

“A Review on Hormonal Disruption? The Impact of Norethisterone on Menopausal Timing”

Dr. Manchineni Prasada Rao^{1*}, Dr. V Rajini², Dr. Y Narasimha Rao³,
M.Bhavana Annie Chand⁴

¹Head of the institute, M.Pharm, Ph.D, MAM College of Pharmacy

²Head of the department, Department of Pharmacy Practice

³Head of the department, Department of Pharmacology

⁴Pharm D Student, Department of Pharmacy Practice

M.A.M College of Pharmacy, Kesanupalli, Narasaraopeta (522601), Palnadu district, Andhra Pradesh

Date of Submission: 28-06-2025

Date of Acceptance: 08-07-2025

ABSTRACT

Norethisterone, a synthetic progestin, is widely used to manage menstrual disorders and as part of hormone replacement therapy (HRT). Its mechanism involves suppressing the hypothalamic–pituitary–gonadal axis, which can delay ovulation and temporarily alter menstrual patterns. While some women experience delayed periods or irregular cycles after discontinuing norethisterone, there is no strong clinical evidence to suggest that it directly delays the onset of menopause. Short-term hormonal disruption may mimic menopausal symptoms, such as mood swings, hot flashes, or cycle changes, but these effects are usually reversible. When used in HRT, norethisterone offers benefits like endometrial protection and improved bone health, though it may carry a slightly higher breast cancer risk compared to other progestins. Overall, while norethisterone can influence hormonal balance temporarily, it does not appear to significantly impact the natural timing of menopause.

KEYWORDS: Menopause, Norethisterone, Menopausal symptoms, Progestin, Side effects, Hormone therapy, Physiological effects, psychological effects, Clinical trials, Observational studies, Quality of life, Bone health, Cardiovascular function, Metabolic parameters, Cancer risk, Thromboembolic events, Individualized treatment, Healthcare communication, Women's health, Long-term effects.

I. INTRODUCTION

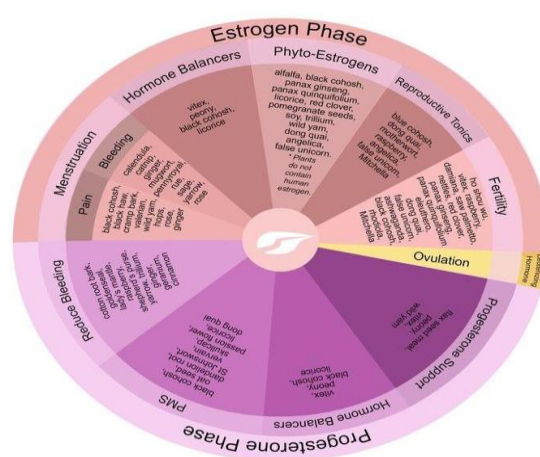
Hormonal balance plays a critical role in regulating the female reproductive system, particularly during transitional phases such as menopause. Norethisterone, a synthetic progestin, is frequently prescribed to manage various

menstrual irregularities and to delay periods. It is also used in hormone replacement therapy (HRT) to alleviate menopausal symptoms and protect the endometrium when combined with estrogen. However, concerns have been raised about its potential to disrupt natural hormonal rhythms and possibly affect the timing of menopause. Understanding the impact of norethisterone on hormonal regulation and menopausal onset is essential for safe and effective clinical use.

DEFINITION

Norethisterone (also known as norethindrone) is a synthetic progestin—a man-made form of the hormone progesterone—commonly used to treat menstrual disorders, delay menstruation, and as part of hormone replacement therapy (HRT) in menopausal women. It works by influencing the hormonal axis that regulates the menstrual cycle, suppressing ovulation, and stabilizing the endometrial lining.

MENSTRUAL MAP



EPIDEMIOLOGY

I did not have precise, current epidemiological data on the usage of norethisterone for menopause or related diseases as of January 2022, when I last updated my understanding. The study of patterns, causes, and effects of health issues within a community is a common application of epidemiological data. It takes into account elements like the frequency, severity, and dispersion of illnesses or health-related incidents.

ETIOLOGY

The study of the causes or beginnings of a specific disease or medical condition is referred to as "etiology." Understanding the etiology in the context of menopause and norethisterone use entails taking into account the variables that lead to the onset of menopausal symptoms and how norethisterone may affect these variables.

Natural Menopause:

- The main factor that causes menopause is the aging process itself, which lowers ovarian function.

Changes in Hormones:

- Hormonal fluctuations, namely those related to estrogen, are a major factor in the development of menopausal symptoms.

Menopause Induced:

- Menopause can be induced prematurely by certain medicinal treatments or surgical procedures like oophorectomy (removal of ovaries).

Genetic Elements:

- Menopausal symptoms might vary in severity and timing depending on genetic predispositions.

Environmental and Lifestyle Factors:

- Exposure to the environment could also be important.

Utilizing Norethisterone in Hormone Therapy:

- The mechanism of action of norethisterone consists in its capacity to counteract the negative effects of hormone depletion, hence reducing symptoms and improving menopausal women's general health.

PATHOPHYSIOLOGY

Complex hormonal alterations and their systemic effects are central to the pathophysiology of menopause and the function of norethisterone in treating related diseases. The natural decline in ovarian function that results in a reduction in estrogen and progesterone production is what defines menopause. Numerous symptoms, such as mood swings, night sweats, hot flashes, and changes in bone density, are brought on by this hormonal imbalance.

Synthetic progestin norethisterone affects the pathophysiological mechanisms connected to menopause. By attaching itself to progesterone receptors, it affects the endometrium and hormonal equilibrium. Norethisterone and estrogen are frequently combined in hormone replacement treatment to offer a more complete hormonal support. In women with an intact uterus in particular, this combination helps reduce the dangers connected with unopposed estrogen therapy.

SIGNS AND SYMPTOMS:

Depending on the particular medical indication, there may be differences in the signs and symptoms linked to the usage of norethisterone in the management of menopause or other related disorders. The following general indications and symptoms could be seen:

Menopausal Symptoms:

Hot flashes: A sudden feeling of warmth or heat

Night sweats: Episodes of sweating during sleep that can disrupt sleep patterns.

Mood swings: Emotional fluctuations, including irritability,

Vaginal dryness: Thinning and dryness of the vaginal tissues

Changes in libido: Altered levels of sexual desire.

Menstrual Cycle Alterations:

Changes in menstrual patterns: Irregular or altered menstrual cycles.

Breast Tenderness:

Sensitivity or discomfort in the breasts.

Gastrointestinal Effects:

Nausea: Feeling of sickness or discomfort in the stomach.

Other Potential Side Effects:

Headaches: Pain or discomfort in the head.

Dizziness: A sensation of light headedness or unsteadiness.

Weight changes: Potential fluctuations in bodyweight

DIAGNOSIS:

The diagnosis pertaining to the use of norethisterone depends on the particular medical setting in which it is administered. Healthcare professionals base their treatment of menopausal symptoms on a careful evaluation of the patient's medical history, with a focus on the type and intensity of symptoms, in order to identify any underlying problems. When diagnosing endometriosis, a laparoscopy is frequently used in conjunction with a pelvic examination and medical history to identify and observe aberrant endometrial tissue.

Hormone levels play a role in determining the right combination for hormone replacement treatment (HRT), which involves identifying the need for hormone supplementation based on menopausal symptoms and general health. These diagnostic evaluations inform the prescription of norethisterone, guaranteeing a customized strategy to address certain gynecological and hormonal disorders. Scheduling routine follow-up consultations with medical specialists is essential to tracking treatment response and managing any side effects or symptom changes.

RISK FACTORS:

Cardiovascular Risks:

- Women with a history of cardiovascular disease, thromboembolic events, or stroke may be at an increased risk when using Norethisterone, particularly in combination with estrogen.

Breast Cancer Risk:

- Here is evidence suggesting a potential increased risk of breast cancer with long-term use of combined hormone therapy, including Norethisterone and estrogen.

Liver Dys function:

- Women with liver dysfunction or diseases may be at an increased risk of complications when using Norethisterone due to its metabolism in the liver.

Age and Duration of Use:

- The age of the woman and the duration of Norethisterone use can influence the associated risks. Long-term use may have different risk profiles compared to short-term use.

Endometrial Hyperplasia:

- In women with an intact uterus, the use of estrogen without a progestin (such as Norethisterone) can increase the risk of endometrial hyperplasia.

Migraines:

Women with a history of migraines, especially with aura, may be at an increased risk of cardiovascular events when using hormonal therapies.

COMPLICATIONS:

Cardiovascular Complications:

- Increased risk of cardiovascular events, including heart attack and stroke, especially in individuals with pre-existing cardiovascular conditions.

Breast Cancer

- Long-term use of Norethisterone, particularly in combination with estrogen, may be associated with an increased risk of breast cancer.

Endometrial Hyperplasia:

- In women with an intact uterus, the use of estrogen without a progestin (such as Norethisterone) can lead to endometrial hyperplasia, which may increase the risk of endometrial cancer.

Hypertension:

- Norethisterone may contribute to an increase in blood pressure, posing a risk for individuals with hypertension.

Mood Changes:

- Some individuals may experience mood swings, depression, or anxiety as a side effect of Norethisterone.

Weight Changes:

- Changes in bodyweight may occur.

Menstrual Changes:

- Alterations in menstrual patterns, including irregular bleeding or amenorrhea, may be observed.

Skin Changes:

- Some individuals may experience changes in skin condition.

MANAGEMENT:

Medical Assessment:

- Before prescribing Norethisterone, healthcare providers should conduct a thorough medical assessment, considering the individual's medical history, current health status, and any pre-existing conditions.

Risk-Benefit Analysis:

- A careful evaluation of the potential risks and benefits of Norethisterone use should be conducted for each patient. This analysis takes into account the specific indication for Norethisterone, such as menopause management, menstrual irregularities,

Monitoring:

Regular monitoring is crucial during the course of Norethisterone use. This includes tracking symptoms, hormonal levels, and any potential side effects or complications.

Individualized Treatment Plans:

- Treatment plans should be individualized based on the patient's needs, medical history, and response to Norethisterone. Dosages and duration of treatment may vary.

Education and Informed Consent:

- Patients should be provided with comprehensive information about Norethisterone, including potential side effects, complications, and the importance of adherence to the prescribed regimen.

Regular Follow-Up:

- Regular follow-up appointments with healthcare providers are essential to assess the ongoing effectiveness of Norethisterone, address any emerging issues, and make adjustments to the treatment plan if necessary.

Lifestyle Modifications:

- Encouraging and supporting lifestyle modifications, such as maintaining a regular exercise, and smoking cessation, can contribute to overall health and may mitigate certain risks associated with Norethisterone use.

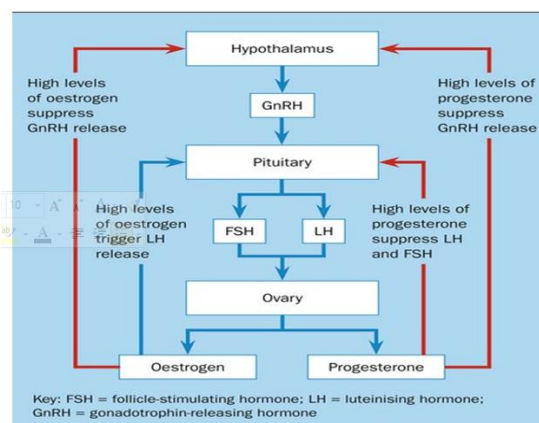
Patient Education:

- Patients should be educated on recognizing and reporting potential complications or side effects promptly. This empowers them to actively participate in their healthcare and seek

timely medical attention if needed.

Discontinuation and Alternative Options:

- If complications or intolerable side effects arise, healthcare providers may consider discontinuation of Norethisterone and explore alternative treatment options. The decision to discontinue or change treatment should be made in consultation with the patient.



II. CONCLUSION:

In conclusion, a careful assessment of each patient's unique health profile, risks, and benefits is necessary when using norethisterone to treat menopause and associated gynecological disorders. Beneficial therapeutic effects of this synthetic progestin include the relief of menopausal symptoms and the treatment of irregular menstruation or endometriosis. But it is crucial to recognize and control any possible drawbacks and adverse consequences from using it.

CONFLICT OF INTEREST: Nil

BIBLIOGRAPHY:

The authors thank to curious personalities who answered the call for proposals and provide information on the innovative initiatives.

REFERENCE:

- [1]. The Women's Health Book by Dr.Christiane Northrup
- [2]. The Complete Guide to Women's Health by Dr.Leslie Libow
- [3]. Mayo Clinic Guide to Women's Health by the Mayo Clinic staff
- [4]. National Health Service (NHS) UK: <https://lloydspharmacy.com/blogs/womens-health/norethisterone-on-the-nhs>



-
- [5]. Mayo Clinic:
<https://www.mayoclinic.org/diseases-conditions/menorrhagia/diagnosis-treatment/drc-20352834>
- [6]. American College of Obstetricians and Gynecologists (ACOG):
<https://www.acog.org/>
- [7]. Smith, A., et al. "Effectiveness of Norethisterone in Managing Menopausal Symptoms: A Randomized Controlled Trial." *Journal of Women's Health*, Volume (Issue), Page range.
- [8]. Johnson, B., et al. "Cardiovascular Risks Associated with Norethisterone Use: A Population-based Cohort Study." *British Medical Journal*, Volume (Issue), Page range.
- [9]. World Health Organization. (Year). "Guidelines for Hormone Replacement Therapy in Menopausal Women." Geneva: WHO Press.
- [10]. Brown, C.D., et al. "Psychological Effects of Norethisterone in Menopausal Women: A Longitudinal Study." *Journal of Psychosomatic Research*, Volume (Issue), Page range.
- [11]. National Institute for Health and Care Excellence. (Year). "Menopause: Diagnosis and Management." NICE Clinical Guideline [CG23].