Don’t sweat it: treatments for hyperhidrosis

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Director Dermatology Clinical Trials Unit
Emory University School of Medicine
April 1, 2017
<table>
<thead>
<tr>
<th>External Industry Relationships *</th>
<th>Company Name</th>
<th>Role</th>
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<tr>
<td>Equity, stock, or options in biomedical industry companies or publishers</td>
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<tr>
<td>Board of Directors or officer</td>
<td>Coquille Economic Development Corp (CEDCO)</td>
<td>William S. Rice MPA, Husband, Board Member</td>
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<td>Mith-ih-kwuh Economic Development Corp (MEDCO)</td>
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<td>Royalties from Emory or from external entity</td>
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<td>Industry funds to Emory for my research</td>
<td>Sanofi-Genzyme/Regeneron Pharmaceuticals, Inc. (AD)</td>
<td>Principal Investigator (PI)</td>
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<td>Anacor Pharmaceuticals, Inc. (AD)</td>
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<td>Celgene Pharmaceuticals, Inc. (AD/PsO)</td>
<td>PI/ Co-Investigator (CI)</td>
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<td>Menlo (CP)</td>
<td>PI (partial salary support, PSS)</td>
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<td>Incyte (Vitiligo)</td>
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<td>Janssen (Neurology)</td>
<td>CI (PSS)</td>
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<td>Other</td>
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<td>Honorarium</td>
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<td>Global Pointe</td>
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<td>Georgia Physicians Assistants Society</td>
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<td>International Hyperhidrosis Society</td>
<td>Honorarium/Distinguished Faculty</td>
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Objectives

1) Review the quality of life (QoL) impact of hyperhidrosis (HH)
2) Review the known pathophysiology of HH
3) Review the treatment options for HH
Outline

Defining HH (reviewing classification)
Epidemiology of HH
QoL in HH
Pathophysiology of HH
Treatment of HH
Outline

Defining HH (reviewing classification)
Epidemiology of HH
QoL in HH
Pathophysiology of HH
Treatment of HH
ID: A 21 year old female

HPI: 8 year history of excess sweating of her palms bilaterally

MEDS: NONE

ROS: Negative

Question #1
Her diagnosis is most consistent with:

A) Generalized HH  
B) Regional HH  
C) Primary focal HH  
D) Aquagenic palmar keratoderma  
E) None of the above (this is degree of sweating is normal)
What is Hyperhidrosis?

Sweating that is more than required to maintain normal thermal regulation

Hornberger et al. JAAD. 2004.
Diagnosis of Primary Focal Hyperhidrosis

- Focal, visible, excessive sweating of at least 6 months duration, *without apparent cause*, with at least 2 of the following characteristics:
  - Bilateral and relatively symmetric
  - Impairs daily activities
  - Frequency of at least one episode per week
  - Age of onset less than 25 years
  - Positive family history
  - Cessation of focal sweating during sleep

# Primary vs. Regional vs. Generalized

<table>
<thead>
<tr>
<th>Type</th>
<th>Clinical presentation</th>
<th>Causes</th>
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<tr>
<td><strong>Primary</strong></td>
<td>Focal, bilateral, <em>symmetric</em> sweating</td>
<td>Idiopathic</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td>Focal sweating, <em>asymmetrical</em></td>
<td>Neurological disorders (i.e. Frey syndrome), Neoplasms, Trauma</td>
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<tr>
<td><strong>Generalized</strong></td>
<td><em>Generalized</em> sweating</td>
<td>Endocrine disorders (i.e. Pheochromocytoma, thyrotoxicosis etc.), Drugs, Tumors, Febrile diseases, Spinal cords injury, Cutaneous diseases</td>
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Aquagenic palmar keratoderma
Outline

Defining HH (reviewing classification)

Epidemiology of HH

QoL in HH

Pathophysiology of HH

Treatment of HH
Question #2
What is the prevalence of HH?

A) 0.03%
B) 1%
C) 2.8%
D) 10%
E) 28%
Prevalence of HH

• 2.8% of the United States Population (7.8 million)
  – Comparable to psoriasis
  – Underestimate (widely undiagnosed and untreated)

Strutton et al. JAAD. 2004.
Prevalence of HH (Cont.)

• 2/3\textsuperscript{rd} of HH patients do not consult their physician

• HH patients wait for a mean of 8.9 years before seeking treatment
  – Not knowing treatment options
  – Not able to find a provider familiar with HH treatment options
  – Not knowing insurance coverage options
  – Embarrassment

Walling et al. JAAD. 2009.
Outline

Defining HH (reviewing classification)
Epidemiology of HH
QoL in HH
Pathophysiology of HH
Treatment of HH
“Never let them see you sweat!”
QoL in HH

“I usually wear black and try not to lift my arms.”
“My feet are always infected with fungus and are sore.”
“My pen slips out of my hands and my paper is always wet.”
“I am not able to play baseball (my favorite sport) because the bat flies out of my hands”
“I have not taken a job outside my house.”
“I would do anything to improve my sweating!”
QoL in HH (Cont.)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dermatology Quality Life Index</th>
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<tbody>
<tr>
<td>Hyperhidrosis</td>
<td>10.1</td>
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<tr>
<td>Severe acne</td>
<td>9.2</td>
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<tr>
<td>Pruritus</td>
<td>9.2</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>8.9</td>
</tr>
<tr>
<td>Atopic Dermatitis</td>
<td>7.3</td>
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<tr>
<td>Hailey- Hailey</td>
<td>6.1</td>
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<tr>
<td>Darier’s Disease</td>
<td>5.9</td>
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<tr>
<td>Vitiligo</td>
<td>4.8</td>
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</table>

Outline

Defining HH (reviewing classification)
Epidemiology of HH
QoL in HH
Pathophysiology of HH
Treatment of HH
The underlying pathophysiology of HH is due to an:

A) Increased density of eccrine glands
B) Increased size of eccrine glands
C) Increased activity of the eccrine glands
D) Increased release of the acetycholine (ACh)
E) Increased uptake of the ACh
Pathophysiology of HH

• Poorly understood
• Normal density and size of eccrine glands
• Overstimulation of the eccrine glands innervated by postganglionic cholinergic sympathetic fibers

• Cartoon of post synaptic Eccrine cell

Pathophysiology of HH (Cont.)

• Probably genetic
  – Gene unknown
  – AD, variable penetrance
  – 30-50% have a known family history of HH

Haider et al. CMA. 2005.
Outline

Defining HH (reviewing classification)
Epidemiology of HH
QoL in HH
Pathophysiology of HH
Treatment of HH
Question #4
Topical anti-perspirants mechanism of action (MOA) is:

A) Physical blockade of eccrine ducts
B) Decreased release of ACh
C) Increased destruction of ACh
D) Decreased uptake of ACh
E) Thermolysis of eccrine cells
Treatment of HH

<table>
<thead>
<tr>
<th>Non-invasive</th>
<th>Minimally invasive</th>
<th>Moderately invasive</th>
<th>Surgical</th>
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<tr>
<td>Topical medications</td>
<td>Iontophoresis</td>
<td>Microwave Thermolysis</td>
<td>Excision</td>
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<tr>
<td>Systemic medications</td>
<td>Botulinum toxin injections</td>
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<td>Liposuction</td>
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<td>Sympathectomy</td>
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</table>
Treatment of HH

• Topical
  – Aluminum/Zirconium salts
  – Used all locations, **most effective axillae**
How Anti-Perspirants Work...

1) Anti-perspirant matrix with active particles is applied to skin.

2) Perspiration grabs and dissolves active particles... pulling them back into the sweat duct.

3) Active works with perspiration to form a temporary gel plug near the surface of the skin. Underarm wetness is prevented.

Question #5
The most common side effect after use of topical anti-perspirant is:

A) Irritation
B) Dry eyes and mouth
C) Muscle paralysis
D) Dysesthesia
E) Compensatory hyperhidrosis
**Treatment of HH**

\[ M^{+n}Cl + n \text{ moles Base} \rightarrow M(\text{base})_3 \text{ ppt} + n\text{HCl} \]

Base may be OH from water, lactate, or protein

*Best applied to dry area in the evening before bed.*
Question #6
Glycopyrrolate’s MOA:

A) Physical blockade of eccrine ducts
B) Decreased release of ACh
C) Increased destruction of ACh
D) Decreased uptake of ACh
E) Thermolysis of eccrine cells
Treatment of HH

• Systemic medications
  – Anticholinergics (glycopyrrolate>> oxybutynin)
  – Beta-blockers
  – Calcium Channel Blockers
  – Alpha andrenergics
  – Benzodiazepines
• Cartoon of post synapse

Eccrine cell

Treatment of HH

• Systemic anticholinergics are best to use:
  – Generalized HH
  – Multiple areas of involvement
  – Large areas of involvement
  – Craniofacial
  – Multi-therapy approach with other agents
Question #7
The most common side effect after the use of a systemic anticholinergic is:

A) Irritation
B) Dry eyes and mouth
C) Muscle paralysis
D) Dysesthesia
E) Compensatory hyperhidrosis
Treatment of HH

• Anticholinergic side effects
  – Ocular: **Dry eyes**, mydriasis, cycloplegia
  – GI: **Dry mouth**, reduced gastric secretions
  – RESP: **Bronchodilation**, reduced secretions
  – GU: **Urinary retention** (relaxes smooth muscle ureters a bladder wall)
  – CARD: Cardiac arrhythmias (bradycardia at low doses and tachycardia at high doses)

Paller et al. JAAD. 2012.
Treatment of HH

• Anticholinergic Contraindications
  – Absolute
    • Glaucoma
    • Impaired gastric emptying
    • Urinary retention
Treatment of HH

• Anticholinergic caution
  – Outdoor occupation/ athlete
  – Pediatric patients
  – Age >65 years old
    • Systemic anticholinergics associated with dementia

Gray et al. JAMA Internal Med. 2015.
Question #8
The MOA of iontophoresis is:

A) Physical blockade of eccrine ducts
B) Decreased release of ACh
C) Increased destruction of ACh
D) Decreased uptake of ACh
E) Thermolysis of eccrine cells
Treatment of HH

- Iontophoresis
  - Passing of ionized substance through intact skin by use of electrical current
  - For primary focal palmar/plantar HH
    - One of the best options
Treatment of HH

• MOA of Iontophoresis
  – Blockage of sweat glands from ion deposition
  – Blocking of sympathetic nerve transmission
  – Decrease in pH due to accumulation of hydrogen ions

Question #9
The most common side effect after the use of iontophoresis is:

A) Irritation
B) Dry eyes and mouth
C) Muscle paralysis
D) Dysesthesia
E) Compensatory hyperhidrosis
Treatment of HH

• Adverse events from Iontophoresis
  – Stinging/tingling/ “pins and needles” during treatment
  – Erythema along the waterline of the hand
  – Dermatitis, vesiculation
Question #10
The MOA of botulinum toxin (BTX) is:

A) Physical blockade of eccrine ducts

B) Decreased release of ACh

C) Increased destruction of ACh

D) Decreased uptake of ACh

E) Thermolysis of eccrine cells
Eccrine cell

Acetylcholine (ACh) in vesicles

Treatment of HH

• BTX A
  – Onabotunilumtoxin A (Botox®)
    • FDA approved July 19, 2004 for severe primary axillary HH
  – Abobotulinumtoxin A (Dysport®)
    • Not FDA approved for HH
  – Incobotulinumtoxin A (Xeomin®)
    • Not FDA approved for HH
    • May be stored at room temperature

Lowe et al. JAAD. 2007
Treatment of HH

• Injections of BTX
  – Office procedure
  – Pain gating techniques
  – Craniofacial, axillary, palmar, infra-mammary, groin, plantar
  – Q4-6months
Treatment of HH

• 100 units of Botox®
• Dilute 4ml sterile NS
• 2.5 units per 0.1ml
- 30gauge, 1ml syringe
- 1.5-2cm apart
- 2.5units to each site

Videos

http://www.sweathelp.org/education-and-resources/online-learning.html
Question #11

A worrisome side effect after the use of BTX for palmar HH is:

A) Irritation
B) Dry eyes and mouth
C) Muscle paralysis
D) Dysesthesia
E) Compensatory hyperhidrosis
Treatment of HH

• BTX side effects
  – Injection site pain
  – Injection site bleeding
  – Compensatory HH
  – Muscle weakness (craniofacial and palmar)
Question #12
The MOA of miraDry is:

A) Physical blockade of eccrine ducts
B) Decreased release of ACh
C) Increased destruction of ACh
D) Decreased uptake of ACh
E) Thermolysis of eccrine cells
Treatment of HH

- miraDry System
  - Manufactured by Miramar
- Axillary HH (and hair removal)
- FDA approved January 2011
- Uses microwave energy (580MHz) resulting in the thermolysis of eccrine glands

Treatment of HH

• miraDry side effects
  – **Dysethesia** (transient altered sensation in treatment arm)
  – Local swelling
  – Compensatory hyperhidrosis (rare)
  – $3K

Treatment HH

• Additional topicals
  – Astringents (formaldehyde, gluteraldehyde, tannic acid, acetic acid)
  – Glycopyrrolate (wipes and gel)*
  – Oxybutynin
  – Botulinum toxins

www.clinicaltrials.gov

*Available Canada
Investigational Anticholinergic Topical Gel May Be Safe, Effective For Treatment Of Axillary Hyperhidrosis, Study Suggests

- Medscape (3/9, Tucker) reports that research presented at the American Academy of Dermatology meeting suggested “an investigational anticholinergic topical gel is safe and effective for the treatment of axillary hyperhidrosis.” The gel, Sofpironium bromide (BBI-4000), “is a specially formulated ‘soft’ topical anticholinergic designed to block sweat production, and its rapid metabolic deactivation and excretion reduces the adverse effects associated with anticholinergic agents.”
Objectives

1) Review the quality of life impact of hyperhidrosis (HH)
2) Review the known pathophysiology of HH
3) Review the treatment options for HH
Patients with hyperhidrosis are a JOY to care for!
http://www.sweathelp.org/

- Diagnosis and treatment algorithms
- Informed consents
- Videos
- Brochures and posters
- Clinical research postings
- CPT and ICD-10 codes (insurance letters)
- Literature references
- And MUCH MORE...

*Ms. Lisa Pieretti*
Questions:
zpressL@emory.edu
Treatment of HH

• Glycopyrrolate (PO)
  – Adults
    • 1 and 2mg tablets
    • Start 1mg PO BID
    • Increase 1mg every 2 weeks, depending on clinical side effects
    • Max 8mg/day
  – Children
    • Oral suspension 0.5mg/mL
    • Start 0.02mg/kg PO TID
    • Increase 0.02mg/kg every 1-4 weeks, depending on clinical side effects
    • Max 3mg/day
Billing and Coding

- E&M 99212-99213
- ICD-10 Primary Focal Hyperhidrosis
- L74.512 axilla
- L74.513 palms
- L74.514 soles
- R61 Craniofacial
- CPT
  - 97033, iontophoresis, each 15min
    - Typically bill for 2-4 units, depending on how many areas are treated
  - 64650 chemodenervation of eccrine glands, axillae
  - 64653 chemodenervation of eccrine glands, other areas (i.e. scalp, face, neck),
  - 64999 unlisted procedure, nervous system (i.e. hands and feet)
    - J0585, per unit of onabotulinumtoxinA
# HDSS

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<tr>
<th>How would you rate your HH</th>
<th>Score</th>
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<tr>
<td>Sweating noticeable, never interferes</td>
<td>1</td>
</tr>
<tr>
<td>Sweating tolerable, sometimes interferes</td>
<td>2</td>
</tr>
<tr>
<td>Sweating barely tolerable, frequently interferes</td>
<td>3</td>
</tr>
<tr>
<td>Sweating intolerable, always interferes</td>
<td>4</td>
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