Toward Optimized Practice

# LABORATORY ENDOCRINE TESTING: AMENHORRHEA (WITHOUT HIRSUTISM) AND MENOPAUSE

**Clinical Practice Guideline | January 2008**

**OBJECTIVE**

Clinicians in Alberta optimize laboratory tests for investigation of amenorrhea (without hirsutism) and suspected menopause

**TARGET POPULATION**

Women with primary amenorrhea

Girls with the lack of breast development by age 14 years, or by the lack of menses by age 16 in the presence of normal secondary sexual development, or by the lack of menses by three years after the larche

Women with secondary amenorrhea (more than six months without menses after prior establishment of menses)

**EXCLUSIONS**

Pregnant women

# RECOMMENDATIONS

## PRIMARY AMENORRHEA

- ✓ Refer for appropriate medical consultation

## SECONDARY AMENORRHEA

Defined as no menses ≥ six months or fewer than three menses in six months.

- ✓ Rule out pregnancy
- ✓ Order a follicle stimulating hormone (FSH) and a prolactin level, to determine the amenorrhea disease category
- ✓ Follow endocrine testing algorithm (see Appendix A)
- ✓ Repeat endocrine testing if necessary to confirm a diagnosis

## MENOPAUSE

- ✓ Order FSH to confirm menopause – this is the ONLY TEST NEEDED
- X DO NOT test for luteinizing hormone (LH), FSH, estradiol and progesterone for diagnosis or monitoring treatment
- X DO NOT order follow-up testing for patients receiving hormone replacement therapy as results do not reflect the adequacy of treatment

# BACKGROUND

## PRIMARY AMENORRHEA

Primary amenorrhea indicates a significant medical disorder including genetic, anatomic, or endocrine causes[1,2] and has a prevalence of 1 to 2%. It occurs in the setting of delayed puberty as defined by the lack of breast development by age 14 years, or by the lack of menses by age 16 in the presence of normal secondary sexual development, or by the lack of menses by three years after the menarche.[3]

## SECONDARY AMENORRHEA

Secondary amenorrhea is defined as more than six months without menses after menses is established. Mechanisms responsible include anatomic (e.g., endometrial scarring by infections or curettage) and, most commonly, anovulation.[4] Anovulation may occur because of ovarian failure estrogen and progesterone secretion due to a variety of disorders. The most common cause of secondary amenorrhea in a premenopausal woman is pregnancy and this diagnosis must be excluded before further investigation is undertaken.[5] For those women who are estrogen replete, the most frequent cause is polycystic ovarian syndrome.[1] For those women who are estrogen deficient, hypothalamic disorders (including emotional stress, intercurrent illness, excessive exercise or weight change) are the most common causes.[1,6,7]

Non-prolactin secreting pituitary adenomas may also result in gonadotropin deficiency and amenorrhea. In women with known autoimmune disease (e.g., Type 1 Diabetes Mellitus, Hashimoto's thyroiditis or Addison's disease) premature ovarian failure should be considered.[8] Premature ovarian failure is defined as secondary amenorrhea, hypoestrogenemia, and elevated gonadotropins before age 40 years.[9,10] Prolactin levels are elevated in 10 to 20% of women with secondary amenorrhea and consequently serum prolactin should be measured in all cases of amenorrhea.[6,7,11]

## MENOPAUSE

The average age of menopause is 51 years.[12] However, in general, one year or more of amenorrhea after age 40 is commonly accepted as a diagnosis of menopause.[13] Symptoms of menopause begin in premenopausal years and progress as hormone levels decrease.[14,15] During the perimenopausal period, FSH becomes elevated while LH may remain normal, and FSH elevation precedes both the sustained loss of estrogen and progesterone secretion and of menses.[16,17] Elevated serum FSH (but not LH) levels completely separate women with and without ovarian follicles (ovarian failure) therefore best diagnose the menopause.[18,19,20] Doses of estrogen adequate to control menopausal symptoms do not fully suppress gonadotropins,[21,22] due to regulation of FSH by hormones other than estradiol, principally inhibin.[3] Thus, FSH levels cannot be used to monitor effectiveness of therapy. Therapy effectiveness should be based on the clinical status of each patient. Similarly, in patients receiving estrogen therapy, estrogen effects do not correlate with serum levels due to varying biologic potency and inability of estrogen assays to detect different estrogen metabolites.[22,23] Measurement of estrogen levels thus are not useful in determining adequacy of therapy.

## SUMMARY

This evidence and data indicate that initial laboratory investigation of amenorrhea to establish categories of disease should include FSH and prolactin. Laboratory tests (serum LH, FSH, estradiol, progesterone) do not have a role in monitoring therapy of ovarian failure.

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## *SUGGESTED CITATION*

Toward Optimized Practice (TOP) Endocrine Working Group. 2008 January. Laboratory endocrine testing: amenorrhea (without hirsutism) and menopause clinical practice guideline. Edmonton, AB: Toward Optimized Practice. Available from: http://www.topalbertadoctors.org

For more information see www.topalbertadoctors.org

## *GUIDELINE COMMITTEE*

The committee consisted of representatives of family medicine, general medicine, medical biochemistry, pathology, internal medicine, endocrinology, laboratory technologists and the public.

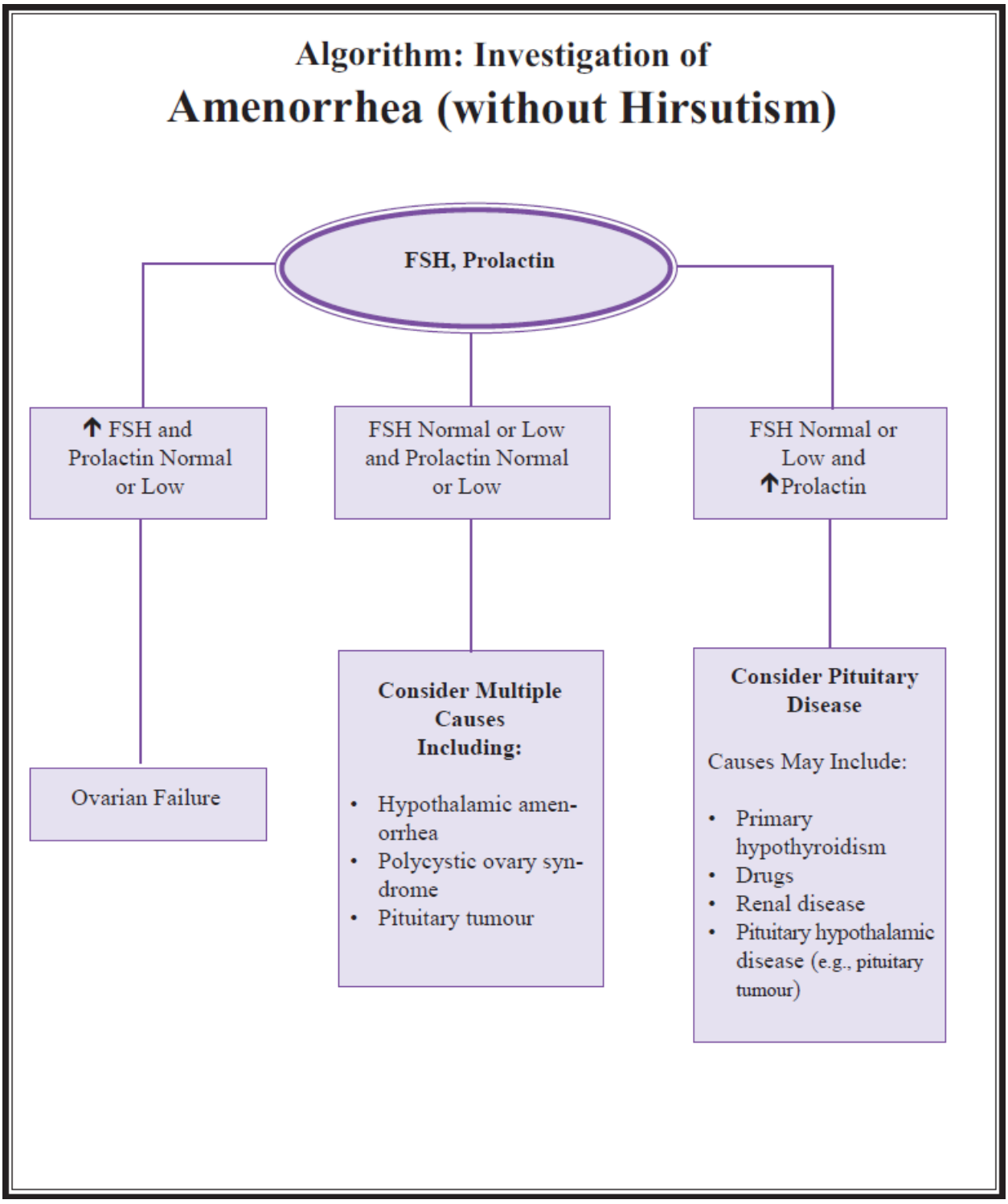
April 1998

Revised June 2001

Reviewed January 2008

Reviewed May 2014

# APPENDIX A


Algorithm: Investigation of
Amenorrhea (without Hirsutism)
FSH, Prolactin
↑ FSH and Prolactin Normal or Low
FSH Normal or Low and Prolactin Normal or Low
FSH Normal or Low and ↑Prolactin
Ovarian Failure
Consider Multiple Causes Including:
• Hypothalamic amenorrhea
• Polycystic ovary syndrome
• Pituitary tumour
Consider Pituitary Disease
Causes May Include:
• Primary hypothyroidism
• Drugs
• Renal disease
• Pituitary hypothalamic disease (e.g., pituitary tumour)