dutch®

MINI GUIDES

Third Edition

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CREATORS OF THE DUTCHTEST®

DUTCH Mini Guides

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PLEASE NOTE:

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DUTCH Mini Guides

Introduction

The educational DUTCH Mini Guides have been designed to help the medical practitioner learn more about a specific health condition and to identify patterns and markers noted on the DUTCH Test® commonly associated with these conditions. The Mini Guides are designed to be a concise resource about various health issues and include a brief overview of the medical condition, signs and symptoms, diagnosis and etiology, potential support considerations, resources for further exploration, and a unique DUTCH checklist for medical professionals to assess for patterns and markers associated with the health condition seen on the test.

The Mini Guides are intended to be used in combination with the DUTCH Interpretive Guide, the DUTCH Treatment Guide, and other DUTCH education resources. We recommend using the DUTCH Interpretive Guide first to interpret the DUTCH Test results, the DUTCH Mini Guides to further understand how various conditions may impact the results, and finally the DUTCH Treatment Guide to evaluate support considerations.

LET'S GET STARTED

AMENORRHEA

WHAT IS AMENORRHEA?

Amenorrhea is the absence of menstrual periods in a female who should be cycling. Amenorrhea affects 3-4% of reproductive-age women.

DUTCH RESOURCES ON AMENORRHEA

Webinar: "Diagnosing & Managing Secondary Amenorrhea" with Tori Hudson, ND

Case Study: "Hypothalamic Amenorrhea & Osteopenia" with Kelly Ruef, ND

Case Study: "Post-Pill Amenorrhea: In Search of a Cycle" with Kelly Ruef, ND

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

- Absence of menses is the key feature of amenorrhea.

Other signs and symptoms can vary widely and relate to the etiology (see below).

DIFFERENTIAL DIAGNOSIS & ETIOLOGY

Rule out other causes: Pregnancy, lactation, natural menopause (Age > 45), hysterectomy, uterine ablation history

Primary Amenorrhea

Primary amenorrhea is delayed or absent initiation of menses by age 15. If a girl does not show development of secondary sex characteristics by age 13, a diagnostic workup for primary amenorrhea should be initiated. Primary amenorrhea is usually due to a genetic or anatomical anomaly, but lifestyle and environment are also important. Examples:

- Congenital absence of reproductive structures (e.g., Turner syndrome, others)
- Delayed puberty due to chronic illness or physical stress (including young female athletes)

Secondary Amenorrhea

Secondary amenorrhea occurs in cycling females, with at least a two-year history of regular or irregular menses (if shorter, considered primary). Consider secondary amenorrhea in a regularly cycling female who has not menstruated in three months or in an irregularly cycling female who has not menstruated in 6 months.

Hypothalamic (35%) or Pituitary (17%)

- Functional hypothalamic amenorrhea (physical/emotional stress)
- Negative energy balance (hypometabolic, calorie and body fat deficit)
- Metabolic disease affecting pituitary signals (polycystic ovary syndrome (PCOS))
- Hormone secreting brain tumors such as in prolactinoma or Cushing's Disease

Ovarian (40%)

- PCOS
- Premature ovarian insufficiency (POI)
- Iatrogenic (surgery or damage to reproductive structures)

Uterine (7%)

- Blockage of the uterine opening through neoplasm, infection, damage, or trauma

Other

- Adrenal (Cushing's, 21-hydroxylase deficiency) (excess adrenal androgens)
- Early menopause (40-45) occurs naturally in 5% of women but should be worked up for secondary amenorrhea and is a diagnosis of exclusion

DUTCH CHECKLIST

Test patterns & markers associated with amenorrhea

Hypothalamic Amenorrhea, Primary Amenorrhea

- [ ] **Low estrogen** (in the menopausal range): HPO axis dysfunction
- [ ] **Low progesterone** (in the menopausal range): Anovulation, HPO axis dysfunction
- [ ] **High androgens:** High androgens can block the HPO axis, leading to irregular or absent periods
  - [ ] **High testosterone:** ovarian origin (PCOS, insulin resistance)
  - [ ] **High DHEA:** adrenal origin (21-hydroxylase deficiency, prolactinoma, adrenal PCOS, obesity, insulin resistance)
- [ ] **High 5a-metabolism:** Seen with obesity, high insulin, and PCOS
- [ ] **High free cortisol** (acute stress)
- [ ] **Low free cortisol** (chronic stress)
- [ ] **Cortisol metabolism issues:**
  - [ ] **Slow cortisol clearance rate (CCR):** Metabolized cortisol is LOWER relative to free cortisol and free cortisone. This is seen with hypothyroidism, anorexia, sluggish bile, and low metabolic function (hypothalamic or hypometabolic type amenorrhea).
  - [ ] **Fast cortisol clearance rate (CCR):** Metabolized cortisol is HIGHER relative to free cortisol and free cortisone. This is seen with hyperthyroidism, obesity, and inflammation (PCOS type amenorrhea).

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Identify and address the cause of amenorrhea
- Initiation/Re-initiation of cycle if possible
- Support foundational health

Other support may include, but is not limited to:

- Increase calorie intake and/or reduce exercise to levels that support reproductive hormones
- Consider herbal cycle support such as chaste tree, black cohosh, maca, etc.
- Further workup for Cushing's Disease, thyroid disease, etc.
- Treatment of underlying diseases such as thyroid disorders, hormone secreting tumors, etc.
- Surgery to remove barriers to menstruation
- Hormone replacement therapy (HRT) when necessary. When hormones are low and recovery is not possible, as in POI or other disorders, hormone replacement therapy is strongly suggested at least until the onset of natural menopause (age 52 and beyond) to normalize risks associated with chronically low sex hormones.
- If other disorders are found, such as prolactinoma, Cushing's Disease, hyper- or hypothyroidism, structural anomalies, address the root cause. HPO axis support may benefit cycle regulation if interfering conditions are treated but the cycle does not resume.

BREAST CANCER RISK FACTORS

WHAT IS BREAST CANCER?

Breast cancer (BC) occurs when breast cells begin to grow out of control and do not function as normal, typically due to DNA damage. Cancer cells can interfere with the function of other neighboring cells or spread (metastasize) to other tissues and interfere with essential body functions, leading to serious health concerns and death. BC is the most common type of cancer in females, accounting for 30% of all female cancer diagnoses. Breast cancer may be influenced by estrogen and how it is metabolized.

DUTCH RESOURCES ON BREAST CANCER

Webinar: "An Integrative Approach to Breast Cancer" with Tara Scott, MD

Webinar: "Breast Cancer Insights" Important Markers to Watch Using the DUTCH Test" with Carrie Jones, ND, FABNE, MPH

Case Study: "Elevated 4-OH Metabolites and Breast Cancer" with Kelly Ruef, ND

DUTCH Podcast: Summer School Episode 6: "Estrogen Metabolism and Breast Cancer Risk" with Lindsey Szczepanski, NP

Blog: "Breast Cancer, Nutrigenomics, and Estrogen Detoxification" by Christina O'Brien, DC, RDN, LD, DACNB, IFMCP

Blog: "Breast Cancer Risk Factors to Look for on the DUTCH Test" by Kelly Ruef, ND

Blog: "Evaluating Estrogen Detoxification to Understand Breast Cancer Risk" by Debbie Rice, ND, MPH

Blog: "Breast Cancer Awareness Month: How DUTCH Testing Helps Manage Risk" by Carrie Jones, ND, FABNE, MPH

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS, SYMPTOMS, AND RISK FACTORS

Breast cancer may be difficult to detect, and early identification reduces morbidity and mortality significantly. Routine screening of asymptomatic women based on age dramatically reduces BC mortality. BC is often found on routine screening tests with no signs or symptoms.

The patient may have a palpable breast mass, unilateral change in breast shape or movement, abnormal nipple discharge, or skin changes on the breast.

Risk factors that cannot be changed include female sex, advancing age, and genetics.

Modifiable risk factors:

- Sedentary lifestyle
- Being overweight or obese
- Drinking alcohol
- Smoking
- Poor estrogen metabolism

Diagnosis

Performed via imaging and biopsy. Procedures vary by type and history.

Differential Diagnosis

Breast masses can also be benign. Breast changes and symptoms should be thoroughly assessed in each case.

DUTCH CHECKLIST

Test patterns & markers associated with increased BC risk

- [ ] **High estrogens, in particular high estradiol** Due to obesity, insulin resistance, poor detoxification, or other based on patient history. Studies show that women with higher parent estrogens (estrone, estradiol) are significantly more likely to be diagnosed with BC in their life.
- [ ] **Poor phase 1 estrogen detox:**
  - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar)
  - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar)
- [ ] **Low phase 2 estrogen methylation** (slider bar)
- [ ] **Low melatonin** from increased nighttime light exposure may increase the risk of breast cancer
- [ ] **High free cortisol and diurnal rhythm issues** are associated with poor outcomes in breast cancer patients. This may be due to the high blood sugar and obesity response to high cortisol, lack of sleep, and impairment of the immune system (both high and low cortisol are associated with immune function changes).
- [ ] **Cortisol metabolism issues:**
  - [ ] **Fast cortisol clearance rate (CCR): metabolized cortisol is HIGHER compared to free cortisol and free cortisone.** This is seen with hyperthyroidism, obesity, and inflammation.
- [ ] **Circadian rhythm issues: High bedtime free cortisol** and/or **high middle-of-the-night free cortisol, absent/low CAR,** and **circadian rhythm dysfunction** can impair immune function and promote oxidative stress and metabolic disease
- [ ] **High Inflammation.** These patterns are associated with high inflammation on the DUTCH Test. The more patterns the patient has the higher the likelihood of high inflammation contributing to breast cancer:
  - [ ] High 5a reductase activity
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Cortisol metabolism favoring THF (acute) or THE (chronic)
  - [ ] High free cortisol (acute) or low free cortisol (chronic)
  - [ ] High kynurenate
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Prevent or reduce BC mortality
- Reduce modifiable risk factors
- Normalize long term BC risk by optimizing hormone levels and metabolism

Other support may include, but is not limited to:

- Follow guidelines on early identification of BC, screening, and diagnosis
- Due to the high mortality rate, patients at high genetic risk should review a plan with an oncologist or genetic counselor and follow oncology treatment plans

DYSMENORRHEA

WHAT IS DYSMENORRHEA?

Dysmenorrhea is the diagnostic term for painful menses. Dysmenorrhea consists of painful cramps in the lower abdomen or neighboring areas shortly before menses or during menses.

DUTCH RESOURCES ON DYSMENORRHEA

Case Study: "Optimizing the Menstrual Cycle: Painful Periods & Insulin Resistance" with Kelly Ruef, ND

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

Dysmenorrhea symptoms occur during or just before menstruation:

- Lower abdominal pain, most commonly aching or cramping
- Pain in pelvic region and/or low back
- Abdominal bloating
- Nausea
- Diarrhea

DIAGNOSIS & ETIOLOGY

Symptom Assessment

Dysmenorrhea may accompany serious infection or disease processes. Consider urgent care if menstrual pain is severe or associated with fever, chills, urethritis, severe bleeding, or any other urgent symptom that may be present.

Symptom Diary

Patient records the pattern, severity, and quality of symptoms throughout the menstrual cycle for 2-3 cycles. Key points include the age of menarche (first menstrual period), the regularity of cycles, the timing and duration of pain, its characteristics (e.g., sharp, dull, throbbing), and any factors that relieve or worsen the pain, especially NSAIDS or hormonal contraceptives. A history of pelvic pain outside of menstruation is also important.

Primary Dysmenorrhea

Primary dysmenorrhea is characterized by pain or cramping that begins a day or two before menstruation and lasts for 2-3 days. The pain is often described as cramping in the lower abdomen, and it may be accompanied by nausea, vomiting, fatigue, diarrhea, and headaches.

Secondary Dysmenorrhea

Secondary dysmenorrhea is distinguished from primary by pain and associated symptoms during other times in the cycle or lasting significantly longer than 2-3 days, indicating another medical condition is present and contributing to the menstrual pain.

Diagnosis

- Diagnosis of dysmenorrhea is based on history and exclusion of other causes
- Physical Examination
- Diagnostic imaging

Differential Diagnosis

- Sexually transmitted infection (STI)
- Pelvic inflammatory disease (PID)
- Endometriosis
- Uterine fibroids or uterine adenomyosis
- Adnexal mass

DUTCH CHECKLIST

Test patterns & markers associated with dysmenorrhea

- [ ] **High estrogen, in particular, high estradiol:** Not always present but may cause the endometrial lining to thicken excessively and contribute to menstrual pain
- [ ] **Poor phase 1 estrogen detox:** 16- and 4-OH-E1 may also cause the endometrial lining to thicken excessively, and additionally contributes to inflammation and oxidative stress
  - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar)
  - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar)
- [ ] **Low phase 2 estrogen methylation** (slider bar) may prevent oxidative phase 1 metabolites from being neutralized, contributing to oxidative stress and increased estrogen receptor activity
- [ ] **Low progesterone** and a **low progesterone/estrogen (P/E) ratio** can contribute to pain as progesterone is unable to adequately "oppose" estrogenic effects on the endometrium
- [ ] **High Inflammation.** These patterns are associated with high inflammation on the DUTCH Test. The more patterns the patient has the higher the likelihood of high inflammation contributing to dysmenorrhea:
  - [ ] High 5a reductase activity
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Cortisol metabolism favoring THF (acute) or THE (chronic)
  - [ ] Fast cortisol clearance rate (CCR)
  - [ ] High free cortisol (acute) or low free cortisol (chronic)
  - [ ] High kynurenate
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Reduce or eliminate dysmenorrhea
- Normalize hormone levels
- Reduce inflammation

Other support may include, but is not limited to:

- Exercise or movement has compelling evidence for reducing dysmenorrhea
- Heat applied to the lower abdomen
- Optimize nutritional support, especially minerals like magnesium, zinc, copper, and antioxidants. Vitamin supplements shown to decrease dysmenorrhea include vitamin E, vitamin B1, vitamin D3, and omega-3s.
- Diet high in plant foods, especially fruits and vegetables, but also dairy products
- Pain-reducing herbs: ginger, Boswellia, turmeric, chamomile
- Progesterone support such as Chaste Tree, Black cohosh, maca
- Physiotherapy including TENS, acupuncture
- Medications that may benefit include: NSAIDs (short term, around menses), birth control pills, oral or vaginal progesterone. Stronger medications are available for severe cases

ENDOMETRIOSIS

WHAT IS ENDOMETRIOSIS?

Endometriosis is the presence of endometrial tissue outside the uterine cavity. Lesions are typically present in the pelvic organs such as the bowels, bladder, and diaphragm, but other areas are possible. The presence of and hormonal changes in the lesions result in significant inflammation, oxidative stress, and pain.

DUTCH RESOURCES ON ENDOMETRIOSIS

Webinar: "Endometriosis and the DUTCH Test" with Jaclyn Smeaton, ND, MPH

Case Study: "Endometriosis and the Estrobolome" with Christina O'Brien, DC, RDN, LD, DACNB, IFMCP

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

Mostly found in women ages 25-35 years old. Some females are asymptomatic. Lesions can affect the function of the structure and organs they attach to; therefore, symptom history is important for driving diagnostic imaging.

Common symptoms include:

- Chronic pelvic pain (70%)
  - Dysmenorrhea
  - Dyspareunia
- Infertility (50%)
- Palpable ovarian mass
- Bowel movement symptoms

DIAGNOSIS

Surgical Diagnosis

Surgical diagnosis (gold standard) is done by laparoscopy and biopsy and is helpful because lesions are removed during the process, serving as a simultaneous treatment.

Diagnosis Nonsurgical

- Visual inspection and biopsy of visual lesions in the vaginal fornix and rectovaginal space
- Ultrasound, Cystoscopy (if bladder symptoms present)

Endometriosis diagnosis is accompanied by staging and description, including the location and size of lesions that may contribute to symptom severity.

DUTCH CHECKLIST

Test patterns & markers associated with endometriosis

- [ ] **Low progesterone:** Progesterone can limit endometrial lesion growth and low progesterone may be associated with worse symptoms
- [ ] **High estrogens, particularly high estradiol:** When present, they can contribute to more aggressive lesion growth and oxidative stress
- [ ] **Poor phase 1 estrogen detox:**
  - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar) may result in increased oxidative stress and inflammation
  - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar) may cause increased endometrial tissue growth, increased oxidative stress and inflammation
- [ ] **Low phase 2 estrogen methylation** (slider bar) may prevent oxidative phase 1 metabolites from being neutralized, contributing to oxidative stress and increased estrogen receptor activity
- [ ] **Any abnormal cortisol findings:** Cortisol helps with pain and inflammation and can contribute to worse endometriosis symptoms when high or low
- [ ] **High Inflammation.** These patterns are associated with high inflammation on the DUTCH Test. The more patterns the patient has the higher the likelihood of high inflammation contributing to the endometriosis:
  - [ ] High 5a reductase activity
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Fast cortisol clearance rate (CCR)
  - [ ] High free cortisol (acute) or low free cortisol (chronic)
  - [ ] Cortisol metabolism favoring THF (acute) or THE (chronic)
  - [ ] High kynurenate
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Reduce high estrogens
- Reduce oxidative stress
- Refer when appropriate

Other support may include, but is not limited to:

- Exercise or movement
- Heat applied to the lower abdomen
- Diet high in plant foods, especially fruits and vegetables, avoid red meat
- Pain-reducing herbs: Ginger, Boswellia, turmeric, chamomile
- Physiotherapy including TENS, acupuncture
- Medications that may benefit include: NSAIDs (short term, around menses), birth control pills. Stronger medications are available for severe cases

FEMALE INFERTILITY

WHAT IS FEMALE INFERTILITY?

Female infertility is defined as the absence of conception or successful pregnancy after one year of unprotected, properly timed intercourse. The timeframe is shortened to 6 months if the female partner is over 35 to expedite fertility assessment as infertility is more common in this age group.

DUTCH RESOURCES ON FEMALE INFERTILITY

Webinar: "Understanding Fertility" with Jaclyn Smeaton, ND, MPH

Webinar: "Ask Me Anything: Women's Health & Fertility" with Debbie Rice, ND, MPH and Kelly Ruef, ND

Case Study: "Fertility Optimization" with Lindsey Szczepanski, NP

Case Study: "Infertility, Irregular Cycles & Elevated Estrogen" with Kelly Ruef, ND

DUTCH Podcast: Season 1 Episode 15 "Fertility & Cycle Mapping" with Jaclyn Smeaton, ND, MPH

Blog: "Fertility Basics" by Lindsey Szczepanski, NP

Blog: "Symptoms and Support of Low Progesterone" by Brook Ahnemann, ND

Blog: "DUTCH, Oura Rings, and Predicting Fertility" by Bryan Mayfield, PharmD, BCGP

Blog: "Supporting Optimal Timing for a Successful Pregnancy" by Debbie Rice, ND, MPH

Blog: "Fertility and the DUTCH Test" by Carrie Jones, ND, FABNE, MPH

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

Signs and symptoms of hormone imbalance that might be the cause of infertility include:

- Irregular or short cycles
- Low libido
- PMS
- Menstrual abnormalities: pain, clotting, color, shade, odor, or amount (heavy or light)
- Bleeding/spotting outside of menstruation
- Dry cervical mucus
- Fatigue, low motivation, brain fog

Symptoms of optimal fertility include:

- Consistent cycles
- Cervical mucus pattern over the cycle: Dry → sticky → creamy → egg white → sticky → dry
- Healthy libido, especially surrounding ovulation

DIAGNOSIS

History

Detailed information about the woman's gynecological history, medications, lifestyle factors, and any symptoms suggesting hormonal imbalances.

Menstrual Cycle Tracking

- Basal body temperature (BBT) to determine when ovulation occurs
- Ovulation predictor kit (OPK) to determine when ovulation occurs
- DUTCH Cycle Mapping Test to identify cycle patterns

Lab Tests

Day 3 of the menstrual cycle:

- Follicle stimulating hormone (FSH)
- Luteinizing hormone (LH)

Day 19-23 of a 28-day menstrual cycle:

- DUTCH Test or
- Serum estradiol, progesterone

Other tests not related to cycle day:

- Thyroid Function Tests
- Prolactin: Elevated levels can disrupt menstrual cycles and ovulation
- AMH: anti-mullerian hormone is a measure of ovarian reserve. Low levels may indicate low ovarian reserve. Very high levels can be a marker for PCOS (polycystic ovary syndrome).

Imaging

- Several imaging procedures can help identify fibroids, scar tissue in the fallopian tubes, or underlying diseases such as endometriosis. These include pelvic ultrasound, hysterosalpingogram, and others.

DUTCH CHECKLIST

Test patterns & markers associated with infertility

- [ ] **DUTCH Cycle mapping findings:**
  - [ ] **High or low estradiol (E2)**
  - [ ] **Low progesterone**
  - [ ] **Anovulation,** early ovulation, or late ovulation
  - [ ] **Short luteal phase**
  - [ ] Short cycle length (<21-25 days) or long cycle length (>35 days)
- [ ] **High or low estrogen, particularly estradiol (E2),** can indicate abnormal ovarian hormone output or poor endometrial environment that can impair ovulation
- [ ] **Low progesterone:** Progesterone plays a role in the uterine lining thickening to prepare for fertilization and implantation
- [ ] **Low phase 2 estrogen methylation** (slider bar) can indicate nutrient deficiencies that can impair healthy ova development
- [ ] **Low or high testosterone and/or DHEA:** Androgens benefit the maturation of follicles. High androgens can suppress LH + FSH secretion and inhibit ovulation. High androgens may indicate PCOS.
- [ ] **High free cortisol** can impair sex hormone production and endometrial implantation
- [ ] **Cortisol metabolism issues:**
  - [ ] **Slow cortisol clearance rate (CCR): metabolized cortisol is LOWER relative to free cortisol** and free cortisone, may be the result of hypothyroidism, metabolic adaptation from chronic under eating, iron deficiency anemia, mitochondrial dysfunction, and poor liver / gallbladder health
  - [ ] **Fast cortisol clearance rate (CCR): metabolized cortisol is HIGHER relative to free cortisol and free cortisone,** can indicate hyperthyroidism, inflammation, or insulin resistance, factors that may impair fertility
- [ ] **Low melatonin** is associated with low implantation rates and difficulty maintaining pregnancy
- [ ] **High inflammation:** These patterns are associated with high inflammation on the DUTCH Test:
  - [ ] High 5a reductase activity
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Poor phase 1 estrogen detox
    - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar)
    - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar)
  - [ ] Fast cortisol clearance rate (CCR)
  - [ ] High free cortisol (acute) or low free cortisol (chronic)
  - [ ] Cortisol metabolism favoring THF (acute) or THE (chronic)
  - [ ] High kynurenate
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Identify and treat obstacles to conception and successful pregnancy
- Balance hormones, stress, and lower inflammation

Other support may include, but is not limited to:

- Specific nutrients of focus: Vitamin A (consider beta-carotene form, avoid synthetic retinoids), vitamin E, vitamin D, B12, B6, Folate (B9), magnesium, zinc, selenium, iodine, choline, CoQ10, and vitamin C
- Mitochondrial support may include CoQ10, ALA, potassium, NAC, and antioxidants
- Moderate exercise routine
- Healthy weight loss
  - Rule out other contributors to weight gain / weight loss resistance
  - Rule out past eating disorders or significant disordered eating
  - Consider referral to a dietitian
- Treat underlying conditions, such as hypothyroidism, insulin resistance, gut dysbiosis, etc.

HAIR LOSS

WHAT IS HAIR LOSS?

Hair loss, also known as alopecia, is the thinning or absence of normal hair growth in both males and females. Hair loss can present on the head and/or on the body diffusely or more localized in patches. It can be permanent or temporary, depending on the cause. Hair loss is different from normal hair shedding - on average 50-100 hairs per day.

DUTCH RESOURCES ON HAIR LOSS

Webinar: "Stress-Induced Hair Loss: Make it Stop!"
with Carrie Jones, ND, FABNE, MPH

DUTCH Podcast: Season 2 Episode 16 "Understanding Hair Loss & Minimizing the Impact" with Marcelle Pick, OB/GYN, NP

Blog: "Stress, Hair Loss, and the Cortisol Connection"

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

Signs of hair loss may include a receding hair line, noticeable thinning of hair in diffuse of localized areas on the head or body, excessive shedding of hair, bald spots, and skin irritation around hair follicles if the etiology is infectious or autoimmune in nature.

Systemic symptoms may present alongside hair loss depending on the cause of the hair loss; for example, if the hair loss is due to hypothyroidism, the patient may experience symptoms related to hypothyroidism such as fatigue, weight gain, constipation, cold intolerance, etc.

DIAGNOSIS

Hair loss is diagnosed based on physical examination, health history, and further testing if warranted such as the pull test, scalp biopsy, or light microscopy of the hair shaft. Diagnostic testing for underlying causes such as hypo- or hyperthyroidism, autoantibodies, nutrient deficiencies, blood sugar issues, cortisol levels, androgen levels, etc. is also common.

Differential Diagnosis

- Telogen Effluvium (diffuse hair loss) is stress-related hair loss which has many potential causes including thyroid hormone imbalance, blood sugar dysregulation, infections, nutrient deficiencies, stress, elevated prolactin, sudden or extreme dietary changes, eating disorders, malabsorption conditions, inflammation of the scalp or hair follicle, childbirth, major surgery, and certain medications
- Androgenic Alopecia, which is often referred to as "male pattern" or "female pattern" baldness or thinning of the hair due to high androgens and/or high 5a-metabolism
- Other causes include skin infections affecting hair follicles, autoimmune disease (alopecia areata, lupus, etc.), stress damage to the hair follicle such as in chronic pulling or harsh chemical use, and more

DUTCH CHECKLIST

Test patterns & markers associated with hair loss

- [ ] **High total free cortisol** due to acute stressors may disrupt the function and cyclic regulation of the hair follicle
- [ ] **Cortisol metabolism issues:**
  - [ ] **Slow cortisol clearance rate (CCR): metabolized cortisol is LOWER relative to free cortisol and free cortisone.** This is seen with hypothyroidism, anorexia, sluggish bile, low metabolic function which may cause hair loss in some.
  - [ ] **Fast cortisol clearance rate (CCR): metabolized cortisol is HIGHER relative to free cortisol and free cortisone.** This is seen with hyperthyroidism, obesity, inflammation, which may cause hair loss in some.
- [ ] **High testosterone, DHEA, and/or 5-alpha androgens** may contribute to androgen related hair loss. Androgen metabolism that prefers a 5a-reductase balance, leading to high 5-alpha androgen metabolites such as 5a-DHT, 5a-androstanediol, and androsterone, may also contribute to androgen related hair loss.
- [ ] **Postmenopausal pattern of low estrogen and progesterone.** These hormones help to promote the growing phase of the hair cycle so their decline may contribute to menopausal changes in hair growth and hair loss.
- [ ] **High b-hydroxyisovalerate may indicate a biotin deficiency.** Because biotin is important for hair and nail growth, correcting a biotin deficiency may help individuals who have experienced hair loss due to a biotin deficiency.
- [ ] **High indican** may indicate hypochlorhydria, pancreatic insufficiency, or dysbiosis that may be affecting the absorption of nutrients needed for hair growth
- [ ] **High Inflammation.** These patterns identified on the DUTCH Test may all point to elevated inflammation or oxidative stress that can impact the hair life cycle. The more patterns the patient has the higher the likelihood of high inflammation contributing to hair loss:
  - [ ] High 5a reductase activity
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Poor phase 1 estrogen detox
    - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar)
    - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar)
  - [ ] Fast cortisol clearance rate (CCR)
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  - [ ] High kynurenate
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG
- [ ] **Autoimmunity** patterns identified on the DUTCH Test:
  - [ ] **Upregulated CYP3A4 activity:** CYP3A4 converts estrone to 16-OH-E1 and estradiol to estriol and when upregulated may result in a **16-OH-E1 preference** and higher estriol relative to estrone and estradiol

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Address underlying systemic or localized conditions contributing to hair loss

Other support may include, but is not limited to:

- Improve blood circulation to skin and hair follicles via gentle massage, acupuncture, smoking cessation, blood sugar control
- Consider topical treatments containing rosemary essential oil, castor oil, melatonin and/or progesterone
- Avoid harsh chemicals to the scalp, harsh brushing, and hairstyles that pull hair too tightly.
- Address vitamin and mineral deficiencies that may be present
- Address localized infections related to hair loss. Consider antibiotics or antifungals if needed
- Address other systemic concerns by supporting proper immune function, healthy thyroid function, effective digestion, lower inflammation.
- Consider menopausal hormone replacement therapy (MHRT) if peri or post-menopausal
- Other support
  - Low level laser therapy to the scalp
  - Red light/NIR light to the scalp
  - Platelet Rich Plasma (PRP) to the scalp
  - Oral collagen
  - Ensuring adequate Vitamin D3 levels

HEAVY MENSTRUAL BLEEDING

WHAT IS HEAVY MENSTRUAL BLEEDING?

Heavy menstrual bleeding is one condition that falls under the umbrella term “abnormal uterine bleeding” or AUB. AUB can also refer to bleeding or spotting that occurs outside of the menses timeframe (not covered here). Heavy menstrual bleeding occurs during menses and is usually defined as total blood loss of greater than 80 ml or bleeding that lasts for more than 7-9 days.

DUTCH RESOURCES ON HEAVY MENSTRUAL BLEEDING

Case Study: “Heavy Menstrual Bleeding” with Rebecca Clemson, ND

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

- Soaking pad/tampon every 2 hours or less
- Menstrual bleeding lasting longer than 7 days
- Menstrual blood may contain large clots
- Patients may develop iron deficiency anemia from blood loss

ETIOLOGY

Ovulatory Dysfunction Leading to Estrogen Dominance

- Adolescence
- PCOS
- Hypothyroidism
- Hyperprolactinemia
- Perimenopause

Structural Pathologies

- Fibroids
- Adenomyosis
- Endometrial polyps
- Neoplasms

Other Disorders

- Inflammation
- Clotting and bleeding disorders
- Kidney or liver disease
- Low vitamin K
- Cancer

Diagnosis Nonsurgical

- Visual inspection and biopsy of visual lesions in the vaginal fornix and rectovaginal space
- Ultrasound, Cystoscopy (if bladder symptoms present)

DUTCH CHECKLIST

Test patterns & markers associated with heavy menstrual bleeding

- [ ] **High estrogen:** when present can contribute to increased endometrial tissue growth and heavier menses
- [ ] **Poor phase 1 estrogen detox:**
  - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar) may result in increased oxidative stress and inflammation
  - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar) may cause increased endometrial tissue growth, increased oxidative stress and inflammation
- [ ] **Low phase 2 estrogen** methylation (slider bar) may prevent oxidative phase I metabolites from being neutralized, contributing to oxidative stress and increased estrogen receptor activity
- [ ] **Low progesterone** and a **low progesterone/estrogen (P/E) ratio** inadequately opposes estrogen’s proliferative effect on the endometrium, resulting in heavy menstrual bleeding
- [ ] **High inflammation** results in increased prostaglandin signaling and uterine contractions that contribute to heavier menstrual bleeding. Inflammation patterns identified on the DUTCH Test are listed below. The more patterns the patient has the higher the likelihood of high inflammation contributing to heavy menses:
  - [ ] High 5a reductase activity
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Fast cortisol clearance rate (CCR)
  - [ ] High free cortisol (acute) or low free cortisol (chronic)
  - [ ] Cortisol metabolism favoring THF (acute) or THE (chronic)
  - [ ] High kynurenate
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Reduce menstrual bleeding
- Rule out structural causes through exam and imaging
- Correct hormone imbalances
- Improve iron levels if needed

Other support may include, but is not limited to:

- NSAIDs around the time of menses can significantly reduce bleeding
- If NSAIDs are beneficial, Omega-3 fatty acids may be indicated and can reduce bleeding if levels are optimized. Increase Omega 3 fatty acids and limit Omega 6 fatty acids.
- EPO/Borage Oil
- Vitamin C
- Consider liver and detox support
- Decrease alcohol and caffeine intake
- Fiber
- Exercise
- Seed cycling
- Support healthy iron levels through diet or supplementation
- Limit xenoestrogens, polyaromatic hydrocarbons (PAHs) and toxin exposures

INFLAMMATION

WHAT IS INFLAMMATION?

Inflammation is a system of serum proteins, cytokines, and interleukins that compose a part of the innate immune system. The role of inflammation is tissue destruction and immune system signaling, resulting in the mobilization of immune cells and other factors to stabilize or repair resultant tissue damage. Short term inflammation is an essential part of healthy repair and protection from infectious disease and injury. However, chronic inflammation results in poor recovery and chronic disease. Inflammation can be a laboratory-diagnosed condition when high inflammatory markers are present in the serum. Chronic elevations signal persistent, significant, and sometimes irreversible damage to tissues and make up the foundational elements of chronic disease.

DUTCH RESOURCES ON INFLAMMATION

Webinar: "Connecting the Dots Between Cardiovascular Disease, Inflammation, and Hormones"
with Doreen Saltiel, MD, JD, FACC, FAARFM

Blog: "Organic Acids, Cognitive Function, and Brain Health" by Christina O'Brien, DC

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

- Body pain
- Cognitive changes
- Fatigue, lethargy
- Mood dysregulation (depression, anxiety)
- Insomnia

DIAGNOSIS

Blood Laboratory Signs

Elevated serum Amylase, Amyloid A, CRP, ESR, Ferritin, Fibrinogen, hs-CRP, IFNγ, IL-1β, IL-6, IL-8, IL-10, IL-12, Liver enzymes (ALT, AST, GGT), Platelet Count, Procalcitonin, TNFa; Elevated plasma viscosity (PV)

Urine Laboratory Signs

Elevated Quinolinate, 8-OHdG, F2-isoprostanes, Malondialdehyde

Fecal Laboratory Signs

Elevated Calprotectin

Accompanying Conditions

Numerous. Chronic inflammation is involved in autoimmune disease, cancer, cardiovascular disease, diabetes, endometriosis, obesity, chronic viral infection, and many more.

Diagnosis

- The diagnosis of inflammation is primarily made by measuring inflammatory markers.

DUTCH CHECKLIST

Test patterns & markers associated with Inflammation

- [ ] **High estrogen:** Inflammatory cytokines increase expression of aromatase enzyme and its activity in liver and in adipose tissues rather than from gonadal tissues
- [ ] **Poor phase I estrogen detox:**
  - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar) may result in increased oxidative stress and inflammation. Inflammatory cytokines directly upregulate CYP1B1 expression.
  - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar) contributes to increased oxidative stress and inflammation
- [ ] **Low DHEA-S** relative to the other DHEA metabolites, etiocholanolone and androsterone: Inflammation and obesity increase cellular uptake of DHEA-S
- [ ] **5a-preference:** Inflammatory cytokines increase expression of SRD5A genes, increasing 5a-reductase metabolism of androgens and cortisol to 5-alpha metabolites (5a-DHT, 5a-androstanediol, androsterone, and a-THF)
- [ ] **Any abnormal cortisol findings:**
  - [ ] Acute inflammatory stress may initially present with **high free cortisol** and cortisone, divergent diurnal pattern at exacerbated timepoints, and a **THF preference**
  - [ ] Chronic inflammatory stress may present with **low free cortisol** and cortisone, a flattened diurnal curve, and a **THE preference**
- [ ] **Cortisol metabolism issues:**
  - [ ] **Fast cortisol clearance rate (CCR): metabolized cortisol is HIGHER relative to free cortisol and free cortisone)** is seen with hyperthyroidism, obesity, and inflammation
- [ ] **High kynurenate:** associated with oxidative stress
- [ ] **High pyroglutamate:** indicates low glutathione, the body's major antioxidant
- [ ] **High indican:** indicates intestinal dysbiosis
- [ ] **High quinolinate:** associated with neuroinflammation, but may also be associated with general inflammation
- [ ] **High 8-OHdG:** associated with oxidative stress and DNA damage. 8-OHdG is considered pro mutagenic and is a biomarker for various cancer and degenerative disease initiation and promotion states.
- [ ] **Low melatonin** results in lower antioxidant activity

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Find and treat the underlying cause(s) of inflammation
- Decrease inflammatory cytokine levels directly using supplements, dietary interventions, and/or drugs
- Repair oxidative tissue damage

Other support may include, but is not limited to:

- Find and treat acute and/or chronic infections
- Replete and restore gut function if imbalances are present
- Adopt an individualized anti-inflammatory style diet
- Eliminate toxins in the environment and promote detoxification and clearance of accumulated body burden
- Herbal and nutritional supplements studied for decreasing inflammation
- Dietary focus points:
  - Higher Omega 3: Omega 6 balanced dietary intake
  - Rationale: EPA and DHA modulate arachidonic acid-derived eicosanoids and decrease formation of reactive oxygen species
  - Increase intake of foods and/or supplements high in polyphenols and bioflavonoids like resveratrol, EGCG, and quercetin
  - Rationale: These and other antioxidants can promote mitochondrial function, tissue repair, and protect DNA from damage in chronic inflammation
  - Incorporate more fiber
  - High fiber diet is negatively associated with inflammation in studies and also promotes proper phase 3 elimination of hormone metabolites
- Exercise considerations:
- Regular aerobic exercise reduces CRP, TNF-a, and IL-6

INSOMNIA

WHAT IS INSOMNIA?

Insomnia is defined as difficulty falling asleep, staying asleep, or not feeling rested after a night of sleep. Insomnia persists despite having enough time allocated to sleep and a good environment for sleep. Sleep problems can occur from outside influences, such as too many activities, not leaving enough time to try and sleep, or a noisy environment that makes sleeping difficult. Sleep problems can also occur as a side effect of many medications and with health conditions such as depression, anxiety, thyroid disorders, interrupted breathing, stress and importantly, because of the hormonal shifts of the menstrual cycle, menopause, and andropause. Insomnia contributes to many long-term health conditions including metabolic disease, cardiovascular disease, and reduced cognitive function.

DUTCH RESOURCES ON INSOMNIA

Webinar: "Sleep and Cortisol: Beyond the Diurnal Rhythm" with Allison Smith, ND

Blog: "Is Cortisol Causing Your Patient to Struggle With Sleep in the Middle of the Night?" by Carrie Jones, ND, FABNE, MPH

Case Study: "Can't Sleep! Mood Issues! Hot Flashes! Help! A Look Into Low Hormones in a Postmenopausal Woman" with Kelly Ruef, ND

Blog: "Circadian Rhythm and Human Health" by Time Hyatt, ND

Blog: "Sleep Hygiene: Foundational Techniques for Your Best Sleep" by Hilary Miller, ND

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

- Fatigue
- Lethargy
- Cognitive changes/decline
- Mood dysregulation
- Pain
- Perceived stress
- Appetite shifts (lack of AM hunger)
- Weight management problems

DIAGNOSIS

Diagnosis

Chronic insomnia is diagnosed with a sleep diary and in some cases a sleep study (actigraphy). Chronic insomnia occurs for 3 or more nights a week for more than 3 months. Chronic insomnia must exist outside of other sleep disorders, and it must include symptoms in the following categories:

- Sleep initiation
- Sleep maintenance
- Early waking
- Daytime symptoms that are due to poor/inadequate sleep

Common Contributing Factors

- Dysglycemia/Insulin resistance
- Menopause/Perimenopause
- Inflammation
- Sleep apnea
- Pain
- Poor sleep hygiene practices
- Medication side effect
- Stress/Sympathetic activation

DUTCH CHECKLIST

Test patterns & markers associated with insomnia

- [ ] **Low estrogen (female); Low testosterone (male):** contributes to sleep fragmentation and poor-quality sleep in menopause and in andropause. The root cause of low sex hormones is often aging (menopause, andropause) but can be seen with other root causes.
- [ ] **Low phase 2 estrogen methylation (slider bar):** may indicate low catechol-o-methyltransferase (COMT) activity. COMT helps to clear epinephrine/adrenaline from the body
- [ ] **Low progesterone, specifically a-pregnanediol:**
  - [ ] a-pregnanediol binds GABA receptors, a relaxing hormone that benefits sleep
- [ ] **Low total DHEA**
  - [ ] Normal DHEA positively impacts sleep architecture, particularly deep sleep
- [ ] **Diurnal free cortisol abnormalities**
  - [ ] Acute insomnia may present with **high middle-of-the-night free cortisol** and **high waking free cortisol**
  - [ ] Chronic insomnia may present with a reversed diurnal free cortisol rhythm: **high bedtime free cortisol** and/or **high middle of the night free cortisol** and **low waking free cortisol** and/or **low morning free cortisol**; **high afternoon free cortisol** also common
- [ ] **Absent/low cortisol awakening response (CAR)** when sleep problems are chronic and with hippocampal damage
- [ ] **Cortisol metabolism issues:**
  - [ ] **Slow cortisol clearance rate (CCR): metabolized cortisol is LOWER relative to free cortisol and free cortisone**, can clue in about underlying causes of sleep problems like hypothyroid, anemia, and sluggish liver function
  - [ ] **Fast cortisol clearance rate (CCR): metabolized cortisol is HIGHER relative to free cortisol and free cortisone,** can clue in about underlying causes of sleep problems like inflammation, insulin resistance, hyperthyroid, and immune activation
- [ ] **High kynurenate and xanthurenate:** indicates B6 deficiency. B6 is cofactor for the glutamic acid decarboxylase (GAD) enzyme which makes GABA (the primary inhibitory neurotransmitter for the central nervous system), and the COMT enzyme (which helps to clear epinephrine from the body). These ultimately support parasympathetic activity and sleep.
- [ ] **High quinolinate:** Indicates systemic inflammation. Quinolinate enters the brain and is excitotoxic, impairing sleep.
- [ ] **High VMA** may indicate elevated epinephrine
  - [ ] High excitatory epinephrine/norepinephrine impairs sleep
  - [ ] Commonly found in sleep apnea and with high cortisol at night
  - [ ] May see low VMA if sluggish methylation (COMT) activity, as COMT helps to clear epinephrine/adrenaline from the body
- [ ] **Low melatonin**
- [ ] **High 8-OHdG** correlates with insomnia in postmenopausal females

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Find and address the root cause
- Ensure proper sleep hygiene
- Restore appropriate sleep function

Other support may include, but is not limited to:

- Menopausal hormone replacement therapy (MHRT)
- Support GABA formation and inhibitory activity: ashwagandha, bacopa, B6, chamomile, GABA, hericium (lion's mane mushroom), lemon balm, L-theanine, magnolia, Relora®, scutellaria, valerian
- Reduce insulin levels and support proper blood sugar levels throughout the day and night
- Correct B6 deficiency if present
- Treat underlying inflammation and oxidative stress which may be affecting sleep architecture (See DUTCH Inflammation Miniguide)
- Employ strategies to improve sleep hygiene:
  - Dim lights and decrease blue screen exposure 2 hours before desired bedtime, reduce alcohol consumption, avoid large meals within 3 hours of bedtime, darken the room completely or wear an eye mask, cool ambient temperature to be in the 60s oF during sleep
  - Support the circadian rhythm
- Regular exercise improves subjective sleep quality:
  - Moderate intensity aerobic exercise
  - Mind-body exercise which includes yoga, tai chi, and qi gong

INSULIN RESISTANCE

WHAT IS INSULIN RESISTANCE?

Insulin is a cross-functional hormone made in the pancreas. It is well known for its job as a glucose shuttle into cells, where glucose is converted to ATP for energy or fat for storage. Insulin resistance is an impaired biological response to insulin stimulation in target tissues, particularly liver, muscle, and adipose tissue. It most commonly occurs when blood sugar is chronically high, primarily due to diet and lifestyle, but genetics are also involved for some people. Insulin resistance can cause obesity and can lead to the development of type 2 diabetes, metabolic syndrome, PCOS, and nonalcoholic fatty liver disease. Approximately 40% of adults 18-44 in the United States are insulin resistant.

DUTCH RESOURCES ON INSULIN RESISTANCE

Case Study: "Optimizing the Menstrual Cycle: Painful Periods & Insulin Resistance" with Kelly Ruef, ND

Blog: "Metabolic Factors in PCOS" by Tim Hyatt, ND

Case Study: "The Obesity Metabolome Connection to Breast Cancer" with Allison Smith, ND

Webinar: "Sleep and Cortisol: Beyond the Diurnal Rhythm" with Allison Smith, ND

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

- Obesity – particularly central adiposity and fat distribution in muscle and liver
- Acanthosis nigricans and skin tags
- Hyperglycemia
- Hypertension
- Dyslipidemia
- Elevated inflammatory markers
- Hyperandrogenism/PCOS

ASSOCIATED DISEASES

- Non-alcoholic fatty liver disease (NAFLD)
- Metabolic syndrome
- Prediabetes or type 2 diabetes
- Polycystic ovarian syndrome (PCOS)
- Obesity
- Microvascular disease (retinopathy, neuropathy, or nephropathy)
- Macrovascular disease (stroke, PAD, and CAD)

DIAGNOSIS

Insulin resistance is currently diagnosed based on clinical findings corroborated with laboratory results.

Laboratory Studies

- HOMA-IR
- Glucose tolerance test
- Fasting insulin
- Fasting glucose Hba1c, Lipid panel (cholesterol)
- Impaired glucose tolerance or impaired fasting glucose
- Abnormal uric acid metabolism
- Dyslipidemia (increased triglycerides, small, dense LDL-C, or decreased HDL-C)
- Hemodynamic changes, i.e., elevated blood pressure
- Prothrombotic factors (PAI-1, fibrinogen)
- Markers of inflammation (hs-CRP, WBCs)

Other factors associated with an increased risk of insulin resistance:

- Family history of Type 2 Diabetes, hypertension, or CVD (cardiovascular disease)
- Sedentary lifestyle
- Non-white ethnicity
- Age older than 40

DUTCH CHECKLIST

Test patterns & markers associated with insulin resistance

- [ ] **Low progesterone** can be seen when insulin resistance impairs LH (luteinizing hormone), altering ovulation and progesterone production.
- [ ] **High or low estrogens:** High insulin and obesity can increase aromatase activity, leading to high estrogens. Conversely, low estrogens can reduce insulin sensitivity and contribute to insulin resistance.
- [ ] **5a-reductase** preference is often seen in patients with insulin resistance or obesity
- [ ] **Cortisol metabolism issues:**
  - [ ] **Fast cortisol clearance rate (CCR):** metabolized cortisol is HIGHER relative to free cortisol and free cortisone) which may point to inflammation and insulin resistance
- [ ] **High waking-free cortisol** may indicate high overnight cortisol often seen with blood sugar dysregulation and stress
- [ ] **Blunted CAR (Cortisol Awakening Response)** can be seen with obesity leading to sleep apnea, chronic inflammation, or chronic stress
- [ ] **High inflammation.** These patterns are associated with high inflammation on the DUTCH Test. The more patterns the patient has the higher the likelihood of high inflammation contributing to insulin resistance:
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Fast cortisol clearance rate (CCR)
  - [ ] High free cortisol (acute) or low free cortisol (chronic)
  - [ ] Cortisol metabolism favoring THF (acute) or THE (chronic)
  - [ ] High kynurenate
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Identify and address factors contributing to insulin resistance
- Decreasing risk of developing diseases associated with insulin resistance
- Weight loss
- Reversing insulin resistance

Other support may include, but is not limited to:

- Dietary interventions – limit refined carbohydrates, foods high on glycemic load, increasing fiber, healthy fats and protein intake, calorie restriction, time-restricted eating/intermittent fasting
- Increase physical activity: resistance training, concentrating on large muscle groups – hamstrings, quads, and glutes. High intensity interval training
- Weight loss – 7% weight loss resulted in 58% decreased risk of developing Type 2 Diabetes
- Supplements that may help improve insulin sensitivity:
  - Berberine
  - Inositol
  - Alpha lipoic acid
  - Chromium
  - Bitter melon
  - Cinnamon
  - Gymnema
- Pharmacologic considerations:
  - Metformin, and other blood sugar-lowering or insulin-sensitizing medications should be considered if the patient meets the criteria

MALE INFERTILITY

WHAT IS MALE INFERTILITY?

Male Infertility is defined as the absence of conception or successful pregnancy after one year of unprotected, properly timed intercourse. The time to diagnostic testing is shortened to 6 months if the female partner is over 35 to expedite fertility assessment as infertility is more common in this age group.

SIGNS & SYMPTOMS

Signs and symptoms of hormone imbalance that might be the cause of infertility include:

- Low libido
- Erectile dysfunction
- Fatigue, lack of motivation, brain fog
- Poor exercise recovery

DIAGNOSIS

History

Comprehensive medical history, including any past illnesses, injuries, surgeries (especially those related to the reproductive system), medications, sexual history, and lifestyle factors that could affect fertility.

Physical Examination

Physical examination to check for any physical abnormalities that might impact fertility, such as varicoceles (enlarged veins in the scrotum).

Semen Analysis

This is the cornerstone of male fertility testing. A semen sample is collected and analyzed for several parameters, including:

- Volume: The amount of semen produced
- Sperm Count: The number of sperm present in the semen. Low sperm count should be followed up with genetic testing and testicular biopsy if no sperm is found on analysis.
- Motility: The ability of sperm to move effectively
- Morphology: The shape and structure of sperm
- pH Level: The acidity of the semen
- Liquefaction Time: The time it takes for the semen to liquefy

A single abnormal result does not necessarily indicate infertility, so often multiple samples are tested over time.

Hormone Testing

- Serum total testosterone
- The DUTCH Complete or DUTCH Plus Test
- Follicle-stimulating hormone (FSH)
- Luteinizing hormone (LH)
- Prolactin

Ultrasound

An ultrasound of the scrotum can help identify issues like varicoceles, blockages, or other structural abnormalities in the testes and supporting structures.

Further Testing Considerations

- Full thyroid panel
- Blood glucose regulation tests
- Inflammation and immune: High sensitivity C-reactive protein (hs-CRP), homocysteine, sedimentation rate, ANA, total IgA
- Advanced micronutrient panel
- Toxin testing – environmental, heavy metals, mycotoxins if suspected

DUTCH CHECKLIST

Test patterns & markers associated with male infertility

- [ ] **Low testosterone** should always be followed up with serum total testosterone, as urine can underrepresent testosterone in patients with UGT2B17 deletion polymorphism. Low testosterone is associated with low sperm count.
- [ ] **Low 5-alpha metabolites** (5a-DHT, 5a-androstanediol, androsterone) can indicate low bioavailable androgens
- [ ] **High estrogen** seen with obesity can lower or impair sperm production
- [ ] **Sluggish phase 2 estrogen methylation** can indicate nutrient deficiency that may impair reproductive function
- [ ] **High or low free cortisol** may have a negative impact on the hypothalamic-pituitary-gonadotropic (HPG) axis resulting in lower sperm count and ejaculation volume
- [ ] **Cortisol metabolism issues:**
  - [ ] **Slow cortisol clearance rate (CCR): metabolized cortisol is LOWER relative to free cortisol and free cortisone.** This is seen with hypothyroidism, anorexia, sluggish bile, low metabolic function.
  - [ ] **Fast cortisol clearance rate (CCR): metabolized cortisol is HIGHER relative to free cortisol and free cortisone.** This is seen with hyperthyroidism, obesity, inflammation.
- [ ] **High inflammation.** These patterns are associated with high inflammation on the DUTCH Test. The more patterns the patient has the higher the likelihood of high inflammation contributing to infertility:
  - [ ] High 5a reductase activity
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Poor phase 1 estrogen detox
    - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar)
    - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar)
  - [ ] High free cortisol (acute) or low free cortisol (chronic)
  - [ ] Cortisol metabolism favoring THF (acute) or THE (chronic)
  - [ ] High kynurenate
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Optimize sperm analysis parameters
- Optimize health
- Identify underlying causes of infertility

Other support may include, but is not limited to:

- Avoid exogenous testosterone. Testosterone replacement therapy (exogenous testosterone) blunts the HPG axis, can lower sperm production due to negative feedback loops.
- Nutrient dense diet
- Specific nutrients: Retinol (preformed vitamin A), vitamin E, vitamin D, B12, B6, Folate (B9), magnesium, zinc, selenium, iodine, choline, CoQ10, DHA
- Antioxidants, fiber, adequate calories + pro/fat/carbohydrates ratios
- Mitochondrial support
- Co-Q10, L-carnitine, ALA, antioxidants

MENOPAUSE

WHAT IS MENOPAUSE?

Menopause is the cessation of the monthly hormone cycle and fertility in women. Average age of menopause is 51 (range 40-58). Hormonal changes prior to menopause are gradual, lasting 2-8 years, and often symptomatic. This transition is called perimenopause. For some, menopause comes with severe symptoms and significant changes in overall health. Estrogen provides many benefits for women that may decline with menopause:

- Supports optimal bone density
- Supports sexual and genitourinary health
- Supports cardiovascular health
- Supports insulin sensitivity and weight management
- Supports healthy skin and hair
- Supports mood and sleep

SIGNS

- Patient is over 45 years (average age 51)
- No menstrual cycles for a contiguous 12 months
- Lab testing: low E2, high FSH

SYMPTOMS

- Hot flashes
- Insomnia, disrupted sleep
- Low libido/vaginal dryness
- Depression/irritability/anxiety

DIFFERENTIAL DIAGNOSIS

- Pregnancy
- Hypogonadotropic (low FSH, LH)
- Hyperprolactinemia
- Hyper or hypothyroidism

The list on the left should be ruled out if cessation of menses occurs in women before the age of 45 or with symptoms that do not align with menopause.

DUTCH RESOURCES ON MENOPAUSE

Webinar: "Menopause and HRT" with Debbie Rice, ND, MPH

Case Study: "Hair Loss, Breast Tenderness and Anxiety in a Postmenopausal Woman on HRT" with Kelly Ruef, ND

Case Study: "Can't Sleep! Mood Issues! Hot Flashes! Help! A Look into Low Hormones in a Postmenopausal Woman" with Kelly Ruef, ND

Case Study: "Prescribing Estrogen and Progesterone in a Postmenopausal Woman" with Kelly Ruef, ND

Case Study: "Elevated Androgens in a Postmenopausal Woman" with Kelly Ruef, ND

DUTCH Podcast: Season 2 Episode 7 "Finding Comfort in the Menopause Metamorphosis" with Esther Blum, MS, RD, CDN, CNS

DUTCH Podcast: Season 1 Episode 4 "Understanding Menopause: From Peri to Post" with Tara Scott, MD

Blog: "What to Expect: The Menopause Years" by Rebecca Clemson, ND

Find more DUTCH Education at: https://dutchtest.com/education/

DUTCH CHECKLIST

Test patterns & markers associated with menopause

- [ ] **Low estrogen** and **low progesterone** due to ceased ovarian production
  - [ ] Keep in mind that during perimenopause estrogens are sometimes high. See the perimenopause DUTCH miniguide if patient still has irregular menses and high estrogen.
- [ ] **Low estrogen metabolites** from low parent estrogens, estrone and estradiol. Ratios of estrogen metabolites are still relevant for long-term estrogen detox health and, if estrogen replacement therapy is used, for detoxing the supplemented estrogen.
- [ ] **Low androgens:** Androgens do not decline significantly at menopause but are in steady decline after about age 30. Low androgens can compound the negative impact of menopause and are implicated in poor sexual health, low mood, low energy, and loss of muscle mass. Androgens, especially DHEA, are primarily excreted by the adrenal glands in women and are the source of postmenopausal estrogens.
- [ ] **High cortisol** can make some symptoms of menopause worse, such as weight gain, and mood and sleep issues. Optimizing the circadian rhythm and cortisol levels can improve menopause symptoms.
- [ ] **Low melatonin:** melatonin does not decline significantly with menopause, but low melatonin in menopause may worsen insomnia and disrupted sleep, two major complaints of menopause
- [ ] **High quinolinate:** associated with neuroinflammation but may also be associated with general inflammation. Quinolinate can cross the blood-brain-barrier (BBB) and is stimulating, impairing mood and sleep, as well as long term brain health. High quinolinate in menopause suggests that improvement in mood and sleep can be found by reducing inflammation.

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Optimize health for longevity during menopausal transition
- Hormone replacement therapy (HRT): Improve metabolism and levels of hormones.

Other support may include, but is not limited to:

- Sleep hygiene
- Exercise: build muscle and improve stamina
- Mediterranean diet
- Monitor and support optimal glycemic control
- Stress management techniques

MENSTRUAL MIGRAINES

WHAT ARE MENSTRUAL MIGRAINES?

Menstrual migraines are a specific type of migraine headache that is linked to the fluctuations of hormones in the menstrual cycle. Symptoms typically occur in the perimenstrual period, which can range from two days before the onset of menstruation to three days after.

SIGNS & SYMPTOMS

Menstrual migraines tend to be more severe, last longer, and are more resistant to treatment compared to non-menstrual migraines.

- Often unilateral, pulsating, with a moderate-to-severe pain intensity that worsens with physical activity
- Can be accompanied by nausea and/or light and sound sensitivity
- Aura may also be present; however, most menstrual migraines occur without aura

PATHOPHYSIOLOGY

The pathophysiology of menstrual migraines is primarily related to the natural decline in estrogen levels that occurs around the onset of menstruation. Estrogen affects the processing of pain, in part by altering vascular inflammatory cytokine and prostaglandin levels, and by modulating the activity of various neurotransmitters that are implicated in migraine pathology, such as serotonin, norepinephrine, and dopamine.

DIAGNOSIS

To diagnose a menstrual migraine, the attacks must fulfill the criteria for a migraine without aura, occur 2 days before and up to 3 days after the onset of menses (and at no other times in the cycle) in at least 2 out of 3 cycles. Diagnosis of menstrual migraines typically is made from a detailed medical history and a headache diary to track the timing and characteristics of the migraines in relation to the menstrual cycle. Laboratory tests, imaging, and consultation with a headache specialist may be necessary to rule out secondary causes (see differential diagnosis).

Differential Diagnosis

To arrive at a diagnosis of menstrual migraines, healthcare providers must distinguish them from other types of headaches and conditions with similar presentations. Here are some differential diagnoses to consider:

- Tension-Type Headaches: These headaches present as a constant, dull, aching pain, often described as a tight band around the head, and lack the pulsating quality of migraines. They are not typically associated with the menstrual cycle.
- Cluster Headaches: These are intensely painful headaches that occur in clusters or cyclical patterns. They are also not typically associated with the menstrual cycle.
- Migraine without Aura: While menstrual migraines can occur without aura, the key differentiator would be the timing in relation to the menstrual cycle
- Migraine with Aura: This type of migraine is accompanied by visual or sensory disturbances that precede the headache phase. Menstrual migraines less commonly present with aura, and again, the timing of the headache in relation to menstruation is a critical distinguishing feature.

DUTCH CHECKLIST

Test patterns & markers associated with menstrual migraines

- [ ] **DUTCH Cycle mapping findings:**
  - [ ] **Estrogen fluctuations:** steep premenstrual decline in estrogen levels. Estrogen influences the tone of cerebral blood vessels, which is why its sudden drop is believed to provoke the onset of migraines in susceptible women.
  - [ ] **Anovulation results** in no progesterone production and a **low progesterone/estrogen (P/E) ratio**
  - [ ] **Short luteal phase results** in less tissue exposure to progesterone
- [ ] **Low progesterone:** While estrogen is often the focus in menstrual migraines, progesterone can also play a role, particularly when it is low. Progesterone has a modulating effect on GABA, a neurotransmitter that can have calming effects on the brain.
- [ ] **Sluggish phase 2 estrogen methylation** leading to an accumulation of estrogen and other hormones which might contribute to hormonal imbalances associated with menstrual migraines
- [ ] **Any abnormal cortisol findings:**
  - [ ] The DUTCH Test provides insight into the adrenal glands' production of cortisol, which can influence migraine activity
  - [ ] Chronic stress can dysregulate cortisol production, potentially exacerbating migraine conditions
  - [ ] An abnormal diurnal pattern of cortisol may suggest adrenal involvement in the migraine pattern
- [ ] **Abnormal HVA and VMA:** may indicate imbalances in dopamine and norepinephrine/epinephrine, respectively, which are closely linked to migraine pathophysiology
- [ ] **DUTCH OATs indicating low B vitamins.** Low levels of B-vitamins can affect the detoxification of neurotransmitters and estrogen, and B6 is a cofactor in the synthesis of neurotransmitters such as serotonin, dopamine, norepinephrine/epinephrine, and GABA.
  - [ ] **High MMA:** indicates B12 deficiency
  - [ ] **High xanthurenate and kynurenate:** indicates B6 deficiency
  - [ ] **High b-hydroxyisovalerate:** indicates biotin deficiency
- [ ] **High 8-OHdG:** indicates high oxidative stress and DNA damage. Oxidative stress is believed to play a role in migraine pathophysiology.
- [ ] **High inflammation.** These patterns are associated with high inflammation on the DUTCH Test. The more patterns the patient has the higher the likelihood of high inflammation contributing migraine incidence and severity:
  - [ ] High 5a reductase activity
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Poor phase 1 estrogen detox
    - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar)
    - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar)
  - [ ] Fast cortisol clearance rate (CCR)
  - [ ] High free cortisol (acute) or low free cortisol (chronic)
  - [ ] Cortisol metabolism favoring THF (acute) or THE (chronic)
  - [ ] High kynurenate
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Improve symptoms
- Reduce estrogen fluctuations: e.g., improve estrogen detox to limit times of excess estrogen, provide phytoestrogenic support to limit extreme lows of estrogen
- Refer for conventional treatment when appropriate – know that some migraines cannot be managed with natural medicine alone

Other support may include, but is not limited to:

- Lifestyle modifications: These include regular sleep, stress reduction techniques, and avoiding known dietary triggers
- Chaste tree
- Nutrient support: vitamin B6 (P5P), vitamin B2 (riboflavin), magnesium
- Antioxidants: CoQ10, vitamin A, vitamin C, vitamin E, alpha lipoic acid
- Hormonal therapy:
  - This might involve estradiol therapy to prevent the decline in estrogen levels, a common trigger for migraines
  - Progesterone therapy to ensure that the decline in progesterone is not as abrupt
- Preventive medications: These are taken regularly to reduce the frequency, severity, and length of migraines and can include beta-blockers, calcium channel blockers, and antidepressants
- Nonsteroidal anti-inflammatory drugs (NSAIDs): These can help in managing the pain and inflammation associated with migraines
- Triptans: These are serotonin receptor agonists that are effective in treating acute migraine attacks

POLYCYSTIC OVARY SYNDROME (PCOS)

DUTCH RESOURCES ON PCOS

Webinar: "The Role of Adrenal Hormones in PCOS" with Kelly Ruef, ND

Webinar: "The Case of PCOS: Evaluating Ovarian and Adrenal Hormones" with Carrie Jones, ND, FABNE, MPH

Webinar: "Functional Medicine Overview of PCOS" with Carrie Jones, ND, FABNE, MPH

DUTCH Podcast: Summer School Episode 8: "PCOS Patterns and Protocols" with Brook Ahnemann, ND

DUTCH Podcast: Season 2 Episode 5 "Rethinking our Approach to PCOS" with Melissa Groves Azzaro, RDN, LD

DUTCH Podcast: Season 2 Episode 6 "Evaluating PCOS with the DUTCH Test" with Melissa Groves Azzaro, RDN, LD

Case Study: "Patient with PCOS and High Cortisol" with Mark Newman, MS

Case Study: "Is it Really PCOS?" with Kelly Ruef, ND

Case Study: "HPA Axis Dysfunction, PCOS and the DUTCH Test" with Doreen Saltiel, MD, JD, FACC, FAARFM

Blog: "The Role of the Adrenals in PCOS" by Kelly Ruef, ND

Blog: "Metabolic Factors in PCOS" by Tim Hyatt, ND

Blog: "Improving Treatment Plans for PCOS and Pregnancy" by Kelly Ruef, ND

Video: "The Doctor is IN: PCOS Awareness Month" by Carrie Jones, ND, FABNE, MPH

Find more DUTCH Education at: https://dutchtest.com/education

WHAT IS PCOS?

Polycystic ovary syndrome is an endocrine and metabolic disorder primarily characterized by hyperandrogenism and ovulatory dysfunction. There are two main types of PCOS: primary functional ovarian hyperandrogenism (the most common) and primary functional adrenal hyperandrogenism (uncommon). PCOS affects up to 21% of women of reproductive age.

SIGNS & SYMPTOMS

- Irregular or absent menses
- Infertility
- Overweight and obesity (approx. half of patients are not obese)
- Cystic ovaries
- Insulin resistance, diabetes mellitus
- Increased lipids and elevated cardiovascular risks
- Hyperandrogenic symptoms: scalp hair loss, increased facial or body hair, acne
- Acanthosis nigricans
- Nonalcoholic steatohepatitis
- Sleep apnea
- Mood disorders

DIAGNOSIS & ETIOLOGY

Etiology

The specific cause of PCOS remains unknown but contributing factors include both genetic and environmental/lifestyle influences:

- Alteration in gonadotropin secretion (LH, FSH)
- Ovarian and adrenal dysfunction leading to hyperandrogenism
- Hyperinsulinemia, disordered insulin action
- Obesity
- Genetic predisposition
- Use of valproic acid as anti-epileptic drug

Diagnosis

After excluding other conditions (see differential diagnosis below), diagnosis is often made by using the Rotterdam Criteria. Two of the following three criteria are required:

- Hyperandrogenism (clinical or biochemical)
- Oligo-anovulation, and/or
- Polycystic appearing-ovarian morphology on ultrasound, with the exclusion of other relevant disorders. Polycystic ovaries are not required for a diagnosis of PCOS and having polycystic ovaries can be a normal finding in women, particular adolescents.

Differential Diagnosis

PCOS is a diagnosis of exclusion, and the conditions listed below must first be ruled out. Laboratory studies are necessary to rule out other diagnoses.

- Hypothyroidism
- Hyperprolactinemia
- Nonclassical congenital adrenal hyperplasia (NCAH)
- Cushing's
- Hypogonadotropic hypogonadism

Androgen-secreting tumors

DUTCH CHECKLIST

Test patterns & markers associated with PCOS

- [ ] **High testosterone**, exacerbated by insulin resistance with primary functional ovarian hyperandrogenism
- [ ] **High DHEA** with primary functional adrenal hyperandrogenism. DHEA may be high even when cortisol is normal due to the adrenal zona reticularis' overresponse to the ACTH signal.
- [ ] **High 5-alpha androgen metabolites** (5a-DHT, 5a-androstenediol, androsterone) suggest higher androgen bioavailability
- [ ] **5a-reductase preference (slider bar)** is often seen in patients with PCOS
- [ ] **Low progesterone** with infrequent menses and anovulatory cycles
- [ ] **Estrogen** may be low, normal, or high
- [ ] **Fast cortisol clearance rate (CCR): metabolized cortisol is HIGHER relative to free cortisol and free cortisone)** may point to inflammation and insulin resistance
- [ ] **High waking free cortisol** may indicate high overnight cortisol often seen with blood sugar dysregulation and stress
- [ ] **High inflammation.** These patterns are associated with high inflammation on the DUTCH Test. The more patterns the patient has the higher the likelihood of high inflammation contributing to PCOS:
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Poor phase 1 estrogen detox
    - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar)
    - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar)
  - [ ] High free cortisol (acute) or low free cortisol (chronic)
  - [ ] Cortisol metabolism favoring THF (acute) or THE (chronic)
  - [ ] High kynurenate
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Address the cause
- Restore ovulation/regular menstruation
- Reduce hyperandrogenic symptoms

Other support may include, but is not limited to:

- Address insulin resistance
  - Dietary interventions
  - Resistance training with focus on large muscle groups (hamstrings, quads, glutes)
  - Supplements: consider myo-inositol, berberine, alpha lipoic acid, chromium, NAC, gymnema
- Herbal support to lower androgens: licorice root, peony, spearmint, chamomile
- Supplemental support to decrease 5a-reductase preference: saw palmetto, nettle root, Pygeum, EGCG, zinc, reishi mushroom
- Stress management techniques and adaptogens to modulate stress response

PERIMENOPAUSE

WHAT IS PERIMENOPAUSE?

Perimenopause is the phase of hormone changes that occurs before menopause, or cessation of fertility. Perimenopause is marked by gradual hormonal changes lasting on average 2-8 years prior to a woman's last menstrual cycle, typically starting after age 40. This transitional process is characterized by menstrual cycle changes, declining fertility, and fluctuations in hormones until a woman reaches menopause.

DUTCH RESOURCES ON PERIMENOPAUSE

Podcast: "Are Your Perimenopause Symptoms Normal? Your Guide to Management, Natural Solutions, and HRT" with Carrie Jones, ND, FABNE, MPH

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

- Irregular menstrual cycles
- Shorter menstrual cycles
- Increases in FSH and LH
- Erratic estrogens that fluctuate from high to low
- Estrogen dominant symptoms
- Lower progesterone
- Unpredictable/absent ovulation
- Heavy menstrual periods/menorrhagia
- Intermittent hot flashes and night sweats
- Mood swings
- Weight gain
- Sleep disturbance

DIAGNOSIS

Diagnosis

Because Perimenopause is a gradual transition, it is typically diagnosed based on age, symptoms, and changes in a woman's menstrual cycle.

Differential Diagnoses

Other causes of irregular cycles include:

- Polycystic ovary syndrome (PCOS)
- Hypo- or hyperthyroidism
- Hyperprolactinemia
- STRESS- mental/emotional/physical
- Endometrial adhesions/Asherman syndrome
- HPO axis dysfunction
- Hypothalamic amenorrhea/ hypogonadotropic/ POI (premature ovarian insufficiency)
  - May typically present with amenorrhea but irregular bleeding is possible
- Need to rule out pregnancy if "missed a period" due to change in cycle length

DUTCH CHECKLIST

Test patterns & markers associated with perimenopause

- [ ] **DUTCH Cycle Mapping findings:**
  - [ ] **Estrogen fluctuations** in the initial stages of perimenopause:
    - [ ] Estrogen on the DUTCH Cycle Mapping test may look like a "roller coaster" with high peaks and low valleys
    - [ ] May see estrogens elevated at times when expected to be lower such as in follicular phase
    - [ ] May see multiple estrogen surges from aberrant signaling
  - [ ] **Anovulation**
  - [ ] **Low progesterone/estrogen (P/E) ratio**
  - [ ] **Short luteal phase results** in less tissue exposure to progesterone
- [ ] **High estrogen:** often seen in the initial stages of perimenopause and can contribute to frequent menses, heavy bleeding, and breast tenderness
- [ ] **Low estrogen:** often seen in the late stages of perimenopause and can contribute to infrequent menses, hot flashes, and weight gain
- [ ] **Low progesterone,** especially as the patient gets closer to being postmenopausal
- [ ] **High waking free cortisol, high middle-of-the-night free cortisol,** and/or **high bedtime free cortisol** can cause disrupted sleep patterns
- [ ] **Low DHEA:** DHEA naturally declines with age but ideally should still be within the reference range for the patient's age
- [ ] **Patterns related to declining insulin sensitivity,** in part due to decline in estrogens
  - [ ] High free cortisol
  - [ ] Fast cortisol clearance rate (CCR): metabolized cortisol is HIGHER relative to free cortisol and free cortisone
  - [ ] Increased 5a-reductase activity
  - [ ] Potentially high 8-OHdG if oxidative stress present from insulin resistance

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Protect the endometrium during high estrogen/low progesterone state
- Support adrenal health through hormone shifts
- Symptom management related to vasomotor symptoms, sleep issues, mood swings, and heavy menstrual bleeding, which are common in perimenopause

Other support may include, but is not limited to:

- Sleep hygiene
- Blood sugar regulation
- Stress reduction
- Metabolic health support
- Strength training to promote healthy body composition, increase/maintain muscle mass, and support bone health
- Whole foods nutrient rich diet
- Phytoestrogen rich diet

PREMENSTRUAL DYSPHORIC DISORDER (PMDD)

WHAT IS PMDD?

Premenstrual Dysphoric Disorder (PMDD) is a severe and sometimes disabling set of emotional and physical symptoms occurring in the luteal phase of the cycle and resolving with menses. It is distinguished from PMS in its intense psychological symptoms, increased severity, and its impact on a woman's life, including work and social relationships.

DUTCH RESOURCES ON PMDD

Case Study: "PMDD: Premenstrual Dysphoric Disorder" with Hilary Miller, ND

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

PMDD is distinguished by the presence of at least one moderate to severe affective symptom in the luteal phase:

- Mood swings
- Irritability
- Anger
- Depression or feelings of hopelessness
- Anxiety or tension
- Decreased interest in usual activities

In addition to emotional symptoms, PMDD often includes physical symptoms such as breast tenderness or swelling, joint or muscle pain, bloating, and weight gain.

PATHOPHYSIOLOGY & DIAGNOSIS

Pathophysiology

The exact pathophysiology of PMDD is not fully understood, but sensitivity to the normal fluctuations of estrogen and progesterone is thought to trigger changes in brain chemicals like serotonin and GABA, which could explain the mood disturbances. This atypical response to these hormonal changes could be influenced by genetic factors, history of other mood disorders, or environmental stressors.

Differential Diagnosis

- Premenstrual syndrome (PMS)
- Psychiatric disorders that are worse in the luteal phase

Diagnosis

The diagnosis of PMDD is clinical, typically made by tracking symptoms across at least two menstrual cycles. The presence of five or more symptoms (see list to the left) that interfere with daily functioning, with at least one being an affective symptom, is required for the diagnosis.

DUTCH CHECKLIST

Test patterns & markers associated with PMDD

- [ ] **DUTCH Cycle mapping findings:**
  - [ ] **Estrogen rapidly increases or decreases**
    - [ ] Estrogen on the DUTCH Cycle Mapping Test may show rapid changes, sharp inclines or declines, which can impact mood
- [ ] **Alpha progesterone metabolites (a-pregnanediol)** within the luteal range: In some women, the alpha progesterone metabolites exert a paradoxical effect on the GABA receptors and instead of promoting a sense of calm, they promote anxiety and irritability. This paradoxical effect has been associated with PMDD. If mood changes coincide with the increase in progesterone during the luteal phase, consider this as a potential cause.
- [ ] **Low progesterone:** Progesterone has a calming effect on the brain, and low levels during the luteal phase may be associated with PMDD symptoms
- [ ] **Estrogen excess or low progesterone/estrogen (P/E) ratio:** can contribute to mood swings and irritability, which are hallmark signs of PMDD
- [ ] **Sluggish phase 2 estrogen methylation:** impaired methylation can lead to an accumulation of estrogen, which might contribute to PMDD symptoms
- [ ] **Elevated androgens:** have not been linked to PMDD but they can contribute to overall hormonal imbalance and have been associated with mood disorders
- [ ] **Any abnormal cortisol findings:** dysregulated cortisol may exacerbate symptoms of anxiety and depression associated with PMDD
- [ ] **High or low HVA (dopamine metabolite) and VMA (norepinephrine and epinephrine metabolite):** imbalances in these neurotransmitters can be associated with mood disorders, although their link to PMDD specifically is not well established
- [ ] **High MMA:** may be seen with vitamin B12 deficiency which could influence serotonin and GABA synthesis, potentially affecting mood and contributing to PMDD symptoms

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Improve symptoms
- Refer when appropriate

Other support may include, but is not limited to:

- Herbal support: chaste tree, black cohosh
- Nutrient support: magnesium, vitamin B6, vitamin C
- Daily Oxaloacetate
- Exercise
- Medications: selective serotonin reuptake inhibitors (SSRIs), combined oral contraceptives (COCs), GnRH agonists, hormone suppressing treatments
- Bioidentical hormone therapy: Oral progesterone
- Cognitive behavioral therapy (CBT)

PREMENSTRUAL SYNDROME (PMS)

WHAT IS PMS?

Premenstrual syndrome (PMS) refers to the physical and behavioral symptoms that occur in the luteal phase of the menstrual cycle due to hormonal changes of the cycle. PMS resolves with the onset of menses.

DUTCH RESOURCES ON PMS

Blog: "Symptoms and Support of Low Progesterone" by Brook Ahnemann, ND

Blog: "Can Seed Cycling Ease Menstrual Cycle Symptoms" by Hilary Miller, ND

Find more DUTCH Education at: https://dutchtest.com/education/

SIGNS & SYMPTOMS

Signs and symptoms are extensive, and may include:

- Mood swings, depression, crying spells, angry outbursts, irritability, anxiety
- Confusion, social withdrawal, poor concentration
- Insomnia, increased nap taking,
- Changes in sexual desire
- Thirst and appetite changes (food cravings)
- Breast tenderness
- Bloating and weight gain
- Headaches
- Swelling of hands and/or feet
- Aches and pains
- Dizziness, fatigue
- Hot flashes
- Skin issues
- Gastrointestinal symptoms, abdominal pain

DIAGNOSIS & DIFFERENTIAL DIAGNOSIS

Diagnosis

According to the American College of Obstetricians and Gynecologists (ACOG), PMS is diagnosed when a woman's PMS symptoms are present in the 5 days before a period at least three menstrual cycles in a row, end within 4 days after a period starts, and interfere with some normal activities.

Differential Diagnosis

- Any symptom ascribed to other cycle phases may be a chronic condition exacerbated by cyclical hormone changes. Clinical outcomes will be improved if the underlying chronic condition is identified and treated rather than addressing hormone imbalance. Due to the high number of symptoms, a complete differential diagnosis is not within this document's scope.

DUTCH CHECKLIST

Test patterns & markers associated with PMS

- [ ] **Low progesterone:** some women experience PMS with normal hormone levels and fluctuations, however, clinically sometimes PMS is associated with low progesterone. This may be due to progesterone's calming effect on the nervous system.
- [ ] **High estrogen and/or low progesterone/estrogen (P/E) ratio:** can contribute to mood swings, breast tenderness, fatigue, headaches, and more, especially when not properly balanced with progesterone
- [ ] **Elevated xanthurenate and kynurenate:** elevations in these two organic acid markers may be seen with vitamin B6 deficiency, and research shows that vitamin B6 supplementation may improve PMS
- [ ] **Any abnormal cortisol findings:** higher perceived stress has been shown to precede an increase in PMS symptoms
- [ ] **High inflammation** can affect the hypothalamus, the 100-day follicle development, hormone receptors and signs and symptoms of PMS. Inflammation patterns identified on the DUTCH Test are listed to the right. The more patterns the patient has the higher the likelihood of high inflammation contributing to the PMS:
  - [ ] High 5a reductase activity
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Poor phase 1 estrogen detox
    - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar)
    - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar)
  - [ ] Fast cortisol clearance rate (CCR)
  - [ ] High free cortisol (acute) or low free cortisol (chronic)
  - [ ] Cortisol metabolism favoring THF (acute) or THE (chronic)
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Rule out other conditions that can mimic or overlap with PMS (see differential diagnosis above)
- Rule out premenstrual dysphoric disorder (PMDD), the most severe form of PMS
- Relieve symptoms and improve functional impairment

Other support may include, but is not limited to:

- Nutrient support: vitamin B6, magnesium
- Regular exercise
- Sleep hygiene
- Heat applied to the lower abdomen for pain, cramping, and bloating
- Chaste tree berry extract can improve mood changes
- Cognitive behavioral therapy (CBT)
- Acupuncture for pain

WEIGHT GAIN

WHAT IS WEIGHT GAIN?

Weight gain is increased storage of adipose tissue which can lead to negative health outcomes and decreased quality of life. Weight gain can occur due to positive energy balance (chronically overeating in relation to energy expenditure), hormonal shifts (thyroid, cortisol, sex hormones), stress, lack of sleep, and poor glycemic control. Once weight has increased it can be difficult to lose. If weight is increasing despite lack of caloric imbalance, it is important to investigate factors that may be affecting metabolism.

DUTCH RESOURCES ON WEIGHT GAIN

Webinar: "Addressing the Connection Between Cortisol and Weight Gain" by Debbie Rice, ND

Podcast: "Metabolic Factors in PCOS" by Tim Hyatt, ND

Blog: "Menopause and Stress"

Blog: "Metabolic Flexibility and Female Hormones" by Hilary Miller, ND

Find more DUTCH Education at: https://dutchtest.com/education/

DIFFERENTIAL DIAGNOSIS AND ETIOLOGY

Diagnosis

- BMI: Overweight (BMI ≥25 kg/m2) or obese (BMI ≥30 kg/m2)
- High waist circumference: Male > 40 inches and female > 35 inches
- High waist to hip ratio: >0.90 for males and >0.85 for females is high
- Body composition: > 25% body fat for men and > 32% body fat for women

Differential Diagnosis and Etiology

- Excess caloric intake for activity level, metabolism
- Age related decline in metabolic rate
- High stress: Stress hormones can contribute to increased fat storage around the abdominal area.
- Poor sleep: Insufficient sleep has been linked to weight gain in part by affecting hormones that regulate hunger, satiety, and blood sugar
- Changes to metabolism and metabolic disease occur with age and genetics
- Insulin resistance
- Inflammation
- Sex hormone changes: The drop in hormones associated with menopause has been linked to increased central adiposity and loss of lean muscle mass. Men can experience similar impacts with the more gradual decline in testosterone seen with age, called andropause.
- Excess dieting or caloric restriction: This overtime can shift metabolic rate to make weight more difficult to lose or easy to gain due to adaptation
- Thyroid disease-Hashimoto's/ hypothyroid
- Cushing's Disease is a serious condition where excess cortisol is chronically excreted due to a tumor. This can look like stress-related weight gain
- Medications contributing to weight gain e.g., antidepressants

Environmental toxins: PFOAs, phthalates, BPA and other chemicals have been linked to weight gain

DUTCH CHECKLIST

Test patterns & markers associated with weight gain

- [ ] **High estrogen** or **low estrogen:** Estrogen helps to regulate insulin sensitivity and metabolic rate
- [ ] **High cortisol** is seen with stress related weight gain
- [ ] **Low cortisol** results from chronic stress. Although low cortisol is not commonly linked to weight gain, cortisol helps with energy balance and mitochondrial function that helps optimize weight loss.
- [ ] **Cortisol metabolism issues:**
  - [ ] **Slow cortisol clearance rate (CCR): metabolized cortisol is LOWER relative to free cortisol and free cortisone,** may be seen in hypothyroidism
  - [ ] **Fast cortisol clearance rate (CCR): metabolized cortisol is HIGHER relative to free cortisol and free cortisone,** may point to inflammation, insulin resistance, seen with excess belly fat
- [ ] **High inflammation.** These patterns are associated with high inflammation on the DUTCH Test. The more patterns the patient has the higher the likelihood of high inflammation contributing to weight gain:
  - [ ] High 5a reductase activity
  - [ ] Low DHEA-S relative to etiocholanolone and androsterone
  - [ ] Poor phase 1 estrogen detox
    - [ ] High 4-OH-E1 (dial) or high *relative* 4-OH-E1 (slider bar)
    - [ ] High 16-OH-E1 (dial) or high *relative* 16-OH-E1 (slider bar)
  - [ ] Cortisol metabolism favoring THF (acute) or THE (chronic)
  - [ ] High kynurenate
  - [ ] High pyroglutamate
  - [ ] High indican
  - [ ] High quinolinate
  - [ ] High 8-OHdG

POTENTIAL SUPPORT CONSIDERATIONS

Review the DUTCH Interpretative Guide for patterns identified on the DUTCH Checklist.

Goals of Functional Medicine Treatment

- Lifestyle interventions to help improve weight management
- Reduce the risk of chronic disease
- Balance hormones

Other support may include, but is not limited to:

- Whole foods diet
  - Ensure adequate caloric intake for activity levels
  - Protein intake during weight loss can prevent loss of muscle mass
- Encourage balanced regular physical activity
  - Strength training can increase muscle mass which can increase metabolic rate over time
  - Aerobic exercise can increase oxygen to tissues and burn more calories per session
  - Proper rest and recovery are essential
- Balance blood sugar
  - Diet
  - Herbal supplements like berberine, gymnema, turmeric
  - Nutrients like B-complex, chromium, magnesium
  - Medication to control blood sugar if needed
- Mitochondrial support: CoQ10
- Liver support
- Thyroid support

READER NOTES

Thank You!

We know that every sample received by our lab comes from a real person, *with a real story.*

We are incredibly thankful for the opportunity to serve healthcare practitioners and their patients around the world, and we love hearing stories about how the DUTCH Test profoundly changes lives. This is why we do what we do!

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Scan the QR code or visit dutchtest.com/dutch-testimonial/ to tell us about how DUTCH has helped you get to the root cause and profoundly change lives, one life at a time.

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