The adrenal hormonal response to increased salt intake

Data from humans living in a controlled environment

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Where does the idea come from?

A simulated flight to Mars

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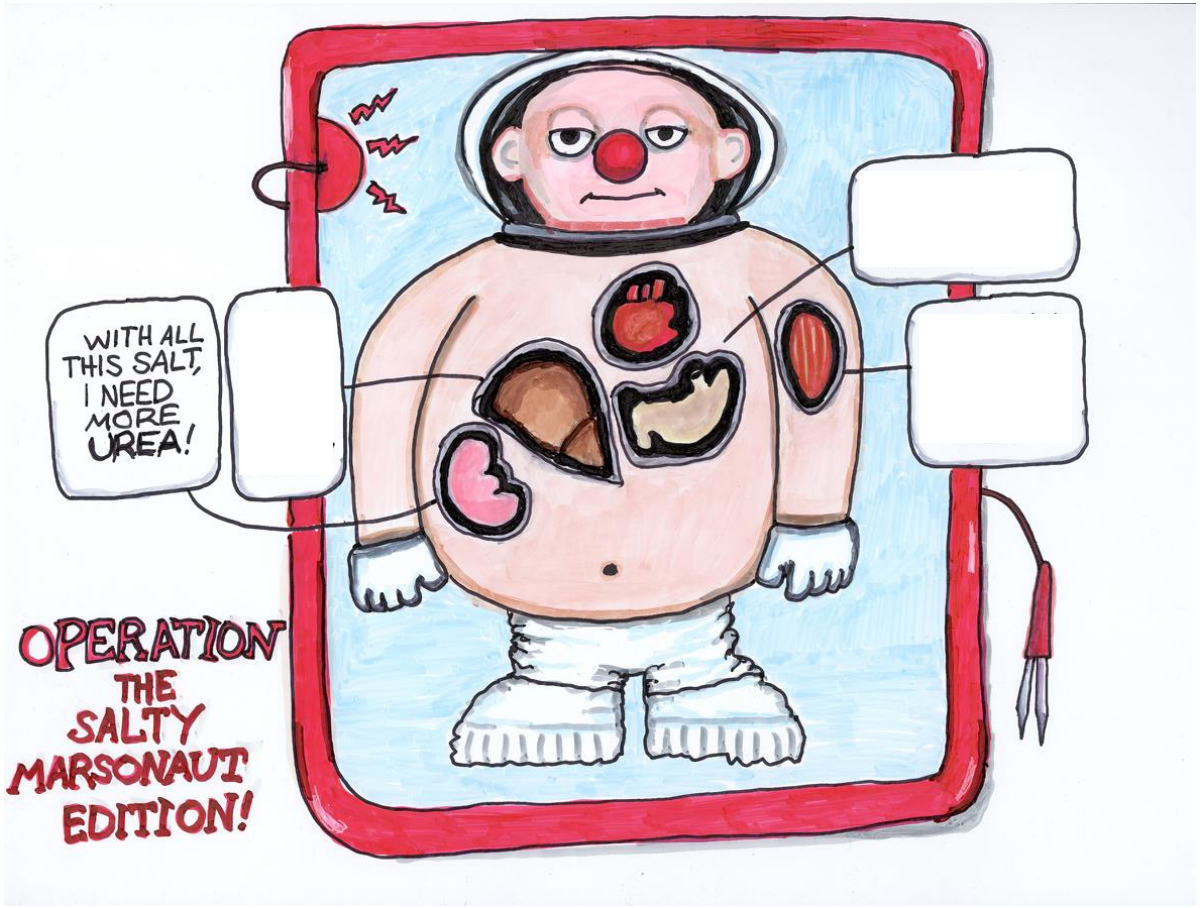
Long-term is not short-term.

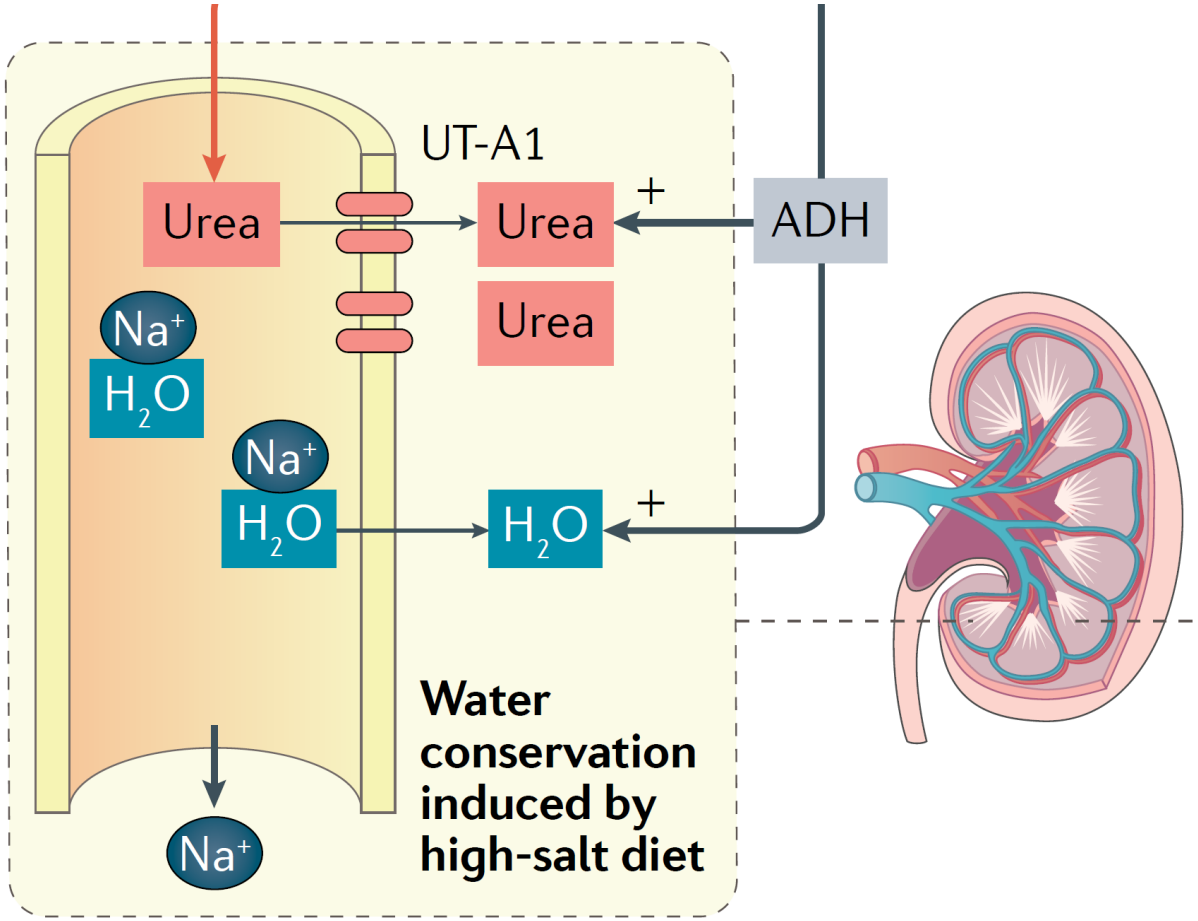
+

Why is there no long-term evidence?

12 people living in the box for 520 days

Natriuretic-ureotelic regulation of body fluid homeostasis





J Clin Invest 127(5):1932-1944, 2017

Natriuretic-ureotelic regulation of body fluid homeostasis

From “bed” to “bench”.

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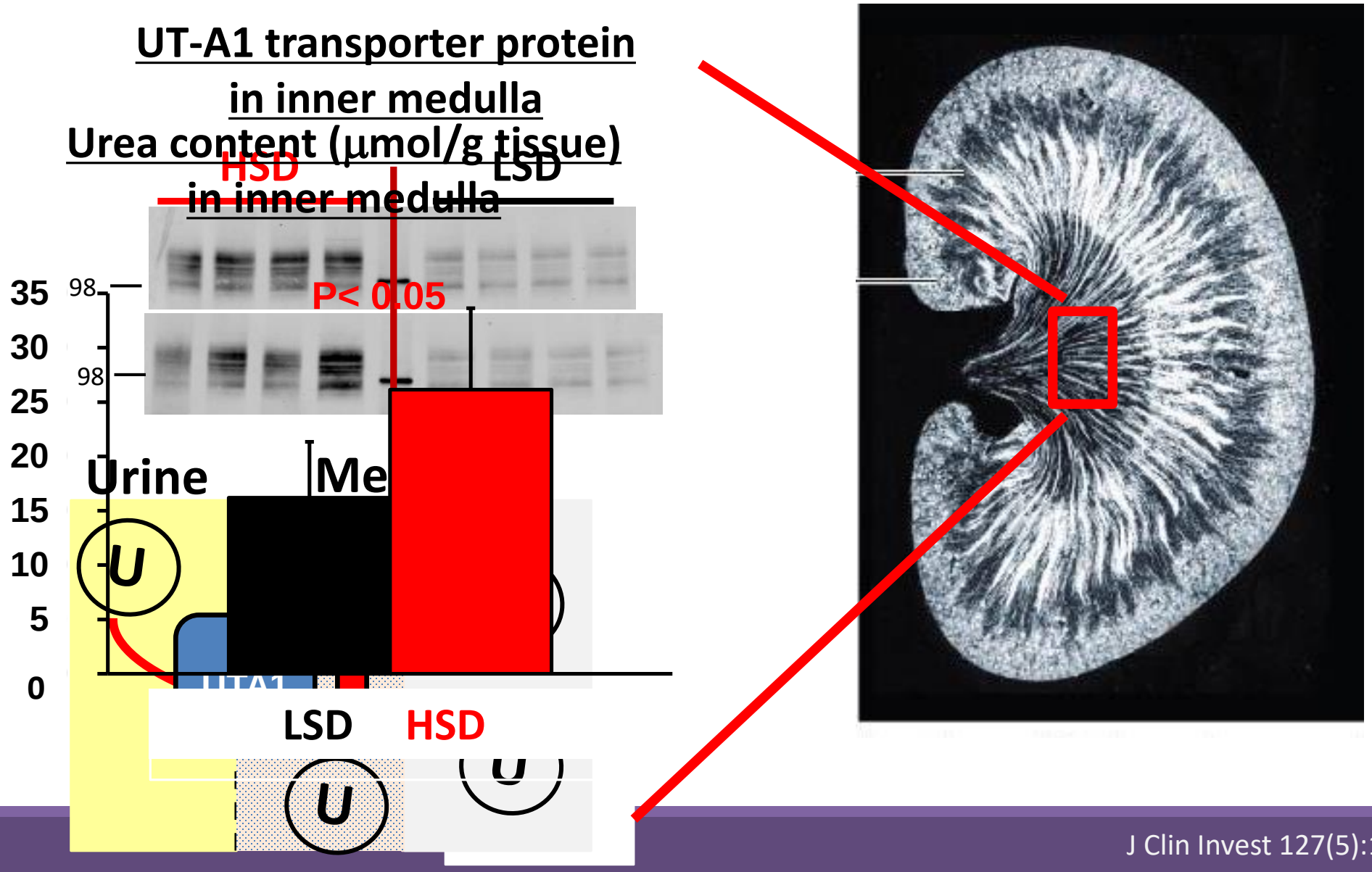
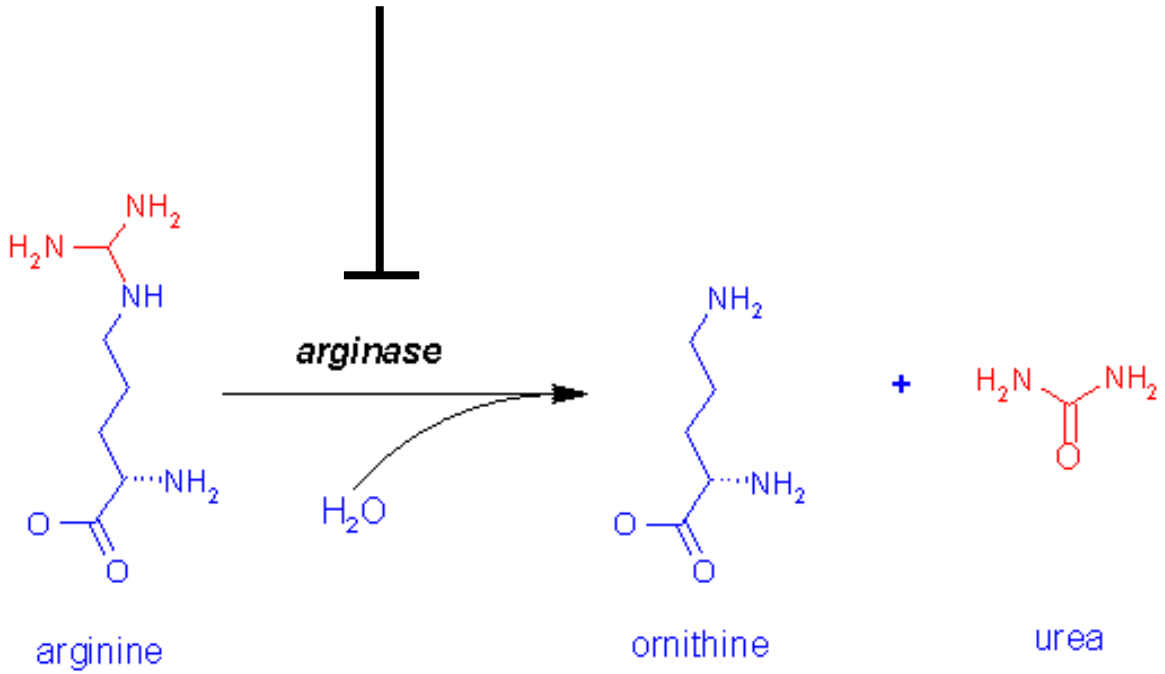
Natriuretic-ureotelic regulation: from men to mice - kidney

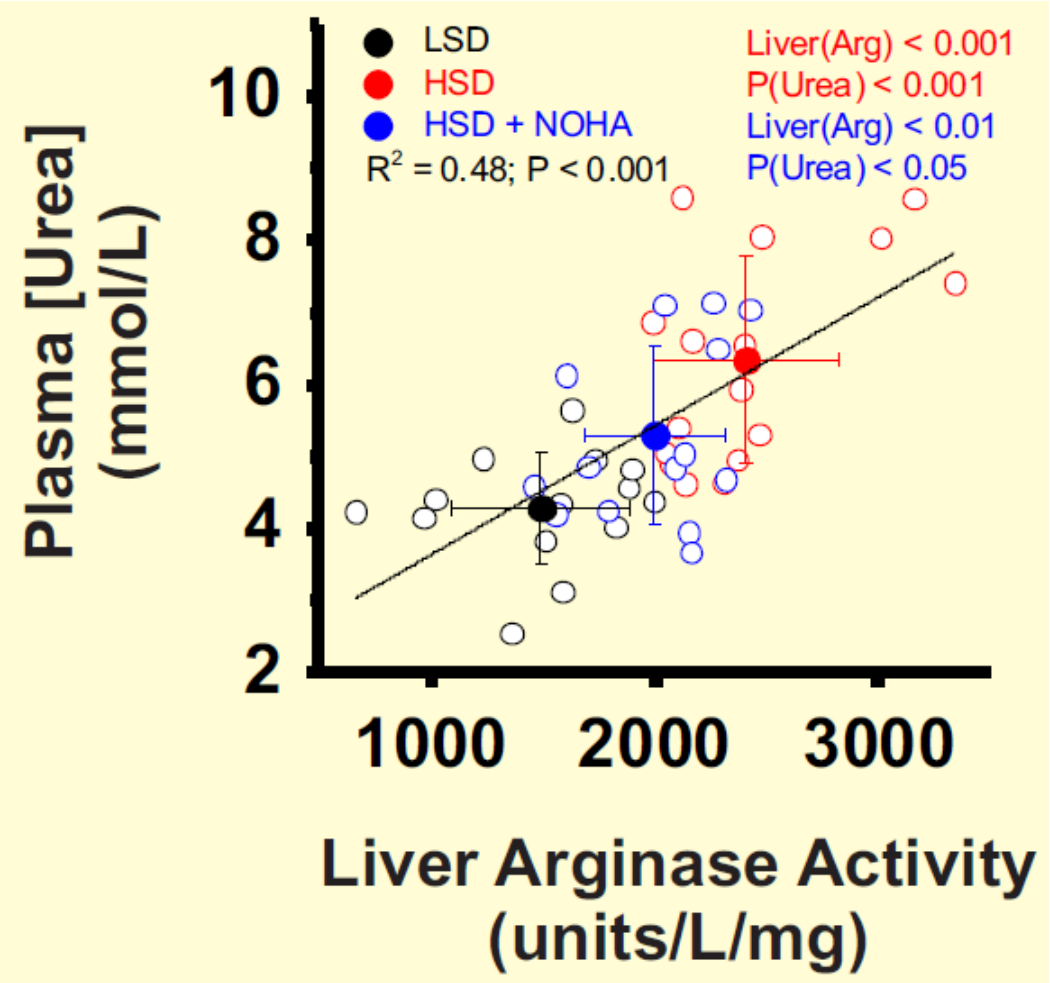


J Clin Invest 127(5):1944-1959, 2017

Natriuretic-ureotelic regulation: from men to mice - liver

N-ω-Hydroxy-L-norarginine

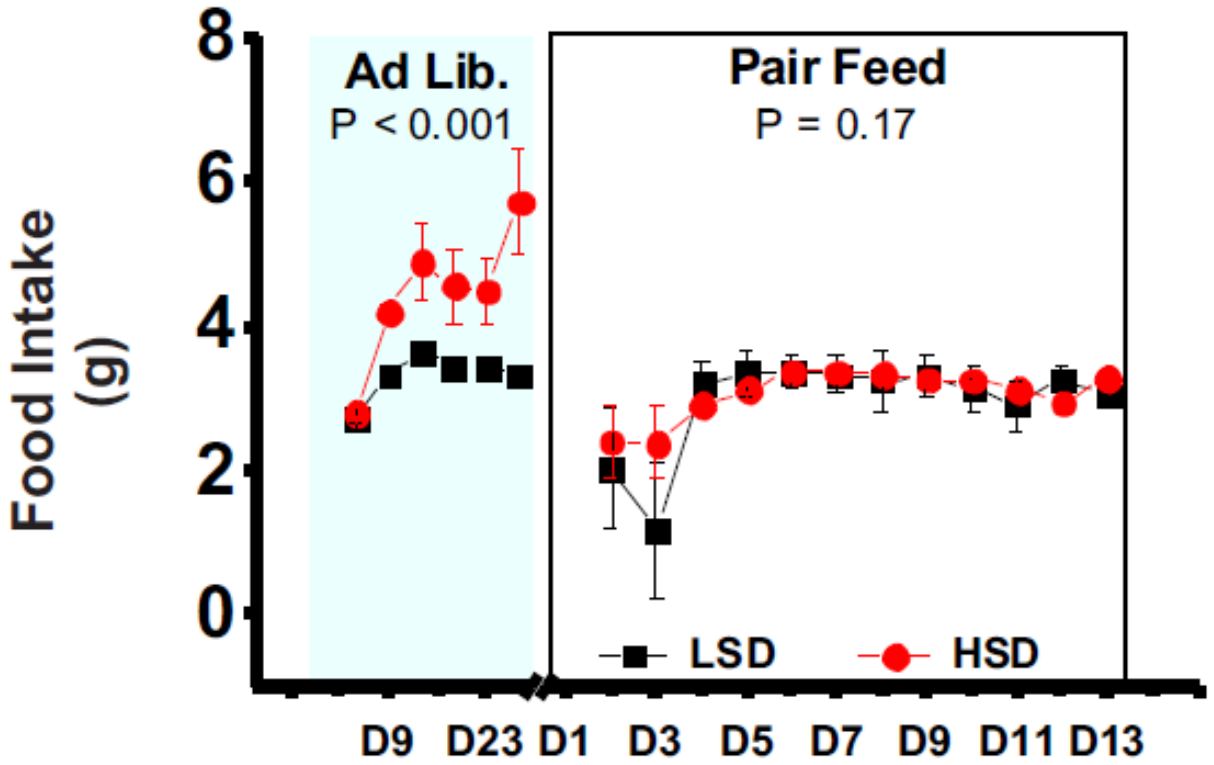




J Clin Invest 127(5):1944-1959, 2017

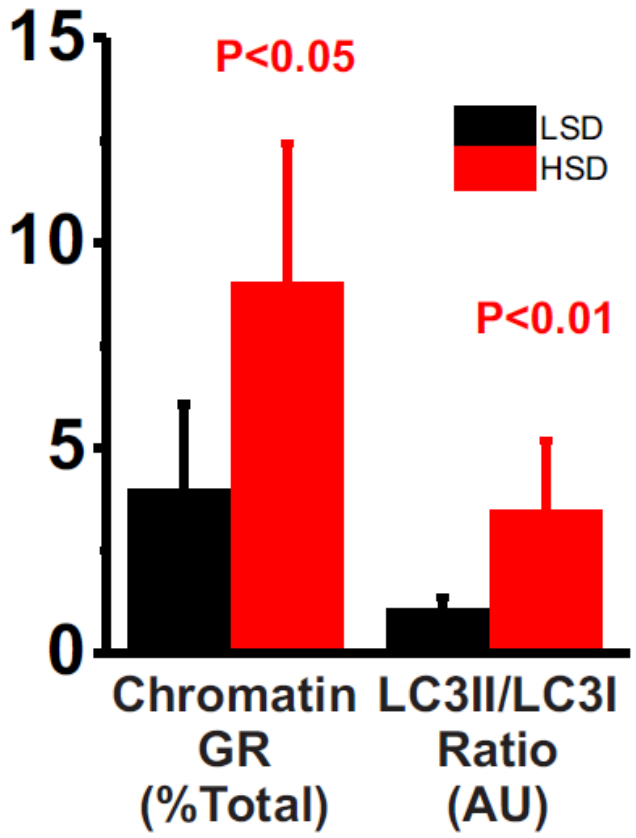
Natriuretic-ureotelic regulation: from men to mice - muscle

A

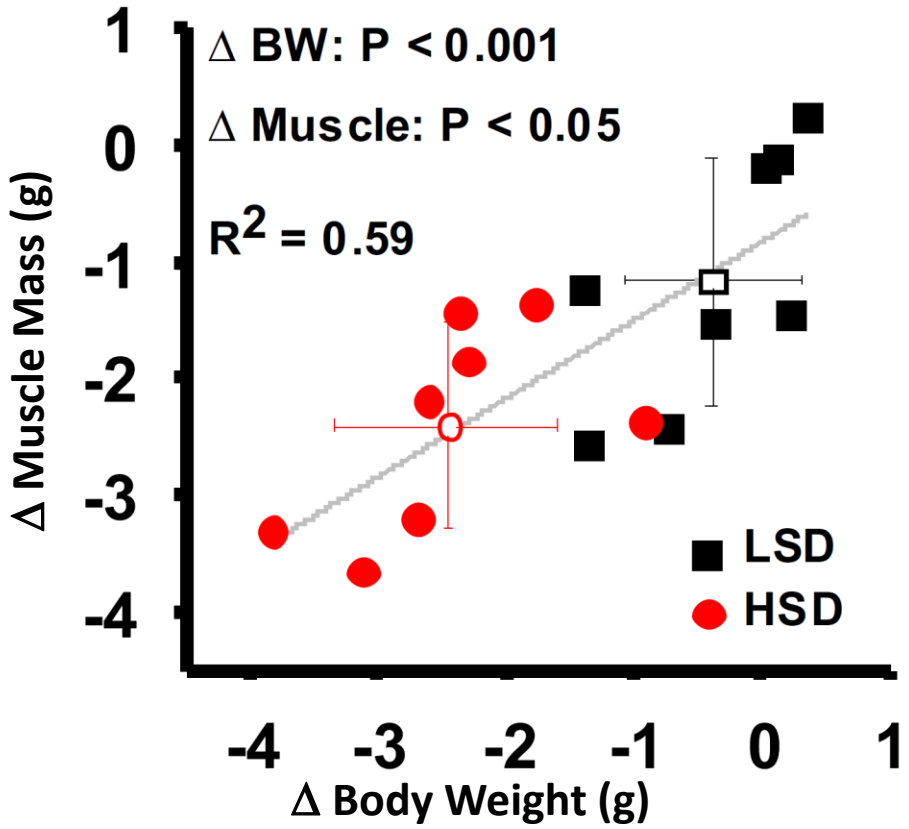


Natriuretic-ureotelic regulation: from men to mice - muscle

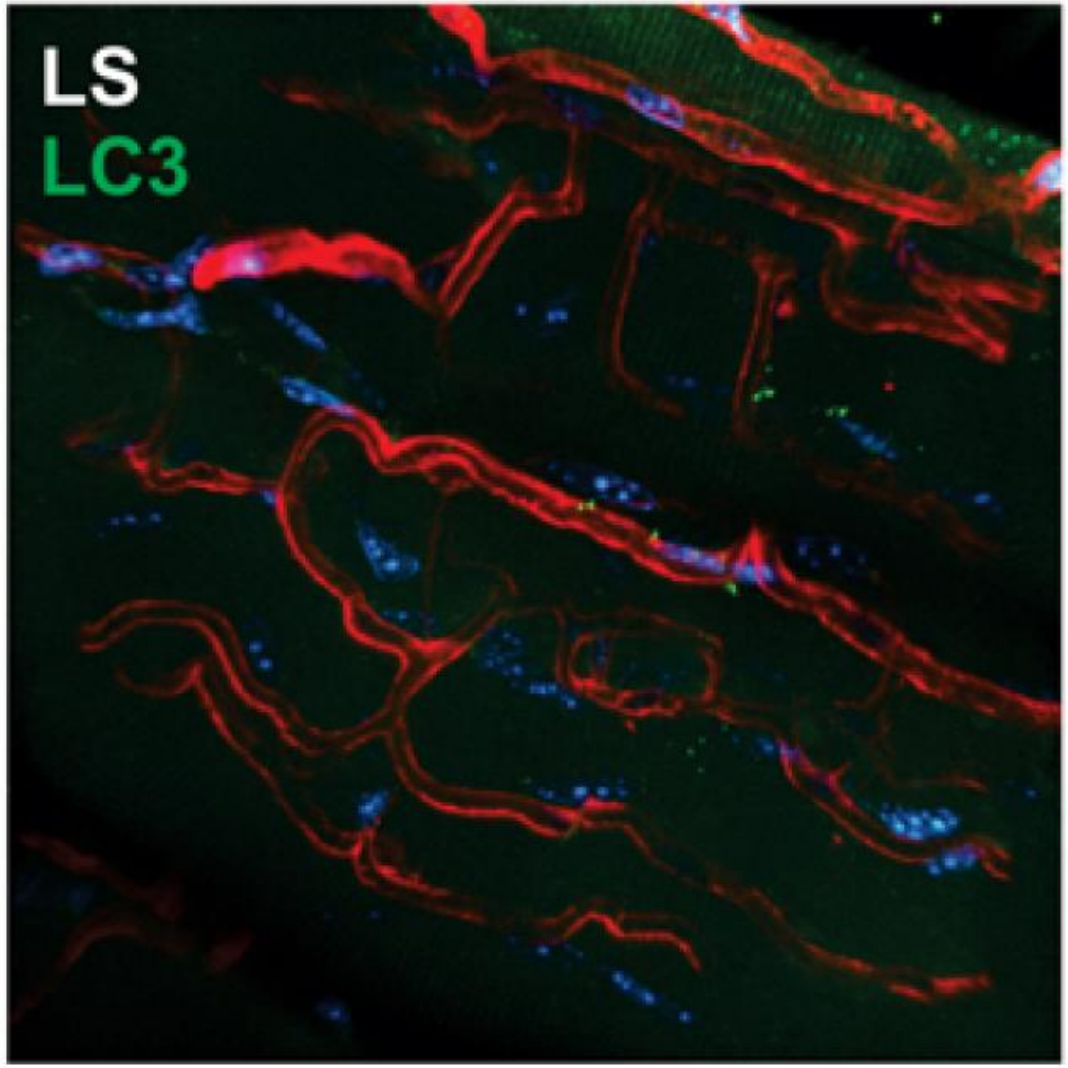
GR chromatin binding

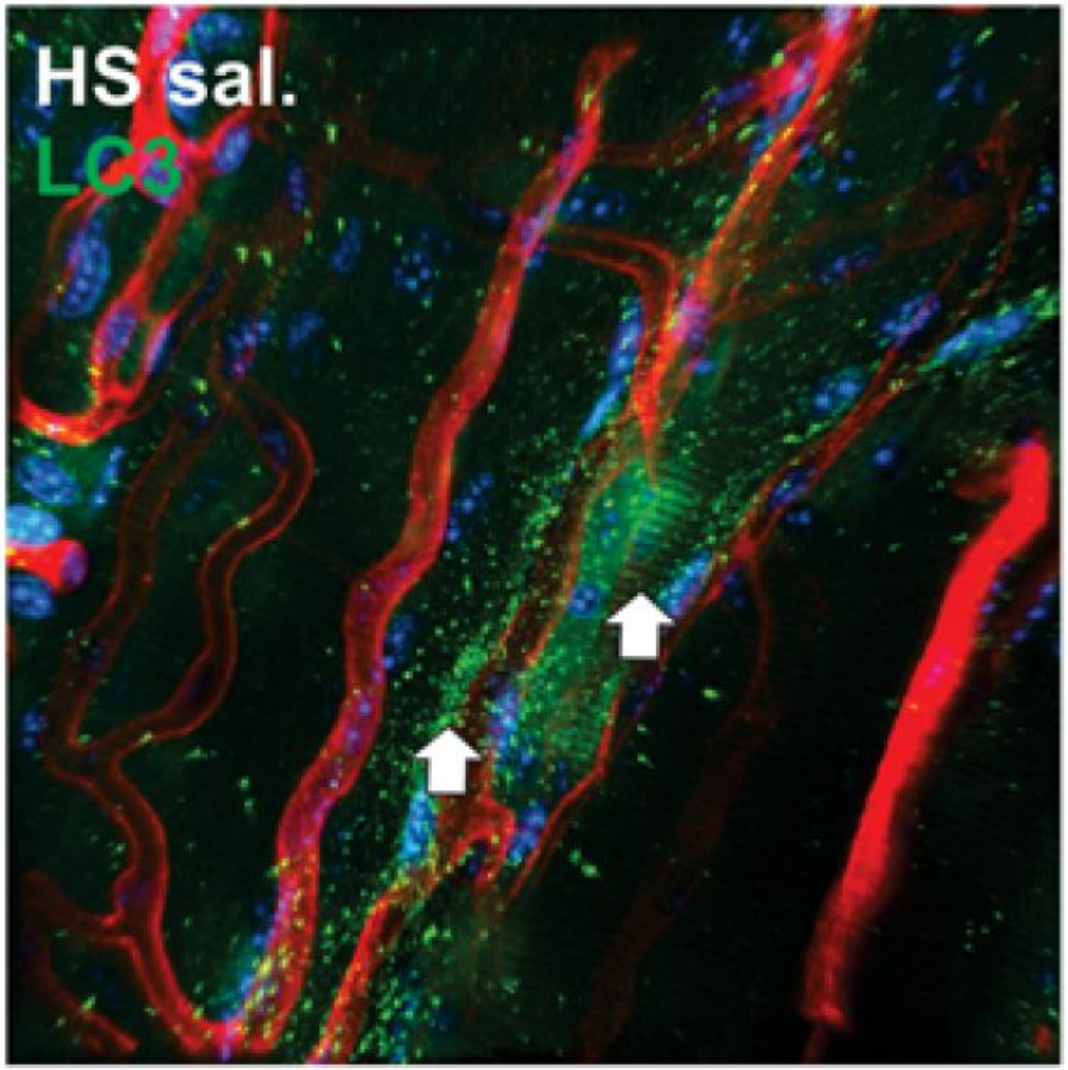


Muscle loss



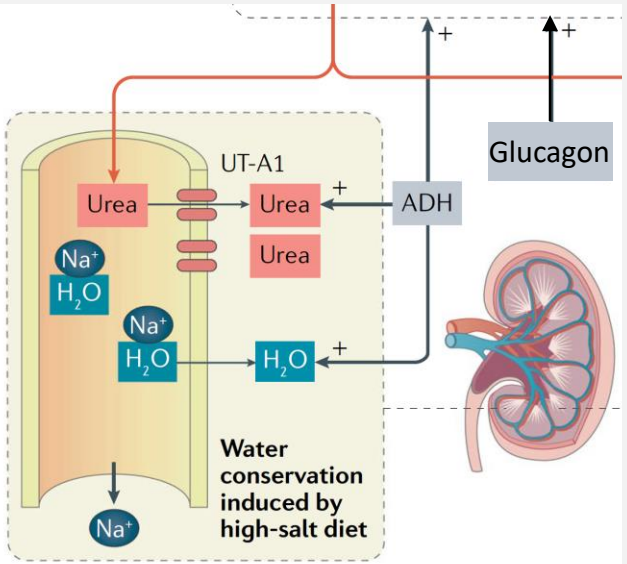
Natriuretic-ureotelic regulation: from men to mice - muscle





J Clin Invest 127(5):1944-1959, 2017

Physiological Water Conservation Eliminates Osmotic Diuresis: Salt



Nat Rev Nephrol . 2021 Jan;17(1):65-77

Natriuretic-ureotelic regulation of body fluid homeostasis

From “bench” to “bed”: does dietary salt increase glucocorticoid levels in humans as well?

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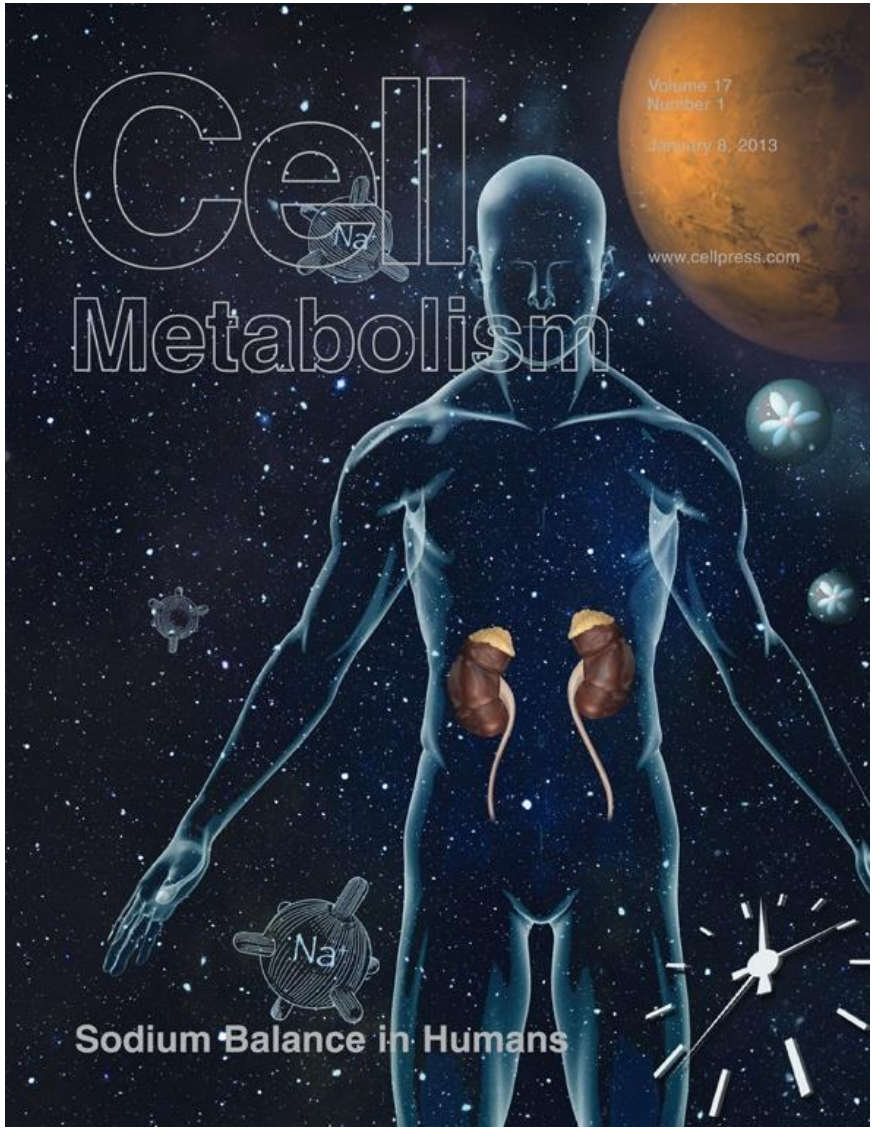
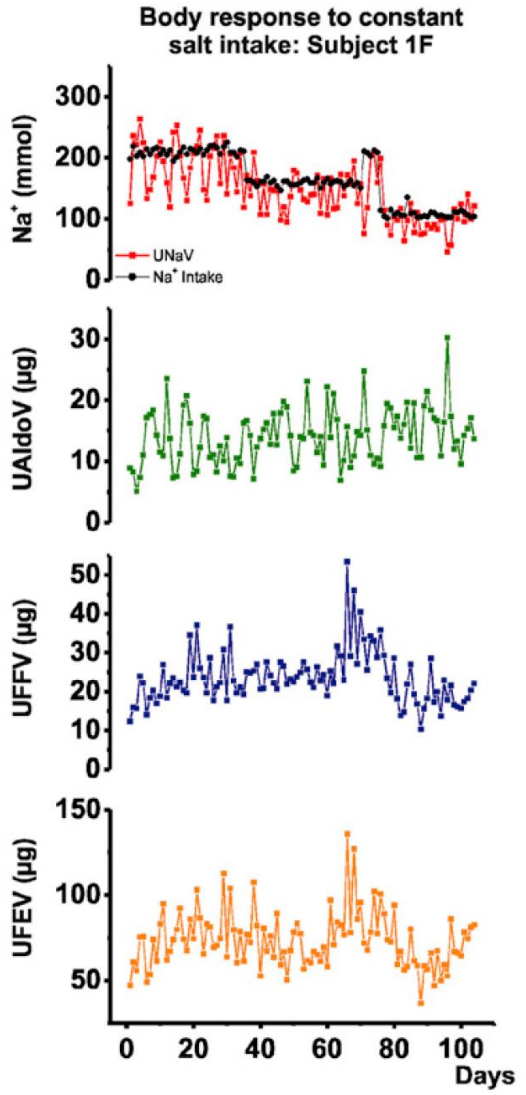
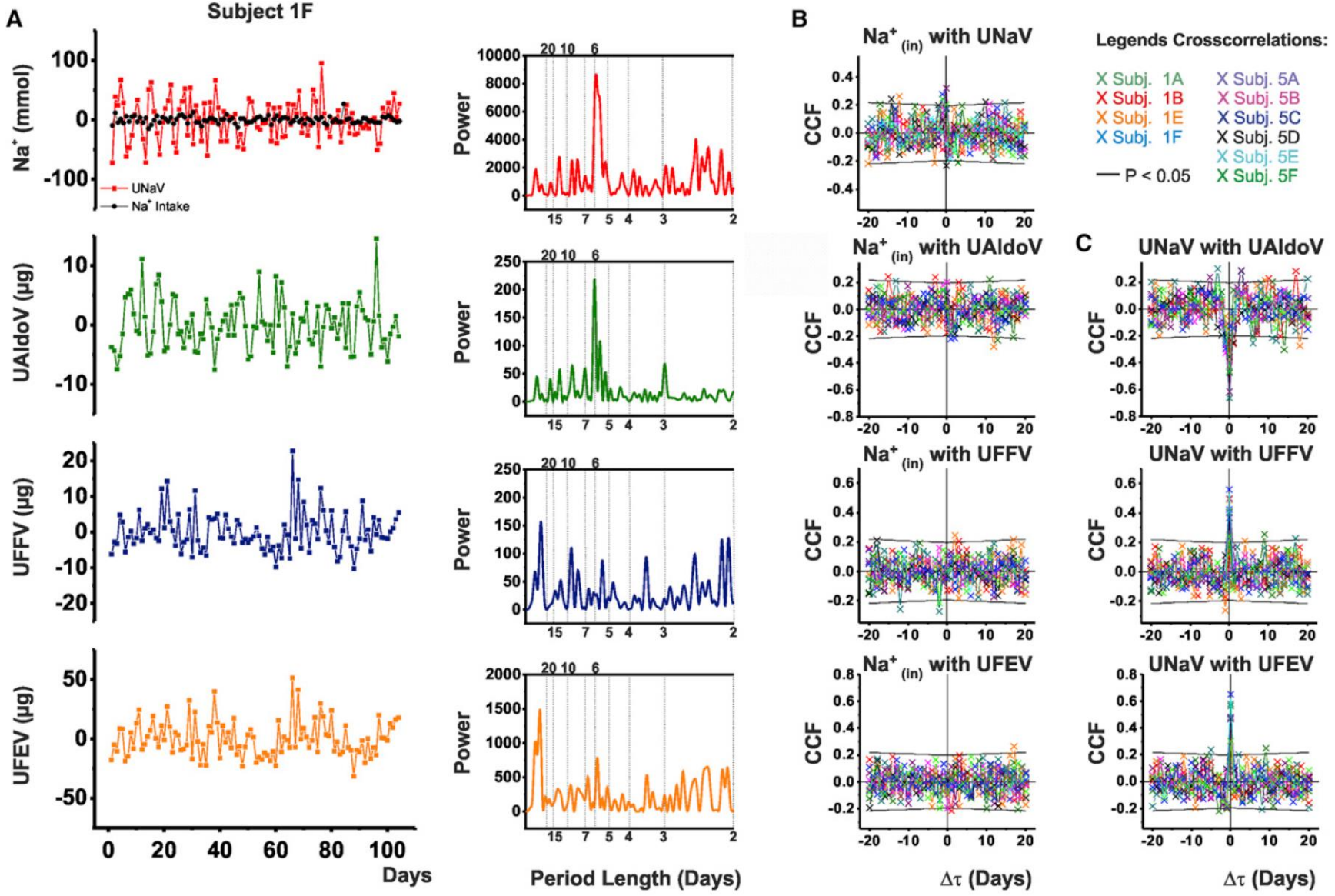
2013: What is the role of Aldosterone vs Cortisol in Na^+ Balance?

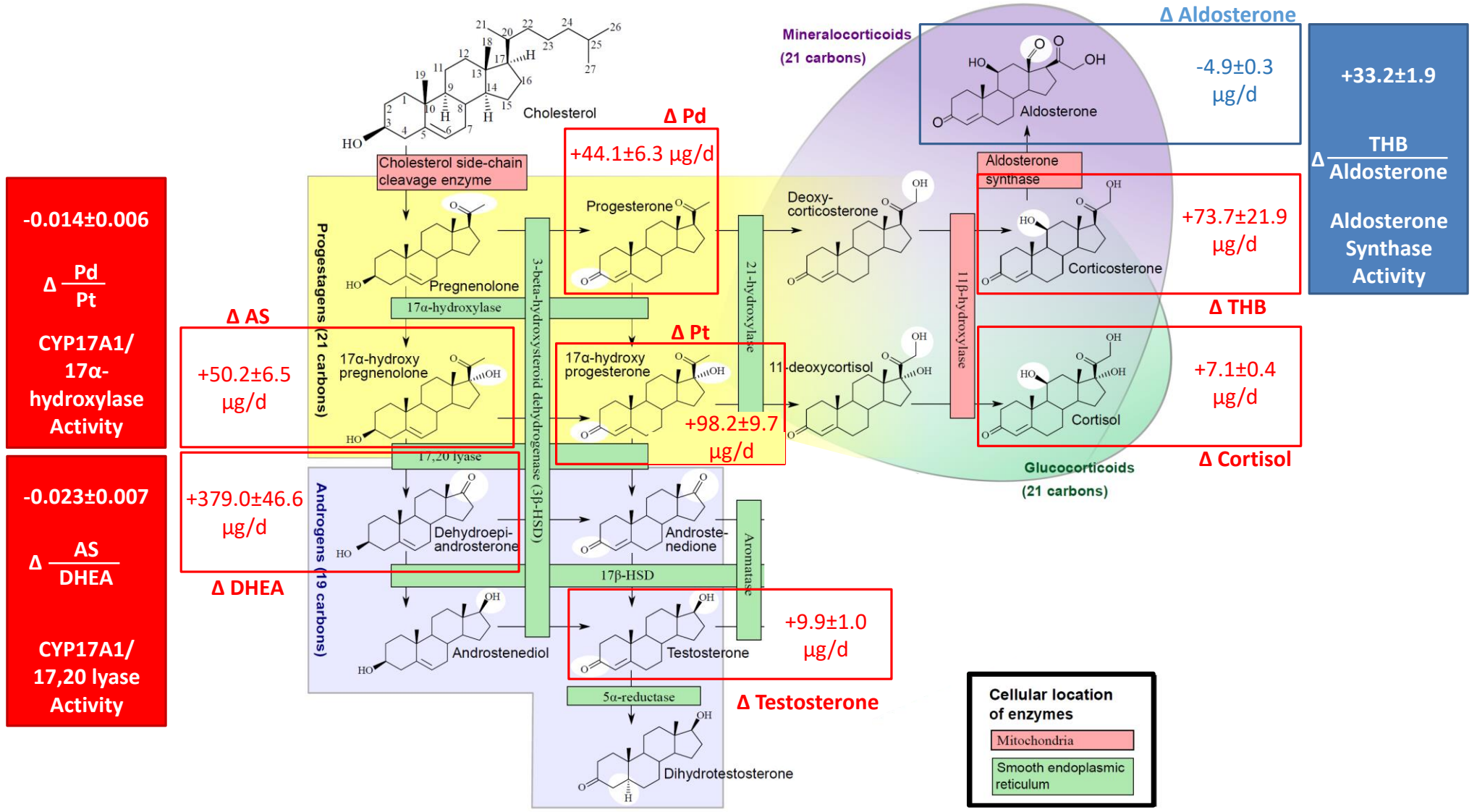




2013: What is the role of Aldosterone vs Cortisol in Na^+ Balance?



Update 2024:
How does dietary salt suppress aldosterone and increase cortisol levels?



Update 2024: Does dietary salt cause a negative nitrogen balance?

EFFECT OF A 6 g/d INCREASE IN SALT INTAKE

Na^+ and water release

Positive nitrogen balance

INTAKE

Water:

ΔWater: -295.4±28.9 ml/d

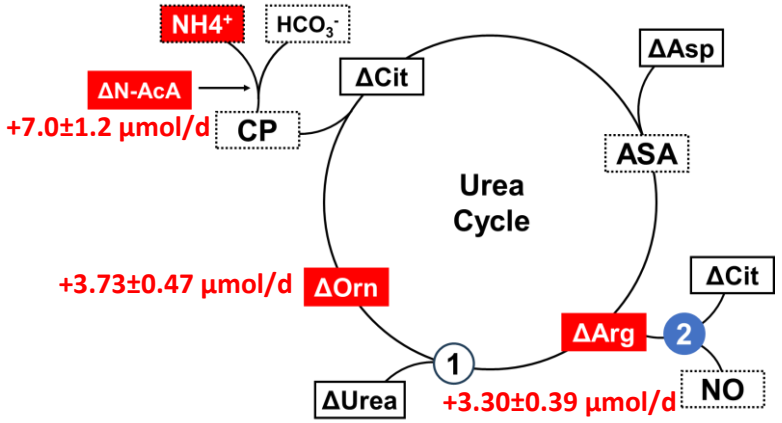
Solute and Energy:

ΔNa⁺: +97.7±1.4 mmol/d

ΔK⁺: no change

ΔProtein: +2.8±0.9 g/d

ΔEnergy: +112.6±16.3 kcal/d



EXCRETION

Water:

ΔUrine Osmolality: +86.2±7.6 mOsm/kg

ΔUrine Volume: no change

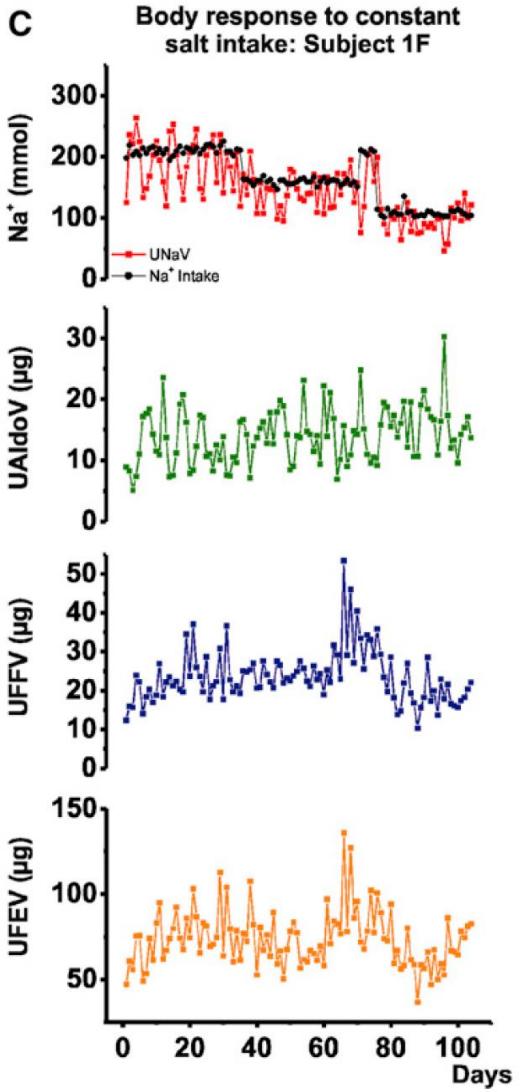
Solute:

ΔUNaV: +96.5±2.2 mmol/d

ΔUKV: -14.4±1.1 mmol/d

ΔUUreaV: no change

ΔBody weight: no change



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Update 2024: What is the role of rhythmical aldosterone and cortisol release for natriuretic-ureotelic homeostasis?

A EFFECT OF ALDOSTERONE (ΔUAldosteroneV: +8.7±0.2 µg/d)

Na^+ and water conservation

Endogenous nitrogen loss

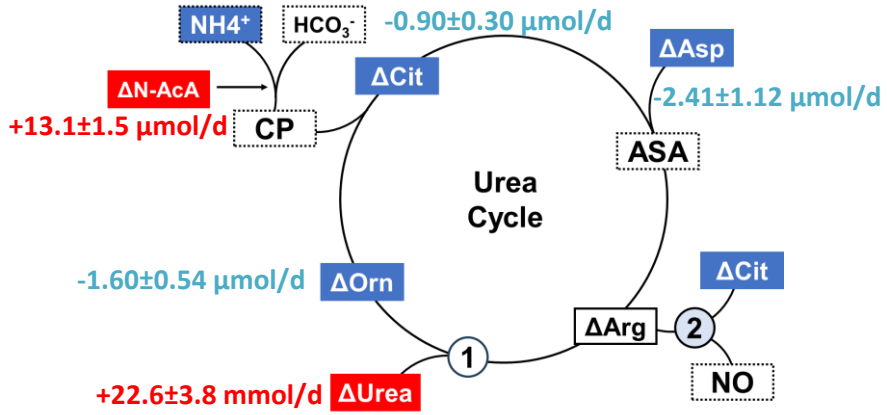
INTAKE

Water:

ΔWater: +95.1±33.2 ml/d

Solute and Energy:

ΔNa⁺: no change
ΔK⁺: +7.3±1.3 mmol/d
ΔProtein: no change
ΔEnergy: +77.3±18.1 kcal/d



EXCRETION

Water:

ΔUrine Osmolality: +67.8±8.8 mOsm/kg
ΔUrine Volume: -302.3±30.1 ml/d

Solute:

ΔUNaV: -37.4±3.7 mmol/d
ΔUKV: +11.7±1.2 mmol/d
ΔUUreaV: +22.6±3.8 mmol/d

ΔBody Weight: +196.9±35.2 g/d

B EFFECT OF CORTISOL (ΔUCortisolV: +13.0±0.4 µg/d)

Solute and water release

Endogenous nitrogen loss

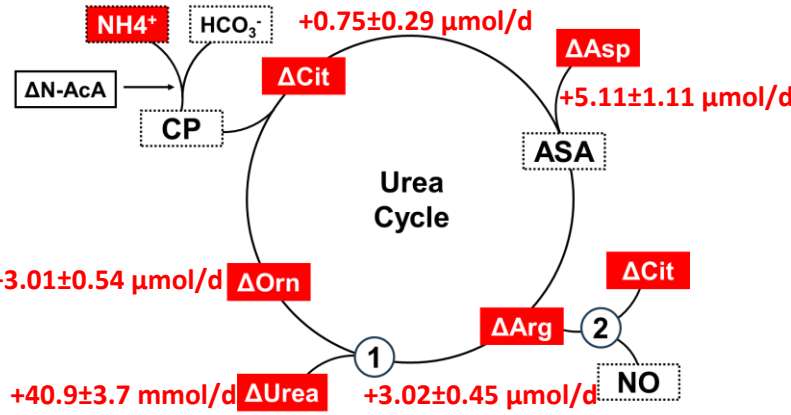
INTAKE

Water:

ΔWater: no change

Solute and Energy:

ΔNa⁺: no change
ΔK⁺: no change
ΔProtein: +3.5±1.0 g/d
ΔEnergy: no change



EXCRETION

Water:

ΔUrine Osmolality: -53.3±8.9 mOsm/kg
ΔUrine Volume: +377.3±29.5 ml/d

Solute:

ΔUNaV: +35.2±3.7 mmol/d
ΔUKV: +9.3±1.2 mmol/d
ΔUUreaV: +40.9±3.7 mmol/d

ΔBody Weight: -150.7±35.4 g/d

Yearly Mars500 progress report

- Cortisol increases with elevated protein intake, activates urea cycle, and promotes urea excretion.
- Aldosterone increases with elevated K^+ intake, suppresses urea cycle, but promotes urea excretion.
- dietary salt increases aldosterone and cortisol/testosterone precursor levels, but suppresses aldosterone synthase activity.
- dietary salt activates urea cycle, but does not increase urea excretion.

Dietary salt causes cortisol-driven urea cycle activation without causing a negative nitrogen balance (e.g muscle catabolism).