Exercise Associated Hyponatremia

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CME ACCREDITED UPDATES IN MEDICINE ELEARNING SERIES

COURSE NAME:
Medicine RSS eLearning Modules

CME eLEARNING ACTIVITY NAME:
Exercise Associated Hyponatremia

PROGRAM DESCRIPTION, EDUCATIONAL GOAL AND RATIONALE:
Evidence based guidelines are constantly changing and being updated for several core areas of Internal Medicine throughout the year. It is important for physicians to practice the most up-to-date standard of care in all specialties to promote patient health and well-being. Our series of lectures at the medicine regularly scheduled series promotes continuing education for the practicing internist and highlights important updates in medical practice in these core areas. Physicians in general practice often and do not have the time to keep themselves up-to-date with medical advances as they are busy seeing patients in the clinical setting. The Medicine Regularly Scheduled Series gives these physicians the opportunity to learn these advances in an academic setting.

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TARGET AUDIENCE:

Physician Partners and Premium Network
community-based providers

LEARNING OBJECTIVES:

- To define epidemiology.
- To identify the risk factors and pathogenesis of Exercise-Associated Hyponatremia.
- To understand the treatment and prevention.
- Learn about clinical features.
- To identify severe and symptomatic Hyponatremia.

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ESTIMATED TIME TO COMPLETE ACTIVITY:
90 minutes

ACKNOWLEDGEMENT OF COMMERCIAL SUPPORT:
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FACULTY DISCLOSURES:

Drs. Sandy Balwan, Mitchell Rosner, George Boutis, John Raimo and Sean LaVine have nothing to disclose.

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Case Series

- In 1990, the US military adopted new hydration guidelines aimed at reducing the risk of heat illness in military personnel.
- Required that US army personnel drink 1.8 liters of fluid every hour that they were exposed to temperatures in excess of 30^{o}C.

- Military Medicine 1990; 164: 502-8

Case Series (cont'd)

- At Fort Benning, Georgia:
- Between 1990 and 1996, 40 cases of severe hyponatremia and 6 fatalities reported
- Led to US military changing fluid consumption guidelines to much lower levels.

Exercise-Associated Hyponatremia

- Epidemiology
- Risk Factors
- Pathogenesis
- Treatment
- Prevention

Exercise-Associated Hyponatremia

- Occurrence of hyponatremia in individuals engaged in prolonged physical activity/endurance events such as marathons, triathlons, and ultradistance races
- Defined by serum [Na+] below the normal reference range of lab performing the test; usually [Na+] of less than 135 mmol/L
- Can occur during or after physical activity

Hew-Butler et al. Clin J Sport Med. 2005;15(4):208-213.

Epidemiology

- First described in Durban, South Africa in 1981
- No reports of EAH before 1981 when athletes were advised to avoid drinking fluids during exercise; rather athletes developed hypernatremia during exercise secondary to dehydration
- Since then, athletes have been generally advised to consume as much fluid as possible during exercise
- In 1985, T. D. Noakes et al reported severe hyponatremia in 4 athletes engaging in endurance events longer than 7 hours
- 2 physicians in 1985 reported their own case histories in JAMA
- Occurs in any endurance activity

Noakes et al. Med Sci Sports Exerc 1985; 17: 370-375

Incidence

- 2002 Boston Marathon: 13% of a sample of 488 runners had post-race hyponatremia and 0.6% had serum sodium values less than 120 mmol/L. (up to 60 runners in the Boston Marathon)
- Other studies have given incidence rates of 16-29%.
- While majority of these athletes are asymptomatic, some sustain life-threatening manifestations such as cerebral edema, non-cardiogenic pulmonary edema and seizures.

- At least 30 reported deaths due to hyponatremia- although database is very limited

- Almond et al. NEJM 2005; 352: 1550-56
- Davis et al. J Emerg Med 2001; 21: 47-57

Risk Factors

- Major risk factor is overhydration:
  - Supported by historical review of cases
  - Several studies documenting that fluid intake greater than 3 liters (marathons), post-race weight greater than pre-race weight and self-reported water loading are all associated with the development of hyponatremia

Speedy et al Emerg Med 2004; 13:17-27

Too much water!

Bad advice!

NATIONAL POST – John Stanton

June 1, 2011

Getting enough water is still the key hydration issue

Recent media reports have made the issue of fluids and hydration very confusing, which is too bad because it is actually a very straightforward issue.

During exercise, athletes should start drinking early and at regular intervals in an attempt to consume fluids at a rate sufficient to replace all the water lost through sweating (i.e., body weight loss), or consume the maximum amount that can be tolerated.

More Interesting Advice

Changes in sodium associated with weight changes

- Studied in 2135 endurance athletes:

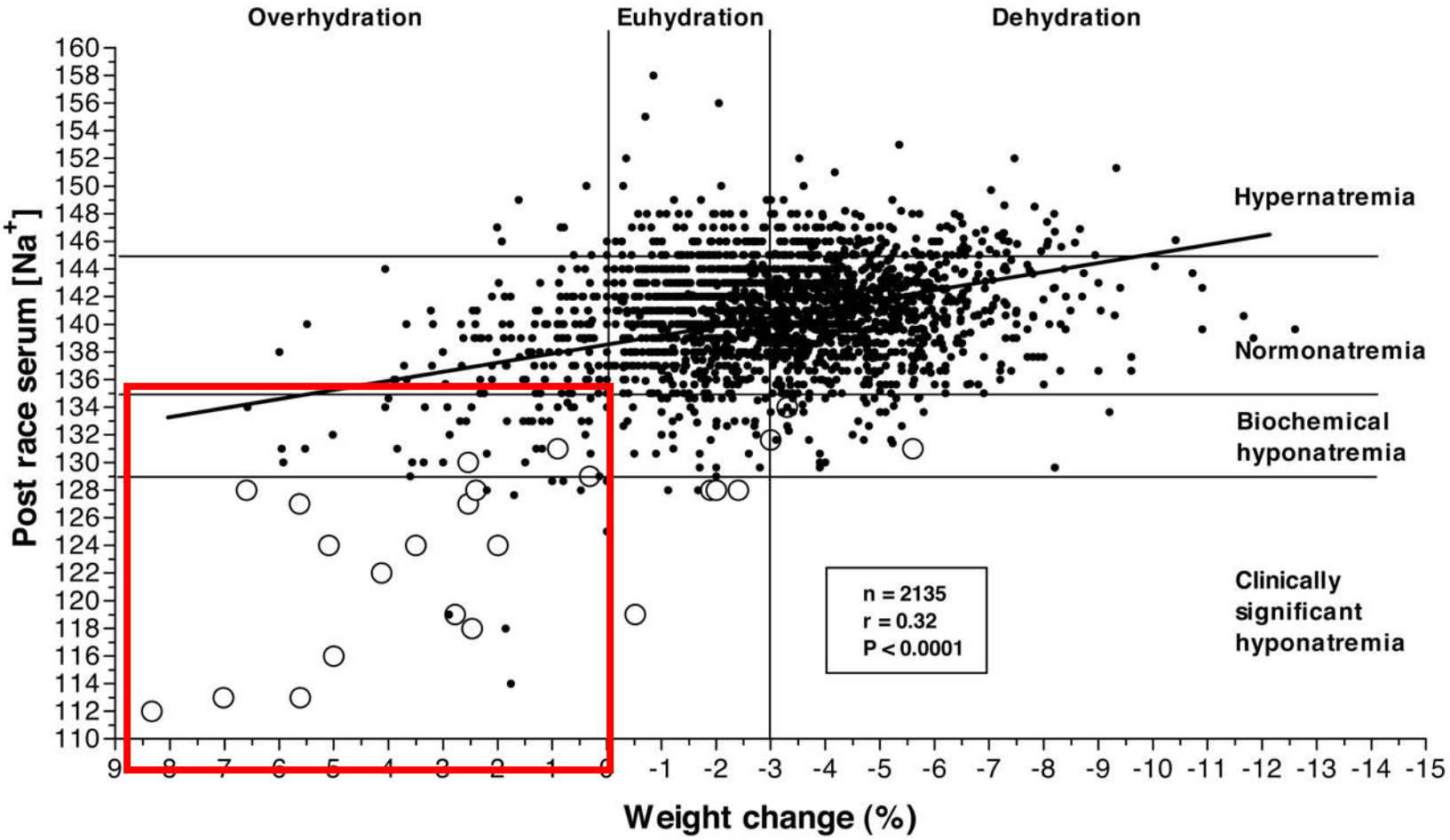
WEIGHT GAIN	SERUM SODIUM
+++	136.1 +/- 6.4
No change	140.5 +/- 3.7
---	141.1 +/- 3.7

Athletes who gained > 4% of their body weight during exercise had a 45% probability of developing hyponatremia.

However, 70% of those who gain weight during exercise do not develop hyponatremia- other factors must be important

Noakes TD, Sharwood K, Speedy D, et al. Proc Natl Acad Sci 102: 18550-18555, 2005

Noakes et al



Noakes T D et al. PNAS 2005;102:18550-18555

Other risk factors

- No correlation with type of fluid ingested
  - Tonicity of sports drinks is 20-30 mmol/L
  - Sports drinks are not protective

Carbohydrate (g/L)	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)	Osmolality (mOsm/L)
62	23	3	14	349

Rosner, MH et al. Clin J Am Soc Nephrol.

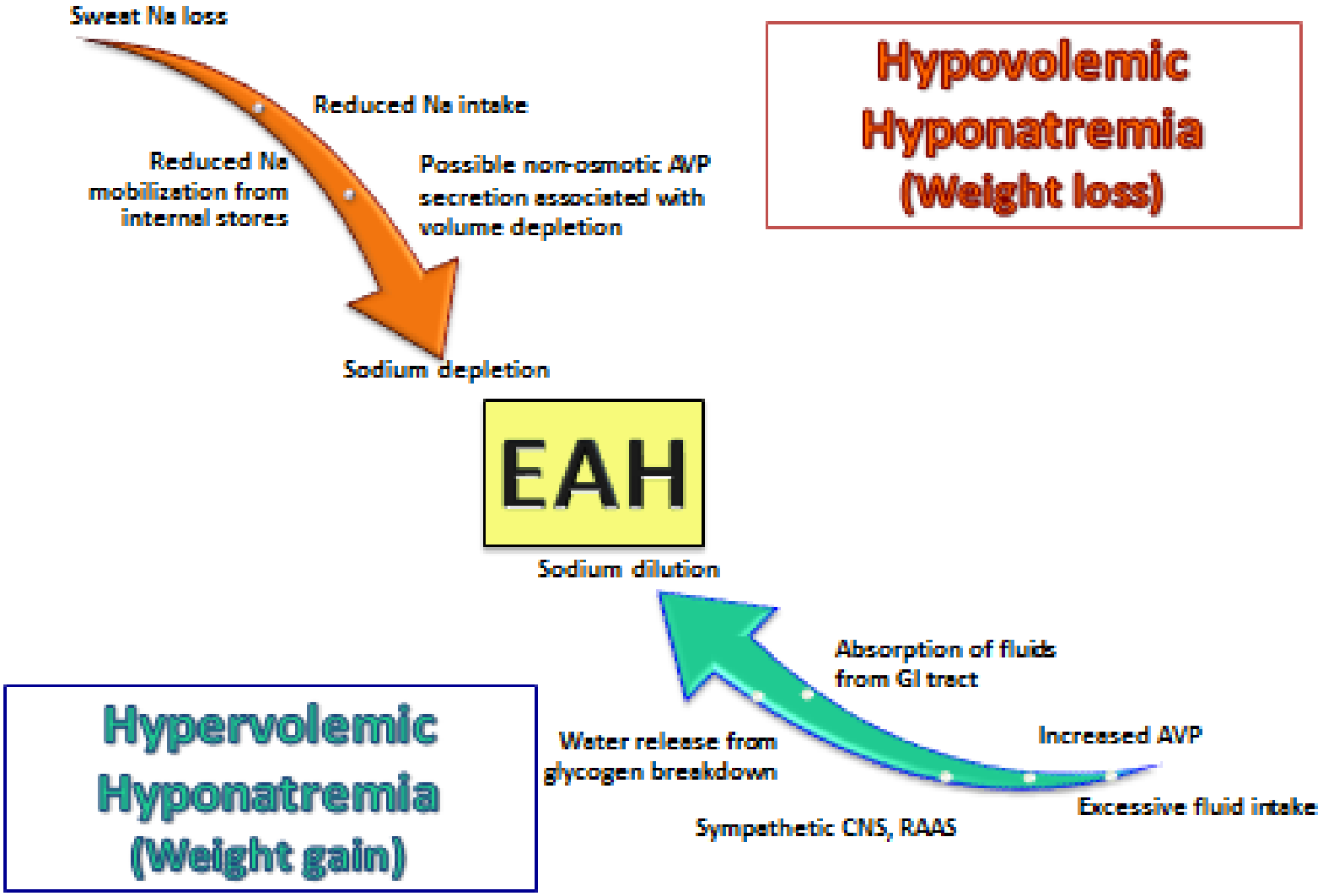
Risk Factors

- Gender: Females much more likely to develop hyponatremia (at least 3x more common) in some studies
  - More susceptible to effects of hyponatremia
  - > 80% of all brain damage associated with hyponatremia occurs in women with an odds ratio of 28:1
  - ? Related to effects of estrogen on Na-K-ATPase

Rosner, MH et al. Clin J Am Soc Nephrol.

Pathogenesis

- Normally, renal and hormonal systems maintain the plasma osmolality within tight limits.
- Hyponatremia reflects some defect in this control mechanism or water ingestion at a level that overwhelms excretory capacity of the kidney.
- In EAH: defects in multiple systems are contributory.


Sweat Na loss
Reduced Na intake
Reduced Na mobilization from internal stores
Possible non-osmotic AVP secretion associated with volume depletion
Sodium depletion
Hypovolemic Hyponatremia (Weight loss)
EAH
Sodium dilution
Absorption of fluids from GI tract
Increased AVP
Excessive fluid intake
Sympathetic CNS, RAAS
Water release from glycogen breakdown
Hypervolemic Hyponatremia (Weight gain)

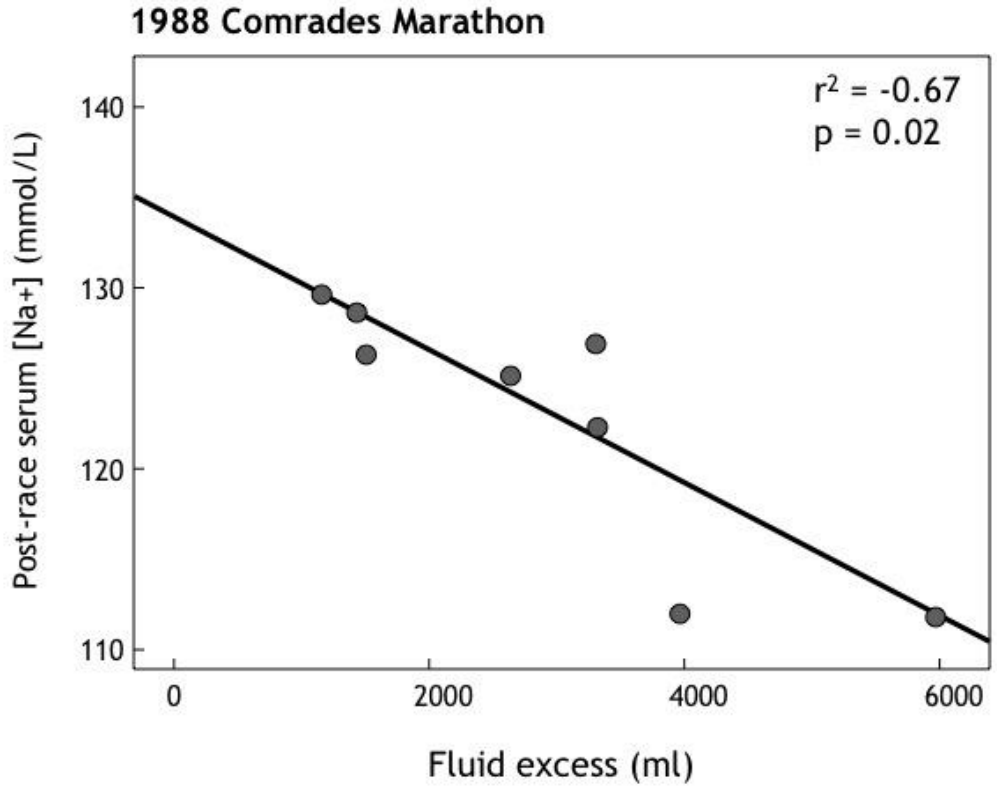
Pathogenesis

- In the majority of athletes with EAH, there is an increase in total body water relative to that of total body sodium.
- Occurs through ingestion of hypotonic fluids in excess of sweat, urine and insensible losses.
- Noakes et al described a linear relationship (with a negative slope) between serum sodium and degree of weight change

Excessive fluid consumption

- Conditioned behavior based upon recommendations/ads stressing the importance of drinking fluids
- Occasionally, may be associated with attempts to dilute the urine to escape detection of banned substances

Over-Hydration Predicts Hyponatremia



Irving RA et al. JAP 70; 342-348, 1991

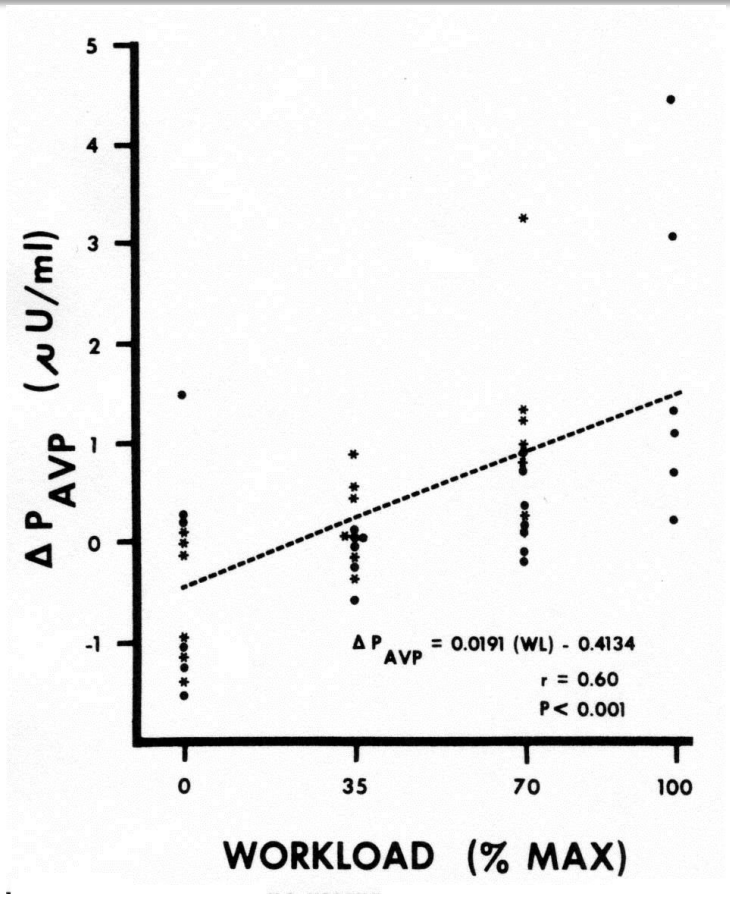
Other factors

- Hyponatremia does not develop in the majority of those who overhydrate
- The maximum water excretory capacity of the kidney is 750 to 1500 ml/hour thus most athletes should be able to consume fluids in excess of 1500 ml/hour.
- Points to the fact that there are concomitant defects in:
  - Renal water excretion
  - Sodium losses
  - Failure to mobilize exchangeable sodium stores

Vasopressin

- The bulk of evidence supports inappropriate AVP stimulation in some athletes.
- Supported by finding of inappropriately high Uosm
- AVP release may be stimulated by:
  - Intense exercise
  - Pain
  - Nausea
  - Hypotension
  - Heat exposure
  - ?Volume depletion (level required to release AVP is in excess of 7-8% of volume loss)

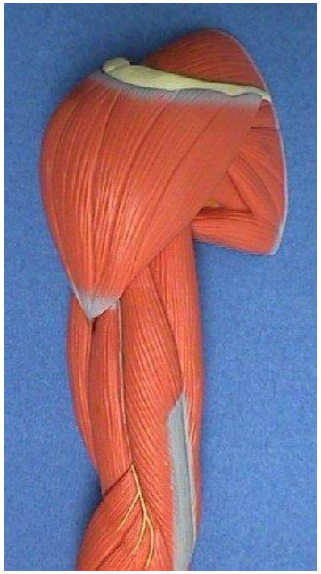
AVP Secretion and Exercise



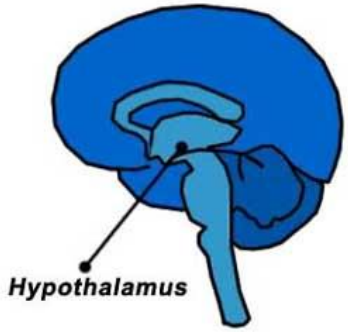
Wade & Claybaugh
J Appl Physiol
49:930-936, 1980

Hypothesis- AVP release

EXERCISE



Release of inflammatory cytokines (IL-6)



Response modulated by:
-Gender -
snps in promotor region]

VASOPRESSIN

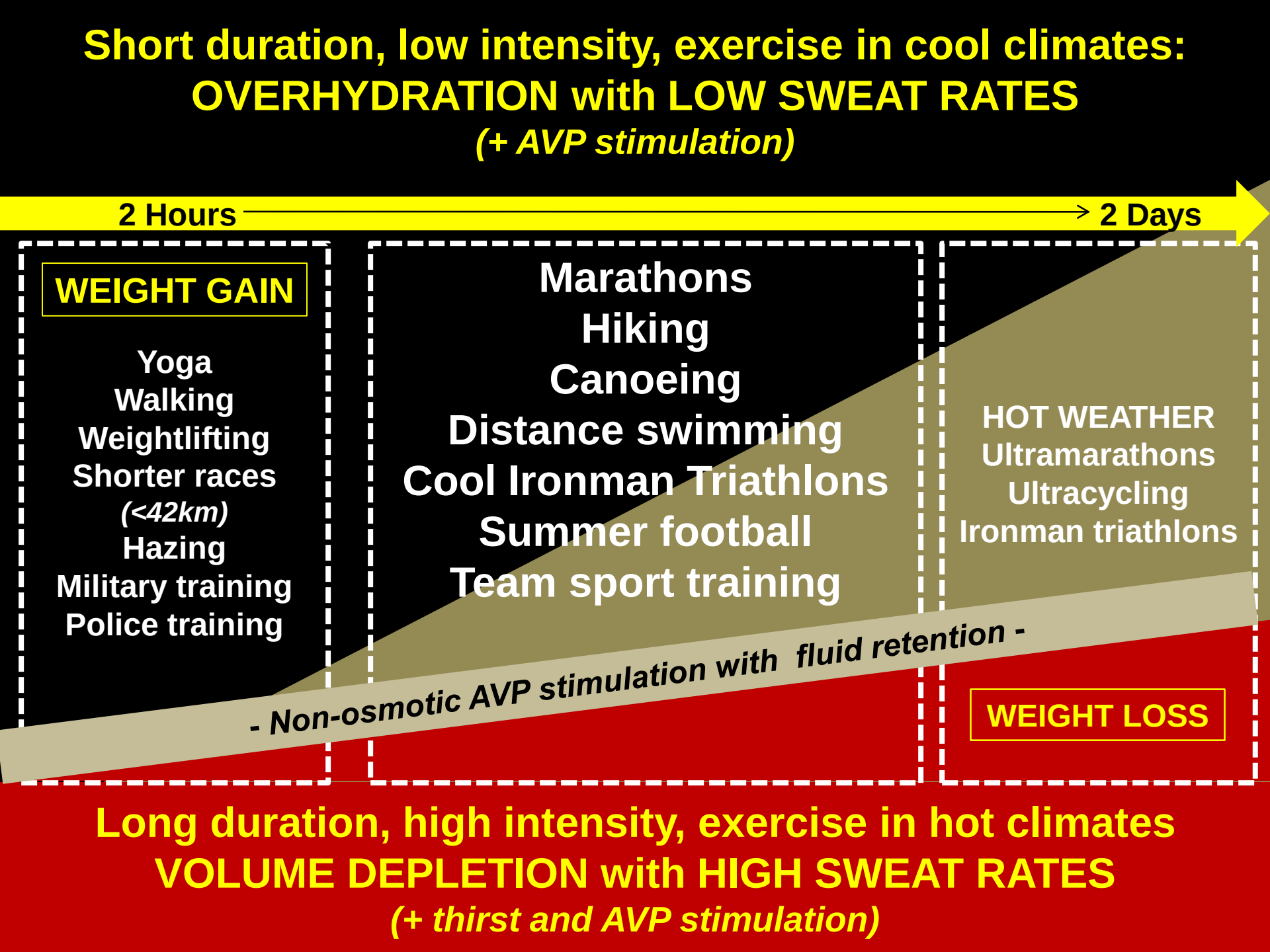
Mastorakos et al. J Clin Endocrinol Metab 1994; 79: 934-9

Sodium Loss

- Concentration of sodium in sweat varies from 15 to 65 meq/L
- Volumes range from 250 ml to 2L/hour
- It would seem that loss of hypotonic fluid would protect against hyponatremia
- However, these losses are replaced by more hypotonic fluids.
- At the extremes, some athletes may lose enough sodium in sweat to cause a substantial sodium deficit and contribute to hyponatremia

Smith HR, et al. Br Med J 1995; 310: 579-580

Weschler LB. Sports Med 2005; 35: 899-922


Short duration, low intensity, exercise in cool climates:
OVERHYDRATION with LOW SWEAT RATES
(+ AVP stimulation)
2 Hours
2 Days
WEIGHT GAIN
Yoga
Walking
Weightlifting
Shorter races
(<42km)
Hazing
Military training
Police training
Marathons
Hiking
Canoeing
Distance swimming
Cool Ironman Triathlons
Summer football
Team sport training
HOT WEATHER
Ultramarathons
Ultracycling
Ironman triathlons
- Non-osmotic AVP stimulation with fluid retention -
WEIGHT LOSS
Long duration, high intensity, exercise in hot climates
VOLUME DEPLETION with HIGH SWEAT RATES
(+ thirst and AVP stimulation)

Clinical Features

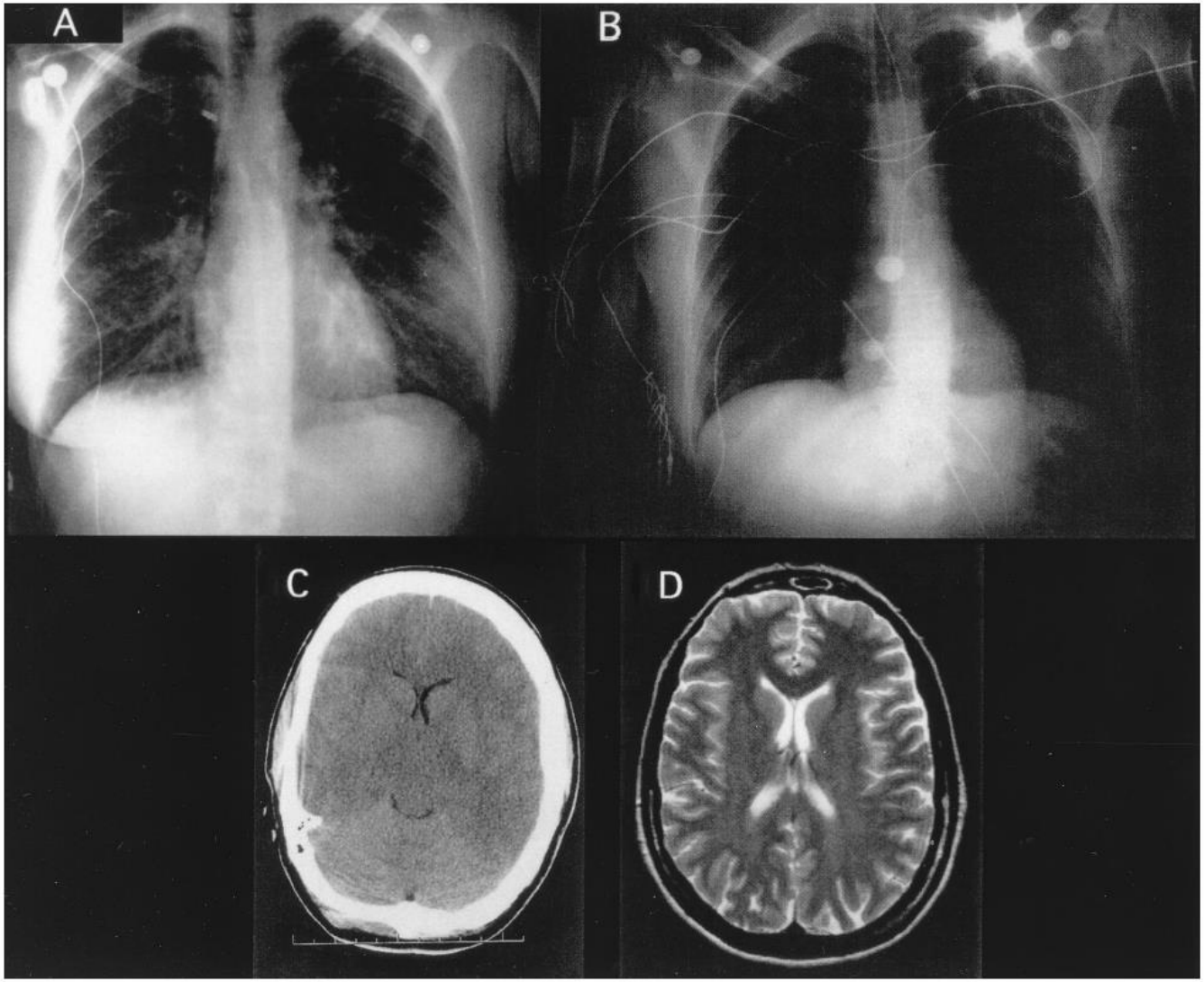
- Range from no or minimal symptoms to severe encephalopathy, respiratory distress and death.
- Related to both rate and the extent of the drop in extracellular tonicity
- In those athletes with sodium < 126 mmol/L there is a higher likelihood of severe manifestations

Pulmonary Edema

- Case series by Ayus et al.: 7 healthy marathon runners with history of NSAID use who collapsed after competing in marathon, hospitalized with pulmonary edema
- All presented with nausea, emesis, obtundation, mean [Na+] 121 mmol/L, O2 sat <70%
- EKG and Echo normal for all patients
- CXR showed pulmonary edema
- CKMB and troponin not elevated
- PCWP not elevated
- CT head showed cerebral edema

Ayus et al. Ann Intern Med. 2000;132:711-714.

Pulmonary Edema



Clinical Features

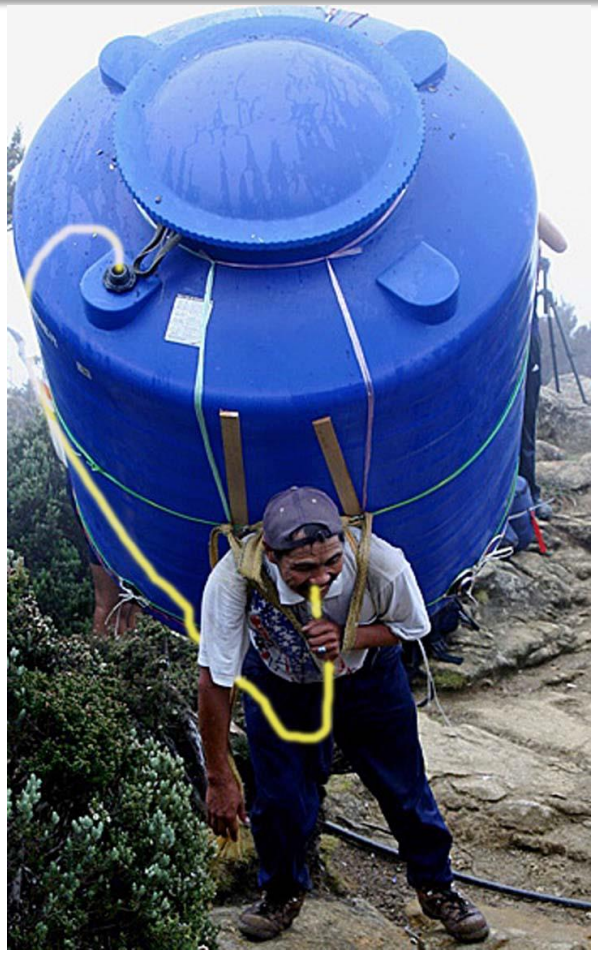
- Difficulty is that these symptoms are non-specific and do not give a clue to the underlying hyponatremia and thus can easily be mis-treated.
- Recommendations have thus been made to have on-site rapid determination of serum sodium levels in those athletes presenting with symptoms compatible with hyponatremia

Possible Signs & Symptoms

	Hyponatremia	Heat Illness or Dehydration
General		
Fatigue/weakness	Possible	Possible
Increased thirst	Possible	Likely
Temperature		
Normal	Possible	Possible
Elevated	Possible	Possible
Cardiovascular		
Tachycardia	Possible	Likely
Orthostasis	Possible	Likely
Gastrointestinal		
Nausea/vomiting	Possible	Possible
Neurological		
Headache/dizziness	Possible	Possible
Blurred vision	Possible	Possible
Confusion/disorientation	Possible	Possible
Obtundation	Possible	Possible
Seizure	Possible	Not likely
Coma	Possible	Possible
Urine Output		
Oliguria	Possible	Likely
Diuresis	Possible	Not present
Respiratory		
Distress	Possible	Not present

Prevention

Not recommended



Prevention

- Because of the primary role of over consumption of fluids efforts focused on limiting fluid intake:
  - Drink according to thirst and no more than 400 to 800 ml/hour
  - USATF recommends serial measurements of weights during and after racing with goal of maintaining weight or even finishing with a slightly lower weight.

www.usatf.org/groups/coaches/library/hydration

Sports Beverages

- Sports beverages do not prevent development of hyponatremia
- May lessen risk slightly as compared to water
- ACSM recommends intake of 0.5 to 0.7 g of sodium/L water to replace usual sodium losses

The IAAF Technical Quarterly 2002; 17: 15-24

Therapy

- Requires rapid and correct diagnosis (ideally, with on-site measurement of sodium)
- Three consensus panels convened to examine the proper course of therapy.

Hew-Butler et al. Clin L Sports Med 2005; 15: 208-215

Mild Hyponatremia

- Levels of Na+ 130-135 mmol/L
- Usually asymptomatic or mildly symptomatic
- Observation
- Fluid Restriction until diuresis occurs.
- Avoid aggressive administration of IV 0.9% saline as this runs the risk of lowering serum sodium concentration if AVP levels are high.
- Serum sodium may continue to fall as water is reabsorbed from the GI tract.

Severe/Symptomatic Hyponatremia

- Serum [Na+] , 120 mmol/L or symptoms requires the administration of hypertonic 3% saline.
  - All EAH is acute- hyponatremia can be safely corrected rapidly
  - No cases of osmotic demyelination reported

Severe Hyponatremia

- In the report by Ayus et al:
- 6 of the 7 patients were treated with 3% saline
- Increase in [Na+] by 10 mmol/L in 12 hours
- Pulmonary and cerebral edema resolved as [Na+] increased
- One patient had unsuspected EAHE, not treated with hypertonic saline; died of cardiopulmonary arrest from brainstem herniation
- All 6 patients treated with hypertonic saline recovered and were well after 1 year follow up
- Although counterintuitive, 3% saline should be used if pulmonary edema and hyponatremia are present

Ayus et al. Ann Intern Med. 2000;132:711-714.

Hypertonic Saline

- In the field:
  - 100 ml of 3% saline
  - Raises serum sodium 2-3 mmol/L
  - Decreases AVP, enhances intravascular volume (equivalent to 1200 ml of 0.9% saline)

Hospital-based therapy of EAH

- Continued use of 3% saline recommended
- Usually at a rate of 1-2 ml/min/kg with close monitoring of both serum and urine electrolytes
- In cases of severe antidiuresis, rate may have to be increased to 3-4 ml/min/kg
- In cases of pulmonary edema, use of 3% saline is imperative.

Acute EAH confirmed by blood test

SYMPTOMS	TREATMENT
Dizziness, lightheaded, fatigue bloating, puffiness, mild nausea, or other non-specific symptoms	Fluid restriction or oral hypertonic solutions *(4 bullion cubes/125mL water or 100mL 3% NaCl)* until onset of urination
Headache, vomiting, confusion, agitation, altered mental status obtundation, dyspnea phantom running	IV bolus 100mL 3% NaCl *(or hypertonic equivalent)* repeated at 10 minute intervals until clinical improvement
Seizures, coma, decorticate posturing, mydriasis	Urgent IV hypertonic saline bolus *(100mL 3% NaCl minimum)* until clinical improvement *(larger boluses may be necessary)*

Summary

- EAH is a preventable complication of endurance athletics
- EAH is associated with a high degree of morbidity and mortality
- The pathophysiology of EAH has brought to light new concepts in the understanding of hyponatremia
- Proper therapy utilizes 3% saline
- Prevention through sensible hydration

My Collaborators

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Tom Myers

Greg Glassman

Tim Noakes