).

The Eshre Guideline Group On Ovarian Stimulation, Bosch E, Broer S, et al. ESHRE guideline: ovarian stimulation for IVF/ICSI†. Hum Reprod Open. 2020;2020(2):hoaa009. Erratum in: Hum Reprod Open. 2020;2020(4):hoaa067. doi:10.1093/hropen/hoaa009.

Kwan, et al.

In "Monitoring of stimulated cycles in assisted reproduction (IVF and ICSI)," the authors re-visited their 2014 review regarding the use of combined monitoring (transvaginal ultrasound and serum estradiol measurements) versus ultrasound only monitoring during ovarian stimulation. They again concluded, based on no new evidence/studies, that combined monitoring is not demonstrated to be more efficacious than ultrasound, alone (i.e., similar rates of clinical pregnancy and ovarian hyperstimulation syndrome incidence). Guidelines generally recommend only ultrasound monitoring, and combined monitoring is controversial, but common in clinical practice (p. 1-2).

Kwan I, Bhattacharya S, Woolner A. Monitoring of stimulated cycles in assisted reproduction (IVF and ICSI). Cochrane Database Syst Rev. 2021 Apr 12;4(4):CD005289. PMID: 33844275; PMCID: PMC8094870. doi:10.1002/14651858.CD005289.pub4.

Follicle Stimulating Hormone (FSH) Tests

Lake, et al.

In a 2013 expert review of pituitary adenomas, Lake, et al. set out a detailed list of diagnostic tests for the evaluation of suspected pituitary adenomas, including an FSH level for patients with "signs or symptoms of pituitary adenoma" (p. 322).

Lake MG, Krook LS, Cruz SV. Pituitary Adenomas: an Overview. Am Fam Physician. 2013;88(5):319-327.

UpToDate

In a 2024 UpToDate review of pituitary adenoma management, Snyder, et al. recommend that patients with "signs, symptoms, or prior imaging suggest[ing] a sellar mass" undergo biochemical evaluation to include a serum FSH level.

Snyder P, et al. Clinical manifestations and diagnosis of gonadotroph and nonfunctioning pituitary adenomas. In: UpToDate. Updated May 2024. https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-gonadotroph-and-nonfunctioning-pituitary-adenomas

National Comprehensive Cancer Network (NCCN): Breast Cancer (4.2025)

This guideline recommends monitoring of estradiol and follicle stimulating hormone (FSH) levels for individuals in whom menopausal status must be assessed to guide selection of endocrine therapy for breast cancer. (p. BINV-O). Frequency of testing should be personalized to the patient (p. 1 of 2, BINV-K).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer 4.2025 https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

American Society for Reproductive Medicine (ASRM)

The "Fertility evaluation of infertile women: a committee opinion" recommends measurement of follicle-stimulating hormone (FSH) for women with infertility due to amenorrhea, to distinguish between ovarian insufficiency (candidacy for oocyte donation) and hypothalamic amenorrhea (candidacy for ovarian stimulation) (p. 1258).

Practice Committee of the American Society for Reproductive Medicine. Fertility evaluation of infertile women: a committee opinion. Fertil Steril. 2021 Nov;116(5):1255-1265. Epub 2021 Oct 2. PMID: 34607703. doi:10.1016/j.fertnstert.2021.08.038.

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The AUA/ASRM guideline "Diagnosis and Treatment of Infertility in Men" (2021) recommends evaluation of follicle-stimulating hormone (FSH) and testosterone for infertile men with impaired libido, erectile dysfunction, oligozoospermia or azoospermia, atrophic testes, or evidence of hormonal abnormality on physical evaluation (p. 38 and 39).

Schlegel PN, Sigman M, Collura B, et al. Diagnosis and treatment of infertility in men: AUA/ASRM guideline part I. J Urol. 2021;205(1):36-43. doi:10.1097/JU.0000000000001521.

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Kaplowitz P, Bloch C; Section on Endocrinology, American Academy of Pediatrics. Evaluation and Referral of Children With Signs of Early Puberty. Pediatrics. 2016 Jan;137(1). Epub 2015 Dec 14. PMID: 26668298. doi:10.1542/peds.2015-3732.

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Dickson G. Gynecomastia. Am Fam Physician. 2012 Apr 1;85(7):716-22. PMID: 22534349.

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The Endocrine Society

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Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Murad MH, Pinkerton JV, Santen RJ. Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015 Nov;100(11):3975-4011. Epub 2015 Oct 7. PMID: 26444994. doi:10.1210/jc.2015-2236.

The Endocrine Society's guideline "Testosterone Therapy in Men With Hypogonadism" (2018) recommends distinguishing between primary (testicular) and secondary (pituitary–hypothalamic) hypogonadism by measuring serum LH and FSH concentrations (p. 1716).

Bhasin S, Brito JP, Cunningham GR, et al. Testosterone therapy in men with hypogonadism: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2018;103(5):1715-1744. doi: 10.1210/jc.2018-00229.

In “Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons” (2017), The Endocrine Society recommends monitoring FSH every 6-12 months during puberty suppression (table 7, p 3883).

Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, Rosenthal SM, Safer JD, Tangpricha V, T'Sjoen GG. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017 Nov 1;102(11):3869-3903. Erratum in: J Clin Endocrinol Metab. 2018 Feb 1;103(2):699. Erratum in: J Clin Endocrinol Metab. 2018 Jul 1;103(7):2758-2759. PMID: 28945902. doi:10.1210/jc.2017-01658.

International PCOS Network

The “Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome,” supported by a partnership with American Society for Reproductive Medicine and the Endocrine Society, recommend measuring TSH, prolactin, 17-OH progesterone, and FSH levels in individuals with irregular menstrual cycles and clinical hyperandrogenism to rule out other causes of these symptoms before confirming PCOS diagnosis (Figure 1, p. G60).

Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, Costello MF, Boivin J, Redman LM, Boyle JA, Norman RJ, Mousa A, Joham AE; International PCOS Network. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Eur J Endocrinol. 2023 Aug 2;189(2):G43-G64. PMID: 37580861. doi:10.1093/ejendo/lvad096.

Luteinizing Hormone (LH) Tests

International PCOS Network

The “Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome,” supported by a partnership with American Society for Reproductive Medicine and the Endocrine Society, recommend measuring LH in individuals undergoing evaluation of PCOS with signs/symptoms of hypogonadotropic hypogonadism (Figure 1, p. G60).

Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, Costello MF, Boivin J, Redman LM, Boyle JA, Norman RJ, Mousa A, Joham AE; International PCOS Network. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Eur J Endocrinol. 2023 Aug 2;189(2):G43-G64. PMID: 37580861. doi:10.1093/ejendo/lvad096.

American Academy of Family Physicians (AAFP)

In their practice resource, "Gynecomastia" (2012), the AAFP recommends a diagnostic algorithm of first testing hepatic function and measuring creatinine and thyroid stimulating hormone levels to determine whether a chronic disease underlies the gynecomastia. Then, if there is no evidence of chronic disease, performing serum hCG, DHEAS, LH, FSH, estradiol, testosterone, and prolactin levels (p. 720).

Dickson G. Gynecomastia. Am Fam Physician. 2012 Apr 1;85(7):716-22. PMID: 22534349..

American Academy of Pediatrics (AAP)

In "Evaluation and Referral of Children With Signs of Early Puberty" (2016), the AAP defines central precocious puberty (CPP) as the full activation of the HPG axis before 8 years of age in girls and before 9 years of age in boys. They suggest considering a CPP diagnosis in girls who display progressive breast development and who cross percentiles upward on the linear growth chart. They state that CPP is much less common in boys but suggest considering a diagnosis of CPP in boys who display both testicular and penile enlargement before 9 years of age. The baseline workup suggested for CPP in a child includes FSH, LH, and either estradiol (for girls) or testosterone (for boys) (p. 4).

Kaplowitz P, Bloch C; Section on Endocrinology, American Academy of Pediatrics. Evaluation and Referral of Children With Signs of Early Puberty. Pediatrics. 2016 Jan;137(1). Epub 2015 Dec 14. PMID: 26668298. doi:10.1542/peds.2015-3732.

The Endocrine Society

In the clinical practice guideline "Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons" (2017), The Endocrine Society recommends monitoring LH every 6-12 months during puberty suppression (table 7, p. 3883).

Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, Rosenthal SM, Safer JD, Tangpricha V, T'Sjoen GG. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017 Nov 1;102(11):3869-3903. Erratum in: J Clin Endocrinol Metab. 2018 Feb 1;103(2):699. Erratum in: J Clin Endocrinol Metab. 2018 Jul 1;103(7):2758-2759. PMID: 28945902. doi:10.1210/jc.2017-01658.

UpToDate

In a 2024 expert UpToDate review on the "Clinical manifestations and diagnosis of gonadotroph and nonfunctioning pituitary adenomas", the authors recommend testing of multiple hormones when a sellar mass greater than 1 cm is detected on MRI. The list of biomarkers to be tested includes luteinizing hormone (LH).

Snyder P, et al. Clinical manifestations and diagnosis of gonadotroph and nonfunctioning pituitary adenomas. In: UpToDate. Updated May 2024. https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-gonadotroph-and-nonfunctioning-pituitary-adenomas

Lake, et al.

In their 2013 review, Lake, et al. recommend LH testing during evaluation for suspected pituitary adenomas to differentiate between hypogonadism and a gonadotroph-secreting tumor (Table 2, p. 322).

Lake MG, Krook LS, Cruz SV. Pituitary Adenomas: an Overview. Am Fam Physician. 2013;88(5):319-327.

Prolactin Tests

Lake, et al.

In a 2013 expert review of pituitary adenomas, Lake, et al. set out a detailed list of diagnostic tests for the evaluation of suspected pituitary adenomas, including a prolactin level for patients with signs or symptoms of pituitary adenoma" (p. 322).

Lake MG, Krook LS, Cruz SV. Pituitary Adenomas: an Overview. Am Fam Physician. 2013;88(5):319-327.

The Endocrine Society

In 2011, the Endocrine Society released a clinical practice guideline with detailed diagnosis and management guidelines for incidentally detected pituitary adenomas. Recommendation 1.0 states

that all patients with an incidentally discovered pituitary adenoma should be evaluated for hormone hypersecretion with laboratory workup, including a serum prolactin level (p. 897).

Freda PU, Beckers AM, Katznelson L, et al. Pituitary Incidentaloma: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2011;96(4):894-904. doi:10.1210/jc.2010-1048

International PCOS Network

The *"*International evidence-based guideline for the assessment and management of polycystic ovary syndrome" (2023), supported by a partnership with American Society for Reproductive Medicine and the Endocrine Society, recommends including prolactin testing in individuals with suspected PCOS (FIGURE 1).

Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, Costello MF, Boivin J, Redman LM, Boyle JA, Norman RJ, Mousa A, Joham AE; International PCOS Network. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Eur J Endocrinol. 2023 Aug 2;189(2):G43-G64. PMID: 37580861. doi:10.1093/ejendo/lvad096.

American College of Obstetrics and Gynecology (ACOG)

ACOG Practice Bulletin Number 194, "Polycystic Ovary Syndrome" (2009; 2018 interim update to treatment sections only, as highlighted), contains a suggested clinical workup to include laboratory assessment prolactin levels (Box 1, p. e159).

American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin No. 194: Polycystic ovary syndrome. Obstet Gynecol. 2018;131(6):e157-e171. doi:10.1097/AOG.0000000000002656. Published correction appears in Obstet Gynecol. 2020;136(3):638. doi:10.1097/AOG.0000000000004069

American Society for Reproductive Medicine (ASRM)

In "Fertility evaluation of infertile women: a committee opinion" (2021), the ASRM lists prolactin as a test that should not be routinely ordered for infertility unless specifically indicated. They recommend prolactin testing for women with infertility who have oligomenorrhea, amenorrhea, or galactorrhea (p. 1258).

Practice Committee of the American Society for Reproductive Medicine. Fertility evaluation of infertile women: a committee opinion. Fertil Steril. 2021 Nov;116(5):1255-1265. Epub 2021 Oct 2. PMID: 34607703. doi:10.1016/j.fertnstert.2021.08.038.

The Endocrine Society

The clinical practice guideline "Diagnosis and Treatment of Hyperprolactinemia" The Endocrine Society recommends single measurement of serum prolactin to confirm a diagnosis of hyperprolactinemia, and recommends against dynamic prolactin secretion testing. Samples subject to excessive venipuncture stress may need to be re-run. They describe hypogonadism, infertility, visual field defects, and galactorrhea as the primary signs and symptoms of hyperprolactinemia, along with secondary bone loss due to hyperprolactinemia-mediated sex steroid attenuation (p. 274-278).

Melmed S, Casanueva FF, Hoffman AR, Kleinberg DL, Montori VM, Schlechte JA, Wass JA; Endocrine Society. Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011 Feb;96(2):273-88. PMID: 21296991. doi:10.1210/jc.2010-1692.

In "Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons" (2017), The Endocrine Society recommends periodically monitoring prolactin levels in transgender females treated with estrogens (p. 3890).

Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, Rosenthal SM, Safer JD, Tangpricha V, T'Sjoen GG. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017 Nov 1;102(11):3869-3903. Erratum in: J Clin Endocrinol Metab. 2018 Feb 1;103(2):699. Erratum in: J Clin Endocrinol Metab. 2018 Jul 1;103(7):2758-2759. PMID: 28945902. doi:10.1210/jc.2017-01658.

American Academy of Family Physicians (AAFP)

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Dickson G. Gynecomastia. Am Fam Physician. 2012 Apr 1;85(7):716-22. PMID: 22534349.

American Urological Society (AUA) and American Society for Reproductive Medicine (ASRM)

In this 2024 joint clinical practice guideline, the authors recommend several follow up tests in males with infertility and a fasting morning total testosterone below 300ng/dL, including a serum prolactin level (p. 22).

Schlegel PN, Sigman M, Collura B, et al. Diagnosis and treatment of infertility in men: AUA/ASRM guideline part I. J Urol. 2021;205(1):36-43. doi:10.1097/JU.0000000000001521.

Progesterone Tests

American Society for Reproductive Medicine (ASRM)

In "Fertility evaluation of infertile women: a committee opinion" (2021), the ASRM lists progesterone as a test that should not be routinely ordered for infertility unless specifically indicated. They recommend progesterone testing to confirm anovulation in women with infertility and regular menstruation (p. 1258).

Practice Committee of the American Society for Reproductive Medicine. Fertility evaluation of infertile women: a committee opinion. Fertil Steril. 2021 Nov;116(5):1255-1265. Epub 2021 Oct 2. PMID: 34607703. doi:10.1016/j.fertnstert.2021.08.038.

American Academy of Family Physicians (AAFP)

In "First Trimester Bleeding: Evaluation and Management", the AAFP proposes consideration of obtaining progesterone level when a hemodynamically stable patient presents with first trimester bleeding (bleeding <12 weeks's gestation), no identifiable cause of the bleeding (i.e., products of conception, non-obstetric bleeding), and has an ultrasound confirmed intrauterine pregnancy with uncertain viability (p. 3, Figure 1).

Hendriks E, MacNaughton H, MacKenzie MC. First Trimester Bleeding: Evaluation and Management. Am Fam Physician. 2019;99(3):166-174.

International PCOS Network

The "International evidence-based guideline for the assessment and management of polycystic ovary syndrome" (2023), supported by a partnership with American Society for Reproductive Medicine and the Endocrine Society, recommends progesterone testing to confirm anovulation in individuals with signs of hyperandrogenism/suspected PCOS and regular menstrual cycles (TABLE 4).

Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, Costello MF, Boivin J, Redman LM, Boyle JA, Norman RJ, Mousa A, Joham AE; International PCOS Network. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Eur J Endocrinol. 2023 Aug 2;189(2):G43-G64. PMID: 37580861. doi:10.1093/ejendo/lvad096.

Stavridis, et al.

Low luteal progesterone has been shown to negatively impact pregnancy outcomes following embryo transfer. The precise progesterone levels that constitute low versus adequate are still inconclusive, and established guidelines around optimal hormone replacement treatment-frozen embryo transfer are still lacking.

In this systematic evidence review, the authors examined studies that reported on the association between use of rescue progesterone and one or more pregnancy outcomes. They concluded that measuring progesterone prior to embryo transfer (day before or day of) may allow for patients with low circulating levels to receive supplemental progesterone, which may in turn reduce adverse reproductive outcomes, resulting in comparable outcomes to pregnancies with adequate progesterone levels.

Stavridis K, Kastora SL, Triantafyllidou O, Mavrelos D, Vlahos N. Effectiveness of progesterone rescue in women presenting low circulating progesterone levels around the day of embryo transfer: a systematic review and meta-analysis. Fertil Steril. 2023;119(6):954-963. doi:10.1016/j.fertnstert.2023.02.007

Monogenic Diabetes (Including Maturity Onset Diabetes of the Young (MODY)) Panels

American Diabetes Association

In 2024, the American Diabetes Association made the following recommendations (p. S32):

- Individuals of any age who were diagnosed with diabetes in the first 6 months of life should have immediate genetic testing for neonatal diabetes (Category A).

- Children and those diagnosed in early adulthood who have diabetes not characteristic of type 1 or type 2 diabetes that occurs in successive generations (suggestive of an autosomal dominant pattern of inheritance) should have genetic testing for maturity-onset diabetes of the young (Category A)

American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: standards of care in diabetes-2024. Diabetes Care. 2024;47(suppl 1):S20-S42. doi:10.2337/dc24-S002

Murphy, et al.

Murphy, et al. (2023) performed a systematic review and issued an expert opinion on how to use precision diagnostics to identify individuals with monogenic diabetes. The article states that the following individuals should be offered testing for monogenic diabetes:

1. All patients diagnosed with diabetes before the age of 6 months should be tested for monogenic forms of neonatal diabetes using the large-gene panel.
2. All patients diagnosed between 6 and 12 months should be tested for monogenic forms of neonatal diabetes using the large-gene panel. No demonstrable yield of monogenic etiology to support reflexive genetic testing patients diagnosed with diabetes between 12-24 months.
3. Women with gestational diabetes and fasting glucose above 5.5 mmol/L without obesity* should be tested for GCK etiology.
4. Those with persisting, mild hyperglycemia (HbA1c 38–62 mmol/mol, or fasting glucose 5.5–7.8 mmol/L) at any age, in the absence of obesity* should be tested for GCK etiology.
5. People without obesity under the age of 30 years who are either autoantibody negative and/or have retained C-peptide levels should be tested for monogenic diabetes using a large-gene panel (p.10).

Murphy R, Colclough K, Pollin TI, et al. The use of precision diagnostics for monogenic diabetes: a systematic review and expert opinion. Commun Med (Lond). 2023;3(1):136. Published 2023 Oct 5. doi:10.1038/s43856-023-00369-8

International Society for Pediatric and Adolescent Diabetes (ISPAD)

In 2022, the International Society for Pediatric and Adolescent Diabetes (ISPAD) released a clinical practice consensus guideline for the diagnosis and management of monogenic diabetes in children and adolescents. The statement includes the following recommendations for genetic testing in the setting of neonatal diabetes and maturity onset diabetes of the young:
"All infants diagnosed with diabetes in the first 6 months of life are recommended to have immediate molecular genetic testing. Genetic testing may be considered in infants diagnosed between 6 and 12 months, especially in those without islet autoantibodies or who have other features suggestive of a monogenic cause" (p. 1190).

"The diagnosis of maturity onset diabetes of the young (MODY) is recommended in the following scenarios: family history of diabetes in a parent and first-degree relatives of that affected parent in persons with diabetes who lack the characteristics of T1D and T2D" (p. 1191).

Greeley SAW, Polak M, Njølstad PR, et al. ISPAD Clinical Practice Consensus Guidelines 2022: The diagnosis and management of monogenic diabetes in children and adolescents. Pediatr Diabetes. 2022;23(8):1188-1211. doi:10.1111/pedi.13426

General Health Panel (Comprehensive Metabolic Panel (CMP), Thyroid Stimulating Hormone (TSH), and Complete Blood Count (CBC))

The "General Health Panel" includes a comprehensive metabolic panel (CMP), complete blood count (CBC), and thyroid stimulating hormone (TSH) test. There are no professional guidelines or recommendations we identified to support the use of this panel test, therefore, coverage requires meeting the established Concert medical policy criteria for the component test: TSH.

Hemoglobin A1C (HbA1c)

US Preventive Services Task Force (USPSTF)

In "Screening for Prediabetes and Type 2 Diabetes," USPSTF recommends screening once every 3 years for non-pregnant adults aged 35 years to 70 years with overweight or obesity and no symptoms of diabetes (p. 736-737).

US Preventive Services Task Force. Screening for Prediabetes and Type 2 Diabetes: US Preventive Services Task Force Recommendation Statement. JAMA. 2021;326(8):736–743. doi:10.1001/jama.2021.12531

American Diabetes Association (ADA)

In "Diagnosis and Classification of Diabetes: Standards of Care in Diabetes" (*2024)*, the ADA recommends HbA1c testing to screen for diabetes or prediabetes for the following (tables 2.4 and 2.5, p. S27-28):

- Those with prediabetes (at least annual screening recommended, with modification based on individual risk)
- Those previously diagnosed with GDM (lifelong testing at least every 3 years recommended)
- Exposure to medications that increase the risk of prediabetes/diabetes, such as glucocorticoids, statins, thiazide diuretics, some HIV medications, and second-generation antipsychotic medications
- History of pancreatitis
- Those with overweight or obesity and at least one of the following additional risk factors for diabetes: first-degree relative with diabetes, high-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander), history of CVD, diagnosis of hypertension or on therapy for hypertension, HDL cholesterol level <35 mg/dL and/or a triglyceride level >250 mg/dL, individuals with polycystic ovary syndrome, physical inactivity, or other clinical conditions associated with insulin resistance
- For children, a first or second-degree relative with diabetes or a history of maternal diabetes or GDM during that child's gestation is an additional risk factor

Regardless of risk factors, screening should begin at 35 years of age and be repeated every 3 years if results are normal, or more frequently in response to a change in signs/symptoms or risk factors (p. S27).

The authors state for diagnostic purposes, unless there is a clear clinical diagnosis, an abnormal A1C must be repeated promptly. The confirmatory/repeat testing can be from the same time point or from a different collection (p. S22).

The A1C test may underestimate glycemia in people with HIV, and is therefore not recommended for diagnosis; it may also present challenges for monitoring in this population (p. S30). A1C has low sensitivity for cystic fibrosis-related diabetes and is therefore not recommended as a screening test in this population (p. S31).

American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: standards of care in diabetes-2024. Diabetes Care. 2024;47(suppl 1):S20-S42. doi:10.2337/dc24-S002

In "Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes" (2024), monitoring A1C in those with diabetes mellitus is recommended at least twice per year for individuals with diabetes who have stable glycemic control and are meeting treatment goals. They recommend quarterly testing for those with diabetes whose treatment has recently changed or who are not meeting treatment goals (p. S112).

The authors also recommend that after an acute episode of pancreatitis it is necessary to screen people for diabetes within 3–6 months and annually thereafter. Screening for diabetes is recommended annually for people with chronic pancreatitis (p. S30).

American Diabetes Association Professional Practice Committee. 6. Glycemic goals and hypoglycemia: standards of care in diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S111-S125. doi:10.2337/dc24-S006

American Urological Association (AUA)

In the AUA's guidelines on erectile dysfunction(2018), it is stated that erectile dysfunction is one of the most common symptoms of diabetes in men and may be a manifestation of undiagnosed diabetes mellitus (p. 634).

Burnett AL, Nehra A, Breau RH, et al. Erectile dysfunction: AUA guideline. J Urol. 2018;200(3):633-641. doi: 10.1016/j.juro.2018.05.004. Published correction appears in J Urol. 2022;207(3):743.

The American College of Obstetricians and Gynecologists (ACOG)

In an ACOG practice bulletin No. 201 titled "Pregestational Diabetes Mellitus" (2018), the authors state that given the alteration of red cell turnover and physiologic changes in glucose parameters, pregnancy warrants the higher frequency of monthly HbA1c testing (p. e231).

American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin No. 201: pregestational diabetes mellitus. Obstet Gynecol. 2018;132(6):e228-e248. doi: 10.1097/AOG.0000000000002960

Parathyroid Hormone (PTH) Tests

American Association of Endocrine Surgeons (AAES)

In the AAES guidelines for definitive management of primary hyperparathyroidism, the evaluation of suspected primary hyperparathyroidism (pHPT) should include serum total calcium, parathyroid hormone (PTH), creatinine, and 25-hydroxyvitamin D levels. The authors note the symptoms of primary hyperparathyroidism as being heterogenous and overlapping with those of aging and disease, ranging from having no recognizable symptoms to profound physical and mental disability. Despite hypercalcemia being a hallmark of this disorder, some patients may also present as normocalcemic. It is stated that the definition of symptomatic disease is still evolving (p. 960-962).

The supplemental document lists some of the common symptoms of primary hyperparathyroidism as nephrolithiasis, osteitis fibrosis cystica, peptic ulcers, fatigue, depression, anxiety, emotional lability, sleep disturbances, worsening memory, inability to concentrate, general weakness, cardiovascular symptoms as well as other psychiatric and neurocognitive symptoms but also states that the "classic" manifestations are rare as the majority, up to 80%, of patients now present with asymptomatic primary hyperparathyroidism (supplemental document attached to publication).

Wilhelm SM, Wang TS, Ruan DT, et al. The American Association of Endocrine Surgeons Guidelines for definitive management of primary hyperparathyroidism. JAMA Surg. 2016;151(10):959–968. doi:10.1001/jamasurg.2016.2310

Bilezikian JP, et al.

In Evaluation and Management of Primary Hyperparathyroidism: Summary Statement and Guidelines from the Fifth International Workshop (2022), it is recommended that for diagnosis of primary hyperparathyroidism, intact parathyroid hormone analysis be performed (utilizing either a second or third generation assay) at least twice over a 3-6 month period after any secondary hyperparathyroidism and alternative causes have been ruled out (p. 2294).

Monitoring of individuals who do not qualify for surgery may include parathyroid hormone, as clinically indicated (p. 2295).

The authors list some of the common "classic" symptoms of hyperparathyroidism as a constellation of skeletal and renal complication, bone pain due to osteitis fibrosa cystica, fractures, chronic kidney disease, neuromuscular manifestations with proximal myopathy, nephrocalcinosis, and renal colic associated with nephrolithiasis. Use of the medication lithium can be a cause of hyperparathyroidism, and lithium-associated primary hyperparathyroidism may also display features of thyroid dysfunction and impaired renal function. Analysis of parathyroid

hormone (PTH) is necessary for differential diagnosis of hypercalcemia of malignancy in cases such as osteolytic metastases, tumors that produce parathyroid hormone like protein, or hypercalcemia due to abnormal levels of vitamin D 1,25(OH)2. PTH analysis is also recommended in the differential diagnosis of granulomatous diseases, such as sarcoidosis and tuberculosis, which may cause hypercalcemia by production of vitamin D 1,25(OH)2 (p. 2298).

Bilezikian JP, Khan AA, Silverberg SJ, et al. Evaluation and management of primary hyperparathyroidism: summary statement and guidelines from the fifth international workshop. J Bone Miner Res. 2022;37(11):2293-2314. doi:10.1002/jbmr.4677

Clarke BL

In "Hypoparathyroidism: Update of Guidelines from the 2022 International Task Force," it is recommended to analyse parathyroid hormone on at least 2 occasions, using a second or third generation test, in the diagnosis of hypoparathyroidism. The common signs and symptoms of hypoparathyroidism may include hypocalcium, hypo-vitamin D 1,25(OH)2, increased serum phosphorus, cataracts, infections, nephrocalcinosis/ nephrolithiasis, renal insufficiency, seizures, depression, ischemic heart disease, cardiac arrhythmias, and on occasion, basal ganglia calcification. Anterior neck surgery and thyroidectomy are risk factors for developing hypoparathyroidism and analysis of parathyroid hormone (PTH) may be used to predict which patients will not develop permanent postsurgical hypoparathyroidism (p. 605-607).

Clarke BL. Hypoparathyroidism: update of guidelines from the 2022 International Task Force. *Arch Endocrinol Metab*. 2022;66(5):604-610. doi:10.20945/2359-3997000000549

Kidney Disease Improving Global Outcomes (KDIGO)

In "Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease", the authors recommend initial testing of parathyroid hormone for diagnosis and serial testing of parathyroid hormone (PTH) due to changes in bone mineral metabolism and alterations of calcium and phosphate homeostasis that may be present in chronic kidney disease (CKD) that worsen as eGFR declines as the condition progresses. For this reason, serial PTH analysis is recommended in those who are in later stages, CKD G3a-G5 (p. S229- S230).

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International. 2024;105(Suppl 4S):S117–S314. https://kdigo.org/wp-content/uploads/2024/03/KDIGO-2024-CKD-Guideline.pdf

Camacho, et al.

The 2020 publication of American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis—2020 Update recommends laboratory evaluation of osteoporosis to include analysis of intact parathyroid hormone (PTH) (p.14).

Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of postmenopausal osteoporosis—2020 Update. Endocrine Practice. 2020;26:1-46. https://doi.org/10.4158/GL-2020- 0524SUPPL

National Comprehensive Cancer Network (NCCN): Neuroendocrine and Adrenal Tumors (2.2025)

This guideline recommends analysis of PTH in the clinical evaluation for the diagnosis of multiple endocrine neoplasia, type 1 and type 2 (p. MEN1-1, MEN2-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. Version 2.2025.
https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf

National Comprehensive Cancer Network (NCCN): Bone Cancer (2.2025)

This guideline recommends routine analysis of parathyroid hormone (PTH) to rule out the differential diagnosis of brown tumor of hyperparathyroidism (p. MS-23).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf

National Comprehensive Cancer Network (NCCN): Thyroid Carcinoma (1.2025)

In this guideline, when the clinical presentation is MEN2A/Familial medullary thyroid carcinoma, additional workup is recommended to include parathyroid hormone analysis (p. MEDU-3).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Thyroid Carcinoma 1.2025 https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf

DEFINITIONS

1. **Autosomal dominant pattern of inheritance** refers to a type of transmission of a genetic condition in which only one mutated copy of a gene (rather than two) is necessary for an individual to manifest the disease. These conditions are generally characterized by the following traits:

    a. There are individuals with the condition in multiple generations of a family

    b. Individuals who do not have the condition do not have children with the condition

    c. Individuals with the condition have a parent with the condition

2. **Conditions associated with increased risk for testosterone deficiency** include unexplained anemia, bone density loss/unexplained fracture, diabetes, exposure to chemotherapy, direct or scatter radiation therapy to the testes, HIV.

3. **Factor known to alter sex hormone binding globulin (SHBG) levels** include aging, obesity, diabetes mellitus, use of glucocorticoids, progestins, and androgenic steroids, use of estrogens, nephrotic syndrome, cirrhosis/hepatitis, hypo/hyperthyroidism, acromegaly, HIV disease, certain anticonvulsants, and polymorphisms in the SHBG gene (according to The Endocrine Society, 2018).

4. **Increased risk factors associated with thyroid dysfunction** may include autoimmune diseases (e.g., type 1 diabetes mellitus, celiac disease, autoimmune gastric atrophy, multiple autoimmune endocrinopathies), heart disease, Down syndrome, Turner syndrome, Addison disease, post-subtotal thyroidectomy, radioiodine treatment, radiation therapy of the neck, and use of medications such as amiodarone, lithium, interferons, and rifampin, tyrosine kinase inhibitors, phenobarbital, interleukin-2, and immune checkpoint inhibitors. Family history of autoimmune diseases such as Grave's Disease may also increase risk.

5. **Signs or symptoms of thyroid dysfunction** are broad, and can be non-specific and highly variable.

a. Common signs or symptoms of *hypo*thyroidism may include infertility, cold intolerance, fatigue, weight gain, depression, dry skin, constipation, voice changes, arthralgias, cognitive impairment/difficulty focusing, edema, hair thinning/loss or dryness, weakness, lethargy, memory impairment, menorrhagia, muscle cramping, myalgia, and bradycardia.

b. Common signs and symptoms of *hyper*thyroidism may include anxiety, jitteriness, palpitations, tachycardia, tremor, hyperdefecation (not diarrhea), onycholysis, vitiligo, patchy skin or hyperpigmentation, heat intolerance, increased eye sensitivity, insomnia, weight loss despite increase in appetite, blurred vision, photophobia, and increased lacrimation.

c. Common symptoms of thyroid cancer or other thyroid dysfunction can include hoarseness, difficulty swallowing, pressure or swelling in the neck, and persistent/chronic cough.

6. **Signs or symptoms of female hypogonadism** include amenorrhea, sexual dysfunction, and vasomotor symptoms.

7. **Signs or symptoms of male hypogonadism** include ambiguous genitalia, small testes/phallus, lack of development of/loss of secondary sex characteristics, decreased muscle mass, and gynecomastia.

8. **Signs or symptoms of parathyroid dysfunction** can vary greatly from no symptoms to severe physical and/or cognitive and physical symptoms. When present, these signs and symptoms may include: hypercalcemia, hypocalcemia, hyper-vitamin D level, hypo-vitamin D level, constellation of skeletal and renal complication, bone pain, fragility/non-trauma fractures, chronic kidney disease, neuromuscular manifestations with proximal myopathy, nephrocalcinosis/ nephrolithiasis, renal colic, osteitis fibrosis cystica, peptic ulcers, fatigue, depression, anxiety, emotional lability, sleep disturbances, worsening memory, inability to concentrate, general weakness, general cardiovascular symptoms, general psychiatric and neurocognitive symptoms, increased serum phosphorus, cataracts, infections, renal insufficiency, seizures, ischemic heart disease, cardiac arrhythmias, and on occasion basal ganglia calcification.

9. **Risk factors for parathyroid dysfunction** can include personal history of chronic kidney disease (CKD), post-total thyroidectomy status, personal history of thyroid cancer, post-anterior neck surgery status, use of certain medications such as lithium,

family history of familial medullary thyroid carcinoma, family history of multiple endocrine neoplasia types 1 and 2.

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2025, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT® Codes	Description
82024	Adrenocorticotropic hormone (ACTH)
82088	Aldosterone
82154	Androstanediol glucuronide
82157	Androstenedione
82160	Androsterone
82163	Angiotensin II
82166	Anti-mullerian hormone (AMH)
82308	Calcitonin
82383	Catecholamines; blood
82384	Catecholamines; fractionated
82528	Corticosterone
82530	Cortisol; free
82533	Cortisol; total
82626	Dehydroepiandrosterone (DHEA)
82627	Dehydroepiandrosterone-sulfate (DHEA-S)
82633	Desoxycorticosterone, 11-
82634	Deoxycortisol, 11-
82642	Dihydrotestosterone (DHT)

CPT® Codes	Description
82670	Estradiol; total
82671	Estrogens; fractionated
82672	Estrogens; total
82679	Estrone
82681	Estradiol; free, direct measurement (eg, equilibrium dialysis)
83001	Gonadotropin; follicle stimulating hormone (FSH)
83002	Gonadotropin; luteinizing hormone (LH)
83003	Growth hormone, human (HGH) (somatotropin)
83006	Growth stimulation expressed gene 2 (ST2, Interleukin 1 receptor like-1)
83498	Hydroxyprogesterone, 17-d
83525	Insulin; total
83527	Insulin; free
83586	Ketosteroids, 17- (17-KS); total
83593	Ketosteroids, 17- (17-KS); fractionation
83727	Luteinizing releasing factor (LRH)
83835	Metanephrines
83970	Parathormone (parathyroid hormone)
84135	Pregnanediol
84138	Pregnanetriol
84140	Pregnenolone
84143	17-hydroxypregnenolone
84144	Progesterone
84146	Prolactin
84206	Proinsulin
84233	Receptor assay; estrogen
84234	Receptor assay; progesterone
84244	Renin
84260	Serotonin
84270	Sex hormone binding globulin (SHBG)
84305	Somatomedin

CPT® Codes	Description
84307	Somatostatin
84402	Testosterone; free
84403	Testosterone; total
84410	Testosterone; bioavailable, direct measurement (eg, differential precipitation)
84432	Thyroglobulin
84436	Thyroxine; total
84437	Thyroxine; requiring elution (eg, neonatal)
84439	Thyroxine; free
84442	Thyroxine binding globulin (TBG)
84443	Thyroid stimulating hormone (TSH)
84445	Thyroid stimulating immune globulins (TSI)
84479	Thyroid hormone (T3 or T4) uptake or thyroid hormone binding ratio (THBR)
84480	Triiodothyronine T3; total (TT-3)
84481	Triiodothyronine T3; free
84482	Triiodothyronine T3; reverse
84681	C-peptide
84703	Gonadotropin, chorionic (hCG); qualitative
84830	Ovulation tests, by visual color comparison methods for human luteinizing hormone

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy developed.	1/26	1/26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of

physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members/enrollees and their representatives are bound to the terms and conditions expressed herein through the terms of their

contracts. Where no such contract exists, providers, members/enrollees and their representatives agree to be bound by such terms and conditions by providing services to members/enrollees and/or submitting claims for payment for such services.

Note: For Medicaid members/enrollees, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.