Tapering Opioids

Minnesota ACP Internal Medicine Meeting

October 11, 2019

Anne Pylkas, MD
Internal Medicine and Addiction Medicine
HealthPartners Pain Program
Sage Prairie Recovery
• No disclosures

• I will use some brand names and off label indications
  • Buprenorphine/naloxone for chronic pain syndromes
Outline

• Why should we taper?
• Who should we taper?
• When should we taper?
• Can we tell if someone is addicted?
• How fast should we taper?
• Which opioid should we use to taper?
• What about the pain?
Why should we taper?

• 2018 JAMA, Krebs et al, VA Study, SPACE Trial
  • 240 pts, chronic back or knee pain
  • Opioid vs non opioid
  • No improvement in pain or function over 12 mo

• 2017 Ann Int Med, Krebs et al, Discontinuation review
  • 67 studies, 11 RCTs, 56 Obs, 8 interventions including interdisp programs, bup, behavioral
  • Most study quality was low
  • Improvement reported in:
    • Pain severity (8/8 fair qual)
    • Function (5/5 fair qual)
    • QOL (3/3 fair qual)
Why should we taper?

• 2019, J Pain Research, Desai et al, Effect on QOL, HC utilization
  • 2011-2015, Retrospective review, CBP, n= 5,203
  • Opioids only (49%) vs NSAIDs only (28%) vs both (23%)
  • Op Only group had lower QOL scores, greater utilization of health services

• 2015, Ann Int Med, Chou et al, Risks of Opioid Therapy for CP
  • Annual incidence overdose increased
  • 256 ODs per 100 000 person-years vs 36 ODs per 100 000 person-years
  • Higher doses associated with increased risk
    • MED 1 to 19 mg/d, 1x
    • MED of 20 to 49 mg/d, 1.44x
    • MED ≥ 100 mg/d, 8.87x
Who should we taper?

• **Definite YES:** High risk, low benefit
  - >65 yo
  - >100 MME (>50mg?)
  - Concurrent addiction to alcohol, opioids, sedative, stimulants, ?THC
  - Aberrant behaviors – is it addiction?
  - Concurrent sedative rx
  - Worsens psychiatric or medical issues, including falls

• **Probably YES:** Moderate risk, low benefit
  - Non-palliative
  - No improvement despite escalating dose
  - Non compliance with adjunctive modalities

• **Maybe NO:** Low risk, moderate benefit
  - Palliative/End of life
  - Low dose
When should we taper?

• When you figure out that the risks outweigh the benefits
• There is **NO WRONG TIME.**
  • When you inherit them
  • After the first inconsistent urine drug screen
  • When the dose just seems to be escalating with no benefit
  • When they overdose
  • When the psychiatrist gives them a benzo
  • When they fall right after a dose change
  • When they are in the ED with a BAC 0.10
  • When they just won’t go to PT
  • When you find out that they are selling
  • When mom calls and says- I think they are addicted
  • When they just won’t stop smoking pot
Can we tell if someone is addicted to opioids?

**TABLE 4.4 DSM-5 Criteria for Substance Use Disorder**

A mild substance use disorder is diagnosed if 3 of the following criteria are met. People meeting 4 or 5 criteria are classified as having moderate substance use disorder, and severe substance use disorder is diagnosed in cases where 6 or more of the criteria are met.

1. Taking the substance in larger amounts or for longer than you meant to
2. Wanting to cut down or stop using the substance but not managing to
3. Spending a lot of time getting, using, or recovering from use of the substance
4. Cravings and urges to use the substance
5. Not managing to do what you should at work, home, or school because of substance use
6. Continuing to use, even when it causes problems in relationships
7. Giving up important social, occupational, or recreational activities because of substance use
8. Using the substance again and again, even when it puts you in danger
9. Continuing to use, even when you know you have a physical or psychological problem that could have been caused or made worse by the substance
10. Needing more of the substance to get the effect that you want (tolerance)
11. Development of withdrawal symptoms, which can be relieved by taking more of the substance


THE MIND’S MACHINE 2e, Table 4.4

- Addiction = Substance use disorder
- Substance Dependence = Withdrawal/physical dependence
Can we tell if someone is addicted to opioids?

• 2018 Review, Martel et al, Substance-related disorders: A review of prevalence and correlates among patients with chronic pain
  • Higher doses
    • Higher risk OD, but not higher risk for addiction
  • Males, younger, personal or FH SUD
  • Weak association between pain “level” and misuse
• Psychological factors
  • Negative affect is the strongest indicator
  • High levels anxiety
  • Catastrophizing
  • Personality disorders
How fast should we taper?

- **Risk** → **Timeline of taper**
  - Higher risk → faster
  - Lower risk → slower
- The risk can be mitigated with buprenorphine products, so the length of the taper can be extended...

<table>
<thead>
<tr>
<th>Exit Strategy</th>
<th>Length</th>
<th>Risk</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate</td>
<td>ASAP</td>
<td>HIGH/DANGER</td>
<td>Opioid addiction, sedative addiction, alcohol addition, and no ACUTE pain</td>
</tr>
<tr>
<td>Short term</td>
<td>10-30 days</td>
<td>HIGH</td>
<td>Multiple aberrant behaviors, but no known addiction, medical/psychiatric risk, other active addictions</td>
</tr>
<tr>
<td>Medium Term</td>
<td>1-6 months</td>
<td>Medium</td>
<td>Aberrant behaviors, no known addiction, less severe med/psych risks, frequent falls, cognitive issues, dose &gt;100MEDS (get down to less and then slow)</td>
</tr>
<tr>
<td>Long term</td>
<td>1-2 years</td>
<td>Low</td>
<td>Age &gt;65, &lt;100 MEDs, low med/psych risks, minor CAD, chem cope, insomnia, little benefit, h/o addiction</td>
</tr>
</tbody>
</table>
Which opioid should we use?

• Considerations:
  • Safety
  • Age/Co-Morbid diagnoses
  • Cost
  • Diagnosis
    • OUD vs No OUD
Which opioid should we use?

- Short vs long acting
  - I always DC all short acting
    - Reinforcing
    - Cycles of withdrawal
  - Schedule vs prn
    - Prn reinforces pain:pill behavior

- Buprenorphine product vs full opioid agonist
  - Safety #1 consideration
    - Aberrant behaviors but not OUD
    - OUD
    - Age/Comorbid dx (OSA, COPD, etc)
Which opioid should we use?

• 1) Long acting, full agonist
  • Profile
    • Young
    • Healthy, no co morbid medical issues
    • Medium or low risk, None/few aberrant behaviors
    • Lower cost, in general than bup products
    • NO OUD diagnosis
  • Choice:
    • Extended release morphine- only lasts 6-8h, dose TID
    • Extended release oxycodone- only lasts 8h, dose TID
    • Methadone- extra caution, dose BID
    • Others: ER hydrocodone, tapentadol, tramadol, fentanyl patches
  • Procedure:
    • 24h dose requirement convert to only one long acting opioid
    • Initially decrease by 10-25%
    • DC all short acting/prns
    • Decrease by 10% q1-3 months
Which opioid should we use?

- 2) Partial agonist/Buprenorphine
  - Profile
    - Medium or high risk and OUD
    - Older, more co morbid dx (OSA, COPD, etc)
    - Higher cost, more PAs
  - Choice
    - Buccal Buprenorphine (Belbuca®)-
    - Transdermal Buprenorphine (Butrans®)-
    - Bup/Nal –
      - Generic Films
      - Generic Tabs
      - Suboxone Films®
      - Suboxone Tabs ®
      - Zubsolv Tabs®
      - Bunavail buccal Films®
    - Bup only

<table>
<thead>
<tr>
<th>Name</th>
<th>FDA appr Dx</th>
<th>Dose Strengths</th>
<th>TDD Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buccal Bup (Belbuca®)</td>
<td>Pain</td>
<td>75-900mcg films</td>
<td>3.6mg</td>
</tr>
<tr>
<td>Transderm Bup (Butrans®)</td>
<td>Pain</td>
<td>5mcg/h-20mcg/h</td>
<td>0.48mg</td>
</tr>
<tr>
<td>SL Bup/Nal</td>
<td>OUD</td>
<td>2-8mg tabs</td>
<td>32mg</td>
</tr>
<tr>
<td>SL Bup</td>
<td>OUD</td>
<td>2-8mg tabs</td>
<td>32mg</td>
</tr>
</tbody>
</table>
Which opioid should we use?

- Partial agonist/buprenorphine
  - Procedure
    - Differs with product and dx
      - OUD: Induction as per protocol
      - Chronic pain
        - 24h dose requirement convert to only bup product (buccal or transdermal)
        - Initially decrease by 10-25%
        - DC all short acting/prns
        - Per package insert:
          - Buccal: Decrease to 30mg OME prior to starting
          - Transdermal: Taper current opioids to 30mg OME or less prior to starting
        - Experience: DC x 12-24h, no need for full withdrawal/full induction
        - Decrease by 10% q1-3 months
What about the pain?

General pain categories overlap with central pain a component in each
RA = Inflammatory synovitis, structural knee damage, pain response modified centrally
What about the pain?

• Central Sensitization:
  • Amplification of neural signaling in CNS
  • Allodynia and Hyperalgesia

• Coexisting symptoms
  • Fatigue
  • Sleep disturbances
  • Mood disturbances
  • Cognitive disturbances
  • Catastrophizing
  • Neuropathic symptoms
What about the pain?

• Chronification of pain
  • Changes occur in
    • 2) Transmission *(Going up)*
    • 3) Inhibition *(Coming down)*
    • 4) Interpretation *(What does it all mean?)*
      • Hyperactive Amygdala
      • Hypoactive Pre-Frontal Cortex
      • Mesolimbic reward center
        • Acute pain: Actives DA in mesolimbic DA reward center
        • Prolonged pain: Prolonged activation of DA in mesolimbic reward center
        • Decrease DA receptor availability in mesolimbic areas

These are the same neurobiological changes that occur in addictions from continued use of a substance!

https://www.change-pain.com/cms/cda/file/cp_com_content_pain_basics.jpg?fileID=310600089&cacheFix=1456495926000&__k=db9f24c77e86cc78296d38ba1ba4c126
What about the pain?

• Now lets give this CS patient some opioids
  • They already have an overstimulated amygdala, hypoactive prefrontal cortex and low mesolimbic DA
    • For a short period of time opioids “cure” these deficits
  • Over time they begin to reinforce these changes
    • But by this time, they are the cure and the affliction
  • Opioids also change transmission and inhibition:
    • Spinal dynorphin (κ agonist) increases
    • Spinal glutamate/NMDA receptor activity increases
What about the pain?

• How do we reverse this in addiction (opioid use disorder)?
  • MAT= buprenorphine or methadone
  • Re-regulates the brain changes
    • Both very long acting
    • Limited tolerance
    • No dysregulation of HPA axis/cortisol

• How can we use this knowledge to help OIH/CS?
  • Bup and methadone can re-regulate the brain changes (same as in addiction)
  • They also can re-regulate transmission and inhibition
    • Buprenorphine is a $\kappa$-receptor antagonist and an NMDA antagonist
    • Methadone is a NMDA antagonist
What about the pain?

- LA opioids or bup products calm down the brain changes and the spinal cord changes
- Calm the hyperactive amygdala
  - EMDR, Somatic Experiencing, Somatosensory therapies, Hypnosis, Biofeedback, Yoga, Breathing, Acupuncture, Mindfulness, Meditation, Tai Chi, Qi Gong
  - Medications that decrease SNS activation: Propranolol, prazosin, clonidine
  - Medications that support serotonin system: SSRIs, duloxetine
  - Medications that support gaba system: Gabapentin, pregabalin, avoid benzos
- Retrain the hypoactive prefrontal cortex
  - CBT, DBT, learning from activities
- Give the mesolimbic DA pathways the ability to regenerate DA receptors
  - Time away from the offending agent/short acting
  - Support with natural reinforcers: nutrition, exercise, time outside/nature, family
Change the plan when stuff happens

- **Overuse**
  - Is this OUD?
  - Does the dx and therefore plan need to change?
  - Does this change the risk profile?
  - Does the product or taper length need to change?

- **Overdose**
  - CHANGE SOMETHING

- **UDS:** No prescribed meds in UDS, Un-Prescribed meds in UDS, Illicit drugs, Falsification
  - Is this SUD?
  - Does this change the risk profile?
  - Does the product or taper length need to change?

- **Missed appts**
  - No refills without appts

- **Not following through with adjunctive therapies**
  - Understand why, change plans if needed
  - Reinforce importance

- **Flare pain**
  - Be prepared to give advice and direct appropriately

- **Flare anxiety, depression**
  - Be prepared to treat!
Case:

- 68 year old female with chronic knee pain related to osteoarthritis and chronic back pain related to spinal stenosis, as well as depression and anxiety and COPD. She is on MS Contin 30mg BID and oxycodone 5mg QID (MME 80-90), here to see you to establish care. You inherited her from a partner that recently retired. She does not want to change anything. She has been on these medications for 14 years.
- She has not been to PT in 3 years, doesn’t exercise. She quit smoking 5 years ago. Her anxiety is treated with lorazepam prn, takes it 1-3x per day, rx from psychiatrist, does not see a therapist. Hospitalization last year for fall, femur fracture. History of alcohol use disorder, but quit drinking 15 years ago.
- No UDS in 3 years, but today UDS shows: Opiates, oxycodone, benzos
- PMP shows refills on time, no providers other than previous PCP
Case

Question 1: Does she meet criteria for an opioid use disorder?
   a) Yes
   b) No

Question 2: Should she be tapered off opioids?
   a) Yes
   b) No

Question 3: Should a buprenorphine product be used to taper?
   a) Yes
   b) No

Question 4: How long should the taper take?
   a) Immediately
   b) 30 days
   c) 6 months
   d) 5 years
Questions or references:
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Supporting Women in Medicine

Anjali Bhagra MD FACP
Disclosures

- None
- Credits: Drs. Julia Files and Sharon Mulvagh and CWHHA
Learning Objectives

- To understand the role of gender in academics and leadership in medicine
- Learn approaches to establish and build networks to support women
- Recognize challenges/obstacles and ways to overcome
First generation gender bias (Overt)
Second Generation gender bias (Covert)

Second-generation gender bias refers to practices that may appear neutral or non-sexist, in that they apply to everyone, but which discriminate against women because they reflect the values of the men who created or developed the setting, usually a workplace.
Elizabeth Blackwell MD
1821-1910

- First woman to graduate from US medical school **first in class!** 1849
- Inspired to pursue medicine by a dying friend who said her ordeal would have been better had she had a female physician.
- Rejected everywhere she applied
- Acceptance letter to Geneva College intended as a practical joke.
- Blackwell faced **overt** discrimination and obstacles in college:
  - professors forced her to sit separately at lectures
  - often excluded from labs
  - local townspeople shunned her as a “bad” woman for defying her gender role.
Women in Medicine

It has been 170 years since Elizabeth Blackwell graduated from medical school and we are STILL experiencing “firsts” for women.
...Between the no longer and the not yet
The story of Women in Medicine...

PERSEVERANCE

Endurance Positive Behavior Plan
Stamina Commitment Dedication
Determination Achieve Grow
Constancy Diligence Persistence
Pertinacity Pursuance Resolution
Attitude Impetus Patience Goal
Steadfast Virtue Tenacity Resolve
Persevere Resolve Success Drive Aim
Historic first, AMA to have three consecutive female presidents

The photo features (L-R): Barbara L. McAneny, M.D., Patrice A. Harris, M.D., M.A., and Susan R. Bailey, M.D.
For the second year in a row, the number of women enrolling in U.S. medical schools has exceeded the number of men:

- 2018: 50.9%
- 2017: 50.7%
- 2016: 49.8%
Women account for 45.6% of active residents training in the U.S.

<table>
<thead>
<tr>
<th>Specialty</th>
<th>% Women</th>
<th>Income ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td>OB/GYN</td>
<td>83</td>
<td>20</td>
</tr>
<tr>
<td>Allergy and Immunology</td>
<td>73.2</td>
<td>*</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>72.3</td>
<td>*</td>
</tr>
<tr>
<td>Medical genetics</td>
<td>67.1</td>
<td></td>
</tr>
<tr>
<td>Psychiatry</td>
<td>66</td>
<td>*</td>
</tr>
<tr>
<td>Dermatology</td>
<td>64.5</td>
<td>6</td>
</tr>
</tbody>
</table>

Among the top specialty choices for female residents, only dermatology, with an annual average compensation of $392,000, ranks in the top 10 highest-paying specialties, according to an online survey of physician compensation conducted by Medscape.

* One of 20 specialties with the LOWEST average annual compensation

Association of American Medical Colleges’ 2017 Report
### Residency

Men account for 54.4% of active residents training in the U.S.

<table>
<thead>
<tr>
<th>Specialty</th>
<th>% Men</th>
<th>Income ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopedic surgery</td>
<td>84.6</td>
<td>3</td>
</tr>
<tr>
<td>Neurologic surgery</td>
<td>82.3</td>
<td>1</td>
</tr>
<tr>
<td>Thoracic surgery</td>
<td>75.2</td>
<td>2</td>
</tr>
<tr>
<td>Radiology</td>
<td>73.5</td>
<td>9</td>
</tr>
<tr>
<td>Plastic surgery</td>
<td>71.8</td>
<td>8</td>
</tr>
<tr>
<td>Vascular surgery</td>
<td>65.2</td>
<td>5</td>
</tr>
<tr>
<td>Otolaryngology</td>
<td>63.8</td>
<td>14</td>
</tr>
</tbody>
</table>

Male physicians, more likely to relocate following their residency program. Figure varies by specialty, 51% of men who completed residency between 2007 and 2016 are practicing in the state where they did their residency, compared with nearly 59 percent of women.
Academic Medicine
Multiple studies over 20 years demonstrated salary inequities disadvantaging female faculty in academic medical careers compared with their male counterparts attributed to factors known to be the major determinants of compensation, including part-time status, specialty choice, and work distribution between administrative, teaching, research, and clinical work.

Even controlling for these differences, women continue to be compensated less for the same work compared to men.

Recent data suggest that for new faculty, even those with similar academic backgrounds and research funding success, gender gaps in compensation early in their careers are already present.

Acad Med. 2016 August ; 91(8): 1068–1073
25.7% of all professors are female
74.9% of all professors are male

<table>
<thead>
<tr>
<th>Rank</th>
<th>Male</th>
<th>Female</th>
<th>Unreported</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professor</td>
<td>28,573</td>
<td>9,501</td>
<td>43</td>
<td>38,117</td>
</tr>
<tr>
<td>Associate Professor</td>
<td>22,248</td>
<td>13,642</td>
<td>42</td>
<td>35,932</td>
</tr>
<tr>
<td>Assistant Professor</td>
<td>43,031</td>
<td>38,151</td>
<td>87</td>
<td>81,269</td>
</tr>
<tr>
<td>Instructor</td>
<td>6,364</td>
<td>9,156</td>
<td>26</td>
<td>15,546</td>
</tr>
<tr>
<td>Other</td>
<td>2,237</td>
<td>2,786</td>
<td>2</td>
<td>5,025</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>102,453</strong></td>
<td><strong>73,236</strong></td>
<td><strong>200</strong></td>
<td><strong>175,889</strong></td>
</tr>
</tbody>
</table>

Source: AAMC Faculty Roster, December 31, 2018 snapshot, as of April 30, 2019.

27% of all male faculty achieve full professor
12.9% of all female faculty achieve full professor
We have still not achieved the % of Full Professors that our male colleagues had achieved in 1979
Leadership inequity

10 /39 specialty societies had equitable or better representation of women among years of presidential leadership.
Causes of Leadership Inequity

These factors encompass the institutional barriers that women face because of the divergent ways in which men and women are perceived and treated by others.

Differences in the perceptions held, decisions made, or behaviors enacted by men and women themselves that contribute to gendered outcomes.

For example, men are more likely than women to engage in dominant or aggressive behaviors, to initiate negotiations and to self-select into competitive behaviors likely to facilitate professional advancement.
Leadership Gap and Women leaving academic medicine:

- lack of career/professional advancement,
- salary inequity
- chairman/departmental leadership issues
  - including harassment and discrimination.\(^{37}\)
  - In a survey on workplace discrimination women were more likely than men to file a complaint of discrimination (14.6% vs 8.1%) but were more likely to report a worsening situation following the complaint as compared to men (26.7% vs 5.3%).\(^{38}\)

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\(^{38}\)Tolbert Coombs AA, King RK, Workplace discrimination: experiences of practicing physicians. J of the NMA 2005;97:467-477
I belong to the following number of medical professional groups:

A. none
B. 1-2
C. 3-5
D. 6-7
E. >8
I belong to a women-focused medical professional group

A. Yes
B. No, and not interested
C. No, but would like to
Interventions and Strategies

- Organizational and Individual
- Physician Engagement Group (Mayo sisterhood)
- Engaging all stakeholders
  - Men as allies (#HeforShe)
Sisterhood PEG
### Sisterhood PEG

<table>
<thead>
<tr>
<th>CONCEPTS</th>
<th>DETAILS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify members</td>
<td>Diverse specialties</td>
</tr>
<tr>
<td></td>
<td>Various stages of career</td>
</tr>
<tr>
<td></td>
<td>Motivated to pursue gender equity</td>
</tr>
<tr>
<td></td>
<td>Establish policy for adding new members</td>
</tr>
<tr>
<td>Meeting specifics</td>
<td>Commit to meeting frequency</td>
</tr>
<tr>
<td></td>
<td>Establish meeting location (ensure privacy)</td>
</tr>
<tr>
<td></td>
<td>Identify group organizer</td>
</tr>
<tr>
<td>Establish ground rules</td>
<td>Confidentiality ('Vegas rules')</td>
</tr>
<tr>
<td></td>
<td>Consider how to handle egregious scenarios (e.g. sexual misconduct)</td>
</tr>
<tr>
<td></td>
<td>Commit to being solution oriented</td>
</tr>
<tr>
<td>Provide framework for discussions that are</td>
<td>Characterize the principles at play (e.g.</td>
</tr>
<tr>
<td>based on personal experiences</td>
<td>gender bias, micro-inequalities,</td>
</tr>
<tr>
<td></td>
<td>communication/language, advocacy,</td>
</tr>
<tr>
<td></td>
<td>unconscious bias etc.)</td>
</tr>
<tr>
<td></td>
<td>Identify resources to augment or</td>
</tr>
<tr>
<td></td>
<td>contextualize discussion (books, articles, TED talks, pod-casts,</td>
</tr>
<tr>
<td></td>
<td>speakers, etc.)</td>
</tr>
<tr>
<td>Actively cultivate trust</td>
<td>Honor the ground rules</td>
</tr>
<tr>
<td></td>
<td>Balance validation and objectivity</td>
</tr>
<tr>
<td></td>
<td>Celebrate member successes</td>
</tr>
<tr>
<td></td>
<td>Foster resilience in the face of setbacks</td>
</tr>
<tr>
<td></td>
<td>Encourage members to reach for stretch assignments</td>
</tr>
</tbody>
</table>
Impact

- Skill acquisition
  - difficult conversations
  - recognize and combat micro-inequities
  - create space to address challenges
- Antidote to isolation
- Trust
- Enhanced resilience
- Contextualization
Impact

- All members were promoted
- All members attributed career advancement in part related to the group
About AMWA

Networking

AMWA has been changing the face of medicine for nearly 100 years. No matter where you go, AMWA has an extensive network of women in medicine both locally and nationally. With these friends and professional contacts in AMWA you will have a powerful local and national network for personal and professional growth. AMWA continues to develop and encourages women to work together to advance their careers. AMWA established the Networking Alliance which pulls together all organizations representing women in medicine including women in specialty organizations.

Connect Online

Become part of our vibrant community online and keep up with networking, mentoring, advocacy, leadership, funding and fellowship opportunities that will change your life through AMWA’s growing networks online. Join the conversation on LinkedIn, Facebook, Twitter, YouTube and the AMWA blog.

https://www.amwa-doc.org/about-amwa/networking/
About the Women Physicians Section (WPS)

The purpose of the AMA Women Physicians Section (WPS) is to increase the number and influence of women physicians in leadership roles.

There are nearly 90,000 female members of the AMA.

As an advocate for women’s health, the WPS identifies issues and communicates through a network of women leaders identified by their state or specialty societies to serve in the role of WPS Associate.

Annual and Interim Business Meetings

Read highlights from the WPS Annual Business Meeting. The WPS Interim Meeting will be held Nov. 14-15 in San Diego, California. Registration for the Interim Meeting will open soon.

Women in Medicine Month

https://www.ama-assn.org/member-groups-sections/women-physicians/about-women-physicians-section-wps
Establish a Governance

Identify Key areas of Focus:

- Knowledge Translation and Mobilization
- Training and Education
- Advocacy
- Health Systems and Policy

Establish Membership, Deliverables and Timelines
- H&S Meeting
- Stakeholder interviews

Nov 2017

- Data analysis
- Draft models, policies

Dec 2017

- Membership selection (EOI)
- Personal invitations

Jan 2018

Initial kick-off meeting

Feb 2018

Canadian Women’s Heart Health Summit - planning meeting

Apr 2018

CWHHA official launch event

Oct 2018
Development of the Canadian Women’s Heart Health Alliance

Priorities for Action:

#1: Establish a formal Alliance of experts and advocates in Women’s Heart Health to promote partnership, collaboration and implementation of best practices across Canada
Growth Resilience Inspiration Tenacity
Intervention

- 3 day leadership conference

THE RITZ-CARLTON, LAKE TAHOE
TRUCKEE, CALIFORNIA
SEPTEMBER 20–22, 2018

COURSE DIRECTORS: ANJALI BHAGRA, MD & SUSAN MOESCHLER, MD

Course Description
This course will empower women and men in medicine with the skills and resources to remove barriers and bias of women in leadership positions specific to the challenges in healthcare. Leaders in business and healthcare will present evidence-based strategies to promote professional development and enhance personal wellbeing. Nationally, there is large number of female clinicians reporting burnout which has a potential effect on patient experience, compliance, and outcomes. This course will address the growing need for improved clinician wellness and development for a gender balanced leadership healthcare team.
**GRIT for WOMEN IN MEDICINE 2019**

**OJAI VALLEY INN**
**OJAI, CALIFORNIA**
**SEPTEMBER 19–21, 2019**

**COURSE DIRECTORS:** ANJALI BHAGRA, MD & SUSAN MOESCHLER, MD

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Successful networks share these 8 common characteristics:

- Strong Coordinating Centre
- Leaders with Strong Interpersonal Skills
- Thorough and Frequent Evaluation
- Early & Frequent Participation
- Ample Leadership and Mentorship Opportunities
- Robust Range of Network Activities
- Diverse Membership
- Solid Governance Structure
Identifying the membership of your network

- “Passive” – Reaching Out:
  - Publications
  - Meeting presentations
  - Research collaborations

- “Active” – Extending Out, Casting the Net:
  - EOI: calls for “Expression of Interest”
  - Personal contact/networking

- Engage “Men as Allies”
Potential detractors from network success

- Lack of
  - **time** for member participation
  - **collaborators** and **support** staff
  - **mentorship** opportunities
- Inadequate **training in research** methods
- Institutional review board **hurdles**
- **Slow adoption** of evidence into policymaking
- Community **resistance to research**
Obstacles

- TIME!!
  - All volunteer effort
  - Requires passion

- DISTANCE
  - e-communication

- ADMIN SUPPORT
  - mission/deliverables

- FUNDING
  - maintenance/growth/sustainability

- POLITICAL
Keys to Success:

- Identify & Engage Passion
- Be:
  - Visible
  - Accessible & Accountable
  - Inclusive & Diverse
- Have a common Vision and Mission
- Develop organizational structure
- Seek and obtain funding
- Avoid Politicization
FIRE UP!

- Find your passion
- Identify your vision and mission
- Reach out and recruit members
- Engage system support
- Develop organizational structure, timelines, deliverables

- Understand obstacles
- Prepare for challenges
Thank You
@anjalibhagramd
bhagra.anjali@mayo.edu

GRIT for WOMEN IN MEDICINE 2020
Growth, Resilience, Inspiration, & Tenacity

THE MERITAGE RESORT & SPA
NAPA, CALIFORNIA
SEPTEMBER 10-12, 2020

COURSE DIRECTORS: ANJALI BHAGRA, MD & SUSAN MOESCHLER, MD

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Relevant Financial Relationships
Royalties for textbook, *Mayo Clinic Medical Neurosciences*

Off-Label Uses
Medications for orthostatic hypotension and POTS
Case 1

A 16-year-old woman with longstanding migraine headaches reports 6 months of feeling dizzy and tipsy when upright. She also describes episodes of pounding heart, shaky hands, and sweating that usually occur while she is standing but have also woken her from sleep. She had the “flu” with low-grade fever and diffuse myalgias for 1 week before onset of the orthostatic symptoms. Her neurologic examination is normal, though she has generalized joint hypermobility.
Which feature suggests hyperadrenergic postural tachycardia syndrome?

A. Age younger than 20 years
B. Comorbid migraine headaches
C. Shaky hands and sweating from sleep
D. Fever and myalgias prior to onset
E. Generalized joint hypermobility
Case 1 – Answer

C. Shaky hands and sweating from sleep
Postural Tachycardia Syndrome

- HR increment \( \geq 30 \text{ bpm} \) (often to \( \geq 120 \text{ bpm} \)) within 10 minutes of head-up tilt or standing

\textit{AND}

- Symptoms of OI without OH

\( \geq 40 \text{ bpm if 12-19 years old} \)
POTS subtypes are not mutually exclusive

**Neuropathic**
- Sudomotor denerv.
- Adrenergic denerv.
- $\alpha_3$-AChR Ab

**Hyperadrenergic**
- ↑ Standing NE
- Autonomic storms

**Chronic Deconditioning**
- Fibromyalgia
- Fatigue

Hypovolemia / Venous Pooling / Joint Hypermobility
## Non-pharmacologic strategies

<table>
<thead>
<tr>
<th>Category</th>
<th>Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical countermoves</td>
<td>Leg crossing, bending forward at waist, slow marching in place, squatting</td>
</tr>
<tr>
<td>Fluid</td>
<td>2 L total daily; 500 mL boluses</td>
</tr>
<tr>
<td>Salt</td>
<td>5-10 g table salt daily = 2-4 g sodium daily (less if cardiac or renal)</td>
</tr>
<tr>
<td>Compression</td>
<td>Abdominal binder ± waist-high stockings</td>
</tr>
<tr>
<td>Exercise</td>
<td>Aerobic + lower limb resistance training</td>
</tr>
</tbody>
</table>

- **Leg crossing, bending forward at waist**
- **Slow marching in place**
- **Squatting**

- **2 L total daily fluid**
- **500 mL boluses**

- **5-10 g table salt daily**
- **2-4 g sodium daily** (less if cardiac or renal disease)

- **Abdominal binder ± waist-high stockings**

- **Aerobic + lower limb resistance training**
Medications to ↓ heart rate or ↑ blood pressure

Drugs* (beneficial in short term; unproven in long term)

• β-blockers (propranolol) for hyperadrenergic POTS
• Low-dose midodrine or droxidopa for neuropathic POTS
• Ivabradine for POTS with inappropriate sinus tachycardia
• Pyridostigmine
• Fludrocortisone

* off-label use

Images from Wikimedia Commons
Cardio

- 30-45 min, 3-5 days/wk
- Long cool down

Weights

- 2 sets x 12 reps, 2-3 days/wk
- Lower limbs and core
Hyperadrenergic POTS is characterized by episodes of prominent palpitations, hand tremulousness, and sweating, even from sleep, and is the subtype of POTS most likely to improve with low-dose propranolol.
Case 2

A 64-year-old man with transthyretin amyloidosis is seen for lightheadedness upon standing. He recognizes immediate relief with sitting and can usually avoid fainting. He also reports early satiety and urinary retention. Blood pressure is 150/94 mmHg when supine and 102/82 mmHg after standing for 1 min. Heart rate rose only from 70 bpm to 74 bpm upon standing. Neurologic examination reveals absent reflexes at the ankles and reduced sensation in a stocking and glove distribution.
Which of the following is the most appropriate intervention for his orthostatism?

A. Fludrocortisone  
B. Inotersen  
C. Midodrine  
D. Patisiran  
E. Pyridostigmine
Case 2 – Answer

E. Pyridostigmine
Orthostatic Hypotension

Sustained reduction of BP…

≥20 mmHg systolic

≥10 mmHg diastolic

…within 3 min of standing or head-up tilt
## Medications to ↑ blood pressure

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midodrine</td>
<td>Peripheral α₁-agonist causes vasoconstriction</td>
<td>Supine hypertension, <strong>scalp paresthesias</strong>, urinary retention</td>
</tr>
<tr>
<td>2.5-15 mg TID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyridostigmine*</td>
<td>Cholinesterase inhibitor amplifies ganglionic signal</td>
<td>Diarrhea, abdominal pain, muscle twitches</td>
</tr>
<tr>
<td>30-60 mg TID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fludrocortisone*</td>
<td>Mineralocorticoid expands plasma volume</td>
<td>Supine hypertension, <strong>hypokalemia</strong>, headache, myocardial fibrosis</td>
</tr>
<tr>
<td>0.05-0.2 mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Droxidopa</td>
<td>Norepinephrine precursor causes vasoconstriction</td>
<td>Supine hypertension</td>
</tr>
<tr>
<td>100-600 mg TID</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* off-label use

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References:

- Byun et al. *Neurology* 2017;89:1078-1086
- Singer et al. *J Neurol Neurosurg PS* 2003;74:1294-1298
Management of Supine Hypertension

Do not lie flat ≥4 h after midodrine or droxidopa
Reduce fludrocortisone

Elevate head of bed
Bedtime snack or alcohol
Losartan 50 mg, Hydralazine 25 mg
Nifedipine 10 mg, Nitroglycerin patch 0.1mg/h
Case 2 – Clinical Pearl

Pyridostigmine improves orthostatic hypotension without causing supine hypertension via amplification of the cholinergic signal at the autonomic ganglia

Singer et al. Arch Neurol 2006;63:513-518
Case 3

A 22-year-old woman is seen after 3 spells of transient loss of consciousness. Each time she has suddenly fallen from a standing position, followed by 5 or 6 jerks of her arms prior to regaining consciousness. Each spell lasted 5-10 seconds. After the spells, she felt tired and did not recall falling, though she was otherwise not confused. She once bit her tongue and lost bladder continence. Neurologic exam, cardiac exam, and electrocardiogram are normal.
Which of the following would suggest epileptic seizure rather than convulsive syncope?

A. Onset only from standing position
B. 5-6 myoclonic jerks of the arms
C. Spell duration 5-10 seconds
D. Lateral tongue bite
E. Urinary incontinence
Case 3 – Answer

D. Lateral tongue bite
Transient Loss of Consciousness

- cardiac arrhythmia
- neurally mediated syncope
- epileptic seizure
- autonomic failure
- pseudo-syncope
- pseudo-seizure
<table>
<thead>
<tr>
<th>Feature</th>
<th>Convulsive Syncope</th>
<th>Epileptic Seizure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of tone</td>
<td>Immediate</td>
<td>At end</td>
</tr>
<tr>
<td>Onset of myoclonus</td>
<td>Follows loss of consciousness</td>
<td>Immediate</td>
</tr>
<tr>
<td>Tempo</td>
<td>Arrhythmic jerks</td>
<td>Rhythmic jerks</td>
</tr>
<tr>
<td>Jerks per event</td>
<td>&lt;10</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Duration</td>
<td>1-15 sec</td>
<td>30 sec – 2 min</td>
</tr>
<tr>
<td>Eye deviation</td>
<td>Upward</td>
<td>Lateral</td>
</tr>
<tr>
<td>Tongue bite</td>
<td>Occasional, tip of tongue</td>
<td>Frequent, side of tongue</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>May occur</td>
<td>May occur</td>
</tr>
<tr>
<td>Postictal period</td>
<td>Fatigue</td>
<td>Confusion</td>
</tr>
</tbody>
</table>
Case 3 – Clinical Pearl

Convulsive syncope can be distinguished from epileptic seizures by the timing and frequency of myoclonic jerks and location of tongue bite.
Case 4

A 55-year-old woman with Parkinson disease takes regular carbidopa/levodopa 25/100 mg tablets and reports that 1.5 tablets every 4 hours during the waking day allows her to function well. A slight tremor appears in her right hand if she is more than 15 minutes late with a levodopa dose. She continues to work as an engineer, though her contract is due for renegotiation. She falls asleep easily at 10 p.m. but often wakes between 2 and 3 a.m. and struggles for at least an hour to fall back to sleep despite feeling tired. Her wife denies hearing snoring, talking, or yelling during the night.
Which intervention is most likely to improve this patient’s sleep?

A. Carbidopa/levodopa 1.5 tabs at bedtime
B. Cognitive behavioral therapy
C. Diphenhydramine 25 mg at bedtime
D. Melatonin 5 mg at bedtime
E. Ropinirole 1 mg an hour before bed
Case 4 – Answer

A. Carbidopa/levodopa 1.5 tabs at bedtime
Levodopa Honeymoon

Long-duration Response

[Levodopa]

ON

C/L  C/L  C/L

During early years, levodopa timing or missed doses matter little because the brain can still buffer the fluctuating blood concentration.
Motor Fluctuations
ON-OFF cycles

When patients notice kick-in and wear-off, shorten the levodopa interval to match the short-duration response.
Insomnia
overnight wearing OFF

• May or may not be aware of other OFF symptoms at night
• “Cannot get comfortable”

If patients wake and struggle to fall back to sleep, add a bedtime dose of controlled-release or an early-morning dose of regular levodopa equivalent to the daytime dose.

Treat RBD with bedroom safety and melatonin 3-12 mg (or clonazepam 0.5-2 mg) to reduce patient and bed partner injury.

Ropinirole and pramipexole are first-line therapy for RLS, which is a frequent comorbidity with Parkinson disease.

1. Urge to move the legs, usually accompanied by discomfort
2. Begins or worsens during periods of rest or inactivity such as lying or sitting
3. Partially or totally relieved by movement, such as walking or stretching
4. Worse in the evening or night

Kurlan et al. *J Gen Intern Med* 2006;21:C1-C4
Szatmari et al. *Sleep* 2017;40: epub
Case 4 – Clinical Pearl

If patients with Parkinson disease wake and struggle to fall back to sleep, add a bedtime dose of levodopa equivalent to their daytime dose to maintain a levodopa ON state.
Case 5

A 78-year-old man began to notice problems walking 1 year ago. His wife describes his gait as stiff and slow. The problem has been progressive, and he began using a cane 3 months ago. Recently he has also noticed weakness in his left hand and urinary urgency.
Which of the following has the greatest sensitivity for detecting cervical myelopathy in this patient?

A. Ankle clonus
B. Babinski sign
C. Hoffmann sign
D. Interosseous atrophy
E. Brachioradialis hyperreflexia
Case 5 – Answer

C. Hoffmann sign
## Cervical Myelopathy

<table>
<thead>
<tr>
<th>Sign</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoffmann</td>
<td>68%</td>
<td>84%</td>
</tr>
<tr>
<td>Biceps hyperreflexia</td>
<td>62%</td>
<td>49%</td>
</tr>
<tr>
<td>Babinski</td>
<td>33%</td>
<td>100%</td>
</tr>
<tr>
<td>Knee hyperreflexia</td>
<td>33%</td>
<td>76%</td>
</tr>
<tr>
<td>Brachioradialis hyperreflexia</td>
<td>21%</td>
<td>89%</td>
</tr>
<tr>
<td>Ankle clonus</td>
<td>13%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Advanced Imaging for Suspected Myelopathy

MRI is indicated upper motor neuron signs are detected in the setting of progressive gait impairment or urinary incontinence.

Transverse pancake-like gadolinium enhancement at or just below level of maximal stenosis suggests spondylosis as the cause of myelopathy.
Case 5 – Clinical Pearl

In a patient with progressive gait impairment, Hoffmann sign is the most sensitive finding for cervical myelopathy and should prompt advanced imaging of the cervical spine.

Parenteral Iron

Any discussion of parenteral iron starts with a discussion of oral iron

- Sir William Osler
How Things Should Work

• Daily diet contains 10-20 mg iron
  • Daily absorption 1-2 mg
• Different iron bioavailability
  • 30% heme-bound
  • 10% non-heme-bound
• Passengers affect absorption
  • Help: pH, vitamin C
  • Hurt: calcium, cereals, teas
• Duodenal, proximal jejunem absorption 90+%
Gastric Bypass: The Tale of Road Construction and Missed Exits

- Pre-op, 20-50% patients w/ IDA
- Post-op mechanisms
  - Lack of duodenal iron access
  - Lack of parietal cell pH
  - Dumping syndrome
  - Oral iron intolerance
  - Ongoing menstrual losses

4 Most Common Weight Loss Surgery Procedures in the United States

- Adjustable Gastric Band (Lap Band)
- Roux-en-Y Gastric Bypass (RYG)
- Vertical Sleeve Gastrectomy (Gastric Sleeve)

nashaware.com
IDA is Common and Ongoing Issue After Gastric Bypass

- 319 patients w/ RYGB 1999-2006 Penn State Hershey
- 58% iron deficiency anemia
  - Hemoglobin <12 W: <14 M
  - Ferritin <10
- 22% required parenteral iron
  - 100% response rate
- Multivariate analysis
  - Menstruating women
  - Pre-operative IDA

Kotkiewicz et al, Libertas Academica 2015
Anemia of Chronic Disease; The Tale of Frozen Bank Accounts

- Inflammation triggers cytokines (IL-6)
  - Infections
  - Cancer
  - Autoimmunity
- Cytokines trigger hepcidin
- Hepcidin “destroys” ferroportin
  - Iron “locked in” marrow macrophages
  - Iron “locked out” from duodenum
- Impaired erythropoiesis

Weiss et al, NEJM 2005
Inflammatory Bowel Disease (IBD) and Parenteral Iron

• 25-80% IBD patients affected
• Multiple mechanisms
  • Poor oral iron absorption
  • Chronic blood loss
• Difficult diagnosis of IDA
  • Ferritin inflammatory marker
• Who really needs it?
  • Active disease
  • Severe anemia
Parenteral Improved Outcomes and Tolerance vs Oral Iron in IBD Patients

- Meta-analysis of 5 RCTs
- 694 patients
- Oral iron more often discontinued due to AEs (OR 0.27; 0.13-0.59)
- IV iron improved Hgb more often ≥ 2.0 (OR 1.57; 1.13-2.18)

Bonovas et al, Medicine 2016
Cautionary Tales About Oral Iron in IBD?

• Small crossover study; 19 patients w/ IBD and IDA
  • Randomized to ferrous fumarate 120 mg daily or venofer 200 mg x 3 over 2 weeks
  • IBD patients receiving oral iron experienced worse disease activity ($p=0.037$), worse well being ($p=0.027$) and more abdominal pain ($p=0.027$)

• Role of the microbiota and oxidative stress

Erichsen et al, Scand Journal of Gastro 2005
Some Cautionary Tales Regarding ACD

• ACD is not “refractory IDA”
  • Like IDA, ACD is a sign and NOT a diagnosis
  • Think autoimmunity, malignancy, smoldering infections
  • Requires “proof of inflammation”

• Treatment
  • Oral iron will almost never work
  • Parenteral iron may work w/ IDA
  • Treat the underlying cause
Distinguishing ACD from IDA

- Soluble transferrin receptor
  - Proportional to erythropoiesis
  - Inversely proportional to iron
- ACD: Normal
- IDA: High
- Can have both conditions

---

**Table 3. Serum Levels That Differentiate Anemia of Chronic Disease from Iron-Deficiency Anemia.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Anemia of Chronic Disease</th>
<th>Iron-Deficiency Anemia</th>
<th>Both Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>Reduced</td>
<td>Reduced</td>
<td>Reduced</td>
</tr>
<tr>
<td>Transferrin</td>
<td>Reduced to normal</td>
<td>Increased</td>
<td>Reduced</td>
</tr>
<tr>
<td>Transferrin saturation</td>
<td>Reduced</td>
<td>Reduced</td>
<td>Reduced</td>
</tr>
<tr>
<td>Ferritin</td>
<td>Normal to increased</td>
<td>Reduced</td>
<td>Reduced to normal</td>
</tr>
<tr>
<td>Soluble transferrin receptor</td>
<td>Normal</td>
<td>Increased</td>
<td>Normal to increased</td>
</tr>
<tr>
<td>Ratio of soluble transferrin receptor to log ferritin</td>
<td>Low (&lt;1)</td>
<td>High (&gt;2)</td>
<td>High (&gt;2)</td>
</tr>
<tr>
<td>Cytokine levels</td>
<td>Increased</td>
<td>Normal</td>
<td>Increased</td>
</tr>
</tbody>
</table>

Weiss et al, NEJM 2005
Heavy Uterine Bleeding: The Tale of Overdraft Bank Accounts

• Iron loss exceeds iron gains
• Menstrual losses can exceed 40-50 mg per month
• RCT; 477 women w/ IDA and HUB
  • Randomized to 1000 mg IV ferric carboxymaltose vs. 325 mg ferrous sulfate TID x 6 weeks
  • 82% hemoglobin response (≥2) w/ parenteral iron vs 62% oral iron (p<0.001)
  • 73% hemoglobin normalized w/ parenteral iron vs 50% oral iron (p<0.001)
  • Subjective improvements in QOL and function

Van Wyck et al, Transfusion 2009
So Where Does that Leave Us?

• Cannot tolerate oral iron
  • Exhaust all oral iron forms and solutions

• Quick repletion
  • Pre-operative, pregnancy, borderline transfusion need

• Pregnancy
  • Third trimester; good for baby

• Iron loss exceeds iron intake
  • Chronic GIB

• Anatomic changes
  • Gastrectomy, celiac, IBD

• Inflammation / ACD
  • IBD, autoimmunity; not chronic infections
Some Thoughts on Various Forms

• All forms are created equal
• All forms are equally safe (except IM)
• Reactions are rare (like really rare)
  • GI, HA, dizziness, hypotension, urticarial / rash, arthralgias < 1%
  • Benadryl likely responsible for some “iron reactions”
  • Premeds unnecessary unless prior reaction
What is Parenteral Iron Anyway?

• Iron core and sugary shell
• 1<sup>st</sup> generation: High-molecular weight dextran
• 2<sup>nd</sup> generation: Iron gluconate and iron sucrose
• 3<sup>rd</sup> generation: Ferumoxytol
Many Parenteral Iron Forms Exist

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Ferumoxytol</th>
<th>Iron Carboxymaltose</th>
<th>Iron Isomaltoside 1000</th>
<th>Low Molecular Weight Iron Dextran</th>
<th>Iron Sucrose</th>
<th>Iron Gluconate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum single dose</td>
<td>510 mg</td>
<td>1000 mg</td>
<td>20 mg/kg</td>
<td>20 mg/kg</td>
<td>200 mg</td>
<td>125 mg</td>
</tr>
<tr>
<td>Minimum administration time (minutes)</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>60</td>
<td>30</td>
<td>30–60</td>
</tr>
<tr>
<td>Replacement dose possible in a single infusion</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Bhandari et al, Pharmaceuticals 2018
Determining Just How Much Iron to Give

• Fancy algorithm to determine iron deficit
  • Iron deficit (mg) = weight (kg) x (14 - Hgb) x (2.145)
  • But... the usual deficit requires 1000-1500 mg
Imagine Anemia Strikes the Set of Jumanji 2

- Kevin Hart (Hgb 7)
- $64 \text{ kg} \times 7 \times 2.145 = 960 \text{ mg}$

- Duane Johnson (Hgb 8)
- $118 \text{ kg} \times 6 \times 2.145 = 1518 \text{ mg}$
What About Oral Iron?

• Oral iron for vast majority of IDA
• Use every trick in the book for oral iron
• Many oral iron formulations w/ gimmicks and angles
  • Check the elemental iron content
  • Prove that it works; recheck retic, hemoglobin, ferritin
• Non-adherence is #1 reason for failure to improve
What is the Optimal Dosing and Frequency of Oral Iron Therapy?

- 40 women w/ mild iron deficiency (ferritin <25) without anemia
- Study 1 (frequency):
  - 60 mg QAM x 14 days
  - 60 mg every other AM x 28 days
- Study 2 (dosing):
  - 120 mg QAM x 14 days
  - 60 mg BID x 14 days
  - 2 week washout then crossover
- Measured iron absorption w/ radiolabeled iron
  - Fractional iron and total iron

Stoffel et al, Lancet Haematology 2017
Alternate-day Dosing Improves Iron Absorption vs. Consecutive-day

• Fractional iron absorption
  • Alternate day superior
  • 21.8% vs 16.3% (p=0.0013)

• Total iron absorption
  • Alternate day superior
  • 175 mg vs 131 mg (p=0.001)

• Less GI symptoms w/ alternate-day dosing!

Stoffel et al, Lancet Haematology 2017
Once-daily Dosing Equivalent Iron Absorption vs. Twice-daily

• Fractional iron absorption
  • Daily equivalent to BID
  • 11.8% vs 13.1% (non-sig)

• Total iron absorption
  • Daily equivalent to BID
  • 44.3% vs 49.4% (non-sig)

Stoffel et al, Lancet Haematology 2017
Conclusions and Concerns

• Conclusions
  • Alternate-day dosing improved iron absorption vs. consecutive-day
  • Daily dosing similar iron absorption as BID
  • Alternate-day dosing decreased GI symptoms

• Concerns
  • Small sample size
  • Restricted patient population
  • Adherence concerns
Final Thoughts...

• Parenteral iron is NOT scary
• Many patients will feel SO MUCH better with it
• Little is known about cost benefit ratio
• Shout out to Greg Vercellotti (U of Mn)
  • Iron man
Thank You
Questions, Comments

Bryan Trottier, MD
October 11th, 2019
CLIMATE HEALTH EMERGENCY: FROM AWARENESS TO ACTION

Dr. Vishnu Laalitha Surapaneni, MD, MPH
Assistant Professor, General Internal Medicine
ACP Minnesota Conference, October 11, 2019
Pluralistic ignorance leads to self-silencing
Disclosure Information

Disclosure of Relevant Financial Relationships
I have no financial relationships to disclose
Climate change is the biggest global health threat of the 21st Century. Climate change will have its greatest impact on those who are already the poorest in the world: it will deepen inequities and the effects of global warming will shape the future of health among all peoples.

THE LANCET
May 2009
OBJECTIVES

Objective 1:
Identify Health Impacts of Climate Damage in the Mid-West

Objective 2:
What can health professionals do about it?
Objective 1:
Identify Health Impacts of Climate Damage in Mid-West
- Extreme Heat
- Air Quality & Asthma
- Allergies
- Vector Borne Illness
- Water Borne Illness
- Mental Health Impacts
1. **CLIMATE DAMAGE & EXTREME HEAT**

Extreme Heat, EPA & CDC, Melillo et al, 2014

Public Perceptions Howe, Leiserowitz 2019
2. **Climate Damage & Allergies**

![Map showing change in ragweed pollen season, 1995-2013](Image Source: Global Health.gov & EPA, 2016)

**Change in ragweed pollen season, 1995-2013**

- Increase
- Decrease

Source: U.S. Environmental Protection Agency
3. **CLIMATE DAMAGE, AIR QUALITY & ASTHMA**

![Diagram showing how climate change influences air quality and health impacts of poor air quality.](image-url)

- **How Climate Change Influences Air Quality**
  - Rising Temperatures Increase the Presence of Pollutants
  - Changes in Weather Patterns (Humidity, Precipitation, and Wind)
  - Longer Allergy Seasons Due to Increase in CO2 (influences the release of Pollen and Hayweed)

- **Ground-level or “bad” ozone is not emitted directly into the air, but is created by chemical reactions between NOx and VOCs in the presence of heat and sunlight.**

- **Emissions from industrial facilities and electric utilities, motor vehicles, gasoline, and chemical solvents are some of the major sources of oxides of nitrogen (NOx) and volatile organic compounds (VOCs).**

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Colorado’s Health & Colorado’s Climate - Examining the Connection, 2017

EPA 2016 Archive, Climate Penalty
Environmental Injustice & Air Quality

Air quality risk

These communities are more likely to be near higher levels of air pollution.

- Statewide average: 32% are above risk guidelines
- Low-income communities: 46% are above risk guidelines
- Communities of color and indigenous communities: 91% are above risk guidelines
4. CLIMATE DAMAGE & VECTOR BORNE ILLNESS

Lyme Disease Reported Cases, Historical Maps, CDC

Source: Globalchange.gov
5. **CLIMATE DAMAGE & WATER-BORNE ILLNESS**

Hamburg, Iowa. Floods of 2019
Photo Credit: Tim Gruber Copyright: New York Times

Mold in a home after Hurricane Katrina,
Credit: Getty Images/iStockphoto Copyright: DarrenTownsend
6. Climate Damage & Mental Health

PTSD after natural disasters

Farmer suicides in drought
RESOURCES
In one word, how does the current climate crisis make you feel?
Objective 2:
How can health professionals take climate action?
INDIVIDUAL’S SPHERE OF INFLUENCE

Source: Elise Amel et al. Science 2017
MITIGATION & ADAPTATION

Building Climate Resilience

MITIGATION
ACTION TO REDUCE EMISSIONS
THAT CAUSE CLIMATE CHANGE

Sustainable transportation
Clean energy
Energy efficiency

ADAPTATION
ACTION TO MANAGE THE RISKS OF
CLIMATE CHANGE IMPACTS

Water conservation
New energy systems
Education
Urban forest

Disaster management & business continuity
Flood protection
Infrastructure upgrades
Complete communities
Local food

Source: Calgary City, Climate Plan
Diet

A planetary healthy diet will prevent 11 million deaths per year globally (19% to 24% of total deaths)
35% of Car Trips are ≤ 2 miles & only 53% of US adults meet 2008 physical aerobic activity guidelines
RIGHT HERE, RIGHT NOW

The health and well-being of Americans are already affected by climate change (very high confidence)

Text- 4th NCA, Image: Medical Society Consortium
VULNERABILITY ASSESSMENT

EXPOSURE
Exposure is contact between a person and one or more biological, psychosocial, chemical, or physical stressors, including stressors affected by climate change.

SENSITIVITY
Sensitivity is the degree to which people or communities are affected, either adversely or beneficially, by climate variability or change.

ADAPTIVE CAPACITY
Adaptive capacity is the ability of communities, institutions, or people to adjust to potential hazards, to take advantage of opportunities, or to respond to consequences.

VULNERABILITY of Human Health to Climate Change

HEALTH IMPACTS
Injury, acute and chronic illness (including mental health and stress-related illness), developmental issues, and death.

Global Change 2016
An 8yr male is presenting to the ER with an asthma exacerbation. It is his 5th admission this year. He lives in North Minneapolis, 55411, next to busy streets, and loves to play in his backyard. He has not been able to fill his inhalers due to financial reasons and mom reports not being able to pay utility bills for two months.
AIR QUALITY & ASTHMA

Source: AirNow
CASE STUDY

- Bemidji, MN

A 78yr female presents to the ER (in June) with syncope while she was gardening. She is admitted for observation. She is on HCTZ and Lisinopril. Labs significant for AKI of 1.8 that resolved with IVF. Orthostatic vitals positive in ER. ECHO is normal, tele for 24 hours is normal. She is discharged w close PCP follow-up.
EXTREME HEAT
AVOID, SPOT, TREAT

Know the Symptoms of Heat-Related Illnesses

HEAT CRAMPS
- Heavy sweating
- Painful muscle cramps or spasms
- Treat:
  - Stop activity for a few hours.
  - Move to a cooler location.
  - Drink water, clear juice, or a sports beverage.
  - Seek medical attention if cramps do not subside within one hour.

HEAT EXHAUSTION
- Heavy sweating
- Weakness
- Fatigue
- Headache
- Dizziness
- Nausea or vomiting
- Paresthesia (sensory disturbance)
- Irritability
- Confusion
- Drowsiness
- Decreased urine output
- Treat:
  - Move to an air-conditioned environment.
  - Lie down.
  - Loosen clothing or change into lightweight clothing.
  - Sip cool, non-alcoholic beverages.
  - Take a cool shower or bath, or apply cool, wet cloths to as much of the body as possible.
  - Seek medical attention if symptoms worsen or last longer than one hour, or if the victim has heat problems or high blood pressure.

HEAT STROKE
- Very high body temperature
- Altered mental state
- Throbbing headache
- Confusion
- Nausea
- Dizziness
- Hot, dry skin or profuse sweating
- Unconsciousness
- Treat:
  - Call 911 immediately and follow the operator’s directions—this is a medical emergency.
  - Reduce the person’s body temperature with whatever methods you can: wrap the person in cool clothes, immersion them in a cool bath, or spray them with cold tap water.
  - After administering cooling methods, move the person to a cooler place.
  - Do NOT give liquids.
  - If there is uncontrollable muscle twitching, keep the victim safe, but do not place any objects in his or her mouth.
  - If there is vomiting, turn the victim on his or her side to keep the airway open.

Source: Climate Change and Extreme Heat, 2016, CDC
RESOURCES

CLIMATE CHANGE, ALLERGIES & YOU

What does climate change have to do with my allergies?

Cars & trucks, industry and power plants all create climate pollution and air pollution.

Climate pollution makes the world warmer and changes our climate.

Climate pollution in the atmosphere causes plants to make more pollen.

Warmer temperatures mean spring comes earlier, so the allergy season is longer.

Pollen from weeds, grasses and trees can cause allergies.

Who is most at risk? People with asthma may experience attacks on high pollen days.

Center for Climate Change & Health, Public Health Institute

Medical Consortium on Climate & Health
US HEALTHCARE’S IMPACT

479.7 Mt Co2


422 Mt Co2

Source: UK Dept of Energy & Climate Change, 2014
HEALTHIER FOOD

Rooftop Garden, Boston Medical Center

Proyecto Jardín- UCLA
GREENING THE OR

Hospitals that pursue these programs could see annual savings of $56,000 per operating room.

- HVAC SETBACK: $7,380
- LED SURGICAL LIGHTING: $618
- REUSABLE STERILIZATION CONTAINERS: $7,575
- MEDICAL DEVICE REPROCESSING: $12,000
- REUSABLE MEDICAL PRODUCTS: $15,611
- OR KIT REFORMULATION: $9,524

Practice Green Health

University of Minnesota Medical Center Team
LEAN & CLEAN ENERGY

Gundersen Health Care System
1st healthcare system in the US to be energy independent

Gundersen, LaCrosse, WI

LED lights- Mayo Clinic, Phoenix

Image credit: Mayo Clinic
ORGANIZATIONAL-ADAPTATION

Spaulding Rehabilitation Hospital, Boston
Southeast Louisiana Veterans Health Care Center
Shorefront Rehabilitation Center, Brooklyn, NY
Healthy Hospitals Initiative

Challenge Areas

Engaged Leadership
Healthier Food
Leaner Energy
Less Waste
Safer Chemicals
Smarter Purchasing

Advancing Sustainability in Health Care, Practice Green Health,
RESOURCES

SUSTAINABILITY SOLUTIONS FOR HEALTH CARE

Practice Greenhealth is the leading membership and networking organization for sustainable health care, delivering environmental solutions to hospitals and health systems across the United States.

SEE HOW WE CAN HELP YOU:
Why Legislative Advocacy?

Source: Frieden T. Am J Public Health; 2010; 100 (4) Image source: Live Healthy Douglas
U.S. CALL TO ACTION: CLIMATE, HEALTH AND EQUITY POLICY ACTION AGENDA
Transition rapidly away from the use of Fossil Fuels

Transition to renewable energy
Coal use is responsible for 460,000 premature deaths from particulate air pollution each year. Coal phase-out is a crucial ‘no-regrets’ public health intervention.

Source: Lancet Countdown, 2018
ADVOCACY

CONTACT POLICYMAKERS
WRITE EDITORIALS
GIVE TALKS

Source: Medical Consortium
Traveling to conferences adds to the carbon footprint of academics. Which would you prefer in the future?

- In-person conference attendance
- Live streaming option for all sessions
Sleep Tips

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Assistant Professor, University of Minnesota
October 11, 2019, ACP Minneapolis
Disclosure of Relevant Financial Relationships

• None
Stages of Sleep

Non REM
N1, N2, N3

REM
Rapid Eye Movement
Sleep Architecture

- Wake
- Stage REM
- Stage N1
- Stage N2
- Stage N3
Function of Sleep

Restoration

Immune Competence

Learning & Unlearning

Brain Detox
Obstructive Sleep Apnea (OSA)
### OSA (Obstructive Sleep Apnea)

<table>
<thead>
<tr>
<th>Category</th>
<th>Men (%)</th>
<th>Women (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Habitual snoring</td>
<td>45%</td>
<td>25%</td>
</tr>
<tr>
<td>Mild</td>
<td>24%</td>
<td>9%</td>
</tr>
<tr>
<td>Moderate</td>
<td>9%</td>
<td>4%</td>
</tr>
<tr>
<td>Symptoms + Mild OSA</td>
<td>4%</td>
<td>2%</td>
</tr>
</tbody>
</table>

- **OSA is undiagnosed in more than 90% of women**

Young T. NEJM 1993; 328:1230
Signs and Symptoms

- Snoring
- Witnessed Apneas
- Nonrestorative sleep or daytime sleepiness
- Morning dry mouth
- Morning headache
- Mood, concentration, memory
Predisposing Factors

- Male Gender
- Post Menopausal
- Obesity **
- Body Position in Sleep
- Alcohol, Sedatives
- Narrowed airway
Normal Anatomy

- Soft palate
- Uvula
- Tonsil
- Tongue
- Nasal turbinate
- Soft palate
- Uvula
Snoring

Vibrating soft palate
Obstructive Sleep Apnea
The Cycle of an Obstructive Apnea

1. Upper airway relaxation
2. Airway collapse
3. Vigorous Inspiratory effort
4. Swings in intrathoracic pressure
5. Hypoxia
6. Arousal from sleep at end of apnea
Anatomy of an Obstructive Apnea

- **Absent airflow**
- **Continued effort**

**Graphical Representation:**
- E1-M2, E2-M2, Fz-Cz, Cz-Oz, C4-M1, Chin EMG, Leg EMG, ECG, Thermal Sensor, Nasal Pressure, Sono, SpO2, Sum, Rib cage, Abdomen, Heart Rate.

**Duration:** 60 sec

Mayo Clinic
<table>
<thead>
<tr>
<th>AHI (Apnea/Hypopnea Index)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>5-14/hr</td>
</tr>
<tr>
<td>Moderate</td>
<td>15-29/hr</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;30/hr</td>
</tr>
</tbody>
</table>

**Degree of oxygen desaturations considered in the severity**
OSA and Coronary Artery Disease

• Associated with nocturnal angina

• Nocturnal ST-T segment depression

• Mechanism:
  • Increased myocardial oxygen demand during post-apneic surges in BP and HR
  • Occurring in an oxygen deprived situation
Nightly Variation of Sudden Cardiac Death in OSA

- NEJM
- Retrospective
- 46% of OSA died between 12-6am vs 21% of No OSA, vs. 16% in general population
- Dose Dependent; based on AHI
- Relative risk of sudden death from cardiac causes from midnight to 6 a.m. was 2.57

Gami, Somers et al NEJM 2005 352;12
Nightly Variation of MI in OSA

- N=92, prospective
- Matched for co-morbidities, meds, age
- Odds ratio of 6 for having OSA if MI between 12-6am

Outcomes

- Population based sample
- Age, BMI matched
- 10 year follow up
- Odds ratio for untreated OSA
  - **Fatal CV**
    - (2.87, 95% CI 1.17–7.51)
  - **Non Fatal CV**
    - (3.17, 95% CI 1.12–7.51)
Hypertension Intervention

- Nocturnal and daytime mean, arterial pressures all reduced by 10 mm Hg

(Becker et al, Circulation 2003; 107)
Therapy

• Weight loss, position therapy

• MAD  Mandibular Advancement Device

• CPAP  Positive Airway Pressure

• Surgical:  -MMA (Maxillary Mandibular Advancement)
             -Neurostimulation
Mandibular Advancement Device (MAD)
CPAP

C = Continuous

P = Positive

A = Airway

P = Pressure
Insomnia
Insomnia

• Trouble getting to sleep or falling back to sleep after awakening

• Waking up frequently through the night

• Nonrestorative sleep
Prevalence of Chronic Insomnia in the General Adult Population

*Sleep disturbance every night for 2 weeks or more, or more stringent criteria.

Risk factors

- Female 2:1 (particularly post- and peri-menopausal)
- Middle age to elderly
- Previous episodes difficulty sleeping in times of stress
- Previous episodes of depression

- Modifiable
  - Medical and Psychological Co-morbidities
  - Acute Insomnia
  - Stress***
Insomnia Management

- Insomnia is largely a problem of a hyperarousal state

- Behavioral changes are more powerful, longer-lasting than medications

- Behavioral changes do not have side effects

- Medications are useful in combination with good sleep habits
Good Sleep Habits

- Go to bed and wake up at the same time every day.
- Make sure that your bedroom is comfortable.
- Use your bed only for sleep
- Exercise regularly
- Consider cutting out all caffeine (coffee, chocolate, tea)
- Avoid alcohol before bedtime
- Avoid looking at illuminated screens (phones, computers, TV) in the 3 hours before bedtime.
- Expose yourself to bright light during the day
CBT-I (Cognitive Behavioral Therapy - Insomnia)

- Relaxation Therapy
- Cognitive Therapy
- Stimulus Control
- Sleep Hygiene
- Sleep Restriction

**Difficult to be done in a primary care setting**
Insomnia

CBT - I Providers

www.behavioralsleep.org
# Benzodiazepine Hypnotics

<table>
<thead>
<tr>
<th></th>
<th>Half-Life (h)</th>
<th>TMAX (h)*</th>
<th>Dose (mg)</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triazolam (Halcion)</td>
<td>2–6</td>
<td>1–2</td>
<td>0.125–0.25</td>
<td>SOI</td>
</tr>
<tr>
<td>Quazepam (Doral)</td>
<td>48–120</td>
<td>2–3</td>
<td>7.5–15</td>
<td>SOI, SMI</td>
</tr>
<tr>
<td>Temazepam (Restoril)</td>
<td>8–20</td>
<td>1–2</td>
<td>15–30</td>
<td>SOI, SMI</td>
</tr>
<tr>
<td>Flurazepam (Dalmane)</td>
<td>48–120</td>
<td>1.5–4.5</td>
<td>15–30</td>
<td>SOI, SMI</td>
</tr>
<tr>
<td>Estazolam (ProSom)</td>
<td>8–24</td>
<td>1.5–2</td>
<td>1–2</td>
<td>SOI, SMI</td>
</tr>
</tbody>
</table>

SOI = Sleep Onset Initiation  
SMI = Sleep Maintenance Insomnia  

FDA APPROVED
## Non-benzodiazepine Hypnotics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Half-Life (h)</th>
<th>TMAX (h)*</th>
<th>Dose (mg)</th>
<th>Indication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ramelteon</td>
<td>1–2.6</td>
<td>0.75 (0.5–1.5)</td>
<td>8</td>
<td>SOI</td>
<td></td>
</tr>
<tr>
<td>Doxepin</td>
<td>15 (10–30)</td>
<td>3.5 (1.5–4)</td>
<td>10-50 (generic)</td>
<td>SMI</td>
<td>FDA APPROVED</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3-6</td>
<td>(Silenor)</td>
<td></td>
</tr>
<tr>
<td>Suvorexant</td>
<td>12</td>
<td>0.5–6.0</td>
<td>10–20</td>
<td>SOI, SMI</td>
<td></td>
</tr>
</tbody>
</table>

* Note: Tmax values are for the peak concentration observed in clinical trials.
# Z-Drugs Hypnotics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Half-Life (h)</th>
<th>TMAX (h)*</th>
<th>Dose (mg)</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zaleplon (Sonata)</td>
<td>(0.8–1.3)</td>
<td>(0.5–2)</td>
<td>5–10</td>
<td>SOI</td>
</tr>
<tr>
<td>Zolpidem: Oral tablet (Ambien)</td>
<td>2.5 (1.4–4.5)</td>
<td>1.6 (0.5–1.5)</td>
<td>5 (&gt;65 yr)</td>
<td>SOI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5–10 (&lt;65 yr)</td>
<td></td>
</tr>
<tr>
<td>Zolpidem: Ext. release (Ambien CR)</td>
<td>2.8 (1.6–4.5)</td>
<td>1.5 (1.5–2.0)</td>
<td>6.25–12.5 SOI, SMI</td>
<td></td>
</tr>
<tr>
<td>Eszopiclone (Lunesta)</td>
<td>6 (5–8)</td>
<td>1.5 (0.5–2)</td>
<td>2–3 (&lt;65 yr)</td>
<td>SOI, SMI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1–2 (&gt;65 yr)</td>
<td></td>
</tr>
</tbody>
</table>

FDA APPROVED (Black Box)
Parasomnias

Things that go bump in the night
Parasomnia

Undesirable behaviors or experiences that arise exclusively upon entry into, during, or arousing from the sleep period

NREM

REM

Miscellaneous
Sleep State Dissociation

---REM Parasomnias---
RBD
Nightmare Disorder

---NREM Parasomnias---
Confusional Arousal
Sleepwalking
Sleep Terrors
Sleep State Dissociation

Epilepsia 2012;53[Suppl. 7]:12–9.)
Patient X

When things go wrong
REM Parasomnia

• REM Sleep Behavior Disorder (RBD)

  • REM sleep exclusive

  • Identified and formally recognized first at HCMC in mid 1980’s by Schenck and Mahowald

  • Early marker for Lewy Body Dementia, Parkinson's Disorder, Multiple System Atrophy
REM Sleep Behavior Disorder

- Elevated muscle tone during REM (abnormal), documented by Polysomnography
- Dream enactment behavior
- If awakened, patient is usually alert and coherent
- Vocalizations and or complex motor behaviors that can be injurious
REM Parasomniah (RBD)
REM Parasomnia (RBD)

87-2 Violent behavior during REM in a 52 year old with Parkinson syndrome (Source: Dr Birgit Högl)

Meir H. Kryger, MD
Thank you

Dr. David Hilden

ACP