UTERINE FIBROIDS: A CLINICAL OVERVIEW OF PATHOGENESIS, DIAGNOSIS, AND MANAGEMENT

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Introduction. Uterine fibroids, also known as leiomyomas or myomas, are the most common benign tumours of the uterus, affecting up to 70-80% of women during their reproductive years. These growths are composed primarily of smooth muscle cells and varying amounts of fibrous connective tissue. Although benign and non-metastatic, fibroids can severely impact the quality of life, fertility, and reproductive outcomes in affected women. The burden of disease is especially significant among women of African descent, where fibroids tend to appear earlier, grow larger, and cause more severe symptoms.

Despite their prevalence, the exact ethology of uterine fibroids remains incompletely understood. Genetic, hormonal, and environmental influences are all believed to play essential roles in fibroid pathogenesis. Advances in imaging and minimally invasive treatment options have improved diagnostic accuracy and individualized care, but challenges remain in management, particularly when fertility preservation is a goal. This paper provides a comprehensive overview of the epidemiology, pathogenesis, clinical presentation, diagnostic tools, and current treatment strategies for uterine fibroids.

Epidemiology and Risk Factors. Uterine fibroids are particularly common among women aged 30 to 50 years. Studies have shown that by age 50, nearly 70% of white women and over 80% of Black women will have developed at least one fibroid. Several risk factors have been identified:

- Age: Prevalence increases with age, peaking before menopause.

- Race: Higher incidence and severity among Black women.
- Genetic predisposition: Family history increases risk.
- Hormonal factors: Estrogen and progesterone stimulate fibroid growth.
- Lifestyle factors: Obesity, early menarche, and vitamin D deficiency are associated with increased risk.

Protective factors include higher parity, long-term use of oral contraceptives, and smoking (which lowers estrogen levels, although it carries many other health risks).

Pathogenesis and Molecular Biology. Uterine fibroids originate from the smooth muscle layer of the uterus (myometrium). Their growth is hormone-dependent, especially influenced by estrogen and progesterone. These hormones promote the proliferation of fibroid cells and increase extracellular matrix (ECM) production, which contributes to fibroid size and stiffness.

Recent molecular studies have identified specific genetic mutations associated with fibroid development, particularly in the MED12 gene, which is mutated in up to 70% of fibroids. Other implicated factors include:

- Dysregulated signalling pathways (e.g., TGF-, Want catenin)
- Epigenetic changes
- Growth factors (e.g., insulin-like growth factor, epidermal growth factor)
- Inflammatory cytokines and ECM dysregulation

These complex mechanisms highlight the multifactorial nature of fibroid development and support the ongoing search for targeted therapies.

Clinical Presentation. While many fibroids are asymptomatic and discovered incidentally, others can cause a wide range of symptoms based on their size, number, and location. Common clinical manifestations include:

- Heavy or prolonged menstrual bleeding (menorrhagia)

- Pelvic pain or pressure
- Urinary frequency or retention
- Constipation
- Infertility or recurrent pregnancy loss

Fibroids are often classified by location: submucosal, intramural, and subserosal, each associated with different symptoms and clinical implications. Submucosal fibroids, for example, are strongly associated with heavy bleeding and infertility.

Treatment Strategies. Management depends on the severity of symptoms, the size and location of fibroids, the womanís age, and her desire for future fertility. Treatment options are divided into medical and surgical approaches.

Medical Therapies:

- Gonadotropin-releasing hormone (GnRH) agonists: Reduce fibroid size temporarily by inducing a hypoestrogenic state.
- Selective progesterone receptor modulators (SPRMs): Such as ulipristal acetate, can control bleeding and shrink fibroids.
- Non-hormonal options: NSAIDs for pain, tranexamic acid for bleeding control.

Emerging Therapies and Research Directions. New therapies under investigation include anti-fibrotic agents, molecular inhibitors, and gene therapy. Advances in stem cell research and targeted drug delivery may eventually revolutionize fibroid treatment. Additionally, long-term studies on the safety and efficacy of SPRMs and GnRH antagonists are ongoing.

Conclusion. Uterine fibroids are a widespread gynecological condition with a significant clinical and public health burden. Although typically benign, they can profoundly affect a womanís reproductive health and quality of life. A multidisciplinary approach that includes accurate diagnosis, individualized treatment, and patient-centered counseling is essential for optimal care. Continued

research into the molecular underpinnings of fibroids promises to improve outcomes through targeted and less invasive therapies.

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