

Spectrum of Exercise-Associated Hyponatremia

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June 24, 2014

MEDICINE & SCIENCE IN
ULTRA-ENDURANCE SPORTS™



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DISCLOSURE

Highest incidences of EAH have been reported in Northern California ultradistance races

51% Lebus D et al CJSM 2010
30% Rogers IR et al CJSM 2011



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Pathophysiology

Diagnosis

Treatment

Prevention

DEFINITION

Exercise-associated hyponatremia is the occurrence of hyponatremia in individuals engaged in prolonged physical activity and is defined by a serum or plasma sodium concentration below the normal reference range of the laboratory performing the test

155

HYPERNATREMIA

150

145

140

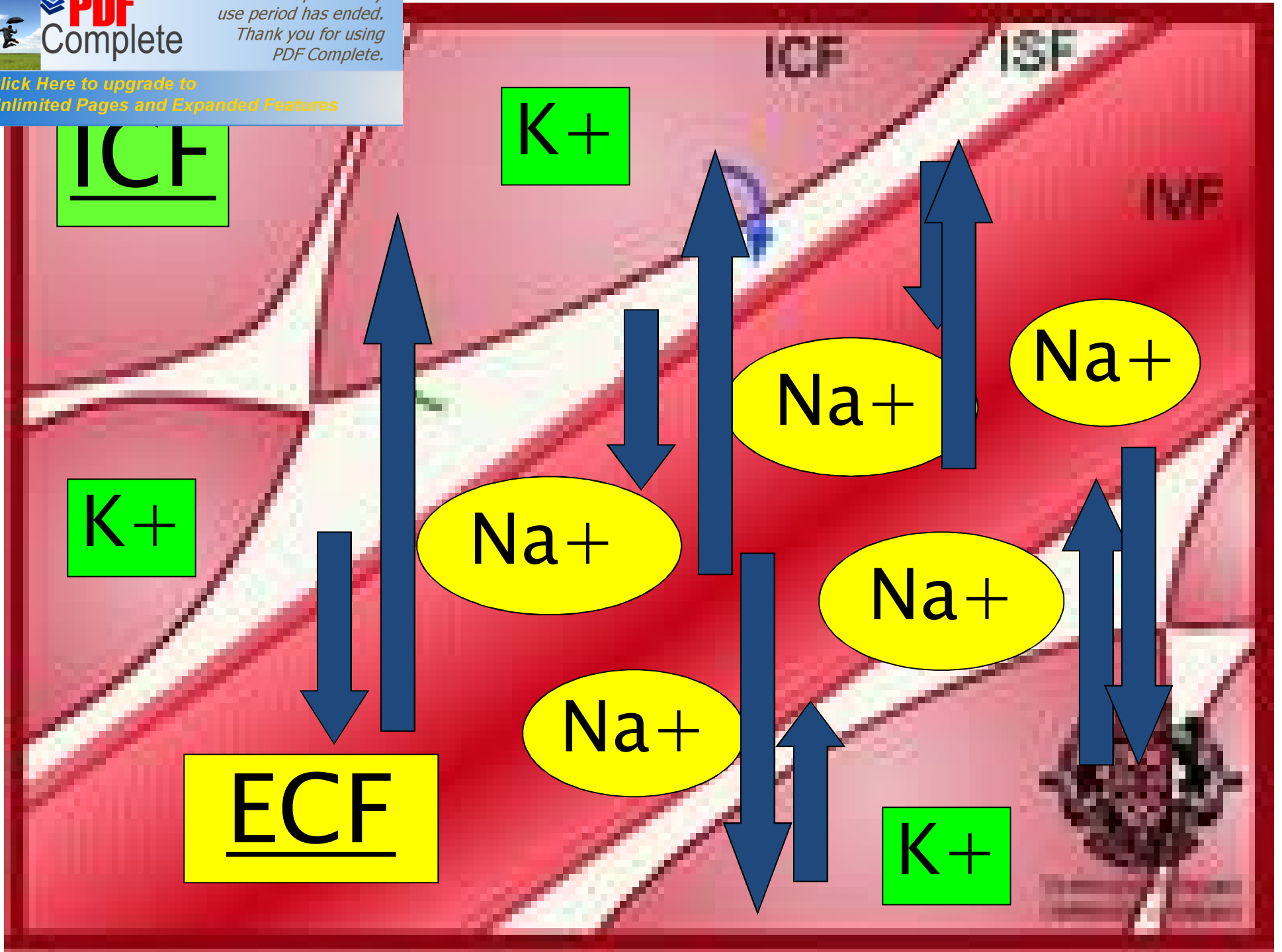
NORMONATREMIA

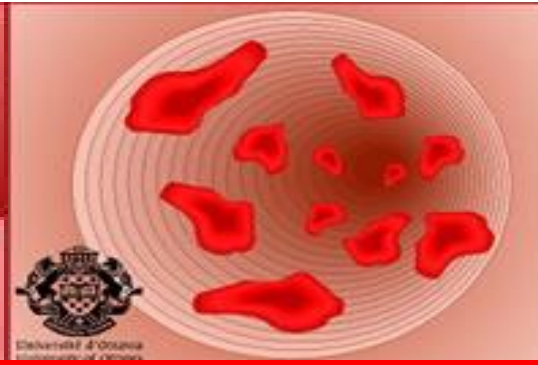
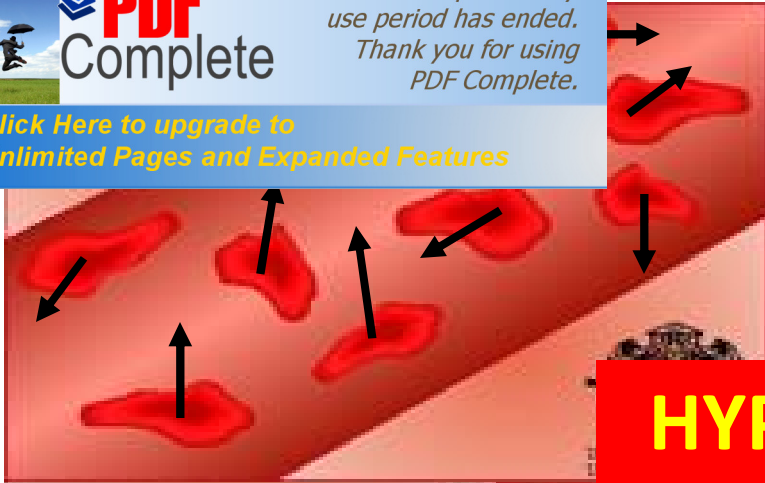
135

130

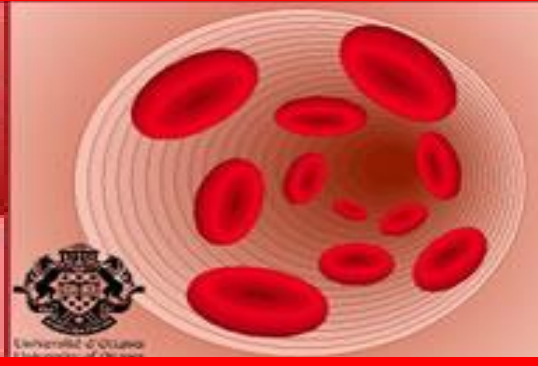
125

HYPONATREMIA

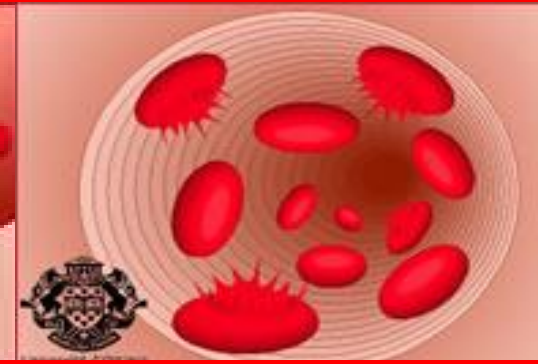
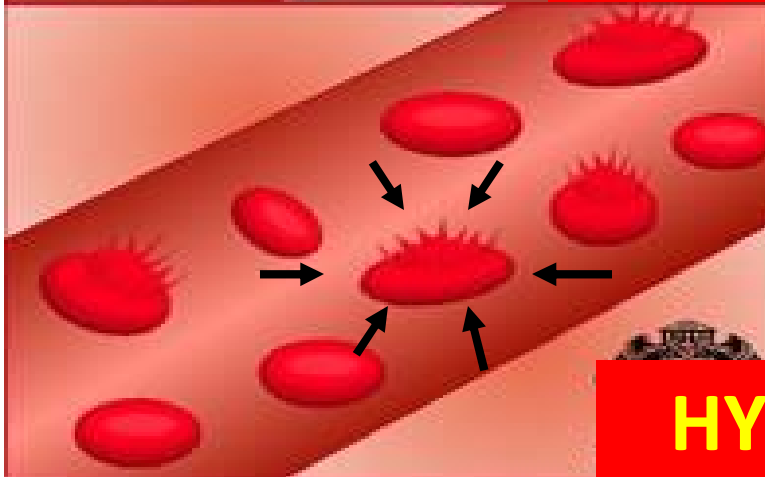




HYPERNATREMIA

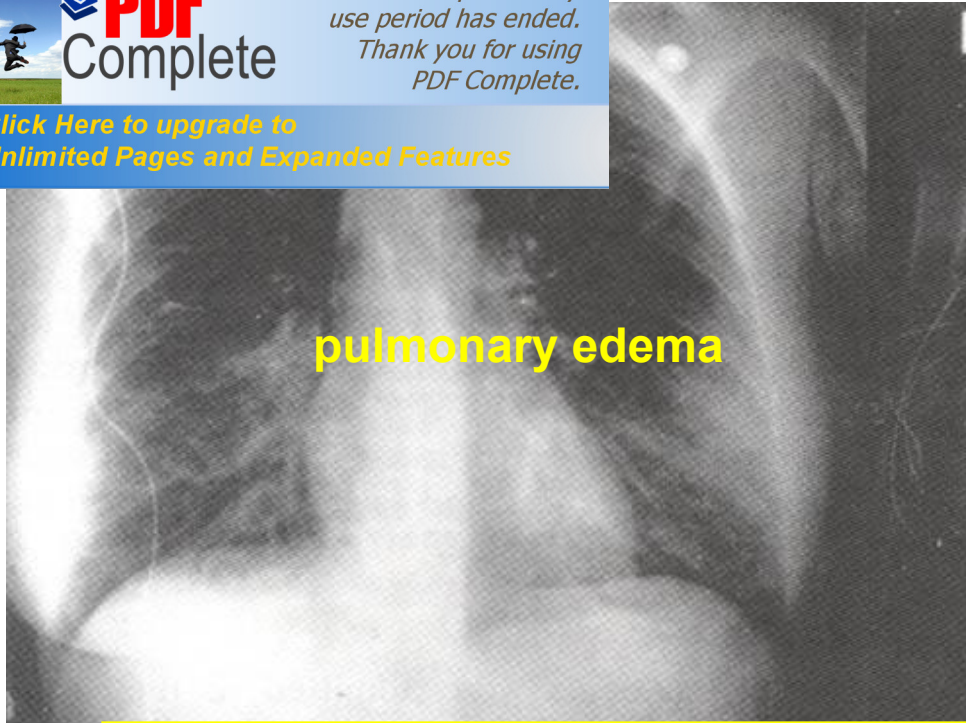


NORMONATREMIA



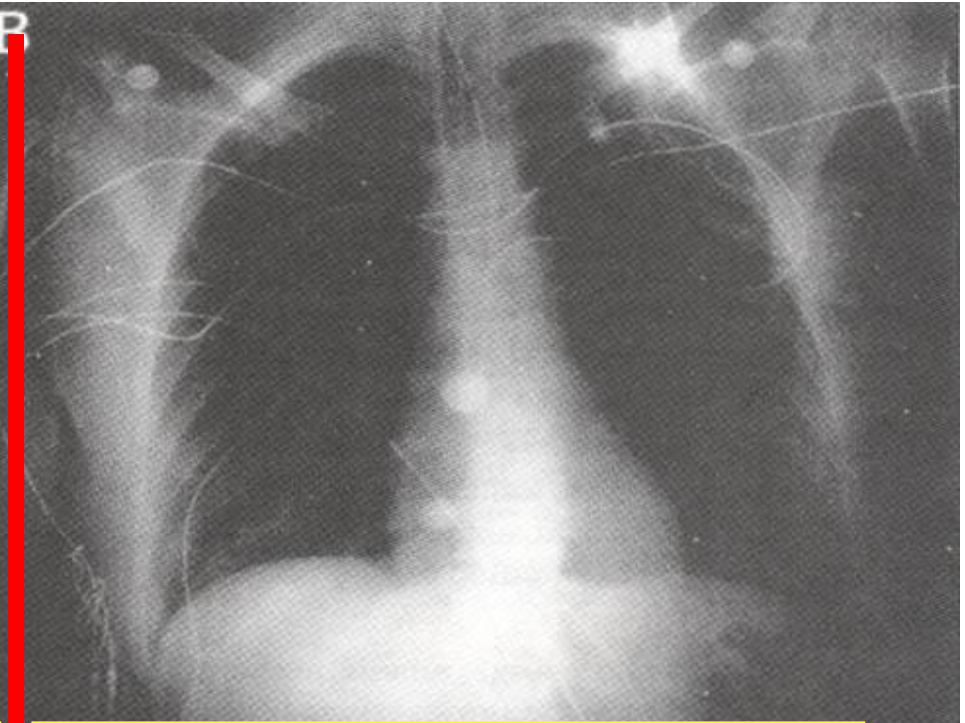
HYPONATREMIA



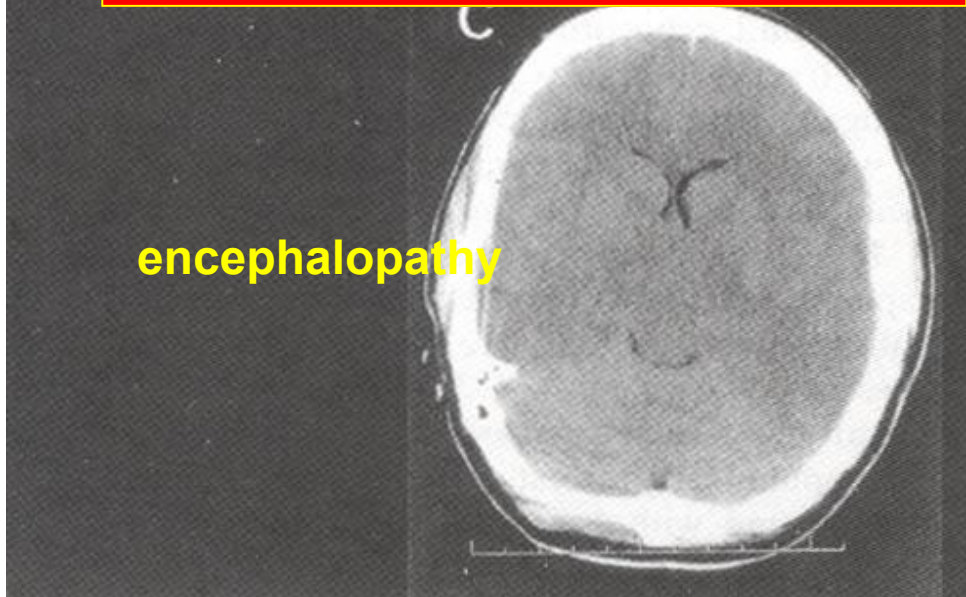


pulmonary edema

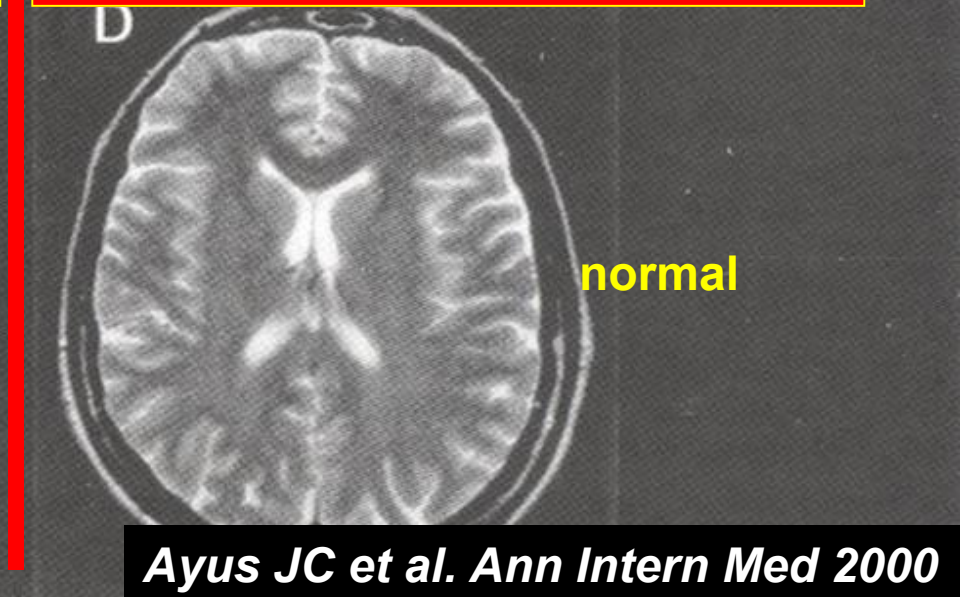
HYPONATREMIA



NORMONATREMIA



encephalopathy



normal

Hyponatremia can be caused by dilution or depletion

↑ Water
Fluid retention



↓ Sodium
Electrolyte losses



SPECTRUM



etiologic possibilities

“pure” water retention from SIADH

mixed solute loss and water retention

“pure” solute depletion from sodium loss

+H₂O

-NaCl +H₂O



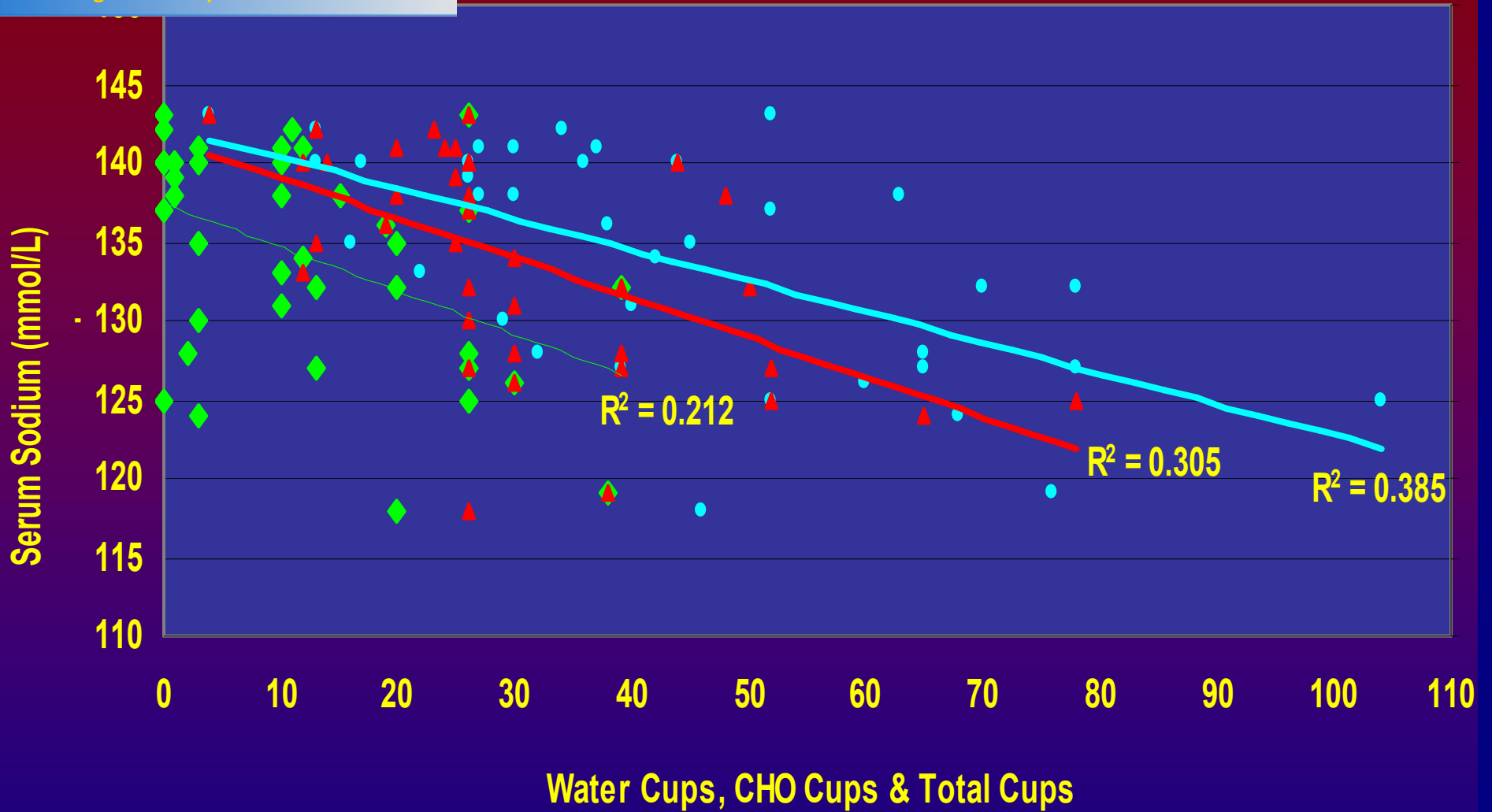
-NaCl

?

**Exercise-induced
Non-osmotic AVP
secretion**

?

CHO Cups & Total Cups vs. Serum Sodium Levels



● Total cups

◆ CHO cups

▲ Water cups

— Linear (Total cups)

— Linear (Water cups)

— Linear (CHO cups)



WHY YOU NEED A

SPORTS DRINK

WATER

Isn't Good Enough

and Availability



...coupled with advice to drink beyond thirst

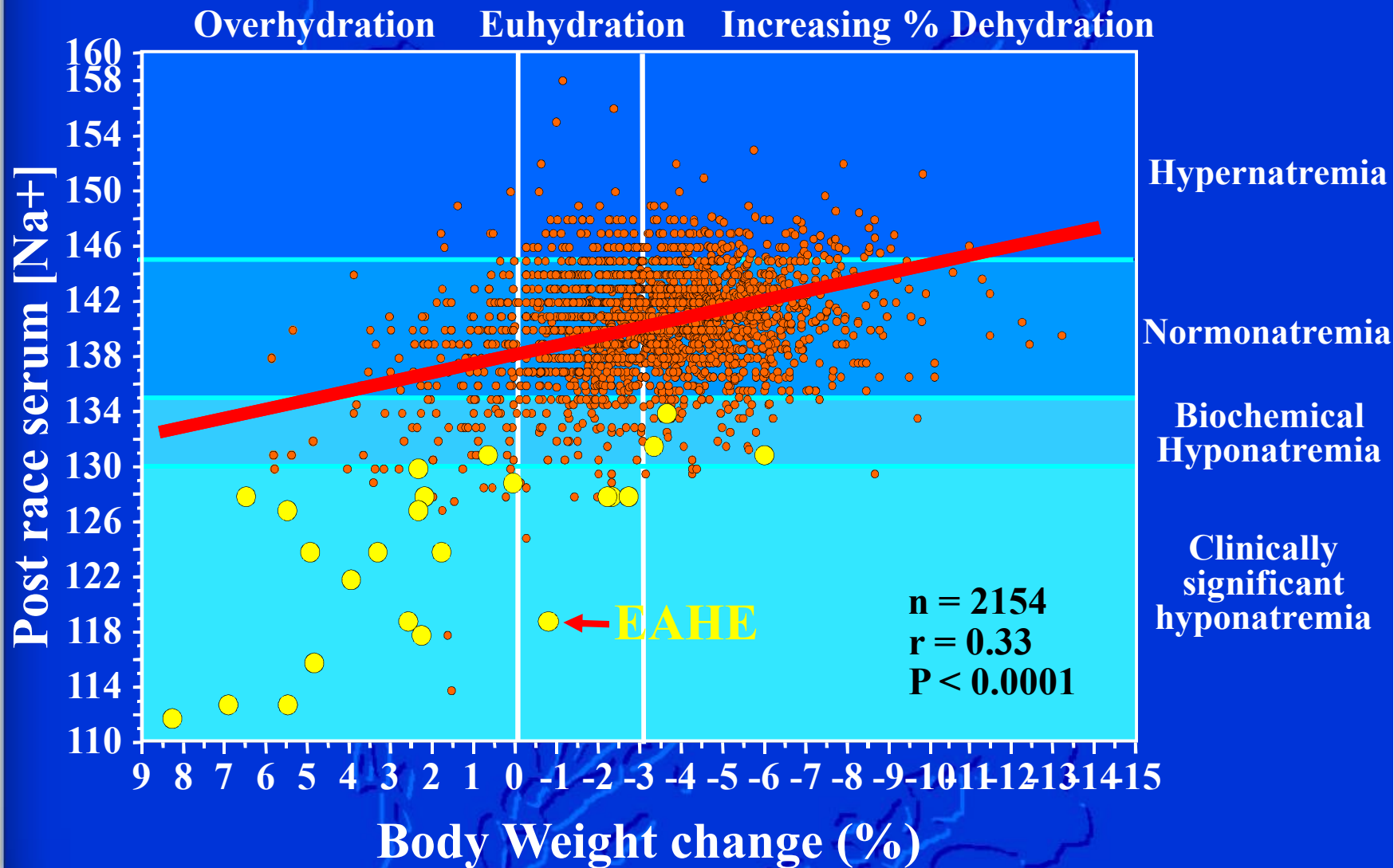


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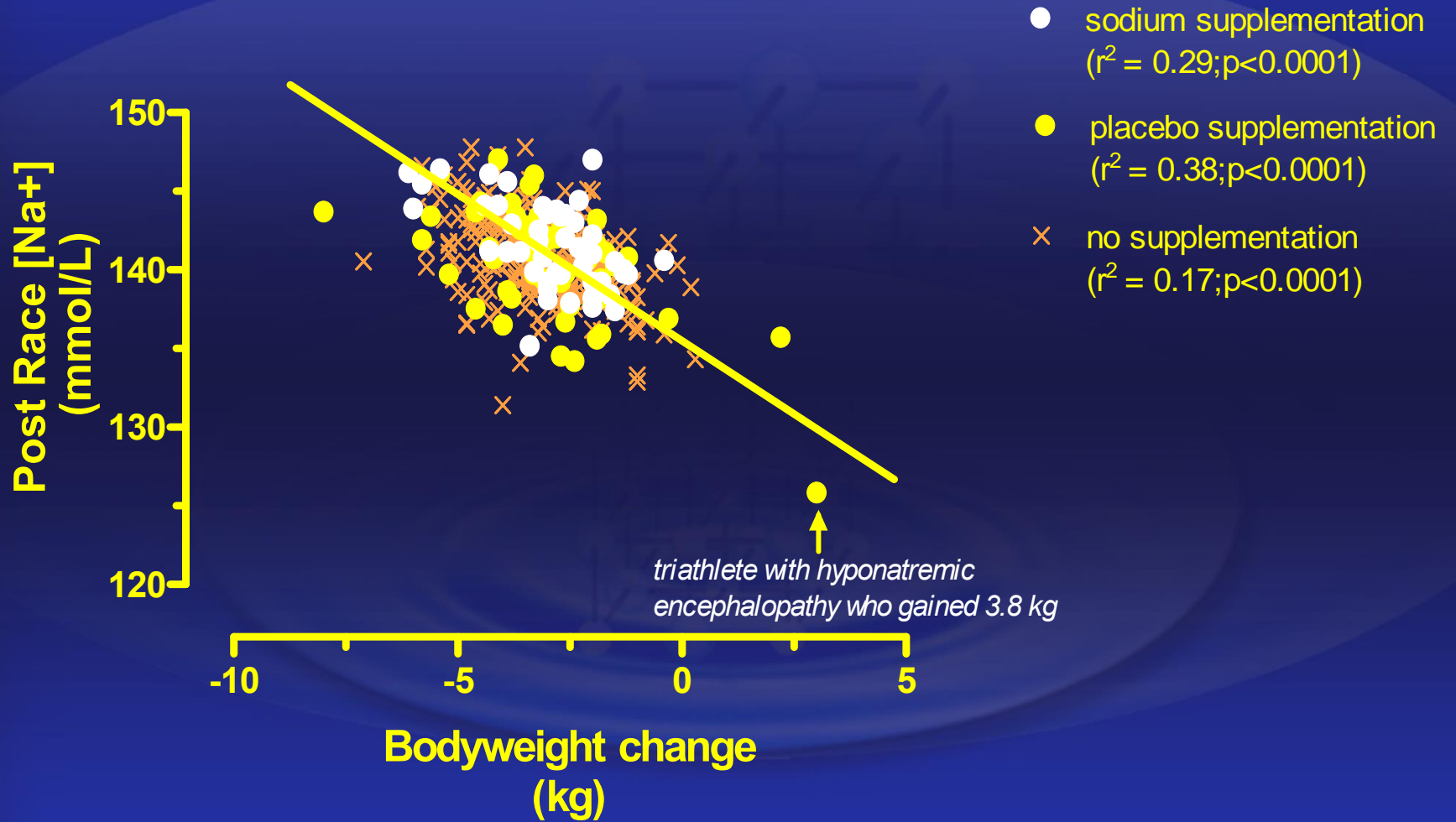
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Relationship between weight changes and post-race serum [Na⁺] in 2154 endurance athletes.



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



Mountain Footraces *a different beast?*

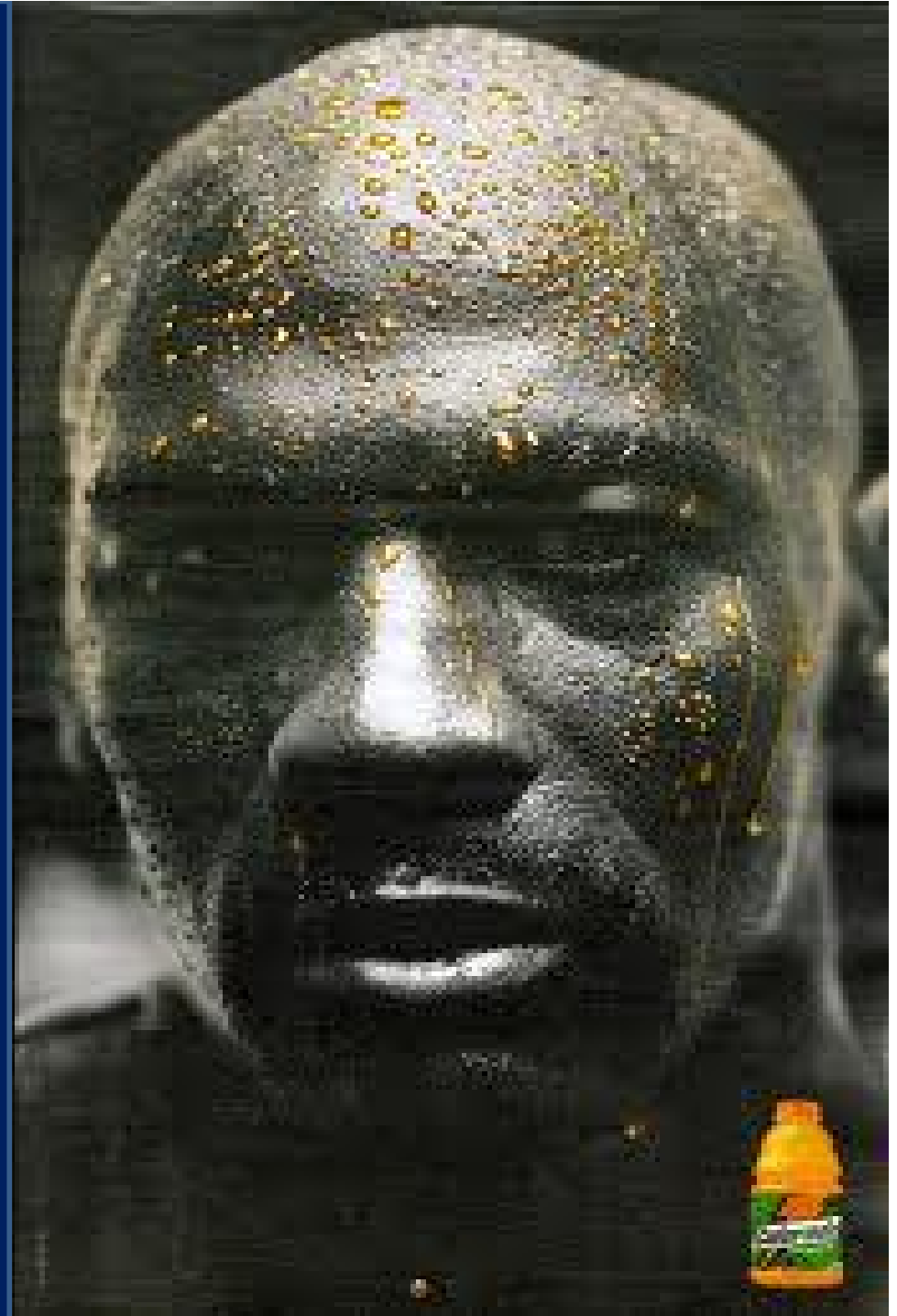


Sweat

Exercise $>40\%$ VO_2 Max
92% water and **87% sodium**
losses derived from sweat

Human sweat is
hypotonic to plasma $[\text{Na}^+]$
(range: 10-70mmol/L)

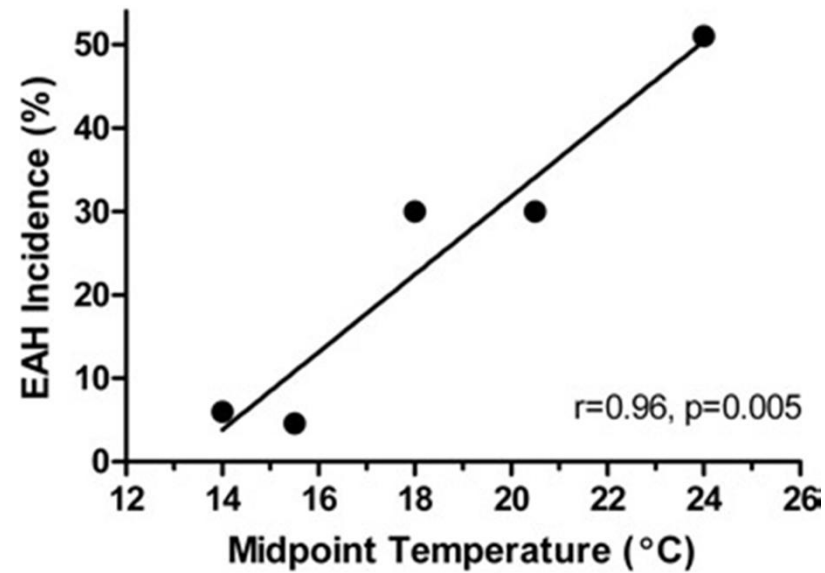
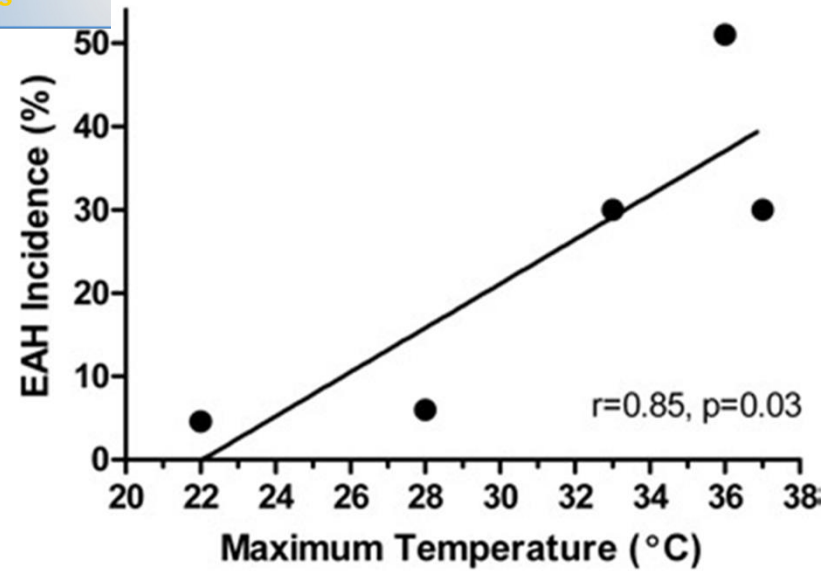
Early hypothesis:
hyponatremia + weight loss
= salt depletion



VARIABLE	24-hour Pre-race (N = 18)	During Race (N = 18)	24-hour Post-race (n = 8)
Total Volume (liters)	3.3 ± 1.7 (0.9 – 6.2)	0.3 ± 0.3 (0.03 – 1.6)	1.7 ± 1.7 (0.5 – 5.6)
Specific Gravity	1.009 ± 0.00 (1.003 – 1.019)	1.017 ± 0.01 (1.003 – 1.030)	1.021 ± 0.00 (1.005 – 1.029)
Total Na+ (mEq)	195.0 ± 79.6 (40.4 – 322.5)	8.8 ± 5.9 (0.3 – 26.2)	44.5 ± 39.5 (11.1 – 118.1)
Total K+ (mEq)	83.5 ± 33.5 (32.4 – 135.0)	25.4 ± 17.5 (2.2 – 74.9)	55.7 ± 33.7 (15.4 – 104.0)

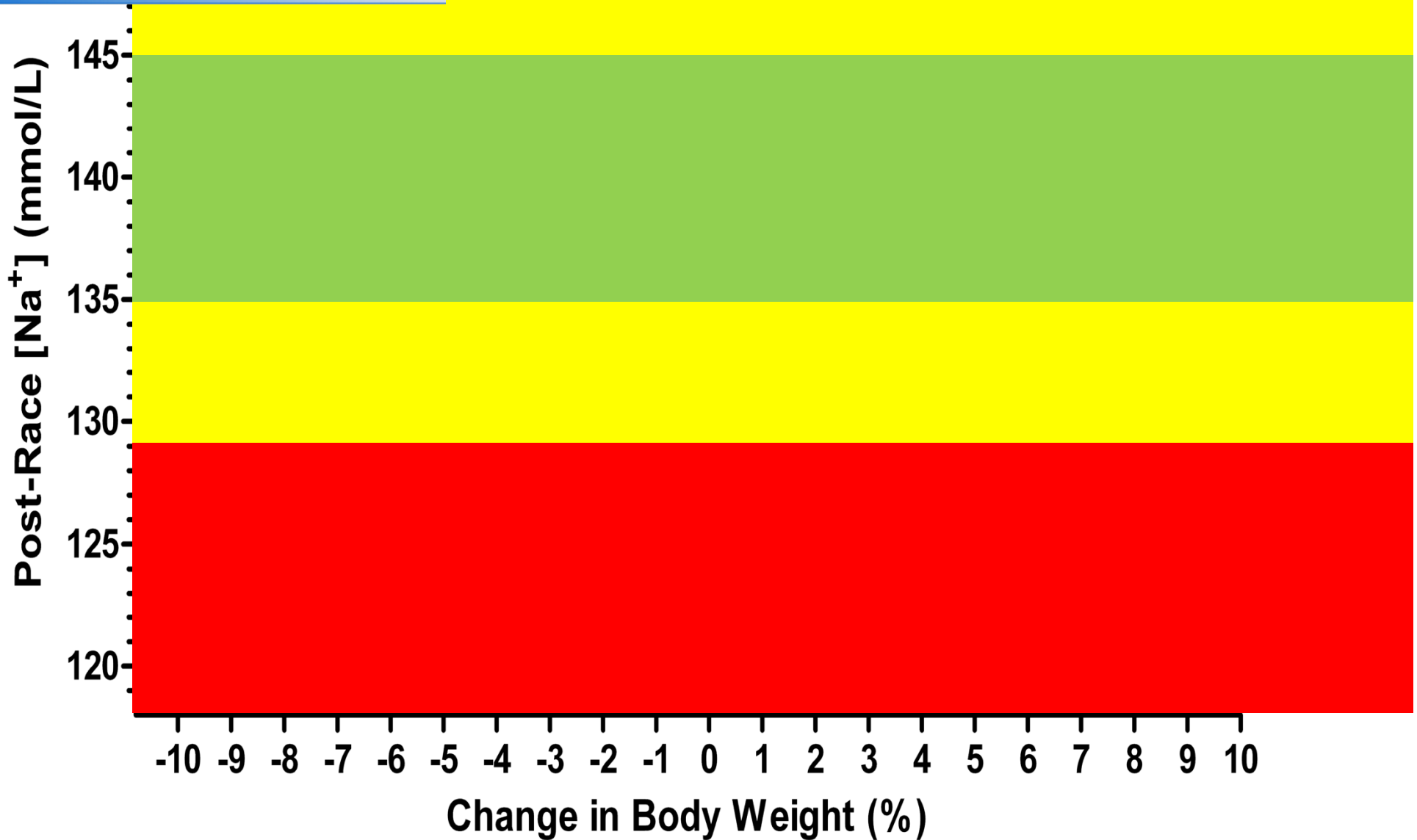
*** No significant differences between finishers versus non-finishers***

er temperature = ↑ contribution sweat [Na⁺] losses



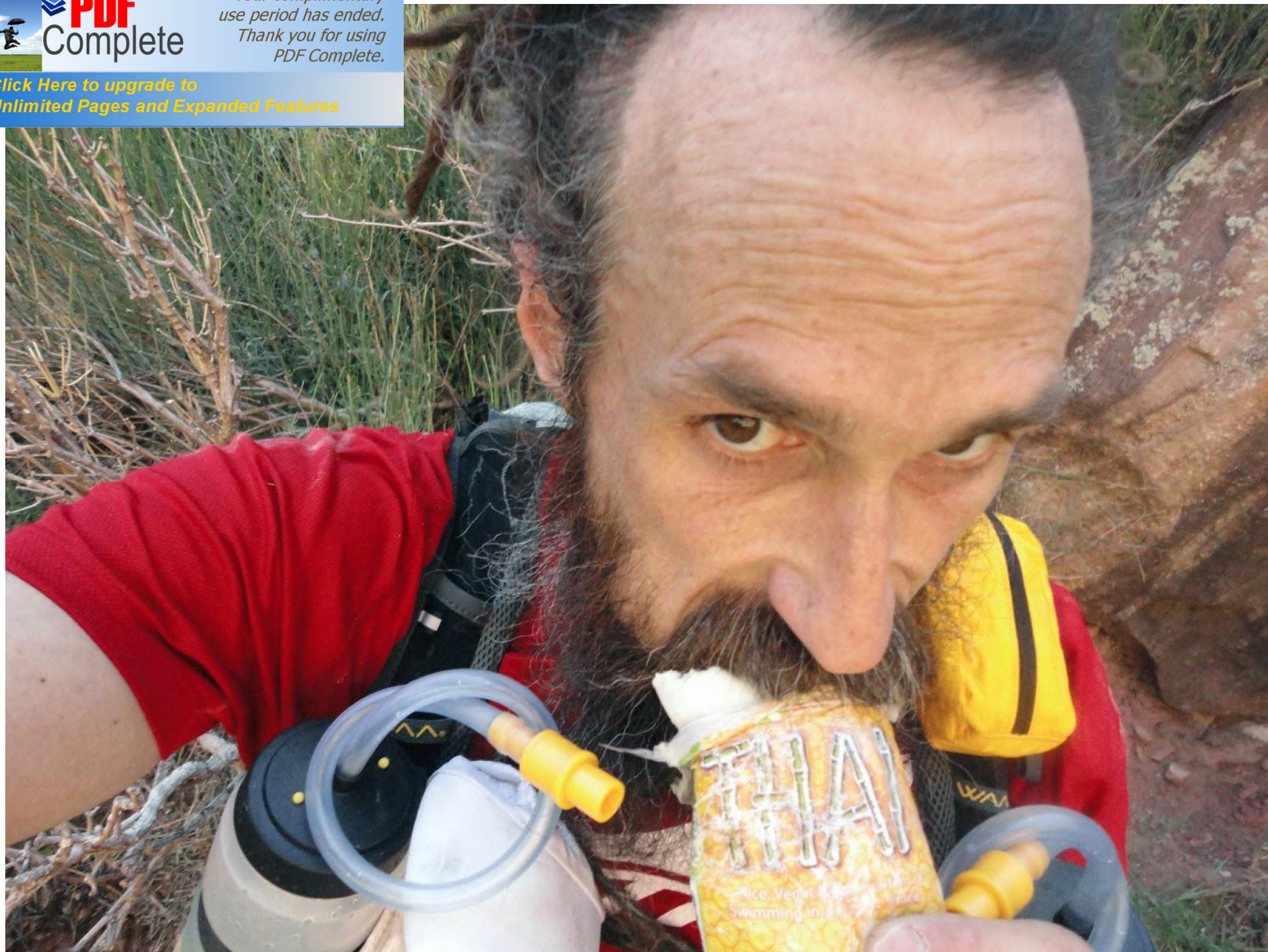
Euhydration

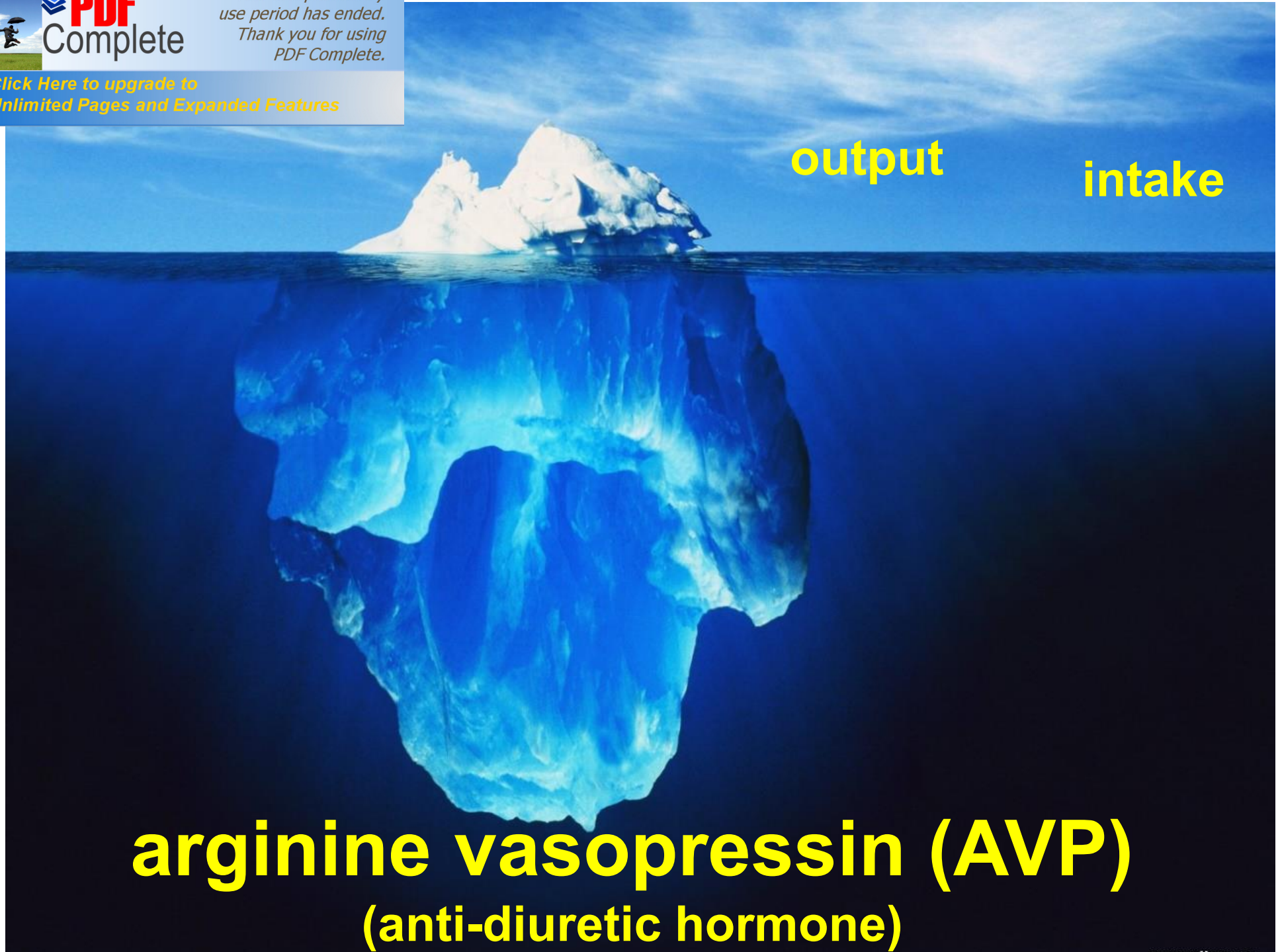
Overhydration



**Body weight changes
during exercise
become less reliable
indicators of fluid balance
as race distance progresses**

*substrate utilization
metabolic water production*



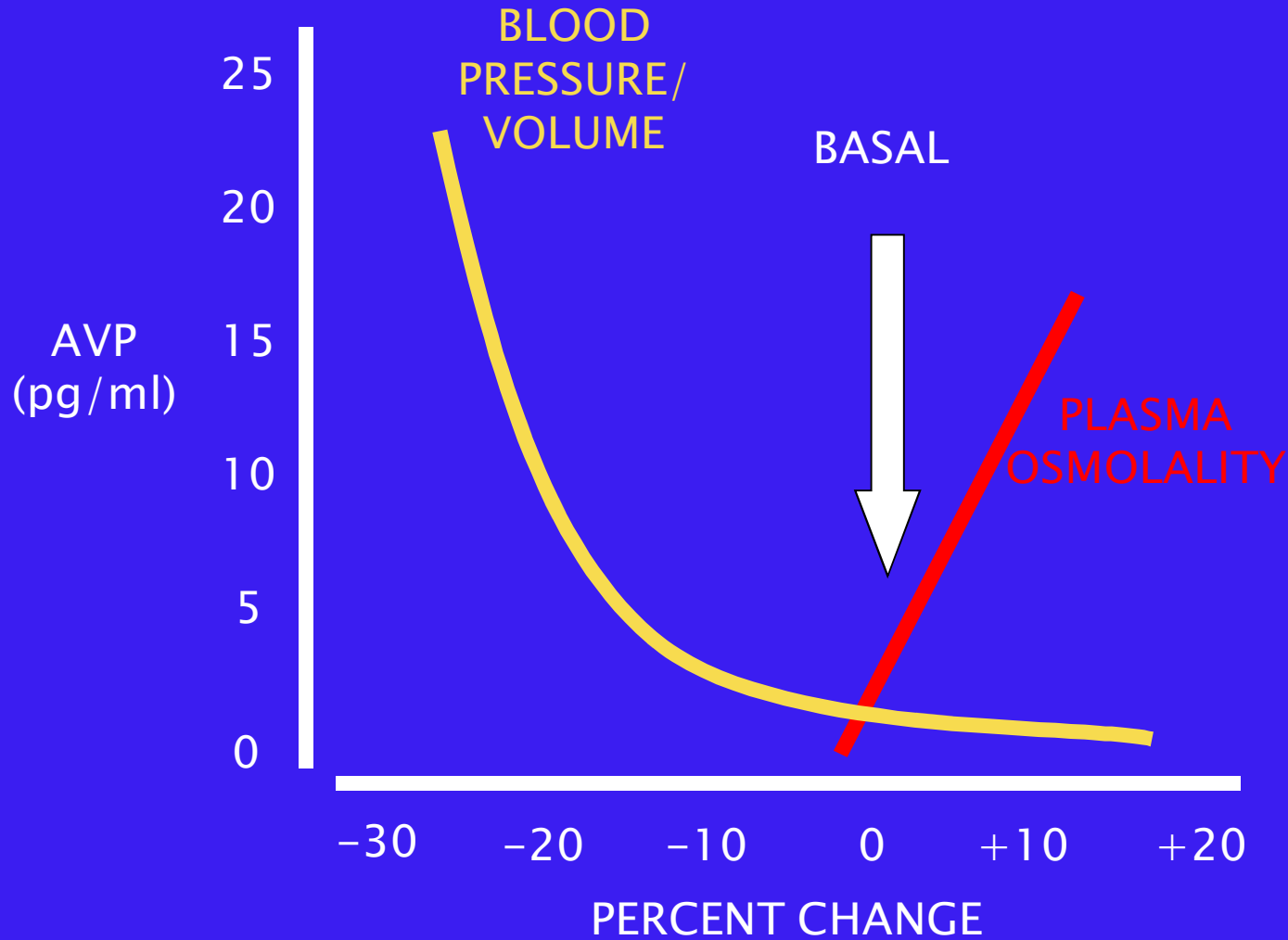


output

intake

arginine vasopressin (AVP)
(anti-diuretic hormone)

ANGIOTENSIN II AND VASOPRESSIN



li to AVP secretion

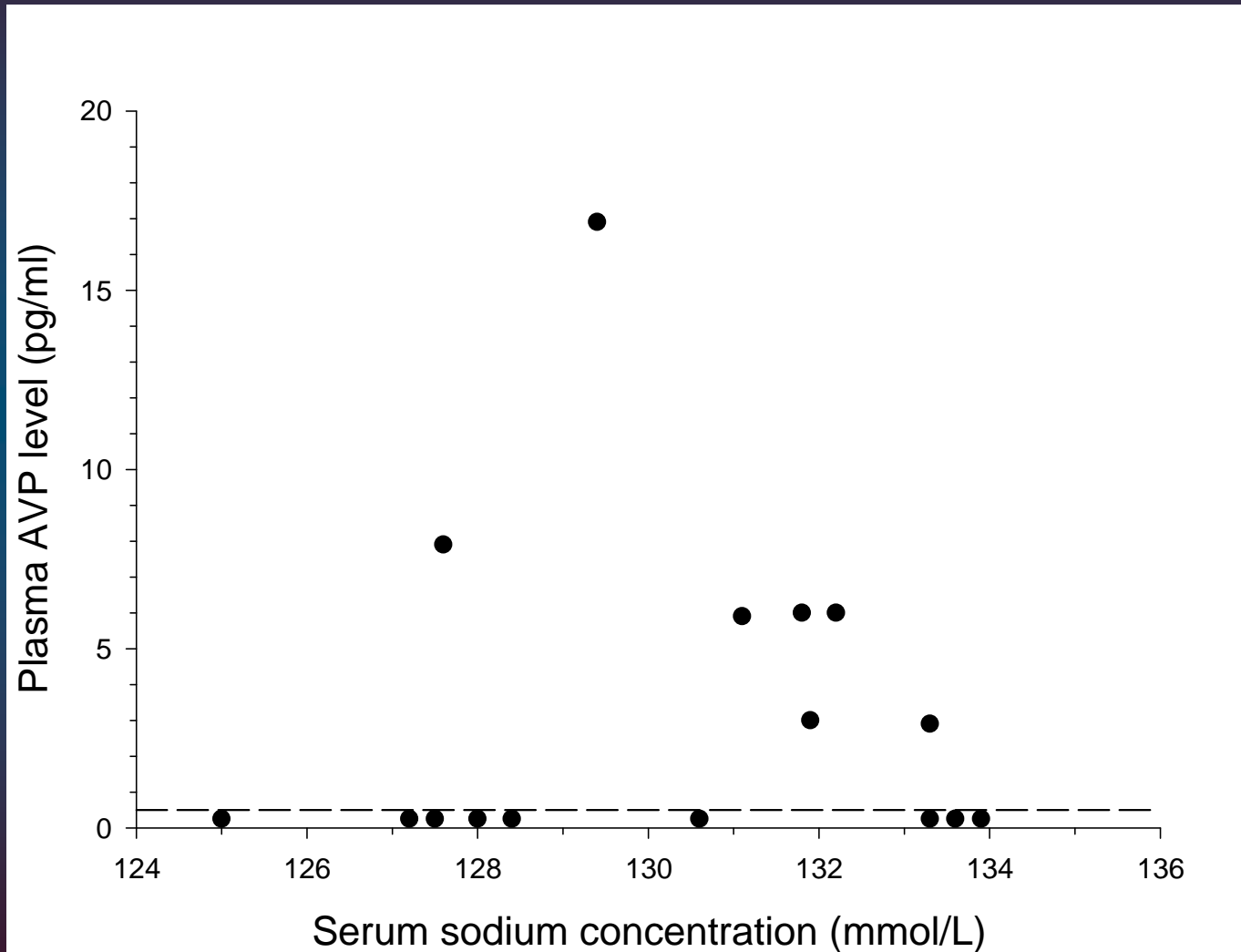
related to fluid homeostasis:

- hyperosmolality
- hypotension
- ✓ hypovolemia
- ✓ angiotensin II

independent of fluid homeostasis:

- ✓ nausea
- ✓ hypoxia
- hypercarbia
- ✓ hypoglycemia
- ✓ stress: cytokines
- ✓ temperature

Marathon: plasma AVP levels in collapsed runners with EAH ($[Na^+] < 135$ mmol/L)



States 100 Mile Run

COHORT

[AVP]_p
(Mean ± SD)

[Copeptin]_p
(Mean ± SD)

[Na⁺]_p
(Mean ± SD)

SODIUM BALANCE TRIAL

Normonatremic
(pre-race)
N=6

0.7 ± 0.4

10.3 ± 12.5

138.7 ± 2.3

Normonatremic
(post-race)
N=6

2.7 ± 1.9

28.2 ± 16.8

136.7 ± 1.6

TREATMENT TRIAL

Hyponatremic
(post-race)
N=6

3.2 ± 2.9

22.5 ± 27.5

130.3 ± 2.6

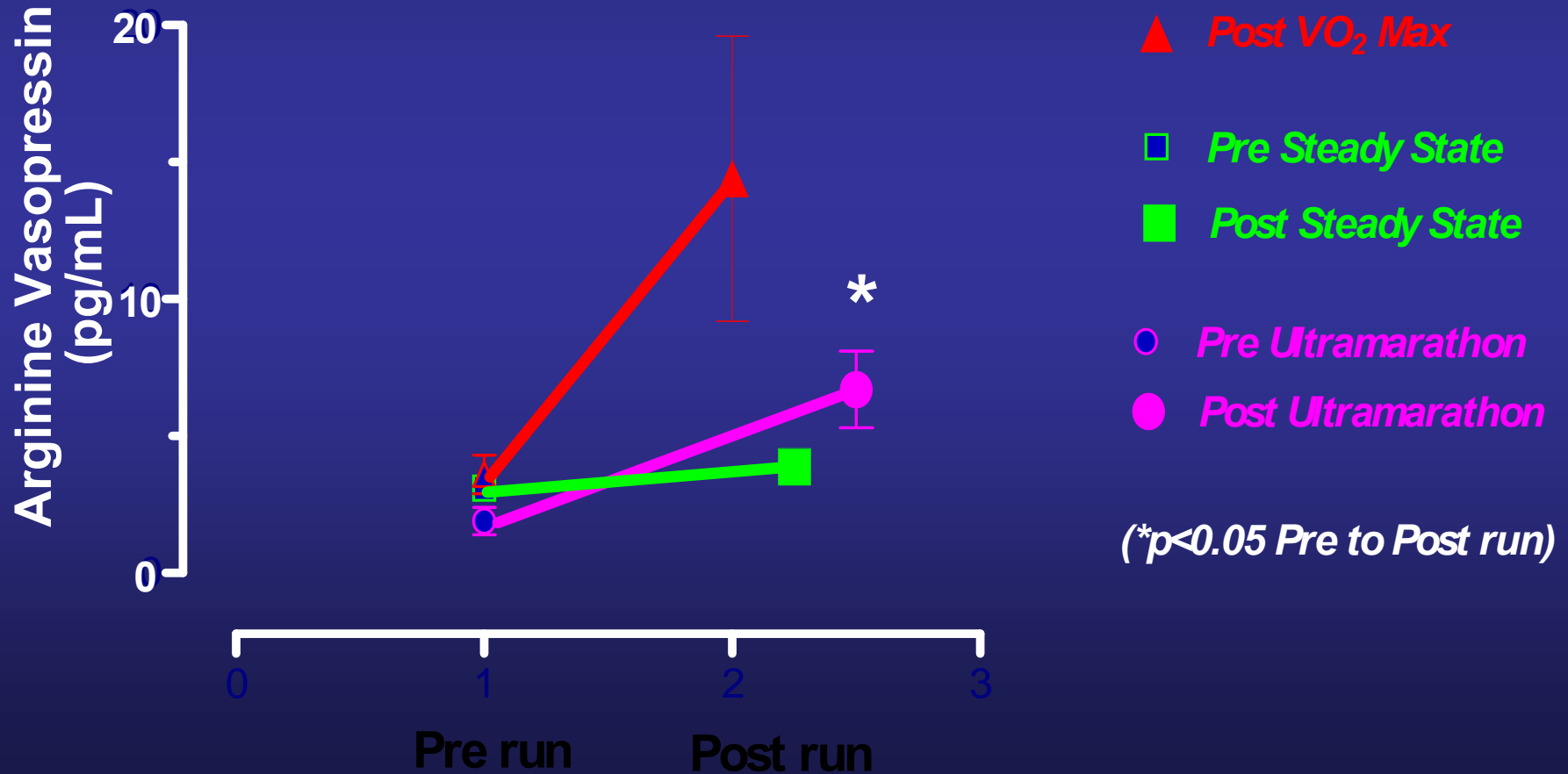
Hyponatremic
(60min post-race)
N=6

2.1 ± 2.5

24.9 ± 39.7

133.5 ± 3.4

Change in AVP during High Intensity, Steady State and Ultradistance Running (N=7)



(*p<0.05 Pre to Post run)

Pathophysiology

CONCLUSION

*EAH is a **spectrum** between
overdrinking and
uncompensated sodium loss*

*Exercise-induced AVP
reduces the ability to excrete
fluid intake in excess of fluid losses*

Pathophysiology

Diagnosis

Treatment

Prevention

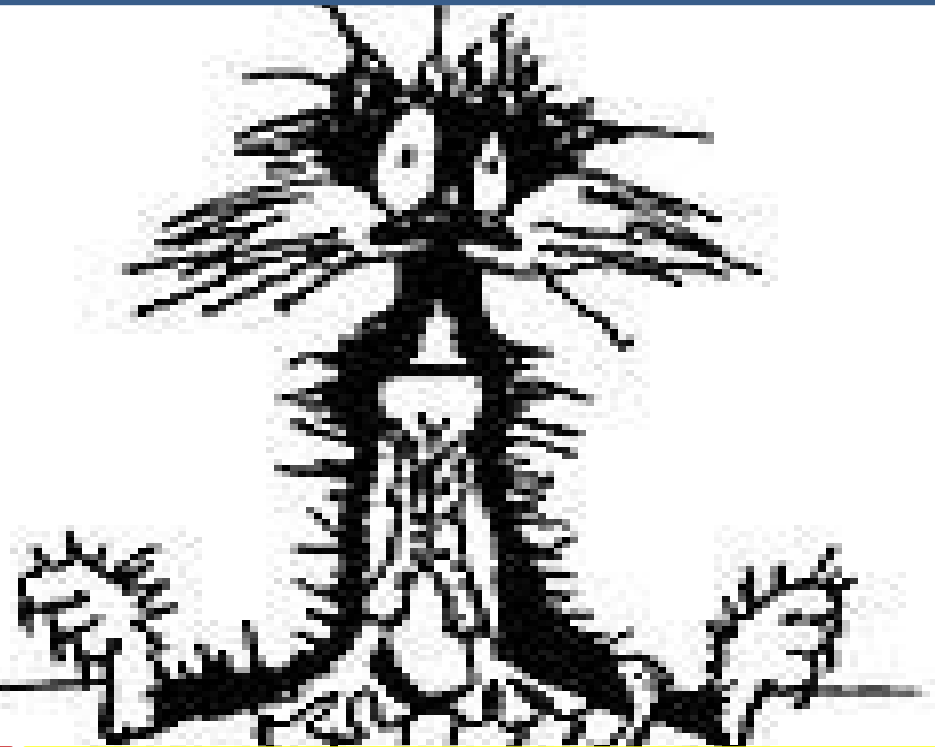
**Hyponatremia is a
biochemical diagnosis
and can only be
determined using a
blood test**

Upper limit of symptoms

Blood $[Na^+] < 135\text{mmol/L}$



Biochemical
(Asymptomatic)



Clinically
Symptomatic

**How would you define
“asymptomatic”
after running a 100 mile race?**

lightheadedness

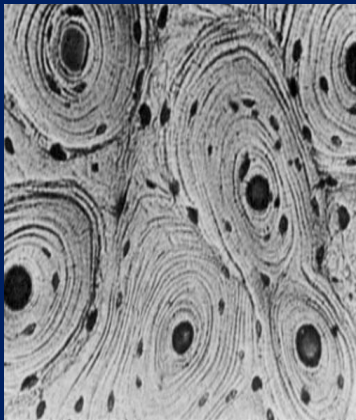
dizziness

fatigue

nausea

*are all non-descript symptoms associated
with many conditions*

Asymptomatic



Symptomatic

symptomatic

EAH with:

altered mental status

seizures

pulmonary edema

is a life-threatening emergency



signs and symptoms

“pure” water
retention from
SIADH

mixed solute
loss and water
retention

“pure” solute
depletion from
sodium loss

+H₂O

-NaCl +H₂O

← -NaCl

h/o overdrinking
bloating
vomiting

↔↑ BP

↑ body weight

↑↔↓ urination?

mixed

“Dehydration”
thirsty, dry mouth
skin tenting

orthostatic hypotension

↓ body weight

↓ urination

etiologic possibilities

“pure” water retention from SIADH

mixed solute loss and water retention

“pure” solute depletion from sodium loss

+H₂O

-NaCl +H₂O



-NaCl

↑ Uosm

↑ pAVP

↓ serum [Na⁺]

↑ weight

↓ BUN

↑ UNa⁺

↑ Uosm

↑ pAVP

↓↓ serum [Na⁺]

↔ ↑ weight

↔ BUN

↓ UNa⁺

↑ Uosm

↑ pAVP

↓ serum [Na⁺]

↓ weight

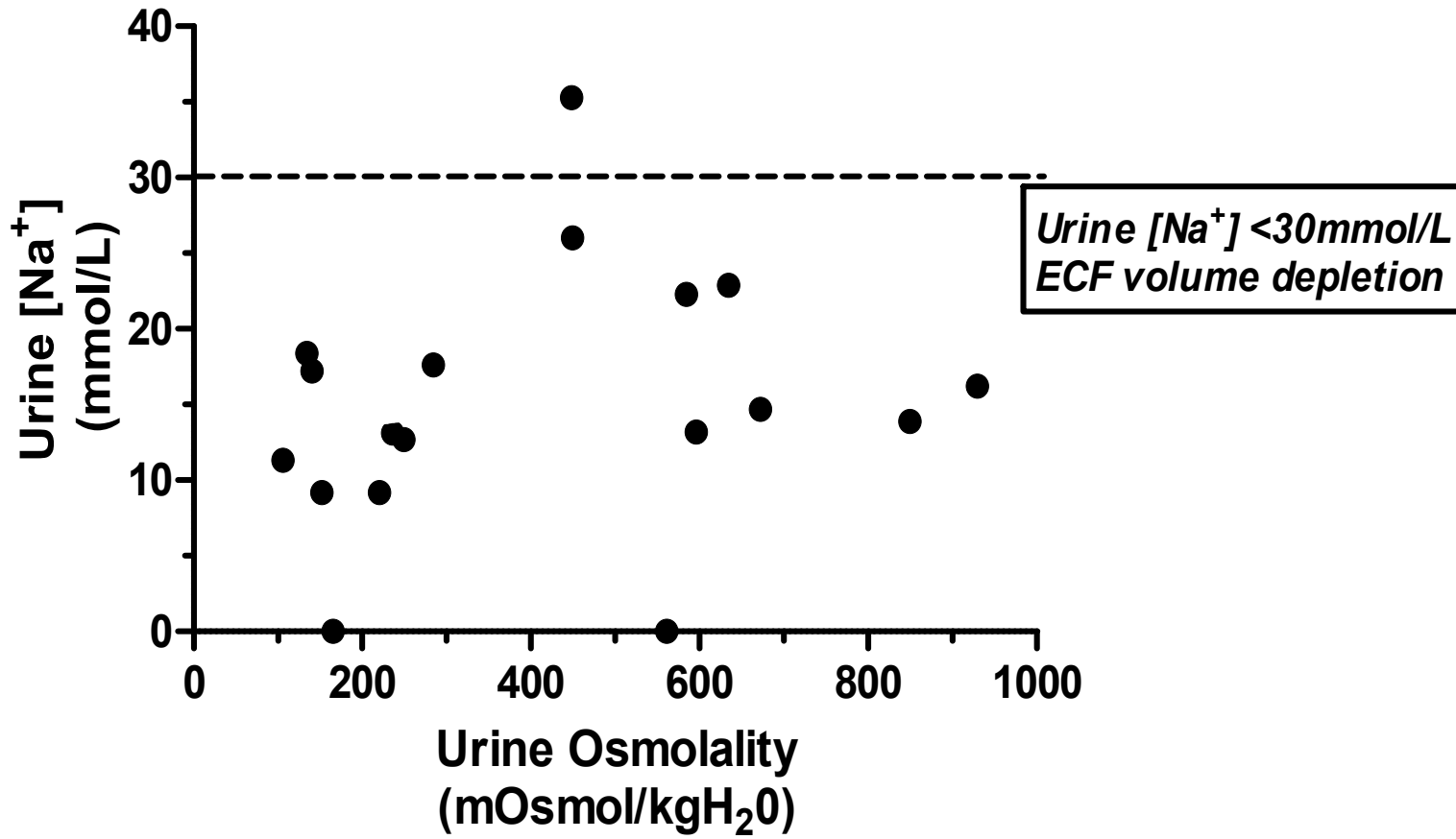
↑ BUN

↓ UNa⁺



etion vs. Dilution

Hyponatremic Finishers Pre-Intervention



Diagnosis

CONCLUSION

EAH is a biochemical determination

Signs and symptoms are non-distinct

*Volemic classification has an
important determination on treatment*

Pathophysiology

Diagnosis

Treatment

Prevention

Upper limit of symptoms

Blood $[Na^+] < 135\text{mmol/L}$

Treat the patient
not the number

Biochemical
(Asymptomatic)

Clinically
Symptomatic

EAH with altered mental status requires emergent treatment with an IV bolus of 3% saline

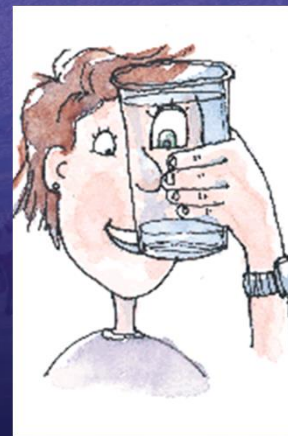
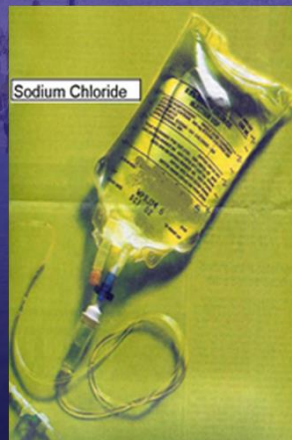
*indicated for hyper and hypovolemic
pathophysiological mechanisms*

*as an acute hyponatremia,
no cases of central pontine myelinolysis
have been documented or expected*

IV Hypertonic Saline Treatment Trial

Primary Aim:

1. Validate if IV hypertonic saline is more efficacious than oral hypertonic saline in the correction of asymptomatic hyponatremia



IV Hypertonic Saline Treatment Trial

307 runners recruited pre-race
Height, weight, body composition

RACE FINISH:
Blood $[Na^+] < 135$ mmol/L
without neurological symptoms
10 mL Blood draw, urine, weight

Randomised

100mL Oral
3% hypertonic saline

100mL IV
3% hypertonic saline

60 Minutes
10mL Blood draw

60 minutes
10mL Blood draw

Randomised Treatment Trial

VARIABLE	ORAL GROUP (n = 15)	IV GROUP (n = 11)
Finish Line [Na+] (mEq/L)	131.5 ± 2.1	129.8 ± 4.2
60 Minutes Post [Na+] (mEq/L)	133.4 ± 2.3	131.8 ± 3.8
Δ [Na+] (post-pre race; mEq/L)	1.9 ± 1.6	2.0 ± 0.9
Finish Line [AVP] (pg/mL)	1.2 ± 1.1	1.7 ± 2.1
Finish Line [BUN] (mg/mL)	30.1 ± 9.6	31.5 ± 12.0
Δ Bodyweight (post-pre race; %)	-3.2 ± 2.7	-1.2 ± 3.4

Mechanism 2010 WSER



Hypovolemia

Urine $[Na^+] < 30 \text{ mmol/L}$

body weight loss $\sim 2\%$

$[BUN] \sim 31 \text{ mg/dL}$

$\sim \text{however} \sim$

only 69% produced urine

lowest blood $[Na^+] (120 \text{ mmol/L})$

5% weight gain

non-suppressed $[AVP]$

most serious case:

Hypervolemia

Spectrum of Hyponatremia

Hypovolemia

“depletional”
most prevalent
**asymptomatic/
mildly symptomatic**

Treatment:
oral or IV
3% saline

Hypervolemia

“dilutional”
less prevalent
symptomatic
emergent

Treatment:
IV 3% saline

Treatment

CONCLUSION

*EAH without altered mental status
can be treated with oral or IV hypertonic
(3%) saline with equivalent increases
in plasma [Na⁺]*

*EAH with altered mental status changes
should be treated with IV bolus
of hypertonic saline (100mL 3%)
and is a medical emergency*

Pathophysiology

Diagnosis

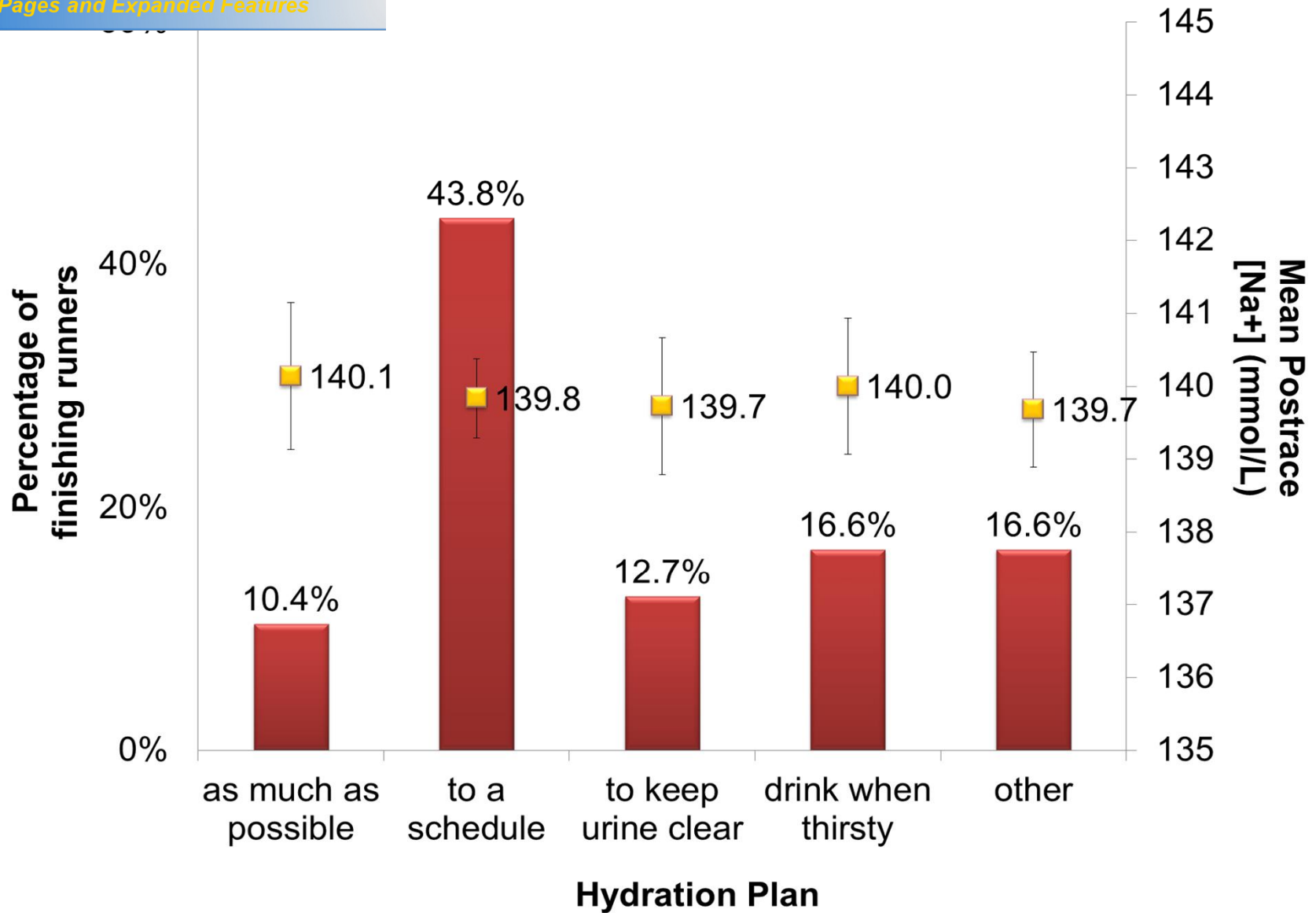
Treatment

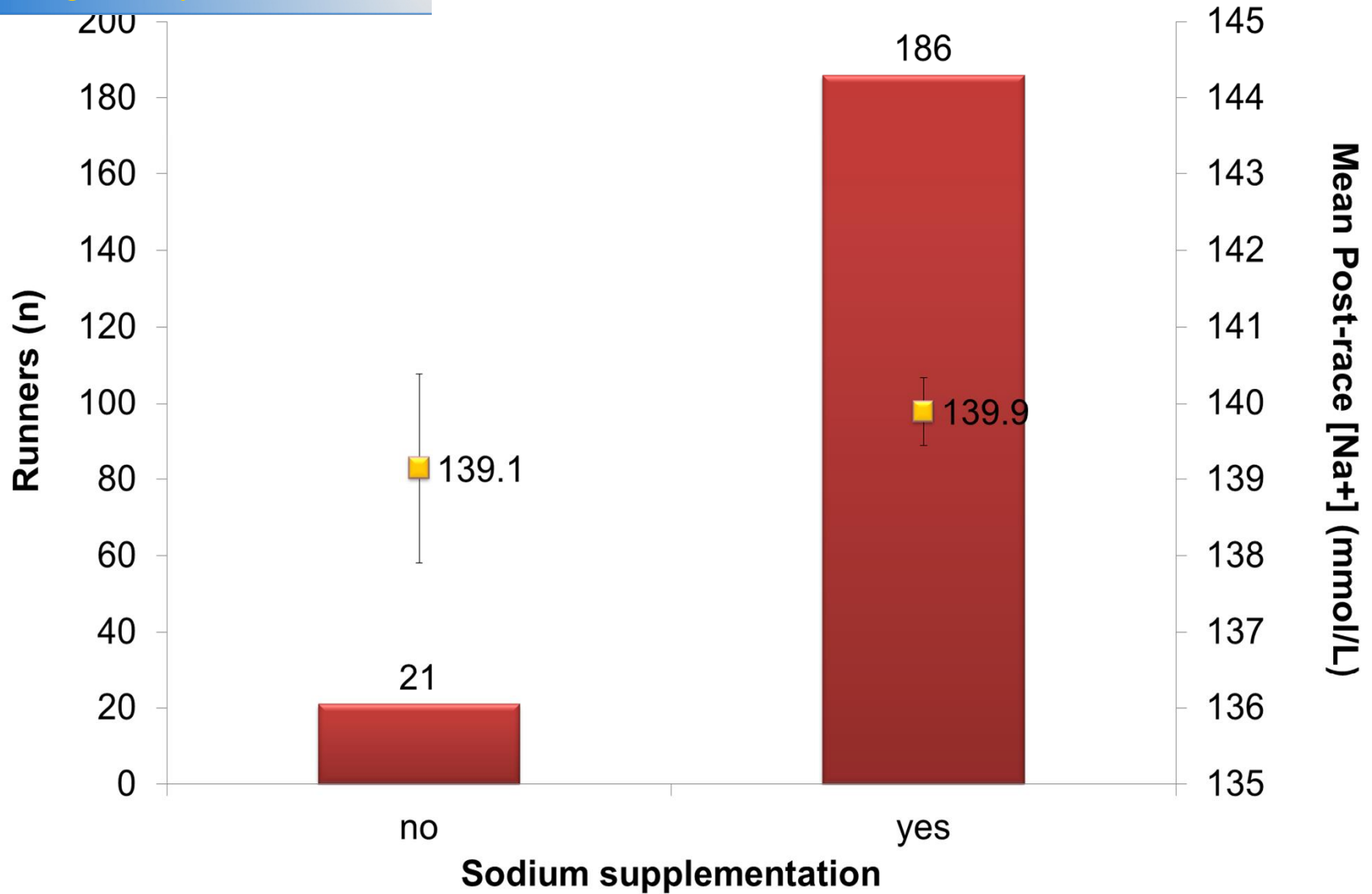
Prevention



How well can our bodies
regulate sodium
during exercise?

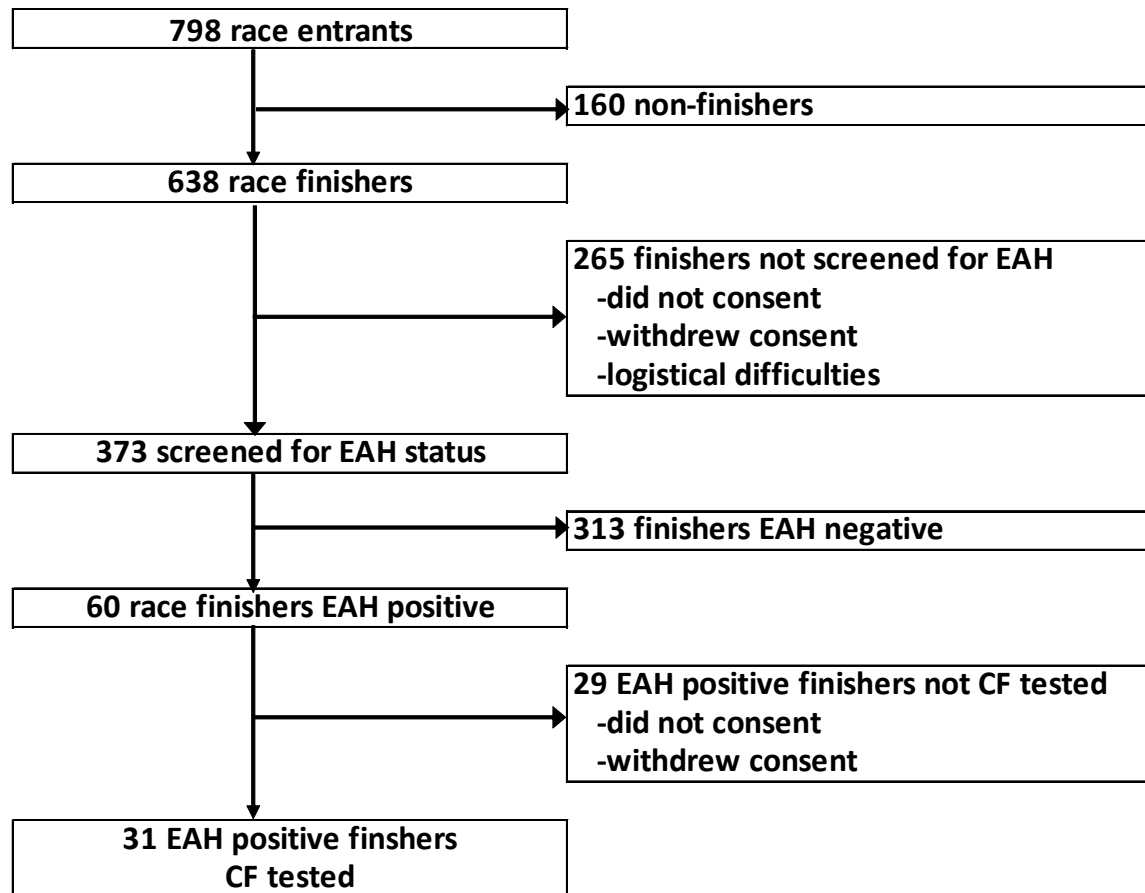






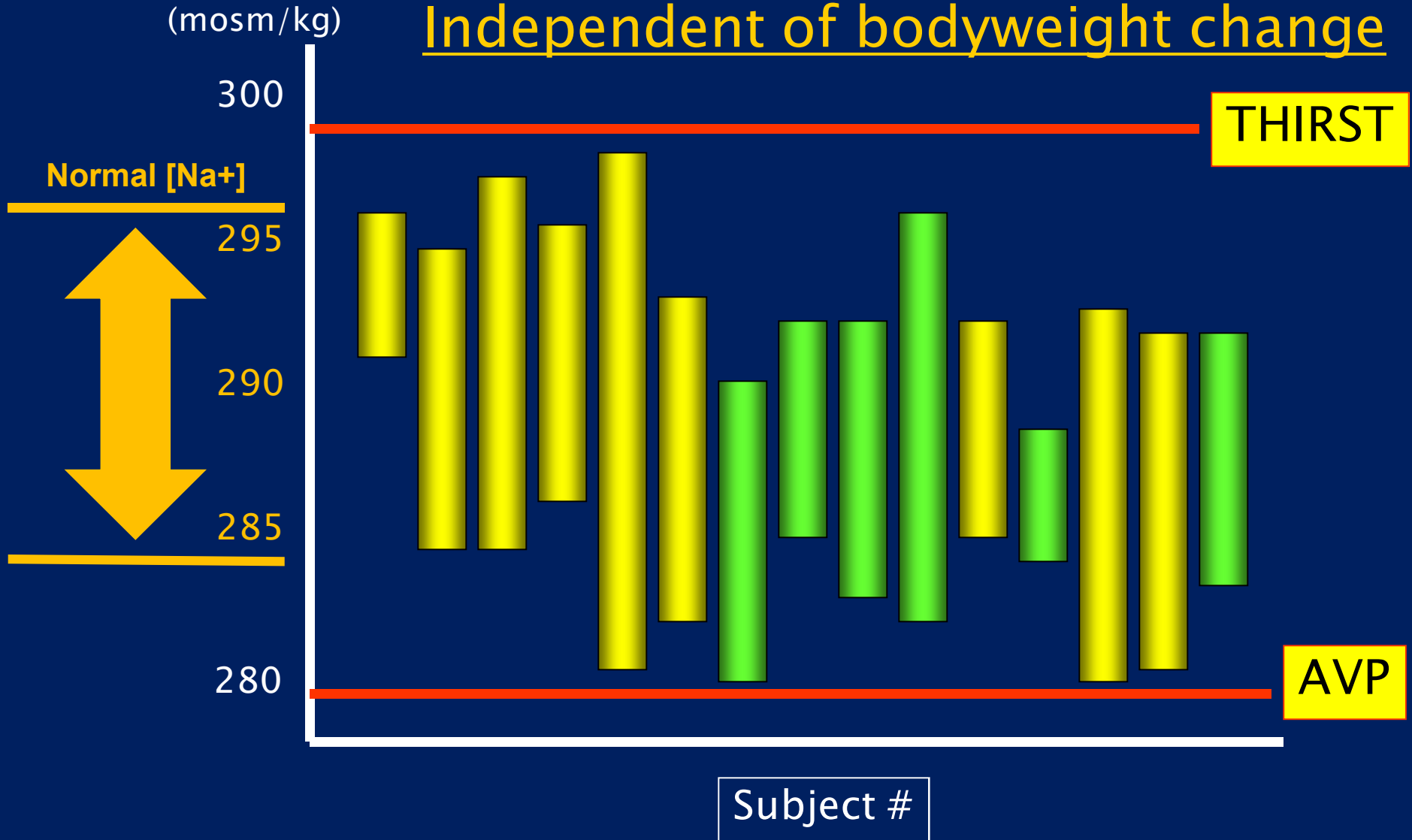
EAH+ or 25 EAH- WSER Finishers tested positive for CF gene mutation

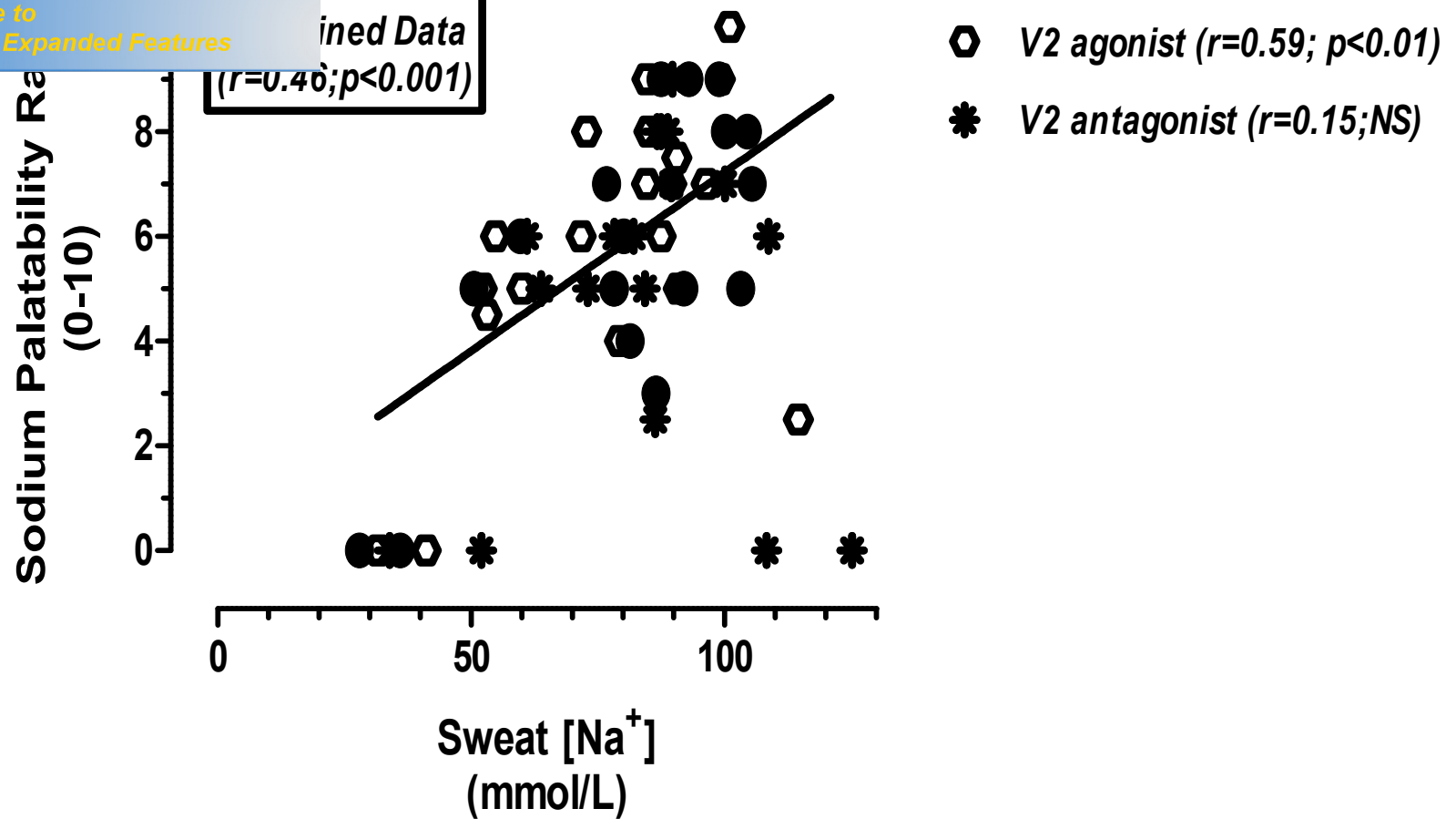
Figure 1:





Thirst is stimulated in humans when the kidneys can no longer protect osmolality Independent of bodyweight change





Sweat [Na⁺] accounted for 21% of variance in sodium palatability

The “saltier” the sweat, the more the subject “craved” salty beverages (increased palatability)

Welcome to Michigan Bluff
Medical Aid Station

Mile 55

What Color is Your Pee?



Coors Light™

GOOD*



Pale Ale

Hydrate*



IPA

Hydrate More*



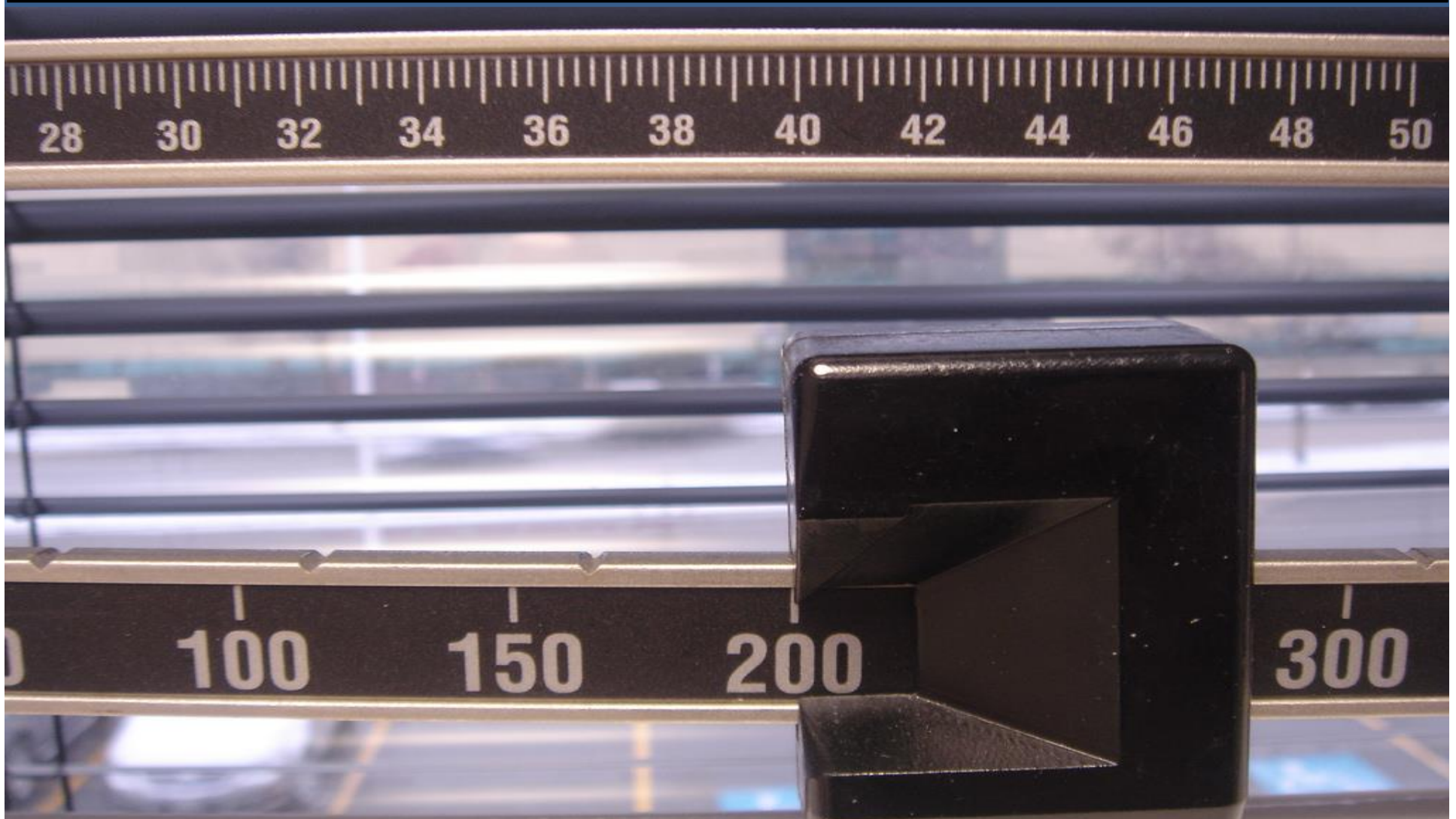
Guinness™

SEE MEDICAL!*

Disclaimer: This poster is only for fun and DOES NOT contain Medical Advice - Individual pee colors may vary.

Created by Deb Paquin | graphics by Robert Seatzrom

body weight \neq fluid



Convention

Drink to thirst

Salt to taste

EDUCATION

FINISHERS:

Time: 27.0 ± 2.3 hours

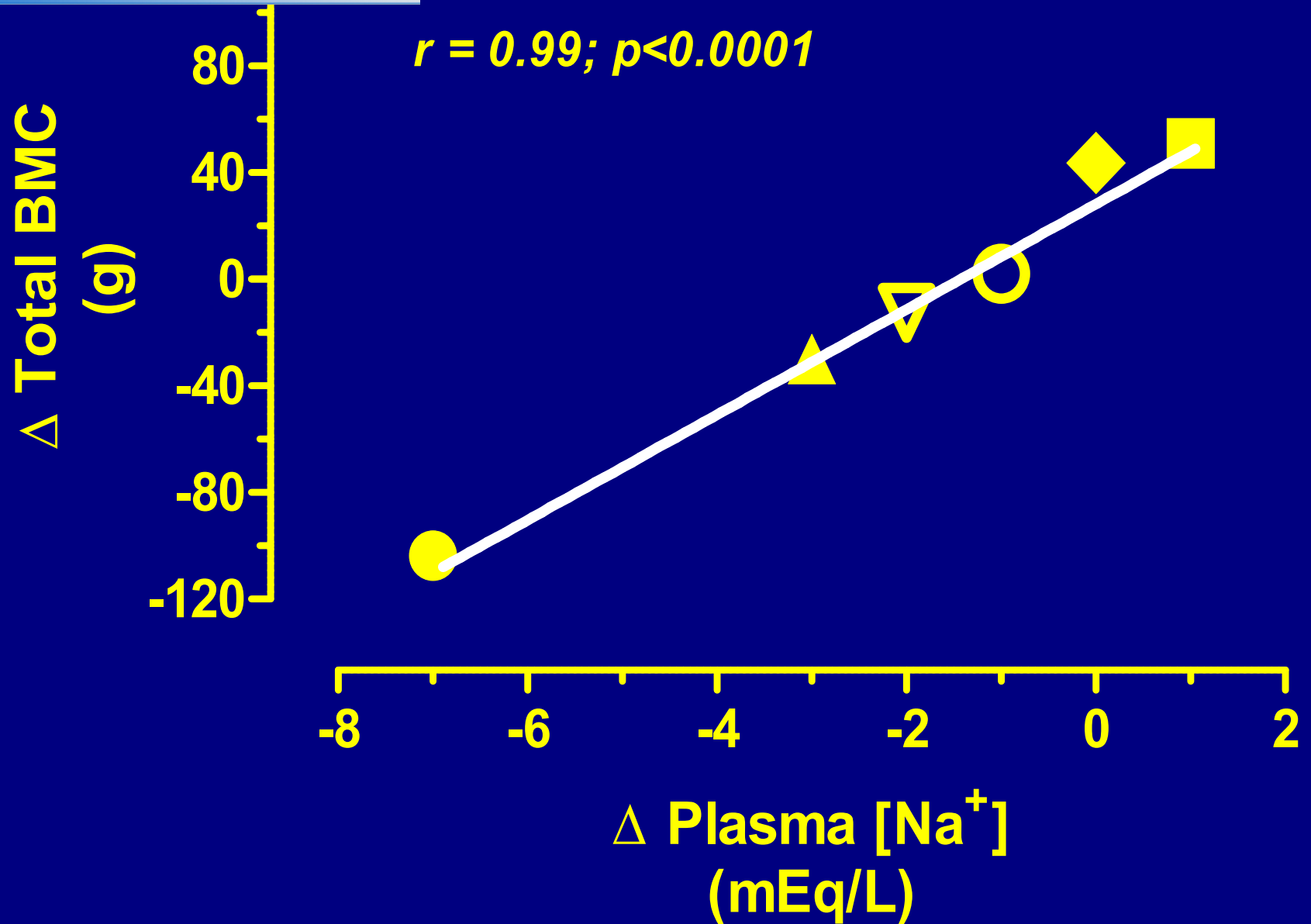
Age: 47.2 ± 4.7 years

VARIABLE (blood)	Pre-Race (n=6)	Post-Race (n = 6)
[Na+] (mEq/L)	138.7 ± 2.3	136.7 ± 1.6
[Ca++] (mEq/L)	1.2 ± 0.2	1.1 ± 0.1
AVP (pg/mL)	*0.7 ± 0.4	2.7 ± 1.9
Aldosterone (pg/mL)	*141.4 ± 38.5	313.6 ± 110.7

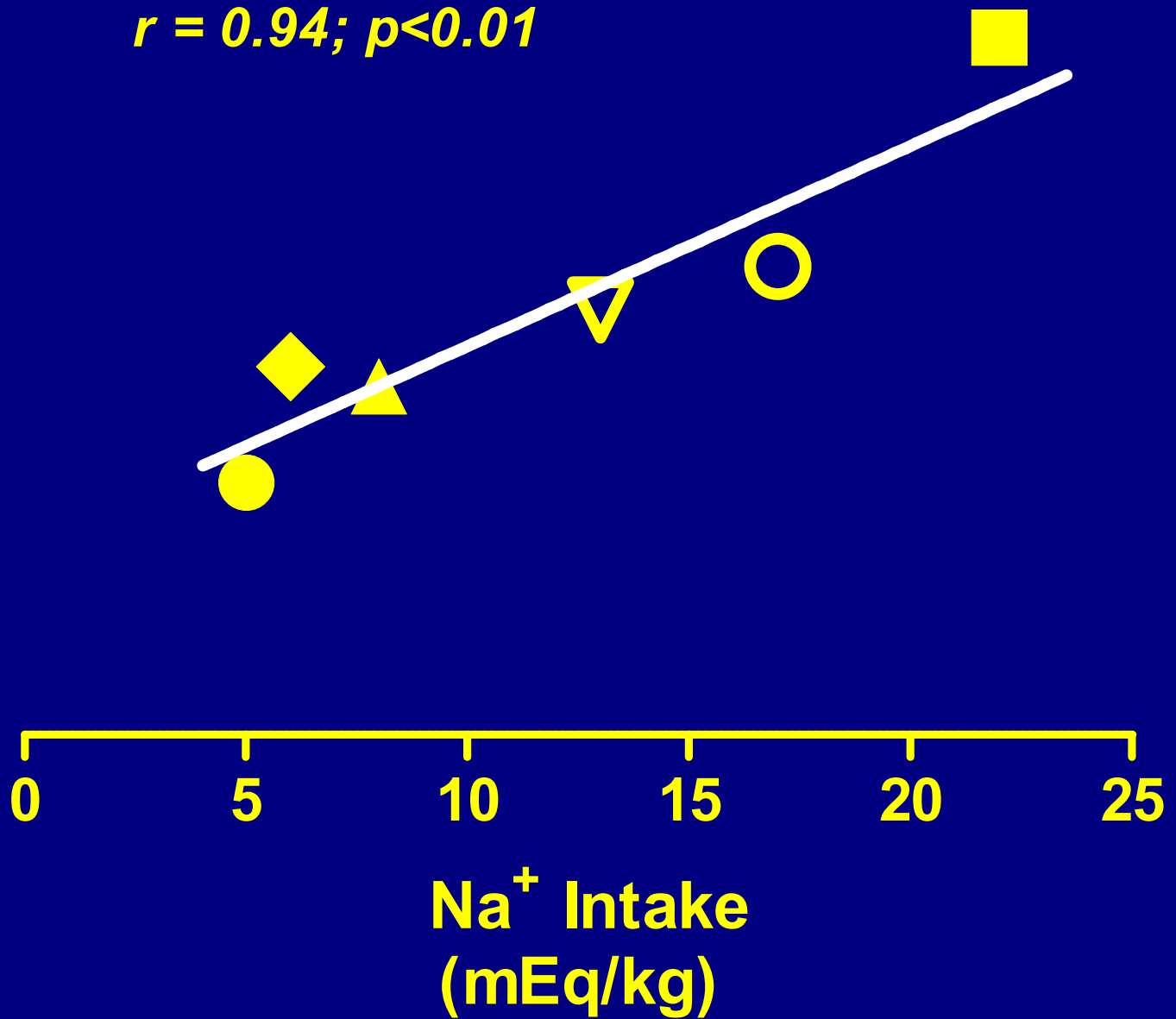
*p<0.05

HERS: DEXA Results

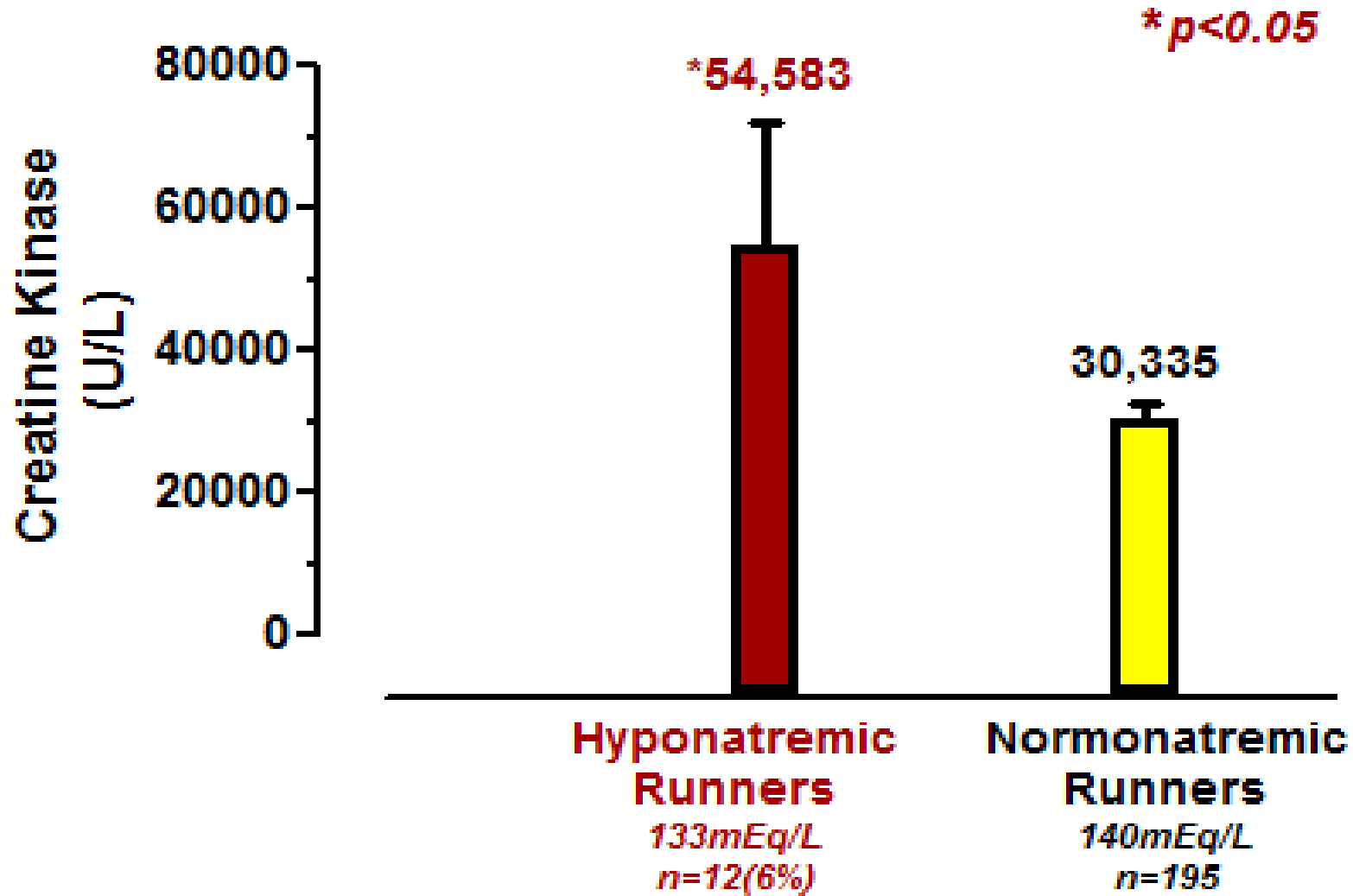
BMC Region	Pre-race BMC (g) (mean ± SD)	Absolute Δ BMC (g) (mean ± SD)	%Δ BMC (mean ± SD)	%CV (range)
Whole Body	2557.6 ± 617.6	-8.2 ± 56.4	0.0 ± 0.0	0.39
Head	521.1 ± 82.7	-18.0 ± 17.5	-3.6 ± 3.4	1.4
Thoracic Spine	94.2 ± 25.5	4.2 ± 12.5	4.6 ± 11.3	2.1
Lumbar Spine	62.8 ± 11.2	0.8 ± 3.5	1.5 ± 6.0	6.3
Pelvis	318.7 ± 84.0	3.0 ± 7.9	1.2 ± 3.2	1.0
Right Leg	507.1 ± 138.8	-3.5 ± 20.2	4.6 ± 11.3	1.7
Left Leg	498.4 ± 132.2	-3.5 ± 17.4	-1.0 ± 3.5	0.6
Right Rib	85.6 ± 23.0	10.3 ± 9.1	9.9 ± 8.7	1.2
Left Rib	85.7 ± 25.5	4.3 ± 7.4	5.1 ± 6.9	1.4



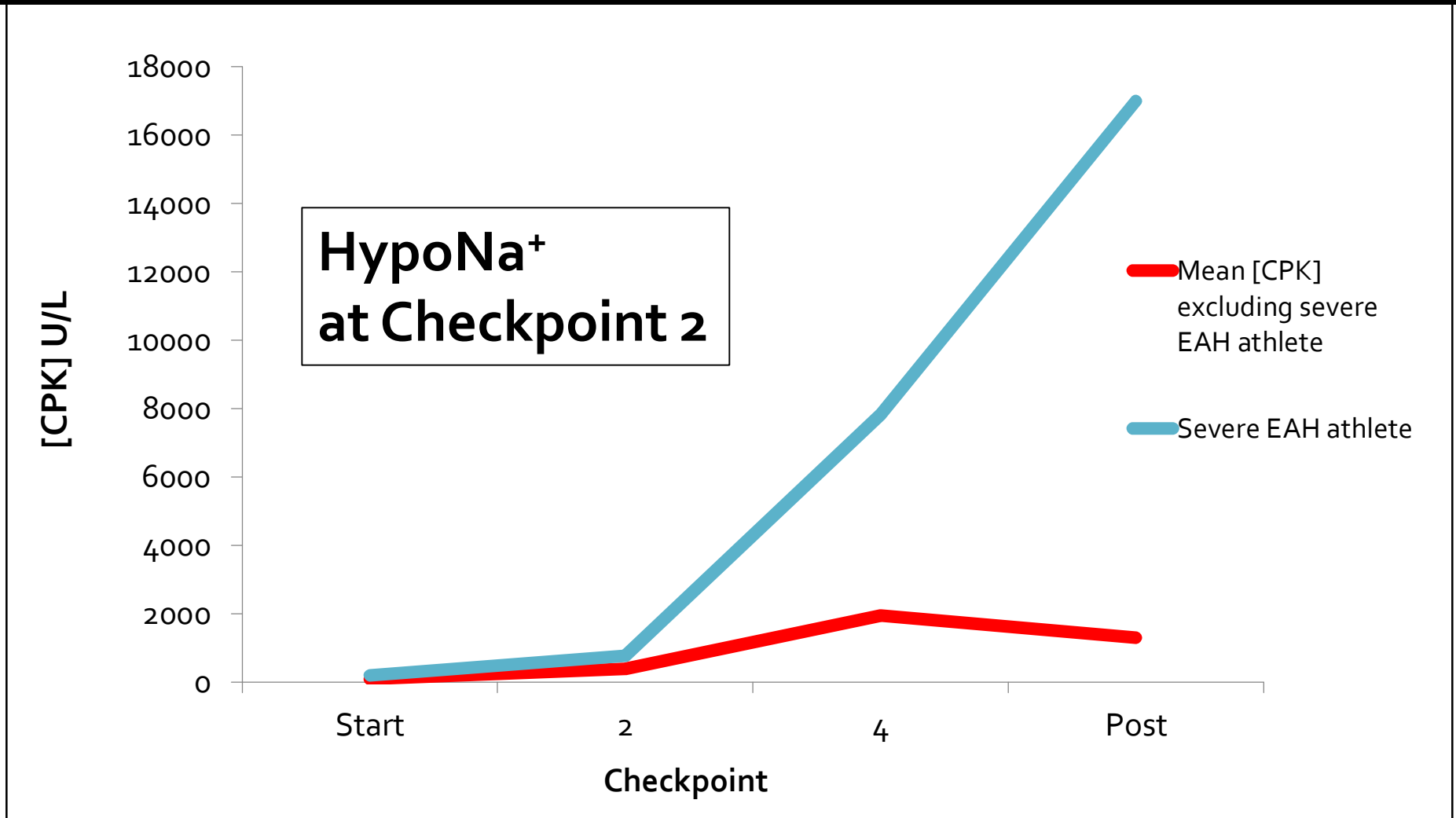
%Δ Lumbar Spine BM
(g/cm²)



WSER 2011



CPK Values in the 100km Race



CONCLUSION

EAH is common in ultramarathons

Hypovolemic variant is more common

***EAH symptoms are vague with
diagnosis confirmed by blood test***

***IV bolus of hypertonic saline
safe in both hypovolemic and
hypervolemic classifications***

Drink to thirst and salt to taste



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THANK-YOU



Joseph G. Verbalis MD

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