

A review of hyperhidrosis: pathophysiology, clinical management, and emerging therapies

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Abstract

Hyperhidrosis is a chronic disorder characterised by excessive sweating beyond the physiological needs of thermoregulation, significantly affecting patients' quality of life. This review explores the epidemiology, pathophysiology, and classification of hyperhidrosis, distinguishing between primary focal hyperhidrosis and secondary generalised hyperhidrosis. Current treatment strategies, including topical agents, systemic medications, botulinum toxin injections, iontophoresis, and surgical interventions, are discussed. Emerging therapies, such as microwave thermolysis, laser treatments, and novel pharmacological agents, are evaluated for their efficacy and safety. Advances in understanding the neural regulation of sweat glands and the impact of hyperhidrosis on mental health have opened new avenues for personalised and minimally invasive treatments. Despite the progress, challenges remain in diagnosis, treatment accessibility, and long-term management. This article highlights the importance of multidisciplinary care and future research to improve therapeutic outcomes for individuals with hyperhidrosis.

Keywords: hyperhidrosis, focal, secondary generalised

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Introduction

Hyperhidrosis, or excessive sweating, is a condition affecting approximately 2–5% of the population.¹ It is categorised into primary focal hyperhidrosis (PFH), which typically affects specific areas such as the palms, soles, axillae, or face, and secondary generalised hyperhidrosis (SGH), which is often linked to systemic conditions like hyperthyroidism or medications.¹ Generally, PFH manifests during adolescence or early adulthood, whereas SGH can occur at any age and requires addressing the underlying cause.¹

Excessive sweating can profoundly impact patients' physical, psychological, and social well-being, leading to stigma, embarrassment, and reduced quality of life.² Understanding the pathophysiological mechanisms behind hyperhidrosis, including overactivity of the sympathetic nervous system and dysregulation of sweat gland function, is critical to tailoring effective treatments.² Hyperhidrosis has a significant impact on many facets of life, including the psychological, social, and even economic spheres, which causes disruptions to day-to-day activities.³ The condition is a significant burden for patients, causing them to withdraw and become more self-conscious.³ Additionally, stress and emotions can exacerbate them, creating a vicious cycle.^{3,4} Researchers have recently found a link between hyperhidrosis and an increased risk of mental illnesses, such as depression.^{3,4}

Epidemiology

Hyperhidrosis is more prevalent in females and is frequently underdiagnosed due to the associated stigma and lack of awareness.⁵ PFH is often familial, with a genetic predisposition noted in approximately 30–50% of cases.⁵ SGH, however, is

usually secondary to conditions like diabetes mellitus, obesity, or neurological disorders.⁵

Pathophysiology

Sweat gland overactivity in hyperhidrosis is mediated by the autonomic nervous system, particularly the sympathetic fibres.⁶ Acetylcholine acts as the primary neurotransmitter, binding to muscarinic receptors on eccrine sweat glands to stimulate sweating, thereby increasing sweat secretion.⁶ In PFH, an exaggerated neural response leads to localised sweating, while in SGH, systemic factors like hormonal imbalances drive generalised hyperhidrosis.⁶

Diagnosis

The diagnosis is based on clinical history and physical examination.⁷ Criteria for PFH include visible, excessive sweating for at least six months without secondary causes and affecting specific areas.⁷ Tools like the Hyperhidrosis Disease Severity Scale (HDSS) are used to evaluate severity and treatment efficacy.⁷

Management strategies

See Table I for pharmacological management.

Iontophoresis

A non-invasive method where electrical currents reduce sweating, primarily used for palmar and plantar hyperhidrosis.¹³

Surgical interventions

- **Endoscopic thoracic sympathectomy (ETS):** Reserved for severe cases unresponsive to other treatments. It involves

Table I: Pharmacological management

Agent	Mechanism of action	Common side effects
Topical Agents Aluminium Chloride	The first-line treatment for mild-to-moderate hyperhidrosis. It works by obstructing sweat gland ducts. ^{8,9}	May cause skin irritation, itching, tingling, rash or dermatitis. ⁸
Glycopyrronium Cloths	An anticholinergic option effective in reducing localised sweating. ^{9,10}	May cause skin irritation, dry skin, contact dermatitis or application site pain. ⁹
Systemic Medications Anticholinergics (e.g. glycopyrrolate, oxybutynin)	Reduces sweat production systemically. ¹¹ Glycopyrrolate is a muscarinic receptor antagonist that blocks acetylcholine from binding, preventing sweat gland activation. ¹¹	May cause side-effects like dry mouth or urinary retention. ¹¹
Beta-blockers	Oxybutynin exerts a direct antispasmodic effect on smooth muscle and inhibits the muscarinic action of acetylcholine on smooth muscle. ¹¹	
Benzodiazepines	Useful for hyperhidrosis triggered by anxiety. ¹¹ Beta-blockers reduce sweating by blocking adrenergic activity, which is part of the body's "fight-or-flight" response. ¹¹	May cause fatigue, dizziness, shortness of breath. ¹¹
	Their effect on sweating is due to their ability to calm the autonomic nervous system. ¹¹	May cause drowsiness, sedation, dizziness and cognitive impairment. ¹¹
Botulinum Toxin Injections	Botulinum toxin A inhibits acetylcholine release at the neuromuscular junction, effectively reducing sweating for up to six months. ¹² It is particularly effective for axillary and palmar hyperhidrosis. ¹²	May cause injection-site pain and haemorrhage, nonaxillary sweating, infection, pharyngitis, flu syndrome, headache, fever, neck or back pain, pruritus. ¹² Numerous factors greatly influence the cost of botox. The cost of the actual Botulinum toxin and the quantity required are the most significant of these. The training and experience of the medical practitioner doing the procedure is the next significant expense. ¹²

cutting or clamping sympathetic nerves but may lead to compensatory hyperhidrosis.¹⁴

- **Local sweat gland removal:** Laser or surgical excision can be considered for refractory axillary hyperhidrosis.¹¹

Emerging therapies

- **Microwave thermolysis:** Destroys sweat glands using controlled microwave energy, offering long-term results.¹⁵
- **Laser treatments:** Targets sweat glands without affecting surrounding tissues.¹⁶
- **Topical novel agents:** Research on new anticholinergic formulations with fewer side-effects is ongoing.^{11,17}

Conclusion

Hyperhidrosis is a debilitating condition with significant physical and psychological implications. While advances in topical agents, botulinum toxin therapy, and minimally invasive procedures have improved outcomes, challenges persist in diagnosis, treatment accessibility, and long-term management. Emerging therapies, including microwave thermolysis and novel pharmacological agents, hold promise for transforming care. A multidisciplinary approach that includes dermatologists, pharmacists, and mental health professionals is critical for optimal management.

Continued research into the pathophysiology of hyperhidrosis and innovative treatments will pave the way for personalised and effective therapeutic strategies.

Conflict of interest

The author has no conflict of interest.

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