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#### Conflict of Interest Statement

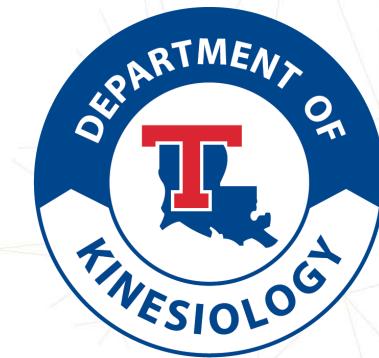
• I have no actual or potential conflict of interest in relation to this presentation.



# Exertional Rhabdomyolysis: What Is **Too Much**?

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# Introduction

- Definition of rhabdomyolysis (rhabdo)
- Definition & physiology of exertional rhabdo (ER)
- Pushing athletes to their limits: case studies for coaches to learn from
- Recommendations for injury prevention in S&C context



# A disclaimer: What this presentation is not.

- A witch hunt
- A detailed investigation of every incident of rhabdomyolysis in every setting
  - Emphasis on athletes; some reference to youth & military settings



# Rhabdomyolysis

Rhabdo ... what?





# Definition

Rhabdomyolysis: massive destruction/disintegration of striated muscle

"rhabdo" = striped, "myo" = muscle, "lysis" = broken (Ramos & Dorgo, 2014)



# What Causes Rhabdo?

Musculoskeletal trauma—damage to cell membrane

- crushing injuries
- burns
- infection
- drugs (including excessive alcohol, cocaine, etc.)
- ingestion of toxins
- heat stress
- cold stress
- sickle cell trait
- excessive [volume of] exercise

Huerta-Alardin, Varon, & Marik (2005); Tietze & Borchers (2014)

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Occurs in 85% of cases of traumatic injury Huerta-Aladin, Varon & Marik (2005)

# Who Else Gets Rhabdo?

- Racehorses
  - genetic tendency for chronic rhabdo in some
- Caged/restrained animals
- Sick people
- Drug addicts & alcoholics
- Crush victims
- ...And other scenarios when muscle tissue is severely damaged

# Definition

- Exertional Rhabdomyolysis (ER): rhabdo brought on by extreme exertion of some kind
  - Sport or military training, punishment, etc.
  - Perfect storm + additional cofactors
  - Numerous case studies exist from injury brought on by personal trainers, coaches, PE teachers, military training instructors, competition, etc.

# Initial Symptoms of ER

- Severe muscle pain, cramps, swelling
- Weakness
- Sometimes tea-colored urine
- Onset follows activity, may lag a day or so



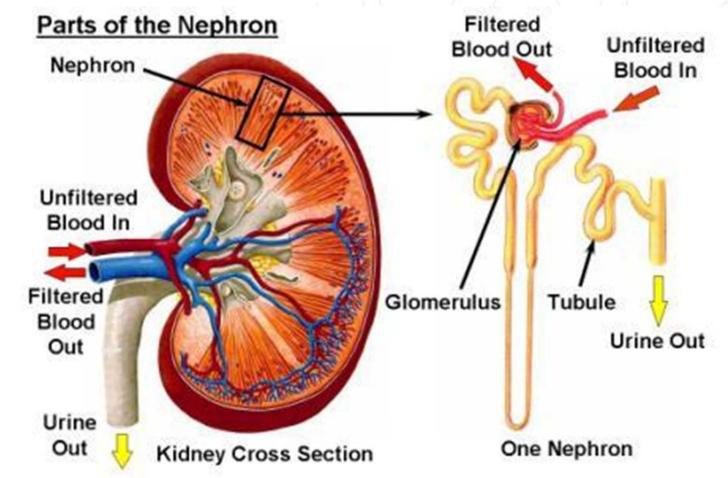
# Diagnosing ER

- Done via formal medical care (Emergency Room)
  - evaluation of blood Creatine Kinase (CK)
    - most sensitive factor
    - Clinical threshold  $\approx$  5X normal limit
      - Some argument ongoing
  - Myoglobinuria: myoglobin (Mb) in urine
    - suggested to not be best indicator due to short half-life
  - Severe pain & cramps
    - Not DOMS

# Why Is ER A Problem?

1. Contents of muscle cells cause problems if they go elsewhere in the body

> heavy concentrations of substances from intramuscular space (i.e. myoglobin) become toxic to kidneys



# Why Is ER A Problem?

2. A certain level of local damage may lead to compartment syndrome

- Medical emergency involving over-pressurized section of tissue within fascia
- May require surgery to prevent further tissue necrosis



# Why Is ER A Problem?

- 3. Cardiovascular problems such as arrhythmia & clotting ... that may lead to <u>DEATH</u>
- Therefore ER is a serious clinical health condition, and has been brought on in athletes usually\* by poor training decisions
  - not always well-explained

\*possibly combined with poor lifestyle decisions, insufficient recovery, or illness

# Possible Local Precipitating Factors Leading to ER

- 1. Cross-bridge & structural sarcolemma damage from lots of eccentric phase
- 2. Muscle cell hypoxia leading to depletion of ATP
  - Anaerobic conditions of shock states
    - vascular occlusion, tissue compression, & inappropriate exercise
  - Membrane pumps, etc. don't function without ATP
    - may compound issue and lead to further necrosis (Huerta-Alardin, Varon, & Marik, 2005)
- 3. Heat injury + extreme exertion

(Szczepanik, Heled, Capaccione, Campbell, Deuster, & O'Connor, 2014)

...or...

4. Other more unusual factors

# With ER In Athletes We Must Consider...

 Possible influence of medication, trace amounts of recreational drugs, and tainted supplements

Huerta-Alardin, Varon, & Marik (2005)



# Athletes With Increased Risk for ER

- Sickle Cell Trait
  - Sickling possibly brought on by stress or ...?
  - Involves cascade of events leading to CV tissue damage
  - Some case reports/studies exist of sudden death in athletes with sicklingrelated ER
    - i.e. One 19 y.o. college football player (Harrykissoon et al., 2007)



# What Causes ER?

- Primary causative factors in preventable cases are <u>acute high volume</u>, with high density, likely involving repeated failure
  - Consider timing of preventable cases in athletes that we'll discuss
  - We have what can be the perfect storm for inducing ER:
    - Massive muscle damage (lots of eccentric action)
    - Heavy sweating due to intramuscular heat production
      - less fluid to transport heat away
    - Environmental heat (see Casa et al., 2012)
    - Rapid ATP degradation
    - Possible electrolyte imbalance

# Dehydration May Increase ER Risk

- Consider the intracellular environment
  - muscle cell is about 75% water (McArdle Katch, & Katch, 2007)
  - water provides the solvent for intracellular biological mechanisms
    - enzymes, electrolytes, etc.
  - the human body has an optimal range
    - if compromised can reduce function

# Is Blood Perfusion Constant?

- Dehydration has been demonstrated to affect blood perfusion between compartments
  - For review see Trangmar & Gonzalez-Alonso (2017)
- Brings about some complexity to training & recovery
- Does this increase value in recovery modalities?



# Context of Blood Creatine Kinase



# Context: American Football

- Many of these cases are seen in football, highlighted by media, so...
- Hoffman et al. (2005) sampled blood of D-III football players over a season
  - Creatine Kinase (CK) average values
    - Pre-camp: ≈ 50 U/L
    - Camp (Day 10; 2-a-days): ≈ 350 U/L starters, ≈ 175 U/L nonstarters \*
    - Inseason (Week 3, 7, 10): ≈ 50 U/L
  - Myoglobin average levels were fairly consistent as measured, averaged around 25 ng/mL
- Hoffman et al. (2002) found in-game CK (starters) ≈ 175 U/L

# Context: more from football

- Smoot, Cavanaugh, Amendola, West, & Herwaldt (2014) observed CK levels of 32 Iowa football athletes during camp
  - Day 1: 285 ± 801 (range: 72 4,659) U/L
  - Day 3: 1,300 ± 2,284 (range: 217 12,067) U/L
  - Day 7: 1,562 ± 1,497 (range: 229 7,453) U/L
    - Positions & practice reps not reported!
  - At days 3 & 7 many athletes met diagnostic criteria for rhabdo, but athletes were asymptomatic

# Context: more from football

- Ehlers, Ball & Liston (2002) monitored CK during 2-a-day camp at Northern Illinois (n = 12, 4 sampling times)
  - Average: 203 3,272 (range: 92 18,823) U/L
  - Some WR & DBs had highest measurements



# Context from multiple sports

- Mougios (2006) reported CK values from large sample of Greek club sport athletes (n = 483 male, 245 female)
  - track & field, swimming, cycling, rowing, kayaking, soccer, basketball, volleyball, handball, water polo, tennis, table tennis, gymnastics, judo, taekwondo, karate, boxing, weightlifting, diving, motocross, snowboarding, and bodybuilding
  - reference limits:
    - males: 82 1,083 U/L
    - females: 47 513 U/L
      - Effects of muscle damage relative to muscle mass

# Note on muscle damage reference limit differences

- Reference limits differ by sport (Mougios, 2006):
  - men's soccer (*n* = 182): **83 1,492 U/L**
  - men's swimming (*n* = 93): **70 523 U/L**
- Why this difference?
  - weight bearing activities with more ECC action
  - harsh environmental conditions may worsen muscle damage

# Context: What about ... "aerobic people"?

Karstoft, Solomon, Laye, & Pedersen (2013)

- Daily recreational marathon running for 1 week (n = 7 males, 1 female) produced CK increases
  - Pre-event 1: **199 ± 48** (range: **75 497**) U/L
  - Post-event 7: 640 ± 99 (range: 329 990) U/L

# Case Studies of ER





Smoot, Amendola, Cramer, Doyle, Kregel, ...& Herwaldt (2013)

- University of Iowa Football, Jan 20-24, 2011
- Following a 3-week break after bowl game...



Smoot et al. (2013) Jan 20, 2011: 15-min dynamic warm up Barbell snatch 3 @ 65%, 3 @ 70%, 3 @ 75% Back squats 100 reps @ 50% Sled pushes 20 yd X 5 (sled load: bigs 240 lb, mids 210 lb, speed 180 lb) Pull ups max reps Dumbbell rows 3 X 12 @ 65% Cable push-aways 10\* Cable ab pulldowns 2 X 10\* Blast strap rollouts 2 X 10

\* Player-selected load

Smoot et al. (2013)

Jan 21, 2011:

15 min dynamic warmup
Barbell bench press 100 reps @ 50%
Back extensions 5 X 10
Ab cable pulldowns 1 X 15 (player-selected load)

#### 5 athletes conducted a punishment run (described only as "extra running assignment"), 3 of these later contracted ER



Smoot et al. (2013) Jan 24, 2011: 15 min dynamic warm up Hurdle hops 3 X 3 Hang clean 2 @ 70%, 2 @ 75%, 3 X 2 @ 80% Barbell incline press 5 @ 70%, 4 X 5 @ 75% Barbell RDL 5 X 5 @ 75% Pull ups 3 X 10 @ body weight Barbell press 3 X 10 @ 60%



Smoot et al. (2013)

- On Jan 24, 3 players (19-21 y.o.) reported to ATC with 3-day history of dark urine, severe muscle soreness & swelling
  - CK range 166,991 233,167 U/L
- ATCs saw 13 total cases
  - 10 athletes permitted researchers to view medical records
  - CK range 96,987 331,044 U/L
- Survey issued to athletes
  - No relationship between injury & size, position, training history, etc.
  - Some athletes did extra squats
- Noted possible protective effect of drinking protein shakes...

# Fallout from the Iowa case...

\$15,000 legal settlement to one athlete (AP, 2016)



Moeckel-Cole & Clarkson (2009)

- Reported ER in a 18 y.o. D-I football placekicker
- Brought on by late summer training led by S&C coach
- The workout:
  - 10 sets of 30 shoulder-band squats (300 reps) with 60s rest between sets
    - No reference to band thickness
  - 30 RDLs using 40-lb dumbbells
  - 30 shrugs using 80-lb dumbbells
- Severe pain presented in quadriceps afterward, difficulty walking the following day
- CK 130,899 U/L upon hospital admission (8 days in hospital)

Shelmadine, Baltensparger, Winson & Bowden (2013)

- 19 y.o. SCT college football player (lineman) diagnosed with ER & heat exhaustion following preseason conditioning test
- Test consisted of 5 X 300 m intervals in > 100° F (4:15pm)
  - Collapsed upon completion
    - Severe muscle pain, cramps, weakness, etc.
  - Hospitalized, CK 408,545 U/L on Day 2, placed on blood dialysis
  - CK values peaked at 880,000 U/L on Day 4

Anzalone, Green, Buja, Sanchez, ...& Eichner (2010)

- 19-y.o. SCT college football player in TX
- Late Sept, 4pm 30-min lift, then ran outdoors in 76° F
- Ran 16 X 100 yd
  - Rest 1 min for 1<sup>st</sup> 4, rest 2 min between next 4, 1 min between last 8
  - Some reports suggested he lagged behind others and was encouraged to continue
  - Collapsed after, given IV fluids by ATCs, lost consciousness
  - Taken to hospital by EMTs, died in hospital 15 h later
  - SCT not known to athlete or family
  - autopsy showed sickling-related rhabdo

Oh, Laidler, Fiala, & Hedberg (2012)

- Aug 17-18, 2010 HS football team from McMinnville HS, Oregon
- 22/43 athletes were diagnosed with ER following a football <u>team-building</u> event, 12 of them hospitalized
- Alternated chair dips and push ups each for 30s, 20s, 10s, 7s, 5s with no rest in hot room, estimated 20-25 min of work for team
  - $\approx$  4 sets each
- Incorrect performances became group punishment
- Reported symptoms 1-3d following workout, pain, weakness, dark urine
- Diagnostic CK threshold used was >2,320 U/L (range 2,434 42,000)
- 3 athletes diagnosed with triceps compartment syndrome, underwent fasciotomy

Stanfa, Silles, Cooper, Arena, Landis-Piwowar,... & Hew-Butler (2017)

- March, 2014 D-I swimmers after 1-week off following league championship
- Week 2 of training 13 swimmers contracted ER, 6 of them hospitalized, male & female
- 3d consecutive workouts prior, ≥ 5,000 m swimming daily + circuit training (no details)
- ER-inducing event occurred on training day 9

Stanfa et al. (2017)

- Novel "team building" competition
- Teams of 3, goal = beat other groups
  - 2 cycles through:
    - Max pull ups
    - Max rows
    - Max bench press
  - 2 groups tied, entered tiebreaker round (details not disclosed)
  - During tiebreaker round, other groups alternated push ups and isometric arm holds horizontal & perpendicular to floor (further details not disclosed)
- Followed by 5,000m swim
- CK values 73 >20,000 U/L
- 6 swimmers hospitalized were "exceptionally motivated"
- Authors linked ER with recovery beverage intake (all 6 had >50% recommended intake of protein shake)

Galvez, Stacy, & Howley (2008)

University of South Carolina Swimming, fall conditioning

- Day 1 workout: alternating 1-min of push ups and body weight squats for 10 mins, then swim practice (no details)
- Day 2 workout: 40-minute weight training circuit (no details), swim practice
- Day 3 workout: max pull ups, unclear ab exercises including "tripods" & bridges, then swim practice (no details)
  - Athletes presented between Days 1-7
  - 7 athletes diagnosed with ER, severe pain & swelling in triceps & pectorals, dark urine
  - CK range: **30,524 81,795** U/L (female) & **38,400 157,700** U/L (male)

Cleary, Sadowski, Lee, Miller, & Nichols (2011)

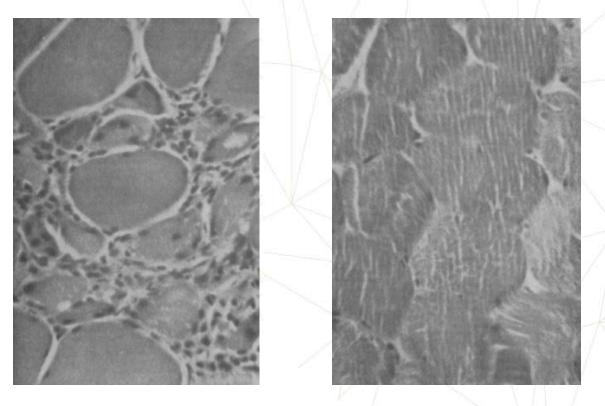
- 16 y.o. high school wrestler in Hawaii, no info on training history
- Day 1: out of camp due to unrelated concussion
- Day 2: 60-minutes of circuit training including wall-sits, squats, sit ups, push ups, lunges, plyometric jumps (played catch up for Day 1 absence)
  - Limited water breaks in training
- Day 3: undisclosed volume of running in practice
- Day 4: presented to ATC with severe bilateral quad pain
- Day 5: practiced with pain, stiffness, difficulty walking
- Day 6: admitted to hospital, peak CK 146,340 U/L

Register, Mihalik, Hirth, & Brickner (2006)

- D-I female lacrosse players at UNC (n = 8, 18-22 y.o.)
- No details about other activities
- First workout back from summer break (most reported no training)
  - Precipitous aspect of workout reported to be:
    - 3 X 20 biceps curls with 15 lb or 10 lb dumbbells
  - CK range: 4,287 20,247 U/L

Greenberg & Arneson, 1967

- Officer Commissioning School, Ft Benning, GA
- Trainee contracted ER from ≈200 push ups in 1.5 - 2 h on Day 2
  - Pain & swelling in pecs & arms
  - Muscle biopsies taken
- 23/586 trainees contracted ER
- Further reduced ER occurrence by ensuring TIs implement progressive activity w/rest



Cross-sectional view of triceps biopsies taken after ER & 3 mo after

Oh, Arter, Tiglao, & Larson (2015)

- Reviewed military injury database for ER injuries 2010-2012 at Tripler Army Medical Center (HI)
- 30 cases identified (not associated with toxins, heat illness, etc.)
- Resulted from
  - Military-style physical training & ruck marches (40%)
  - Nonspecific training including martial arts (43%)
  - High volume training from crossfit (*n* = 4) and P90X (*n* = 1) workouts
  - One case: 300+ lunges for 2 days in a row...
- CK range 697 233,180 U/L

Hummel, Gregory, Desai & Diamond (2016)

- Described 8 cases of diagnosed ER at a hospital in Nashville, TN area
  - 7 high school football athletes (inseason & offseason)
    - 1 case combined with heat exhaustion
  - 1 first-time crossfit participant (15 y.o.)
- Implicated ADHD medication (stimulant) and caffeine in 2 cases
- CK levels ranged from 1,744 to 154,000 U/L between cases

Borrione et al. (2009)

- ER diagnosed following high volume preparation for Nationals in 16 y.o. male swimmer
  - swimming 5d/wk, 2-3 hr/day + school-based PE (4h in week)
  - CK = 9,952 U/L
- Progressive weakness, intermittent muscle aches, malaise, episodic tachycardia, nausea
- poorly controlled vegetarian diet was proposed to be cause
- increased PRO intake & no further issues occurred

Eliakim, Ben Zakin, Meckel, Yamin, Dror, & Yamet (2015)

- 17 y.o. "elite" water polo player underwent 2-day military preselection activity
- primarily endurance, loaded + unloaded movements
- CK values recorded 98,740 U/L
- Genetic testing diagnosed genetic tendency for ER
  - IL-6 174C allele single polymorphism
- Possible that previous water polo activities (goalie) not sufficiently damaging

#### ...So What If We Boost Recovery???

 2 case studies exist of ER exist with steroid-using bodybuilders

Braseth, Allison, & Gough (2001)

Farkash, Shabsin, & Pritsch (2009)

- Neither are very descriptive of onset activities
- Purity of "restorative"?





# Practical Recommendations & Prevention Tips for Coaches



### Key Takeaways for Coaches: Who Is At Risk for ER?

(otherwise healthy)

- Children & adolescents
- Very intrinsically motivated athletes
- Athletes who go to failure with high volume
  - especially repeated failure
- Athletes training in the heat
- Dehydrated athletes

## Key Takeaways for S&C Coaches: Who Is At Risk for ER?

- Athletes coming back from semi-sedentary breaks
  - NCAA rules are *part of this problem* 
    - Supervised active rest period may be better than nothing at all
    - Many sport coaches don't understand training theory or psychology
      - No accountability of what coaches program
      - Athletic Directors need to be aware so they know who to fire or refer to educational resources
  - 2 of 4 possible mechanisms for atrophy are disuse & unloading (Urso, 2009)
    - post-season = sport-specific adaptations
    - not necessarily loading-specific

#### A Progressive Point

- The Repeated Bout Effect is demonstrated following ECC loading (Hyldahl, Chen, & Nosaka, 2017)
  - Rapid protective adaptation to musculature seen after first eccentric (ECC) exposure
  - Results in less muscle damage in subsequent ECC loading due to:
    - possible neural adaptations (follow after >12 h)
    - adapted muscle-tendon complex behaviors
      - including pennation angle changes
    - structural remodeling of extracellular matrix\*
    - modified inflammatory response
  - Part of adaptation!

\*Also supported by high volume eccentric endurance in Hoffman, Cresswell, Carroll, & Lichtwark (2016)

#### Weight Room Wisdom Point #1

- Be careful with volume.
- Amirthalingam et al. (2017) compared 6 weeks of
  - German volume training (10 X 10) primary lifts
  - 5 X 10 primary lifts
    - Both programs performed 3-4 X 10 assistance lifts
    - Both programs 3-day split
  - Greater strength gains for 5 X 10 group
  - No difference in muscle thickness (DEXA) between groups

#### Weight Room Wisdom Point #2

- Dr. Mike Stone:
  - Highest volumes with weightlifters have been 10 work sets of 10 back squats
    - Broken up into 2 sessions in a day
      - AM squats
      - PM squats & a few assistance lifts ≈ 5 sets
- At ETSU, strength-endurance phases don't often exceed 3 X 10 for primary & secondary lifts
  - Athletes doing other stuff
  - It works
  - Advanced strength athletes can handle > 5 X 10 (i.e. weightlifters)...?

#### Weight Room Wisdom Point #3

- Be careful with going to failure
  - Especially through repeated failure
  - Remember Selye's GAS...



#### A Cautionary Note for Coaches

- The CSCS can be revoked ... don't be the first.
- From the NSCA Professional Standards & Guidelines (NSCA, 2009):

"...[An] S&C professional is negligent if he/she is proven to have a duty to act, and to have failed to act with the appropriate standard of care, proximately causing injury or damages to another person."



### Appendix



- 1. Do **<u>NOT</u>** punish your athletes with acute vigorous physical activity
  - Acute high density + high volume = great risk
    - If leaked to press, PR issue <u>could get you fired</u>
    - Coaches should not be programming exercise that may be potentially injurious to athletes
      - NSCA Code of Ethics
      - NCAA Sport Science Institute: <u>http://www.ncaa.org/health-and-safety/medical-conditions/ten-factors-can-increase-risk-exertional-rhabdomyolysis</u>



- 2. Hydrate & Fuel!
  - Smoot et al. (2013) and several other physicians proposed connection between dilution of body fluids and better tolerance to aggressive exercise
  - Is there also a benefit to taking in PRO+ CHO drinks?
    - Anabolic environment vs. further catabolic?
      - Mixed results at this stage regarding reduction in inflammation (Kerksick et al., 2008)
    - Some association in literature of supplements with ER events
  - Immediate treatment for ER = IV hydration

- 3. Get information and use it
  - Sickle cell trait athletes
    - Periodically quiz assistants & GAs on who is SCT
    - Do they know what that means? Are you sure?
    - See Fidler (2012) for review
  - Hydration status
  - Medication status of athletes
    - Many athletes may be on STIMULANTS (ADHD)
    - Requires excellent communication with ATCs

- 4. Teach!
  - Your athletes need to know the consequences of partying extend beyond the party
  - Dehydration may take several days to overcome
    - Basketball athletes?
    - Hot climates?
  - Teach sport coaches about case studies to watch out for

- 5. Have a plan.
  - Annual plan coordinated & agreed upon by sport coaches
  - Best practice in S&C
  - Chronic damage control is bad for the athletes' progression
    - talk to your supervisor (or AD) if you see a problem at your institution
    - being silent about issues may introduce liability to YOU
  - Any team-building, etc. MUST fit into plan
    - athletes should be prepared for it
    - assume NOTHING about athletes' preparedness

- 6. Don't use heat as a "mental toughness" training tool
  - may increase risk for ER via heat illness
  - questionable risk vs. reward intensity of the session WILL decrease and you
    may not get desirable adaptations...
  - adaptation to heat should be considered in context of sport
    - (i.e. introduce in late off-season or preseason for outdoor sports)
    - Do my athletes need this stressor?

#### Key Concepts for S&C Coaches

- Best practice: test often and see if your programming works
  - Once or twice a year may not be sufficient
  - Can test & monitor in many ways
  - Are you able to test thoroughly?
  - Do your results support your programming with ALL athletes on a team?
  - Are there non-responders?

#### NCAA Information for Prevention of ER

- 10 factors that increase risk of ER (NCAA, 2013):
  - Athletes who try hardest
  - Arbitrary programming (not planned)
  - Novel stimuli
  - Irrationally "intense" workouts (high density + volume)
  - Exercise to failure & beyond
  - Fast repetitions to failure
  - Increasing # of sets and time needed to finish
  - Loading as % of body weight
  - Rapid return to fitness goal
  - Using training tools as physical punishment

#### Remaining Questions

- Why do some get rhabdo & others don't?
  - This requires detailed athlete monitoring programs to provide answers
- Some have proposed that mentally tougher athletes are at greater risk—how do we protect them?
  - "Normal" people know when to stop
- Quantify risk increase from dehydration

#### Future Research Opportunities

- Nutritional interventions following high volume
- CK comparison in Northern vs. Southern (U.S.) outdoor sport training
  - i.e. outdoor football conditioning of similar volumes
  - requires collaborative sport science work
- Effect of recovery modalities on perfusion
- Perform case studies when things go wrong!!!
  - Requires collaboration with medical professionals & sport medicine

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ASSOCIATION

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