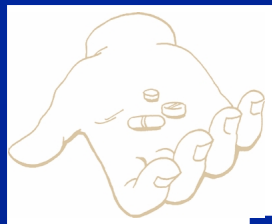
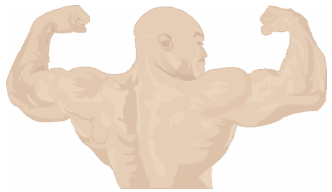
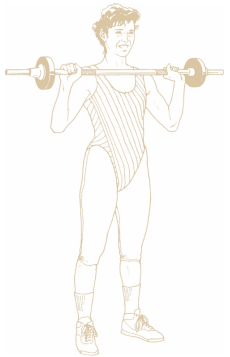


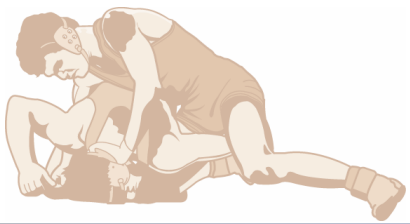
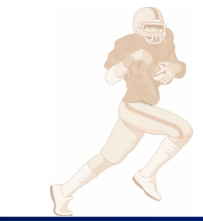


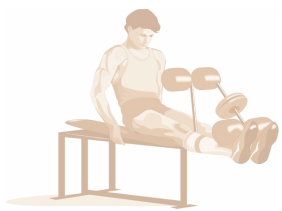











Creatine Supplementation in the 21st Century:

What We Know and What We Don't Know

Jeff S. Volek, PhD, RD, FACN

I. BRIEF BACKGROUND

II. WHY DOESN'T CREATINE ALWAYS WORK?

III. WHAT CAN CREATINE DO?

- Performance
- Body Composition
- Metabolic
- Cardiovascular
- Hormonal
- Other

IV. SPECIFIC POPULATIONS

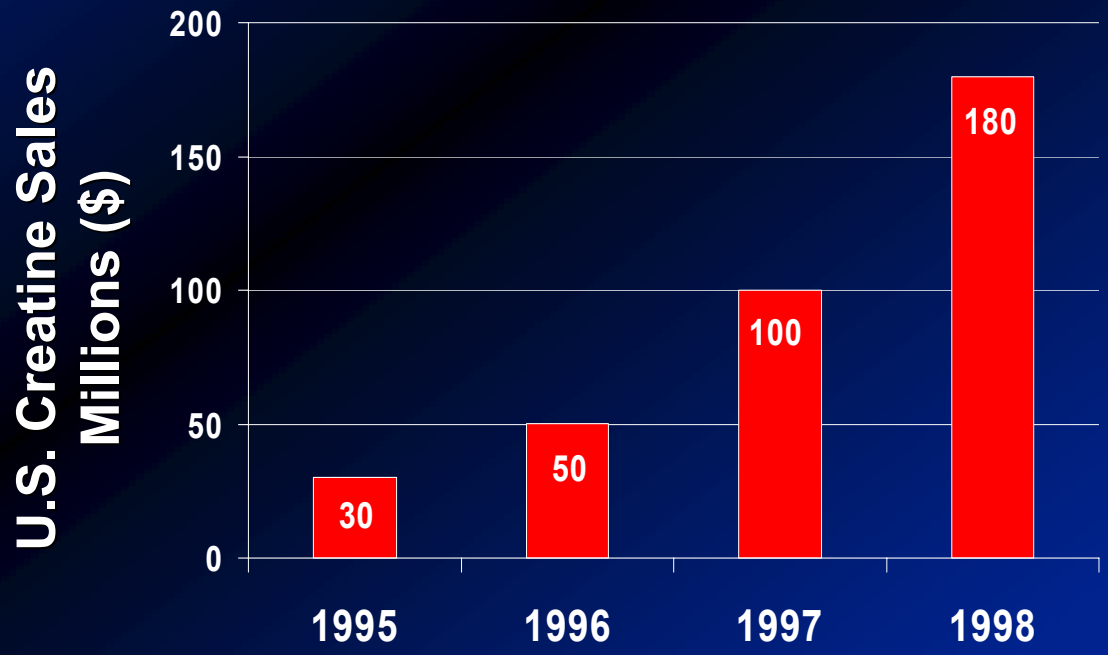
- Adolescents
- Elderly
- Women
- Vegetarians
- Disease States

V. SAFETY ISSUES

VI. FUTURE RESEARCH

USE OF CREATINE

- 16% of high school athletes *(Ray et al, '01)*
- 14% of high school male athletes *(Smith and Dahm, '00)*
- 41% of Division I athletes *(Greenwood et al, '00)*
- 48% (M): 4% (F) Division I athletes *(LaBotz et al, '99)*
- 45% of Norwegian power athletes *(Ronsen et al, '99)*



WHAT IS CREATINE?

- *Cr is NOT a vitamin or mineral*
- *Cr is NOT a steroid*
- *Cr is NOT an amino acid, peptide, or protein*

Creatine is a non-essential, naturally-occurring, organic, nitrogen-containing compound made in the body from amino acids but also obtained in the diet.

SIMPLE YET COMPLEX!

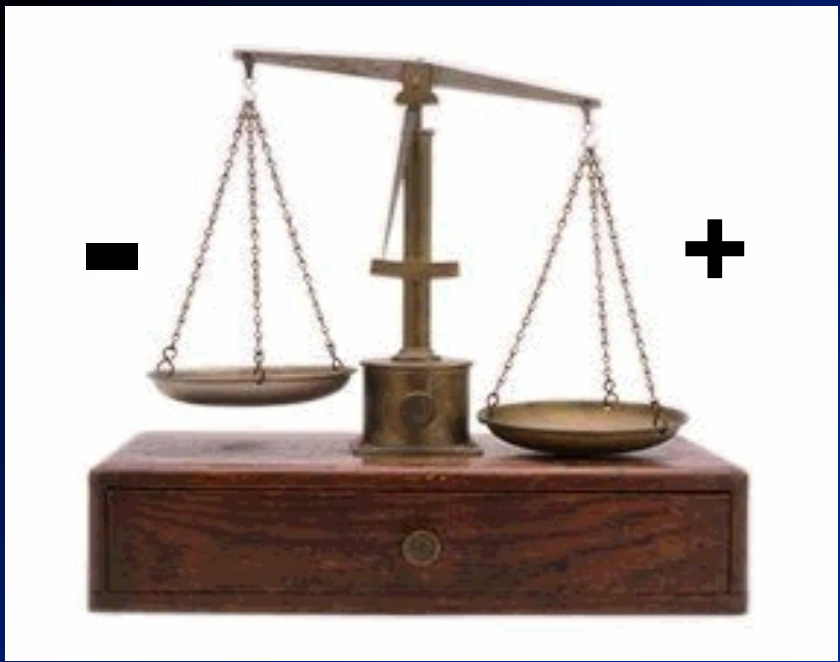
Creatine is involved in one simple chemical reaction and functions to replenish ATP during periods of RAPID energy turnover (temporal energy buffer):

PCr + ADP + H^+ <---*(CREATINE KINASE)*---> Cr + ATP

What can creatine do?
PERFORMANCE

- Cycling protocols
- Running protocols
- Swim protocols
- Loaded/unloaded jumping
- Bench press
- Squat
- Knee extension
- Elbow flexion
- Rowing
- Endurance protocols

- Tennis: No Δ stroke performance
- Soccer: ↑ sprint performance
- Hockey: ↑ spring skating



WHY DOESN'T CREATINE ALWAYS WORK?

RESEARCH VARIABLES IN HUMAN STUDIES

SUBJECTS:
- Age
- Gender
- Number
- Body composition
- Training status
- Motivation
- Genetics
- Circadian rhythms
- Illness
- Learning effects

NUTRIENT PARAMETERS:
- Dosage
- Time of administration
- Mode of administration
- Bioavailability of nutrient
- Single or multiple nutrients
- Form of nutrient

DIET:
- Caloric intake/Diet composition
- Hydration status

STUDY DESIGN:
- Single-Blind/Double-Blind
- Prpoer measurement parameters
- Length of study
- Time-course measurements
- Cross-over/matched

MEASUREMENTS:
- Reproducibilty/Precision/Sensitivity

EXERCISE:
- Type/Duration/Intensity/Frequency

RESULTS:
- Statistical vs. Practical

WHY DOESN'T CREATINE ALWAYS WORK?

- Inadequate statistical power
- Variability in initial muscle creatine stores?
- Performance tests are unreliable?
- Performance tests are the wrong tests?
- Creatine effects are too weak to be detected?
- Failure to increase muscle creatine levels

What can creatine do?

BODY COMPOSITION

(not dependent on training)

Acute (<7 days):

- Body mass *(greater in men)* ↑
- Fat-free mass *(greater in men)* ↑
- Fat mass No Δ
- Total body water ↑
- Intracellular/extracellular water ?

Chronic (>7 days):

- Body mass ↑
- Fat-free mass ↑
- Muscle fiber cross sectional area ↑
- Fat mass No Δ
- Total body water ↑
- Intracellular/extracellular water ?

LONG-TERM CREATINE AND LBM

REFERENCE	DAYS	METHOD	Δ CR	Δ PL
Becque et al. '00	42	HW	1.6	-0.1
Berman et al. '98	52	SF	0.0	0.4
Earnest et al. '95	28	HW	1.6	-0.5
Kelly et al. 98	25	SF	2.5	?NS
Kirksey et al. '99	42	HW	2.6	1.0
Kreider et al. '98	28	DEXA	2.4	1.3
Noonan et al. '98	56	HW	3.2	1.5
Noonan et al. '98	56	HW	2.2	1.5
Pearson et al. '99	70	SF	0.3	-1.3
Peeters et al. '99	42	SF	2.7	0.2
Peeters et al. '99	42	SF	2.2	0.2
Rawson et al. '99	30	HW	0.6	0.1
Stone et al. '99	35	HW	5.3	1.4
Stone et al. '99	35	HW	2.9	1.4
Vandenberghe et al. '97	74	HW	2.6	1.6
Volek et al. '99	84	HW	4.3	2.1

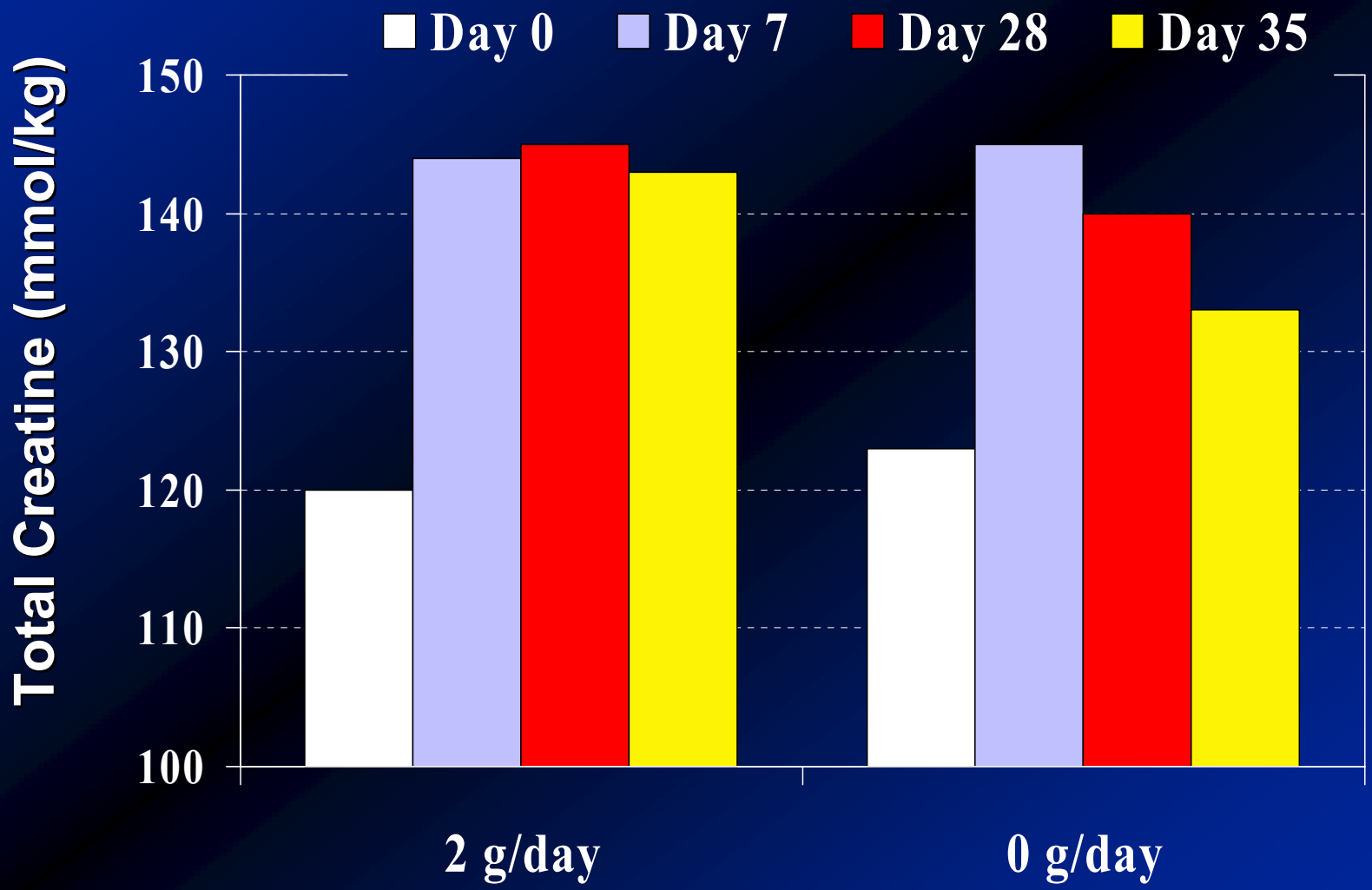
What can creatine do?
METABOLIC

- **Total muscle creatine** ***(↑ by exercise and insulin)*** ↑
- **Muscle glycogen** ↑

  Muscle with ↑ creatine levels can store more glycogen during a 3-day glycogen depletion/repletion protocol

- **Muscle/blood lactate** **Variable**
- **Whole body/mixed muscle PRO synthesis** **No Δ**
- **Leucine oxidation** ***(men only)*** ↓
- **Phosphocreatine resynthesis rate** ↑
- **Amonia/hypoxanthine accumulation** ↓
- **Muscle GLUT 4** ***(insulin sensitivity?)*** ↑

Muscle creatine after ingesting 20 g/day for 6 days followed by 2 g/day or nothing



Modified from Hultman et al. J. Appl. Physiol. 81(1):232-237, 1996.

What can creatine do?

CARDIOVASCULAR

Blood pressure	No Δ
Heart rate	No Δ
Oxygen consumption	No Δ
Cholesterol	↓ or No Δ
Triglycerides	↓ or No Δ

What can creatine do?
HORMONAL

- Growth hormone ↑ ?
- Testosterone No Δ
- Cortisol No Δ
- Others:
  - Aldosterone ↑ ?
  - Renin No Δ
  - Angiotensin No Δ
  - Atrial peptide No Δ
  - Insulin No Δ

PROPOSED MECHANISMS

- Energy metabolism
- Protein metabolism
  - ↓ whole body protrein catabolism
  - ↑ actin & myosin synthesis *in vitro*
- ↑ Cell swelling
- ↑ Satellite cell mitotic activity in rodents
- ↑ Membrane Integrity *(intramuscular or intravenous PCr)*
- ↓ Muscle relaxation time

SAFETY ISSUES

- Kidney/Liver
- Blood Lipids
- GI
- Muscle Cramping
- Cardiovascular

No scientific evidence but anecdotal claims persist

- ↑ Anterior compartment pressure during/after exercise

SPECIFIC POPULATIONS

- Adolescents *(few data)*
- Elderly *(mixed results)*
- Women *(↑ performance and LBM)*
- Vegetarians *(↑ performance and LBM)*
- Disease States

THERAPEUTIC USE OF CREATINE IN DISEASE

- Myopathies & neuromuscular disorders associated w/ ↓ muscle creatine *(gyrate atrophy, mitochondrial pathologies, muscular dystrophy, etc.)*
- Animal models of Parkinson's and Huntington's disease
- Neuroprotective affects from hypoxia and energy-related brain pathologies in animal models
- Guanidinoacetate methyltransferase deficiency
- Heart disease
- Rehabilitation after disuse atrophy
  - ↑ myogenic transcription factor
  - ↑ GLUT 4

FUTURE RESEARCH

- Pharmacokinetic research in order to optimize dosing regimens
- Clinical trials in individuals w/ neuromuscular disorders
- Interaction with other nutrients
- Characteristics of "nonresponders"
- Matrix of delivery, timing of intake, & variability in Cr accumulation
- Long-term safety
- Responses in different populations
- Mechanistic research:
  - Specific myoson & actin-specific fractional synthetic & breakdown rates and isoform-specific mRNA content
  - Cellular hydration

Thank You