GUIDELINE 2T

EXERTIONAL RHABDOMYOLYSIS

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Rhabdomyolysis is breakdown of skeletal muscle. In common use, however, rhabdomyolysis connotes an acute clinical syndrome of major muscle breakdown and leakage into the bloodstream of muscle contents (electrolytes, myoglobin, other proteins) as reflected by a sharp rise in serum creatine kinase (CK). The many causes of rhabdomyolysis can be categorized as: 1) trauma; 2) muscle hypoxia; 3) genetic defects; 4) infections; 5) body temperature changes; 6) metabolic or electrolyte disturbances; 7) drugs or toxins; and 8) exercise. This guideline focuses on rhabdomyolysis from exercise, or exertional rhabdomyolysis (ER). The first case series of ER was in 1960 in Marines doing squat jumps. ER also occurs in police and firefighter trainees, in overeager weightlifters and novice extreme exercise participants, in prisoners who overexert, in fraternity men who endure exercise hazing, in school kids pushed too hard in physical education class, and in recreational athletes who overdo it in training or competition. This guideline will focus on the NCAA student-athlete.

RECOGNITION

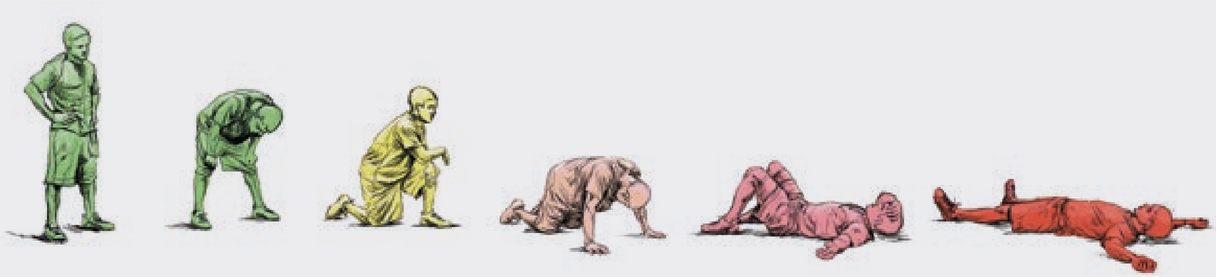
Exertional rhabdomyolysis occurs in the setting of strenuous exercise and can range from mild to severe. Clinical signs are often nonspecific: muscle pain, soreness, stiffness, and, in severe cases, weakness, loss of mobility, and swollen, tender muscles. Severe ER is far more problematic than the milder form known as delayed onset muscle soreness (DOMS), in which muscles become sore and stiff in the first few days after a bout of unaccustomed, moderately strenuous exercise. DOMS is rarely a clinical problem and tends to be self-limited with only relative rest or a cutback in level of training. An even milder form of ER is the physiologic breakdown of muscle that commonly occurs while athletes train. This physiological muscle adaption to exercise overload has few or no symptoms, or only mild muscle symptoms that are generally ignored by the athlete, and so is manifest only by an elevation in serum creatine kinase (CK) – a condition sometimes called hyperCKemia.

Unlike hyperCKemia or DOMS, severe ER is a major health concern for any athlete. A challenge to the early recognition of ER for the athlete and clinician is that signs and symptoms of it during the triggering bout of intense exercise can be few and subtle. But there are clues that coaches and athletic trainers can watch for outlined by case examples involving team outbreaks. Importantly, signs and symptoms of severe ER can begin in the first few hours after the triggering exercise bout and tend to peak over the subsequent two days.

SEVERE EXERTIONAL RHABDOMYOLYSIS

The clinical diagnosis of severe exertional rhabdomyolysis soon after an overly intense exercise bout is a physician's judgment call that hinges in part on the fol-

SERIAL POSTURES OF EXERTIONAL COLLAPSE



- Athletes in active recovery to early fatigue: continue rehydration, rest intervals, cooling and controlled breathing.
- Athletes who are showing signs of physical distress should be allowed to set their own pace while conditioning. Instruct athletes to rest while experiencing symptoms as they may soon feel better and be ready to continue. If symptoms reoccur or progress, the athlete should stop exercise and be assessed by a health care provider.
- Athletes unable to stand on their own from a kneeling position or having trouble walking normally during recovery should raise suspicion of distress, and additional medical intervention should be considered.

lowing features that help separate severe ER from the overlapping but milder DOMS:

- Muscle pain more severe and sustained than expected.
- Swelling of muscles and adjacent soft tissues.
- Weak muscles, especially in hip or shoulder girdle.
- Limited active and passive range of motion.
- Brown ("Coca-Cola") urine from myoglobin.

The clinical diagnosis of ER is commonly confirmed by documenting an elevated serum creatine kinase level. This raises the question of how to interpret CK levels. Several variables must be considered.

First, men tend to have CK levels about twice as high as women, and African-American men tend to have CK levels about twice as high as white men. These gender and ethnic differences in baseline CK level may in part reflect differences in muscle mass, muscle-fiber type and habits of physical activity.

Second, athletes tend to have CK levels higher than nonathletes, and CK can vary by sport and stage of training. For example, in a study of 12 Division I football players during two-a-days, mean CK was normal at the start (about 200 U/L), but by Day 4 had risen 25-fold (to about 5,000 U/L). Despite this sharp rise in CK level, all 12 players practiced football throughout the 10-day study without complications.

Third, there can be a wide range of serum CK elevation among exercising athletes. This was seen in the above football study, and is even more striking in laboratory studies that control the type and duration of exercise. For example, when college men perform the same bout of elbow-flexor exercise, the peak CK response can vary 100-fold, from about 250 U/L to about 25,000 U/L.

Fourth, the rate of rise in CK levels can vary in developing exertional rhabdomyolysis cases. This rate can be slow, over three to four days to a peak CK, as in the elbow-flexor exercise studies; or it can be rapid, as in exertional collapse in athletes or soldiers with sickle cell trait (SCT), where serum CK can reach 100,000 U/L in a few hours and exceed 1 million U/L by the next day.

Given these variables, what level of CK confirms ER that requires action? The U.S. military advises the following action for severe muscle pain if the CK is five times the upper limit of normal (ULN): oral hydration, relative rest and re-evaluation the next day. If the CK is greater than 5,000 U/L, the military advises referral to a medical treatment facility for full clinical and laboratory evaluation, intravenous hydration and possible hospital admission. These low CK values for clinical action cast a wide safety net but seem to conflict with research on ER in basic military training (BMT). In a recent study of 499 recruits during two weeks of BMT in hot and cool climates, none developed "clinically significant" ER (defined by muscle weakness, elevated CK, and myoglobin in serum or urine), although muscle pain and soreness were common, and nearly 90 percent of recruits had elevations in CK. At Day 7 of BMT, the range in CK levels was wide, from about 55 U/L to about 35,000 U/L; just more than 25 percent of the recruits had a CK greater than five times the ULN, and just more than 10 percent had a CK greater than 10 times the ULN.

The military researchers concluded that any ER in recruits in BMT is not "clinically significant" if there is no muscle weakness or swelling, no myoglobin in the urine,

CASE 1: FOOTBALL

Thirteen football players were hospitalized for ER following the first team workout after their three-week winter break. The workout was characterized as some upper body work and sled pushing with 100 timed back squats at 50 percent top weight for one repetition. The institution's investigative committee concluded that the back squats were the likely cause of the ER and said that coaches told the players that the workout would be a tough challenge that "would demonstrate who wanted to be on the team." Within the first two days, players reported with dark urine and severe leg pain, with complaints of difficulty putting on shoes or climbing stairs. These symptoms continued for days until ER was diagnosed in the players. All athletes went home over the next few days as symptoms subsided, and all but one returned to play within the next few weeks.

Another football team outbreak of ER occurred in January out-of-season training at a Division I institution. It was similar in some ways to the previously mentioned outbreak, occurring soon after a winter break transition period and including an intense back-squat drill. Up to five players developed ER, and one player had bilateral fasciotomy for thigh compartment syndrome.

no laboratory evidence of acute kidney injury (AKI) or electrolyte imbalance, and if the CK is less than 50 times the ULN. If this can be translated to sports medicine, given that the ULN for CK tends to be about 200-250 U/L, then any ER in an athlete is not necessarily "clinically significant" if the serum CK is less than 10,000-12,500 U/L. This may be true, but it casts too narrow a safety net, because in fulminant ER from exertional collapse in the athlete with sickle cell trait, for example, the initial CK in the emergency room can be less than 1,000 U/L, but the CK can increase exponentially in a few hours to 50,000-100,000 U/L. The bottom line is that wise and timely clinical decisions in athletes with ER are not easy and require informed physician judgment. Some lessons can be learned from recent NCAA team outbreaks of ER.

LESSONS FROM TEAM OUTBREAKS: 10 FACTORS THAT CAN INCREASE THE RISK OF EXERTIONAL RHABDOMYOLYSIS

1. Athletes who try the hardest — give it their all to meet the demands of the coach (externally driven) or are considered the hardest workers (internally driven).

2. Workouts not part of a periodized, progressive performance enhancement program (e.g., workouts not part of the annual plan).

3. Novel workouts or exercises immediately following a transitional period (winter/spring break).

4. Irrationally intense workouts intended to punish or intimidate a team for perceived underperformance, or to foster discipline and "toughness."

5. Performing exercise to muscle failure during the eccentric phase of exercise such as repetitive squats (e.g. the downward motion of squats) and then pushed beyond to continue.

6. Focusing a novel intense drill/exercise on one muscle with overload and fast repetitions to failure.

7. Increasing the number of exercise sets and reducing the time needed to finish (e.g., 100 squats, timed runs, station drills).

8. Increasing the amount of weight lifted as a percentage of body weight.

9. Trying to "condition" athletes into shape in a day or even over several days, especially with novel exercises or loads.

10. Conducting an unduly intense workout ad hoc after a game loss and/or perceived poor practice effort.

RISK FACTORS FOR ER

Exertional rhabdomyolysis in an NCAA team athlete is commonly linked to three conditions:

- Novel overexertion.
- Exertional heatstroke.
- Exertional collapse with complications in athletes with sickle cell trait.

Novel overexertion is the single most common cause of exertional rhabdomyolysis and is characterized as too much, too soon, and too fast. Team outbreaks of ER in NCAA athletes (refer to case examples) have similarities of irrationally intense workouts designed and conducted by coaches and/or strength and conditioning personnel.

Consistent factors in military service ER cases include low baseline fitness and repetitive eccentric exercises.

Eccentric exercise is when a muscle contracts as an external force tries to lengthen it. Examples include downhill running, squats, push-ups, sit-ups, pull-ups, chair dips, plyometrics and lowering weights. Even though almost every athletic workout has an eccentric component, ER often occurs when exertion is pushed beyond the point at which fatigue would normally compel an individual to stop, such as what can occur during group exercise under demanding supervision or peer pressure.

Exertional heatstroke (EHS) and ER share common risk factors such as history of prior heat illness, elevated environmental heat and humidity, dehydration, or the abuse of stimulants. ER can accompany EHS but is rarely if ever the vital problem. Deaths in EHS are from heat damage to vital organs; the victim dies with some ER, but not directly from ER. In contrast, sickle cell trait is a critical risk factor for ER as deaths have been attributed directly to a seemingly unrecoverable metabolic cascade of ER. How to approach both EHS and sickle cell trait are covered in separate guidelines elsewhere in this handbook.

Other risk factors for ER are either rare or would preclude top athleticism in the first place. These include a severe viral invasion of the muscles, gravely low blood potassium, or an inborn metabolic myopathy. Among the drugs considered risk factors for ER, special consideration should be given to stimulants and pre-workout supplements.

Novel overexertion is by far the most common cause of ER; with early diagnosis and proper therapy, this condition is benign. For example, a recent brief review reported nearly 400 cases of ER (absent EHS or SCT) from novel overexertion in soldiers, athletes or other young people. All were benign. In sharp contrast, both EHS and exertional sickling can be fatal. However, ER from novel overexertion can lead to mild AKI, and/or muscle compartment syndrome, which if not treated promptly can lead to long-term disability.

It is vital that all coaches, strength and conditioning personnel, and athletic trainers prevent ER from novel overexertion, recognize it early and activate their emergency action plan while notifying the team physician for full clinical and laboratory assessment, rehydration to ensure good urine output, pain relief, and monitoring for acute compartment syndrome. After treatment for ER, the physician must assess the athlete for risk of recurrence, consider further testing, and decide on when, if and under what conditions the athlete can safely return to play. A three-phase return-to-play guideline is recommended for athletes deemed as low risk for recurrence (refer to O'Conner et al reference). Athletes with recurrent rhabdomyolysis or cramping should seek additional testing by a specialist.

CASE 2: FOOTBALL SUMMER CAMP

A team outbreak of ER occurred in a small high school. A new football coach introduced an intense, novel, triceps-focused drill, alternating chair dips and push-ups on the first day of a summer camp. This reported workout involved five consecutive bouts, with fast repetitions, competitive motivation and no rest periods. Over the next few days, half of the team members went to the hospital for ER, 12 were admitted, and three had surgery (fasciotomy) to release triceps muscle compartments under high pressure from the ER (compartment syndrome). The risk of ER was higher in the harder working players.

CASE 3: SWIMMING

On a Day 1 practice after a summer break, the 41 members of a Division I swim team met a new coach and a new, grueling drill before their usual two hours of swimming. The drill was as many push-ups as possible in a minute, followed by as many body squats as possible in a minute, with the sequence repeated for 10 minutes. Other upper body workouts continued on Days 2-3, along with swim practice. Beginning on Day 2 and continuing on subsequent days, several swimmers, men and women, presented with severe pain, swelling, and limited motion of the triceps and pectoral muscles, and dark urine. All were hospitalized. All went home in three to six days as their symptoms subsided, and all returned to college swimming.

TIPS FOR PREVENTION AND EARLY RECOGNITION OF ER FROM NOVEL OVEREXERTION

- Moderation. Avoid too much, too soon, too fast. Educate everyone in the athletics department conducting exercise sessions – especially the

CASE 4: LACROSSE

On Day 1, after a three-month hiatus, a women's NCAA lacrosse team did three sets of 20 biceps curls with weights. The next day, several of them had painful, stiff, swollen biceps muscles. They gradually improved and by three weeks were back to full participation. They all completed the competitive season.

CASE 5: LACROSSE

An outbreak of ER in NCAA women's lacrosse occurred after a team lost its first game of the season. The student-athletes' next workout was reported to focus on the upper body and was new to them, with limited recovery on subsequent days. Exercises included many pull-ups, chin-ups and dips. Subsequent complaints included arms feeling "prickly, tingly" and being shaky and stiff; difficulty raising arms overhead to catch balls; and difficulty driving because of sore and stiff arms. Athletes experienced dark urine and were hospitalized for ER three days after the initial workout. All went home over the next three to five days, and all but one soon returned to lacrosse. The athlete who did the most pull-ups had the worst and longest course of ER.

coaches/strength and conditioning personnel – on all aspects of exertional rhabdomyolysis from novel overexertion and the additive effect of all physical exertion on the athlete.

- Strength and conditioning workouts are the highest risk rather than sport skills, drills or competitions. Group workouts in general can be risky if they drive all athletes at the same pace and intensity. Sometimes the athlete who tries the hardest to meet the demands of his/her coach suffers the worst ER.
- Avoid high-intensity conditioning workouts after vacations or seasonal breaks or on returning from injury. Athletes cannot be "conditioned into shape" in a day.
- The design of a workout should reflect a collaborative effort between a strength and conditioning coach and medical staff. However, athlete safety assumes the individual conducting the exercise sessions takes reasonable actions to allow recovery and prevent exertional collapse.
- All training programs should start slowly, build gradually, include adequate rest, and allow for individual differences. Avoid reckless intensity in an effort to make everyone bigger, stronger and faster.
- Workouts are meant to improve fitness, skills and athletic performance. They should be rational, physiologic and sport-specific. Avoid the use of additive physical activity as punishment or for building toughness.
- Athlete's physical readiness changes day to day. Encourage athletes to set their own pace or at least communicate with them frequently to learn if undue symptoms are developing. As the workout ends, watch them closely and ask them how they feel. Athletes who are showing signs of physical distress should be allowed to set their own pace while conditioning.
- Fluids should be regularly available, and frequent breaks should be scheduled.
- Set the right tone. Workouts are to enhance performance, not to punish or intimidate. Never use exercise as a form of punishment in an athlete experiencing physical distress. Athletes should feel free to report any symptom at any time and obtain immediate help. Athletic trainers should be authorized to step in to provide care for an athlete in distress at any time without retribution.
- Encourage athletes to read their body, cut back or stop if they start to struggle, and report immediately any concerning symptom, especially any peculiar, atypical or undue muscle discomfort, pain, swelling, stiffness or weakness.
- Post a urine-color chart in the locker room, athletic training room, and near urinals and restroom stalls. Athletes should report dark urine immediately.
- If one athlete on a team develops early signs or symptoms of possible ER, evaluate all members of the team who participated in the exercise session for ER.
- Design, file and practice an emergency action plan (EAP) for exertional heatstroke (EHS) and for exertional sickling in sickle cell trait (SCT). Coaches should be ready to intervene when athletes show signs of distress. Minutes count in these life-threatening emergencies. See the guidelines in this handbook on EAP, EHS and SCT.
- If you suspect that an athlete is developing ER from novel overexertion (absent EHS or SCT), the EAP should be activated, and the team physician should be promptly notified.

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