Frostbite in January… Amputation in July?

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Objectives

- Summarize the acute care of the frostbite patient from an evidence based focus
- Discuss new and ongoing research
- Case presentation

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Disclosures

- I report no relevant financial relationships that create a conflict of interest for CME purposes
- Pictures may be graphic

Rapid rewarming

- 1961 **Bill Mills out of Alaska** showed that rapid rewarming of the affected tissues resulted in some improvement
- Rapid rewarming helped limit damage by
  - Minimizing the time during phase transition in tissues from solid to liquid
  - Giving cells and tissues the potential to recover
- Little progress was made in the treatment of frostbite from that point on until the late 1980s with the development of a treatment and protocol for frostbite patients using thrombolytics to restore blood flow to the damaged tissues.

Mills JR Jr, Whaley R. Frostbite: Experience with rapid rewarming and ultrasonic therapy. Part I. Alaska Med. 1960;35:6-9. 9.
Mills JR Jr, Whaley R, Fish W. Frostbite: Experience with rapid rewanning and ultrasonic therapy. Part II. Alaska Med. 1960;35:114-124. 10.
Mills JR Jr. Frostbite: Experience with rapid rewarming and ultrasonic therapy. Part III. Alaska Med. 1961;36:28- 36.

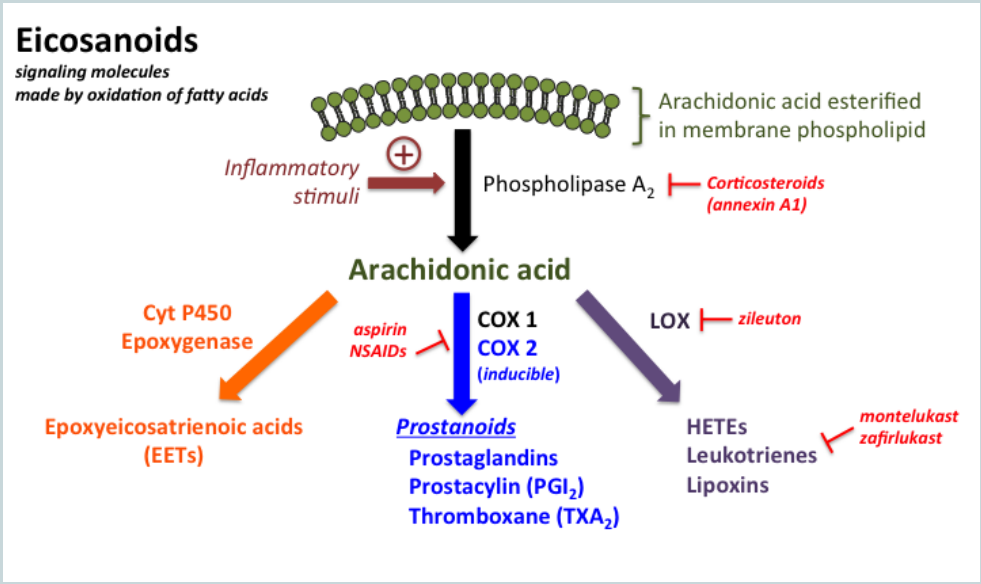
Frostbite Blister fluid

- 1981 Robson & Heggers
- All blisters were found to have:
  - IgM, IgG, IgA, C_3a, and opsonin.
- $PgF_{2\alpha}$ and TxA_2 were markedly elevated.
  - Vasoconstricting metabolites of arachidonic acid
  - Known to mediate dermal ischemia secondary to vasoconstriction

Robson MC, Heggers JP. Evaluation of hand frostbite flister fluid as a clue to pathogenesis. J Hand Surgery. 1981;6:43-47.

Aloe Vera

- **Robson** et al studied the outcomes of inhibiting the arachidonic acid cascade as well as Thromboxane inhibitions in **1987**
  - Ibuprofen
  - Aloe vera
- **32.7% no tissue loss** versus 67.9% control
- **Morbidity was 7%** versus 32.7%
- Debridement of hemorrhagic blister resulted in greater morbidity
- Protocol decreased LOS



Robson MC, Heggers JP. Manavalen K, Weingarten MD, Carethers JM, Boertman JA, Smith DJ jr, Sachs RJ. Experimental and Clinical Observations on Frostbite. Annals of Emerbency Medicine. 1987 Sept;16(9):191-197.

Klein AD, Penneys NS. J Am Acad Dermatol. 1988 Apr;18(4 Pt 1):714-20.

Aloe Vera

- Aloe vera contains several pharmacologically active ingredients:
  - carboxypeptidase that inactivates bradykinin in vitro
  - Salicylates
  - substance(s) that inhibits thromboxane formation in vivo.
- Evidence supporting both an antibacterial and antifungal effect

Robson MC, Heggers JP. Manavalen K, Weingarten MD, Carethers JM, Boertman JA, Smith DJ jr, Sachs RJ. Experimental and Clinical Observations on Frostbite. Annals of Emerbency Medicine. 1987 Sept;16(9):191-197.

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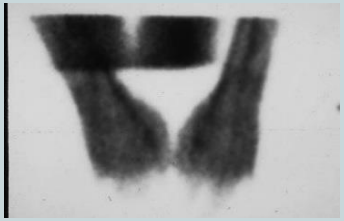
Thrombolytics

- An Open-Label Study to Evaluate the Safety and Efficacy of Tissue Plasminogen Activator in Treatment of Severe Frostbite
  - •Retrospective review **1989-2003**
  - •6 patients intra-arterial and 13 patients intravenous
  - •174 digits at risk in 19 patients
    - -33 were amputated (19% amputation rate)
  - •Historical controls 1985-1989 22 feet & 14 hand – with cutoff on bone scan all had amputations at the cutoff
  - •No or a poor response to thrombolytic therapy in pts with:
    - -> 24 hours of cold exposure
    - -warm ischemia times >than 6 hours
    - -evidence of multiple freeze–thaw cycles
  - •Conclusion -> Safe and effective






Twomey JA, Peltier GL, Zera RT. Journal of Trauma and Acute Care Surgery: Dec 2005. 59(6):1350-1355.

Thrombolytics

- Reduction of the Incidence of Amputation in Frostbite Injury With Thrombolytic Therapy
  - Patients from 2001-2006
  - **32 patients** using intra-arterial tPA
  - Compared to patients from 1995-2006 prior to starting the protocol
  - Decreased amputation rate from **41% to 10%**
  - Conclusion – salvage rates of 85-90% could be expected

- Use of Intra-arterial Thrombolytic Therapy for Acute Treatement of Frostbite in **62 Patients** with Review of Thrombolytic Therapy in Frostbite
  - 1994-2007
  - **Amputation rate of 31.4%**
  - Male predominance 84%
  - Average age 40.4

Bruen KJ, Ballard JR, Morris ST, Cochran A, Edelman LS, Saffle JR. Reduction of the Incidence of Amputation in Frostbite Injury With Thrombolytic Therapy. 2007. *Arch Surg*. 142:546-553.

Gonzaga T, Jenabzadeh K, Anderson CP, Mohr WJ, Endorf FW, Ahrenholz DH. Use of Intraarterial Thrombolytic Therapy for Acute Treatment of Frostbite in 62 Patients with Review of Thrombolytic Therapy in Frostbite. 2016. *J Burn Care & Research*. 37(4):323-334.

Time Matters in Severe Frostbite: Assessment of Limb/Digit Salvage on the Individual Patient Level

Rachel M. Nygaard, PhD, Alexandra M. Lacey, MD, Ashley Lemere, MD, Michelle Dole, DPM, Jon R. Gayken, MD, Anne L. Lambert Wagner, MD, Ryan M. Fey, MD

Journal of Burn Care & Research. Volume 38(1), January/February 2017, p 53–59

The rate of salvage decreases as the time from rewarming to thrombolytic therapy increases.

- Regression analysis demonstrated an additional **26.8%** salvage loss with each hour of delayed treatment

  (P = .006).

- When the amount of tissue at risk for amputation is included in the model, each hour delay in thrombolytic treatment results in a **28.1%** decrease in salvage

  (P =.011).

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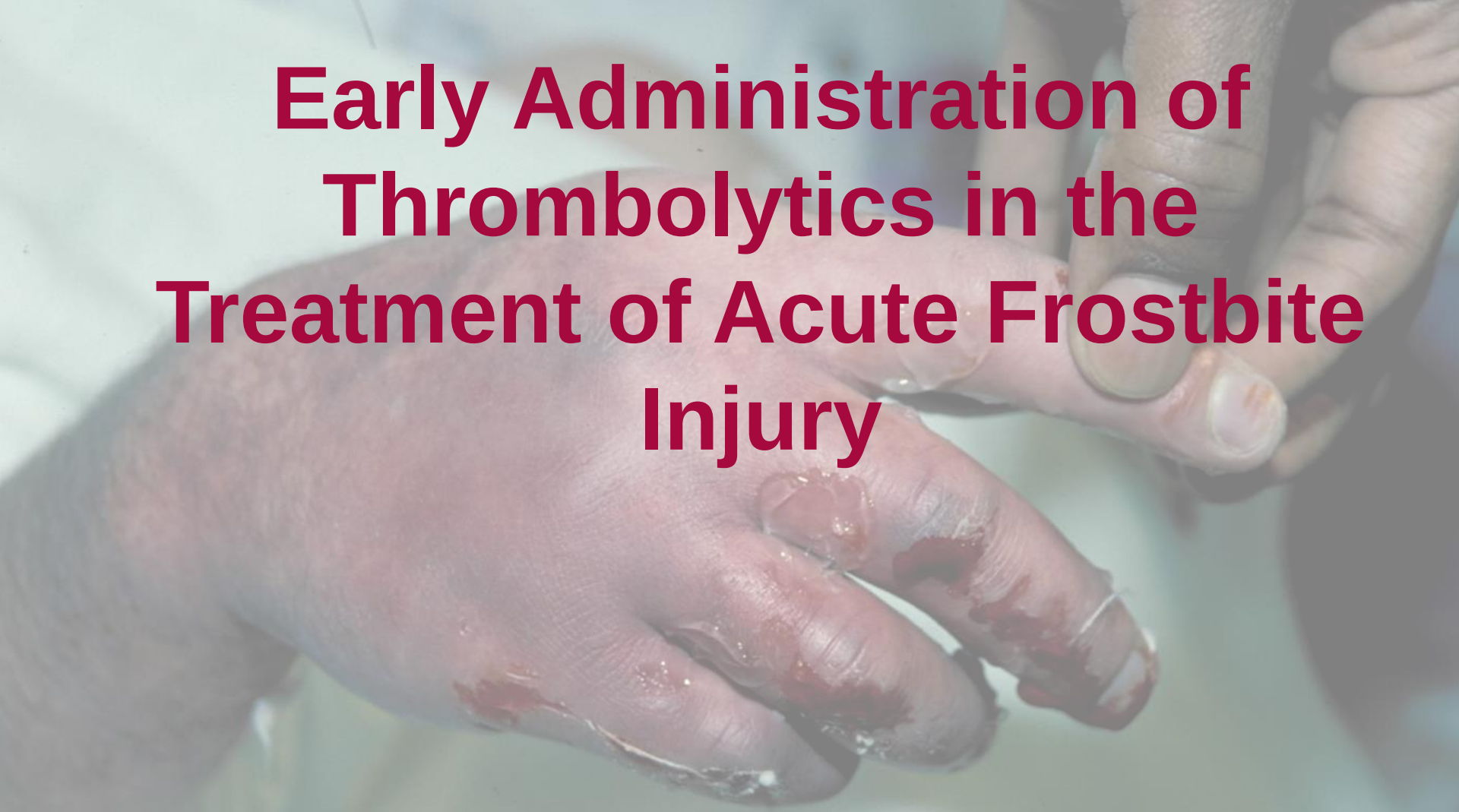
Early Administration of Thrombolytics in the Treatment of Acute Frostbite Injury



Linda Staubli, BSN, RN, CCRN, Tyler Smith, MS,
Samuel Michel, MD, Arek Wiktor, MD,
Anne Lambert Wagner, MD, FACS

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University of Colorado Burn Center
October 2013- October 2017

123 patients with severe frostbite

- 101 males - 22 females (4.6:1)
- Average and median age -> 41
- Age range from 15-86

- Thrombolytic administration:
  - 32 received t-PA at UCH (316 digits affected)
  - 32 patients contraindicated for t-PA due to the timeframe from rewarming to presentation (282 digits affected)
  - 45 patients other contraindications

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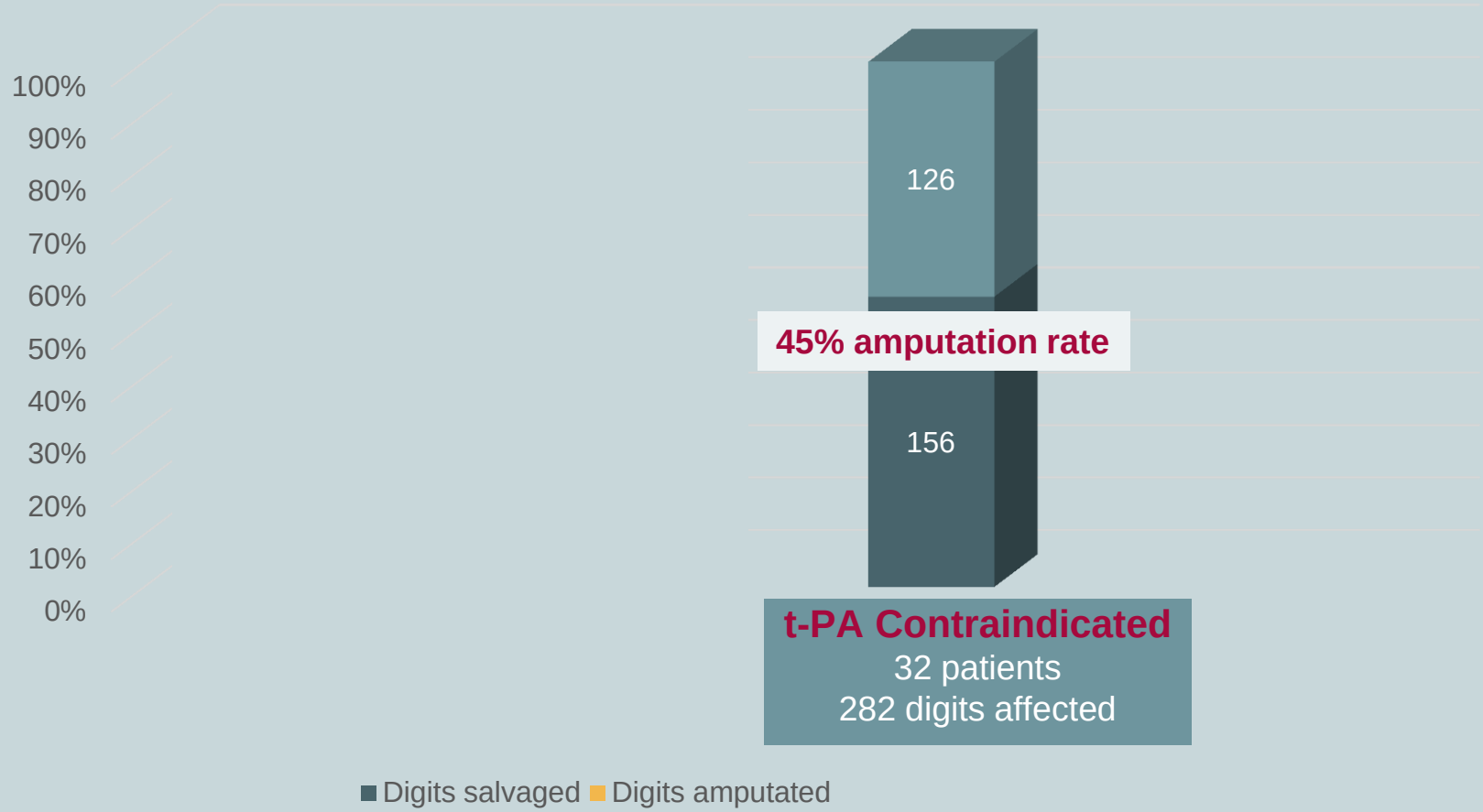
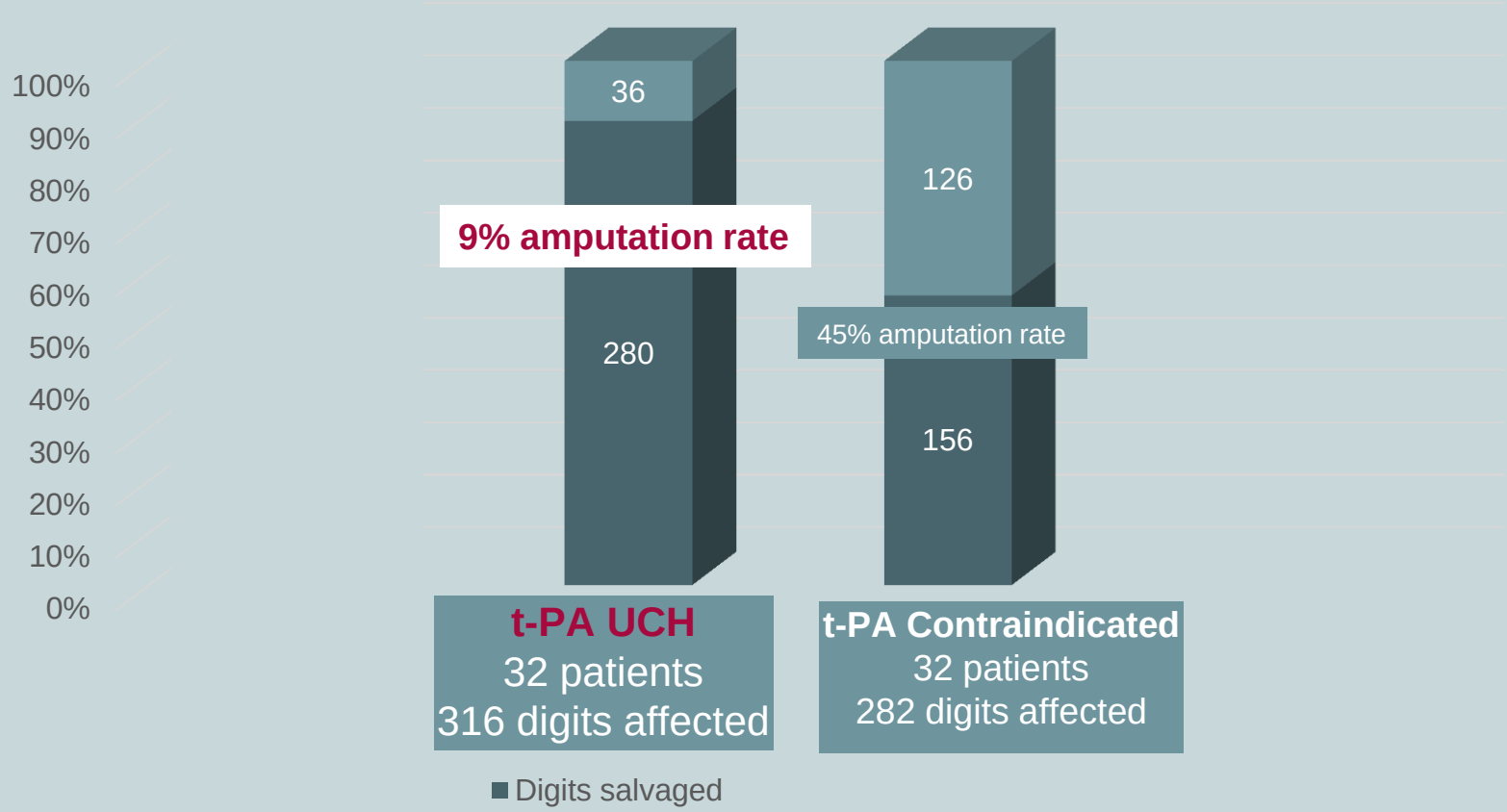
Digit Outcomes



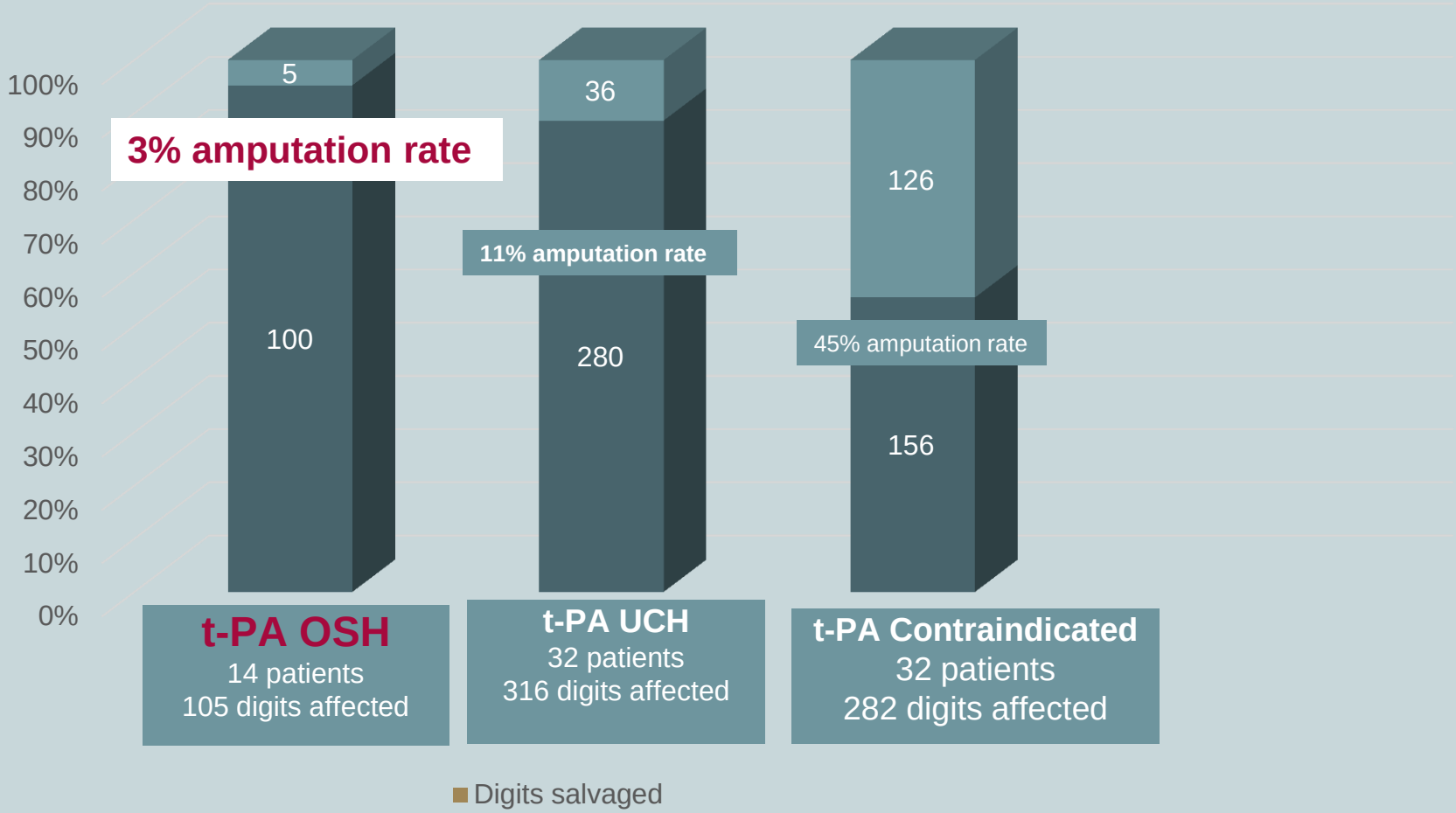
Digit Outcomes



What if our Burn Center partnered with outside hospitals to initiate early administration of thrombolytics in cases of severe frostbite?

- Could t-PA be safely and effectively initiated at outside hospitals?
- Would this improve the rate of amputations?

Digit Outcomes



Case

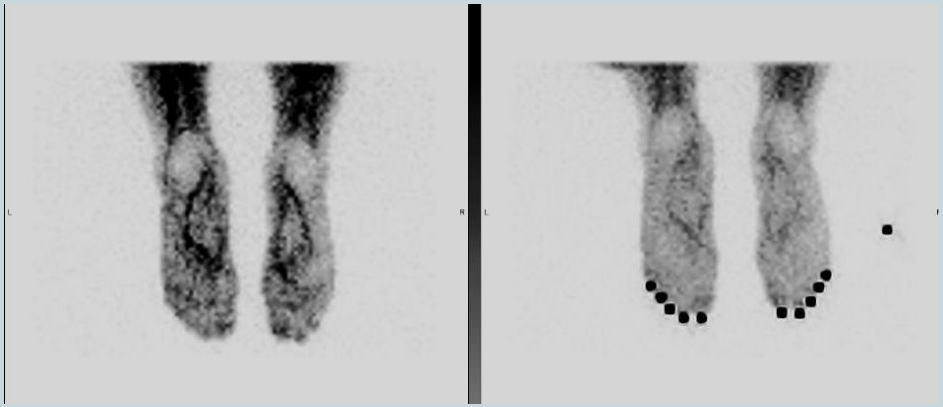
56M found down by a creek following a night of heavy alcohol and marijuana use

Minor abrasions, no significant external trauma, full workup completed

Feet rapidly re-warmed per protocol

Remote TPA protocol initiated at OSH 5 hours prior to arrival at UCH

Case



Conclusions

Early initiation of thrombolytic therapy is an **effective treatment** to increase revascularization and reduce the incidence of amputation.

Burn Centers should **partner with outside hospitals** to effectively and safely initiate thrombolytic therapy prior to transport to a Burn Center.

Specialized protocols and education should be disseminated prior to thrombolytic therapy due to the unique circumstances surrounding administration for severe frostbite injury.

Frostbite

2 components

1. Actual freezing of the tissues
2. Reperfusion injury

This Season 2018-2019

58 Frostbite admissions
Administered tPA 20 times
9 started at outside hospitals
66 threatened digits pre-hospital
6 digits amputations

Frostbite

- Actual freezing of the tissues
  - Ice crystal formation
  - Microvascular occlusion
  - Tissue anoxia

- Initially may present:
  - Hard
  - Cold
  - White
  - Numb
  - Clumsy movements

Frostbite Physiology

- Rewarming
  - RBC, plt, & WBC aggregation
  - endothelial damage
  - Patchy thrombosis
  - Release of O_2 free radicals,
    - PGF_{2a}
    - Thromboxane A_2

Frostbite

Following thawing

24 hours later

- Following thawing
  - Mottled
  - Dark or bright red
  - Can be extremely painful
- Blistering
  - Appear over hours to days
  - Actual character will change after 12-24 hours

Frostbite Classification

1st Degree
- •Hyperemia/edema
- •Non-blistered

2nd Degree
- •Large clear blisters
- •Partial thickness skin necrosis

3rd Degree
- •Hemorrhagic blisters -> dark eschar
- •Full-thickness & subcutaneous skin loss

4th Degree
- •Full-thickness skin necrosis involving bone, tendon or muscle

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Frostbite Wound Management

- Blisters
  - Open only tense clear or serosanguinous blisters
  - Rich in TXA_2 & $PGF_{2\partial}$
    - Vasoconstrictive metabolites
    - Extremely tense
    - Very painful
  - Hemorrhagic – no debridement
- Aloe Vera
  - Counteracts effects of O_2 radicals & Arachadonic acid breakdown products
  - Clinical studies
    - Improved outcomes over topical abx
- Consult PT/OT

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Pre-Hospital Management

- Complete primary survey
  - Airway, Breathing, Circulation
  - Assess for any traumatic injuries using your trauma system protocols
  - Hydration – IV or PO
- Remove jewelry and cold/wet clothing
  - Treat for hypothermia
  - Keep patient warm
- Mechanical protection
  - Pad and/or splint
  - Do not allow the patient to walk or use frozen hands or feet
  - Prevent trauma to frostbitten tissue from direct pressure (blankets, litter straps, etc.)
  - No rubbing or massage
- Do not begin rewarming in the field
  - Unless ability to keep thawed is certain
- Pain Management
  - 800 Ibuprofen unless contraindicated

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Pre-Hospital Management – Field treatment

- **Immediate (<1-2 hrs) evacuation possible:**

- Consider helicopter for anticipated prolonged ground extrication **>1-2 hrs**
- Consider calling your local transfer center to discuss direct transfer to UCH Burn Center
- Do not attempt to rewarm frostbitten tissue.
- **Non-weight bearing** to the affected areas **unless** patient or rescuer in danger
- Elevate frozen extremities above level of the heart if possible

Pre-Hospital Management – Field treatment

Immediate evacuation (> 1-2 hrs) NOT possible:

- **Seek nearest warm shelter** (hut/tent)
- Consider rewarming **only if able to prevent refreezing**
- **Rapid rewarming with water immersion 104 F (40 C)** 30-45 minutes
  - Avoid tissue touching sides or bottom of container
  - Test and circulate warm water with hand
- **Slow rewarming (warm tent/hut, adjacent body heat) if only option**
  - Avoid fire, space heaters, oven
- Anticipate **pain** with re-warming
- **Do not break or drain blisters** that may appear after re-warming
- Apply loose, bulky sterile dressings
- **Elevate** affected areas when able
- When evacuation possible **avoid thawed tissue refreezing**

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Frostbite Management - ED

- Primary assessment
  - Rule out of associated trauma
- Document VS
  - Core body temperature
- Assess and treat for hypothermia
- IV placement
  - Hydration and analgesia
- Supplemental O2
- Start Ibuprofen & Neurontin
- Maintain non-weight bearing status

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Frostbite Management

* Update tetanus
* Scheduled Ibuprofen & Neurontin
* Transfer → protect from further cold
* Keep affected area elevated
* Maintain non-weight bearing status

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Frostbite Management

- **Concerns 3rd or 4th degree frostbite**
  - Consult UCH
  - Specialized treatment unit

- Rapid rewarming
  - Circulating water bath when able
  - **Document start time & completion**
  - Water temp **104 ºF (40º C)** – 30-45 min
  - Continue until frostbitten limb becomes flushed red or purple, and tissue soft and pliable to gentle touch

- Air dry – no aggressive manipulation
  - Elevate
  - Bulky padded dressings

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Indications for Thrombolytics

- Patient presentation with frozen tissue
  - Hard
  - Cold
  - White
  - Numb
  - Clumsy movements
- Absent or weak doppler pulses in limbs and/or digits after rewarming
- Clinical exam
- < 24 hours of warm ischemia time

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Thrombolytic Contraindications

Absolute Contraindications to Alteplase (t-PA):

- ❑ Repeated freeze-thaw cycles
- ❑ >24 hours warm ischemia time

Relative Contraindications to Alteplase

- ❑ Concurrent or recent (within 1 month) intracranial hemorrhage, subarachnoid hemorrhage or trauma with active bleeding
- ❑ Recent intracranial or intraspinal surgery, serious head trauma (within 3 mo)
- ❑ History of or active gastrointestinal bleeding
- ❑ Severe uncontrollable HTN
- ❑ Pregnancy
- ❑ INR > 1.5, PT>50, PTT>40
- ❑ Platelets <50,000

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Thrombolytic Contraindications

Use caution with the following:

- ☐ Age >75
- ☐ Prior ICH, known structural intracranial process, intracranial neoplasm
- ☐ Current or recent use of anticoagulants
- ☐ Non-compressible vascular punctures
- ☐ Traumatic or prolonged CPR (>10 min)
- ☐ Recent internal bleeding (within 2-4 weeks)
- ☐ Dementia or altered mental status
- ☐ Remote history of ischemic stroke (> 3 months)
- ☐ Recent major surgery (within 3 weeks)

Discuss risks and benefits with patient and document consent in medical health record

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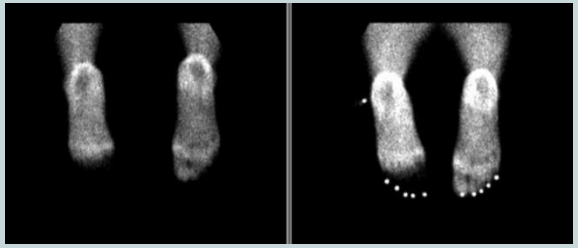
Frostbite Thrombolytic Protocol

* Within 24 hours of rewarming
* Rule out any associated trauma
* Alteplase loading dose 0.15 mg/kg
* Alteplase IVPB 0.15 mg/kg/hr x 6 hr
  * Max dose of 100 mg total
* ICU Status and monitoring
  * Baseline & frequent VS - Hourly neurochecks
* Lovenox 1 mg/kg q 12 hr X 2 weeks



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Future Directions

Future Directions

Hyperbaric Medicine

- Increases RBC deformability
- Decreases edema
- Improves nutritive skin blood flow
- Improves oxygenation
- Helps to reverse the reperfusion injury

Hyperbaric Medicine

Frostbite in a Mountain Climber

Treated with Hyperbaric Oxygen:

Case Report

- 28 yo female mountain climber
- 10 finger involvement
- Delay treatment of 2 weeks
- Hyperbaric treatment over 3 months (21 treatments)

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Hyperbaric Oxygen

- Prospective study utilizing hyperbaric O_2 treatment
  - All patients with evidence of 3rd/4th degree frostbite:
    - presenting outside the thromboltytic window
    - Contraindications for thrombolytics
  - 14 days at 2.4 ATA for 90 min

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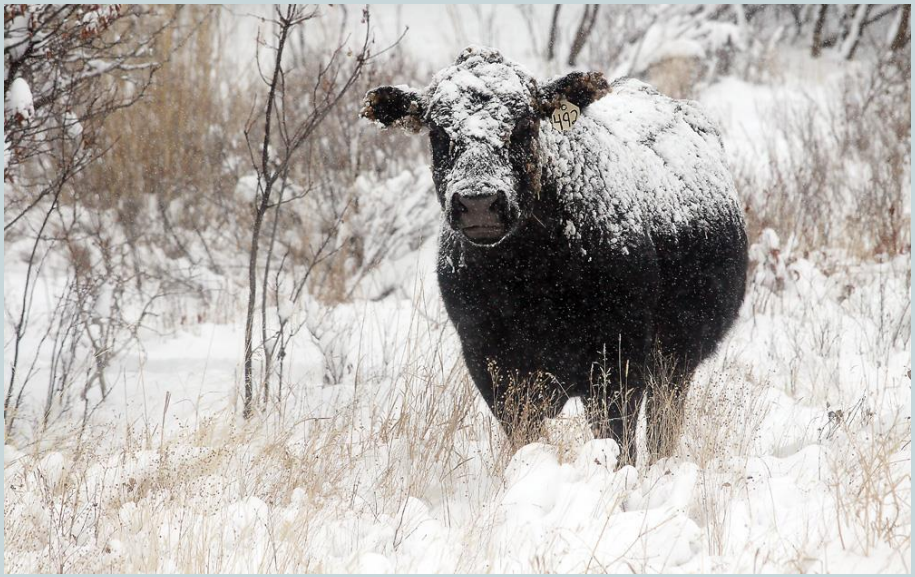
Other research studies



- Dosing and re-dosing of thrombolytics
- Comparing newer devices to bone scans to assess frostbite injury depth
- Surveys to assess long term pain and disability

Challenging Patient Review - JM

-36 yo male - Ski instructor

-Out skiing with another ski instructor

-Skied off trail

-LOST

Challenging Patient Review - JM

-Outside for >48 hours in ski gear

-Build snow cave

-Picked up & transferred to OSH

Challenging Patient Review - JM

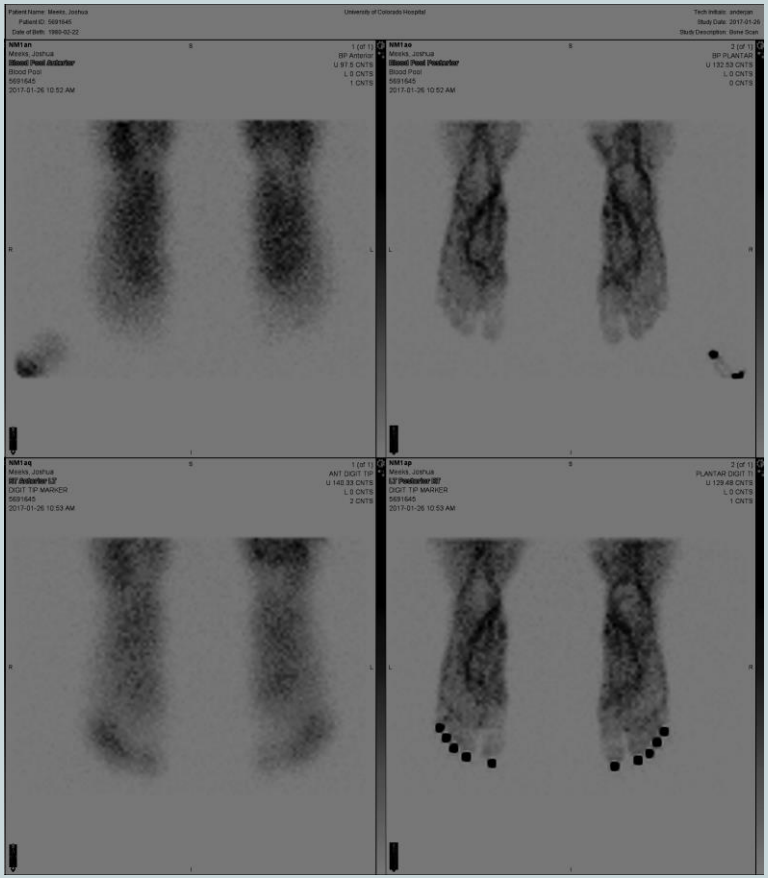
-Rapid rewarming at 14:30 – evidence of 4th degree frostbite to his feet and hands

-tPA started at 19:45

-Transferred to UCH

Challenging Patient Review - JM

-Completed course of tPA
-Underwent triple phase bone scan
-Treated with UCH frostbite protocol



Challenging Patient Review - JM

Challenging Patient Review - JM

Challenging Patient Review - JM

Burn/Frostbite Follow-up

Burn Clinic

720-848-0747

To refer a patient:

1-844-285-4555

(24/7)

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Burn and frostbite consults

are as close as your smart phone

UCHealth burn surgeons will have access to images within seconds to help guide care.

Get expert guidance for all the following injuries:

- Burns of any size
- Frostbite
- SJS/TENS
- Necrotizing fasciitis
- Soft tissue injuries

UCHealth Burn Consult

- The app is a **free** service of **Colorado's only American Burn Association-verified Burn Center.**
- The process is HIPAA-compliant, and images are not stored on your phone.

Get started.

- To register, contact Laura Madsen at 720.848.6054 or laura.madsen@uchealth.org.
- Download the UCH Burn Consult app from the iTunes App Store or Google Play.
- Upload images of the burn area.
- Input a few patient information data sets.
- Call the DocLine at 1.844.285.4555 to get connected with the burn specialists.

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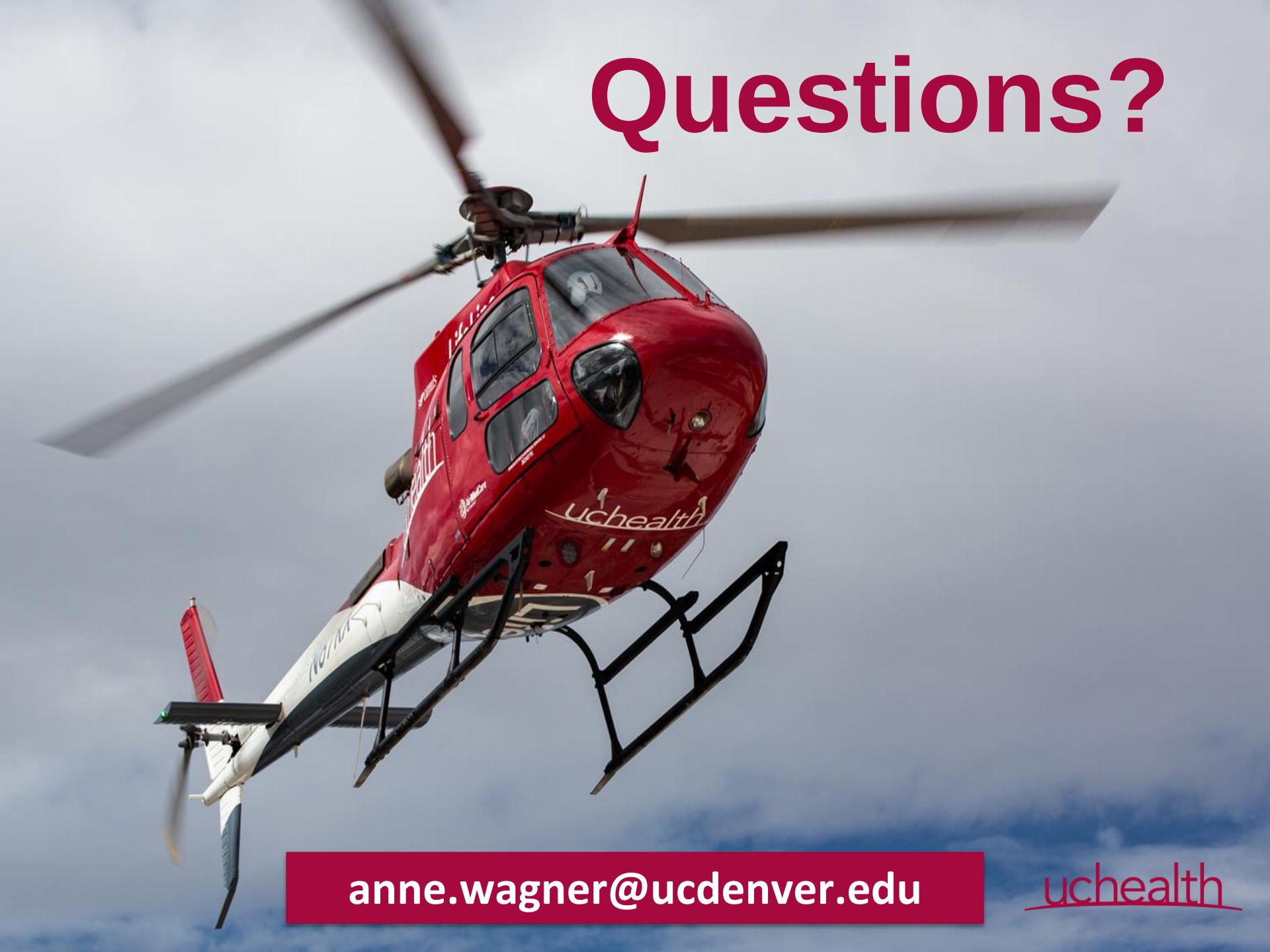
Questions?
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