Erectile Dysfunction in the 21st Century: A Modern Approach to an Old Problem

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Abstract

Erectile dysfunction (ED) is a condition that affects a man's ability to maintain or achieve an erection sufficient for satisfactory sexual activity. The understanding and treatment of this condition have undergone an interesting evolution over time.
In the beginning, it was often associated with spiritual or magical problems, but significant advances in the understanding of ED only began to emerge in the 19th century, with the development of modern medicine.
Today, tests and diagnostics for ED have considerably improved, providing personalized solutions for each case.

The future of erectile dysfunction treatments looks promising, with ongoing research exploring new therapeutic methods: gene therapy, stem cells, and advanced implantable devices.

Key-words: erectile dysfunction, past, present, future

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Editorial

Erectile dysfunction (ED), defined as the persistent inability to achieve or maintain an erection sufficient for satisfactory sexual performance, represents one of the most common male sexual disorders. Affecting millions of men worldwide, ED is not only a physiological problem but also one with profound psychological and social implications. Its impact on quality of life, self-esteem, and interpersonal relationships is significant, making this condition a major topic of interest in men's health.

Historically, the perception and approach to erectile dysfunction have evolved considerably. From mystical explanations and empirical remedies in antiquity to the complex understanding of physiological and psychological mechanisms today, the journey of ED reflects the advancements in medicine and socio-cultural changes. In the past, the subject was often shrouded in shame and stigmatization, leading to underreporting and a lack of appropriate interventions.

In recent decades, with technological advancements and in-depth research, effective methods of diagnosis and treatment have been developed. Revolutionary medications, such as phosphodiesterase type 5 inhibitors, have radically transformed the management of ED, offering practical solutions for many patients. Nevertheless, challenges persist, including addressing underlying causes such as cardiovascular diseases, diabetes, and psychological factors.

Looking toward the future, personalized medicine and therapeutic innovations, such as stem cell therapy and gene therapy, promise to open new horizons in the treatment of erectile dysfunction. Additionally, the increased focus on holistic health and the integration of multidisciplinary approaches can further improve outcomes for patients.

This editorial aims to explore the evolution of erectile dysfunction, analyzing how the understanding and management of this condition have progressed over time. We will examine historical perspectives, current achievements, and future opportunities, highlighting the importance of continued research and an empathetic approach to those affected.

The Past. Historical Understanding of Erectile Dysfunction

Erectile dysfunction has been recognized and discussed since ancient times, although its understanding and approaches have varied significantly throughout history. In ancient civilizations, sexuality and fertility were often linked to divine or supernatural forces.

The Ebers Papyrus (circa 1550 BCE), one of the oldest known medical texts, contains references to sexual problems and offers plant-based remedies and magical rituals for treating impotence [1]. In Mesopotamia and Babylon cuneiform tablets mentioned sexual dysfunctions and proposed incantations and offerings to the gods to restore potency [2].

Hippocrates (460–370 BCE) and Galen (129–216 CE) develop the concept of humors and suggested that impotence could result from bodily imbalances or psychological issues [3].

During the Middle Ages, the medical understanding of erectile dysfunction largely stagnated, and supernatural and religious explanations became predominant, impotence was often attributed to spells or curses. Men suffering from ED could accuse women of witchcraft, leading to notable persecutions and trials during that period [4]. The role of the church, especially the catholic one, was decisive. The catholic church considered sexual intercourse permissible only for procreative purposes. Sexual problems were seen as divine punishment for sins or immoral behaviors [5]. Treatments were largely empirical and included prayers, pilgrimages, the use of talismans, or plants with supposed aphrodisiac properties.

With the Renaissance came a renewed interest in science and medicine, leading to significant advances in understanding human anatomy and physiology. Andreas Vesalius and William Harvey provided a solid foundation for understanding the structure of male genital organs and blood circulation, laying the groundwork for modern physiology [6].

In the 18th and 19th centuries physicians began to investigate physical causes of impotence, including nerve injuries and vascular disorders, interest emerged also in psychological factors influencing sexual function [7]. Sigmund Freud proposed that impotence could have psychogenic causes related to internal conflicts and psychological traumas [8].
The discovery of hormones and their roles in the body opened new perspectives. One of the pioneers of hormone therapy was Charles-Édouard Brown-Séquard (1817–1894). He experimented with injections of testicular extracts to rejuvenate his vitality, sparking interest in hormone therapy, although his methods were unscientific [9].

The isolation and synthesis of testosterone in the early 20th century led to a better understandingof the role of sex hormones in erectile function [10]. Studies of the autonomic nervous system elucidated the neurological mechanisms involved in erection and ejaculation.

Before the 20th century surgical treatments were nearly non-existent. Most interventions involved treating physical deformities or injuries. In ancient civilizations, especially among the Egyptians and Greeks, the treatment of penile injuries often involved amputations and rudimentary reconstruction methods.

The Present

Erectile dysfunction (ED) continues to be a major public health issue in the 21st century, affecting men of all ages, but with increased prevalence among the elderly. Currently, the understanding of ED has advanced significantly due to progress in medicine, psychology, and technology.
Massachusetts Male Aging Study (MMAS) reported that approximately 52% of men aged between 40 and 70 suffer from some degree of ED, and it is estimated that by 2025 approximately 322 million men will suffer from erectile dysfunction [11,12]
The etiology and risk factors of erectile dysfunction are extremely varied.
Organic causes are largely represented by cardiovascular diseases, diabetes and dyslipidemias. Atherosclerosis but also diabetic vascular impairment or elevated levels of cholesterol and triglycerides contribute to endothelial dysfunction [13, 14].
Testosterone deficiency (hypogonadism) can affect libido and erectile function. Obesity is also ssociated with chronic inflammation and hormonal imbalances [15].

Central and peripheral neurological pathologies - acquired brain lesions (stroke, cranial trauma), extrapyramidal symptoms, medullar lesions, multiple sclerosis, peripheral lesions of the cauda equina or more distal- represent determined causes for the appearance of ED, and treating these causes is a challenge. The medication used in the treatment of some neurological diseases can lead to the ED [16].
Psychogenic causes are more and more frequently involved in the etiopathogenesis of ED: stress and anxiety , depression, relationship problems [17] decreased libido and sexual performance and can inhibit erectile response through neuroendocrine mechanisms.

Cigarette smoking is a leading cause of preventable morbidity and mortality all over the world. Relationship between cigarette smoking and erectile dysfunction is relatively well established. The main physiologic mechanism that appears to be affected includes the nitric oxide signal transduction pathway [18]. However, more and more studies show the negative impact of electronic cigarettes on the vascular endothelium and their connection with ED [19].

Excessive alcohol consumption can lead to neuropathy and hormonal disorders. Certain antihypertensives, antidepressants, and antipsychotics may have sexual side effects through the nitric oxide-cyclic GMP pathway in the erectile nervous system [20].

Diagnosis and evaluation
The evaluation of ED requires a holistic approach involving urologists, endocrinologists, psychologists, and other specialists.
The use of standardized questionnaires is mandatory in the assessment of erectile dysfunction. International Index of Erectile Function (IIEF) is a validated tool for assessing erectile function.
Evaluation of signs of hypogonadism, neuropathy, or

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Evaluation of signs of hypogonadism, neuropathy, or cardiovascular diseases during the physical examination can give us information about the possible causes of ED Paraclinical Investigations

Standard laboratory tests must include hormonal profile (total and free testosterone, prolactin, luteinizing hormone, follicle-stimulating hormone), blood glucose and glycated hemoglobin, lipid profile (total cholesterol, LDL, HDL, triglycerides)

In selected cases, specific tests may be necessary: penile doppler ultrasound for evaluation of arterial and veno-occlusive blood flow [21], nocturnal penile tumescence test to distinguish between organic and psychogenic causes .

Current treatment options are represented by: pharmacotherapy, local therapies, mechanical devices and surgical interventions. Psychosexual therapy is added to these.

The main goal of these therapies is to improve erectile function, but especially the impact on quality of life of ED.

The most important drug treatment is represented by phosphodiesterase type 5 inhibitors (PDE5i). By inhibiting the degradation of cGMP the PDE5i improve penile blood flow leading to a good erection. The studies show a high success rate and good safety profile [22].

Replacement testosterone therapy is indicated in confirmed cases of hypogonadism but equires careful monitoring due to potential risks (e.g., polycythemia, adenocarcinoma of the prostate) [23].

Local therapies represent an alternative for patients who are unresponsive to PDE5i or have contraindications for this type of treatment. Intracavernosal injections induce erection through local vasodilation but they are difficult to administer and patient compliance is low. Easier to insert and with similar effects, these vasodilators can also be inserted as intraurethral suppositories [24].

Vacuum erection devices are indicated in selected cases. Often, in the case of surgical interventions in the pelvic area, neurovascular bundle preservation. In these cases, PDE5i therapy is no longer effective. For these groups of patients or for those who, for

various reasons, oral treatment is no longer effective, vacuum erection devices represent an option [25].
The final station in the treatment of ED is represented by penile implants. Whether we are talking about semirigid or inflatable prostheses, these represent a definitive solution for cases refractory to other treatments [26].
Psychosexual therapy should represent a standard in the therapeutic arsenal of erectile dysfunction because every patient with this pathology will at some point associate a psychogenic component of erectile dysfunction. Cognitive-behavioral therapy, relaxation techniques, individual or couple counseling addresses psychogenic factors and relational problems [27].
The treatment of erectile dysfunction must also integrate psychosocial aspects. ED can profoundly affect self-confidence and sense of masculinity with an icreased risk of depression and anxiety. Open communication and partner support are essential for managing ED.
Even if hundreds of years have passed, the social stigmatization of these patients is still present. Many men avoid seeking medical help due to embarrassment or the perception that ED is a normal part of aging. It is important to promote a culture of openness and understanding regarding sexual issues. Proactive questioning and empathetic approach can encourage patients to discuss [28].

The Future. Quo Vadis Erectile Dysfunction?

Erectile dysfunction (ED) represents a continuously evolving field, with research and innovations promising to significantly improve the diagnosis and treatment of this condition. The future management of ED focuses on advanced therapies, personalized medicine, integrative approaches, and health policies aimed at ensuring equitable access to care.
Stem Cell Therapy have the potential to regenerate damaged tissues, including nerves, blood vessels, and muscles involved in erection. Preliminary clinical studies in humans indicate improvements in erectile function without significant adverse effects. The future of stem cell research is constantly being evaluated, although there is a need for protocol standardization and long-term evaluation of safety and efficacy [29].
Gene therapy refers to the use of viral and non-viral vectors to deliver therapeutic genes to tissues via direct or transduced cell-mediated approaches. Anumber of therapeutic gene strategies have been extensively tested and proven to be effective in many animal models. However, only a few of them have been evaluated in clinical trials [30]. The purpose of these gene therapies is to increasing eNOS expression or poromoting angiogenesis and vascular regeneration [31]
The next generation of implantable devices will be represented by "remote controlled" penile prostheses that may be activated without the need for manual compression of a pump or "vibrating" penile implant that may convey vibratory stimulation to a partner
Also, the use of biocompatible materials will reduced the risk of infection and complications [32].
Innovative Pharmacotherapy. Rho-kinase inhibitors are otential agents that relax penile smooth muscles and improve erection. Targeting Rho-kinase may be a possible target for the treatment of ED secondary to specific causes, and Rho-kinase inhibitors may be a new drug family for the treatment of ED. However, this requires further studies for in-depth understanding [33].
Peptide molecule therapy. Apelin, an endogenous circulating peptide, protects corpus cavernosum against fibrosis. Preliminary results suggest an essential protective role of Apelin as a promising candidate for the development of fibrosis-associated erectile dysfunction treatments [34]
Similar to all medical disciplines, the treatment of erectile dysfunction will evolve towards a personalized medicine and the patient's genetic profile may represent the key. Identifying genetic polymorphisms associated with ED to personalize treatment or use of molecular markers to predict therapy response and risk of adverse effects represent the directions towards which medical research is headed [35].
Besides all the current therapies and future discoveries, one thing will always remain relevant: modification of the lifestyle to promote a healthy life. Quitting smoking, aerobic or Kegel exercises, a healthy diet and nutrition, stress management and mental health are milestones that must be reached

by each patient.

At the same time, there is a need for training programs for educating physicians on sensitive and effective approaches to ED-related issues.

The future approach strategy for erectile dysfunction will depend on investments in clinical and preclinical studies, international collaboration for the creation of partnerships between institutions to accelerate progress and standardize practices.

Conclusions. From the mystical beliefs of the past to the pharmacological and technological treatments of the present, and onward to the innovative therapies of the future, erectile dysfunction has come a long way. Current developments in medicine and biotechnology suggest that solutions for this condition will continue to evolve, offering increasingly effective and personalized options for men

Conflicts of Interest. The Authors declare no conflict of interest.

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