Cardiometabolic Risk, Obesity & Inflammation: What Does it all Mean for Individuals Aging with Spinal Cord Injury?

Presented by Suzanne Groah, MD, MSPH
National Rehabilitation Hospital
June 3-4, 2010
Miami, FL

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Cardiometabolic Risk

- The term ‘cardiometabolic risk’ has recently supplanted ‘metabolic syndrome’
- Better defines CVD and endocrine risks
- CMR represents unique combinations of risk factors that may impart a health hazard
- CMR clustering linked to CVD-related morbidity and mortality
  - Worsens non-linearly with the identification of additional risk factors

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Cardiometabolic Risk

- Studies examining cardiometabolic syndrome have found that its principal clinical outcome is cardiovascular disease
- People who develop CVD do so based upon the synergies of multiple risk factors
- Many CMR factors and clustering are disturbingly prevalent in persons with SCI
- But is this commensurate with CVD?

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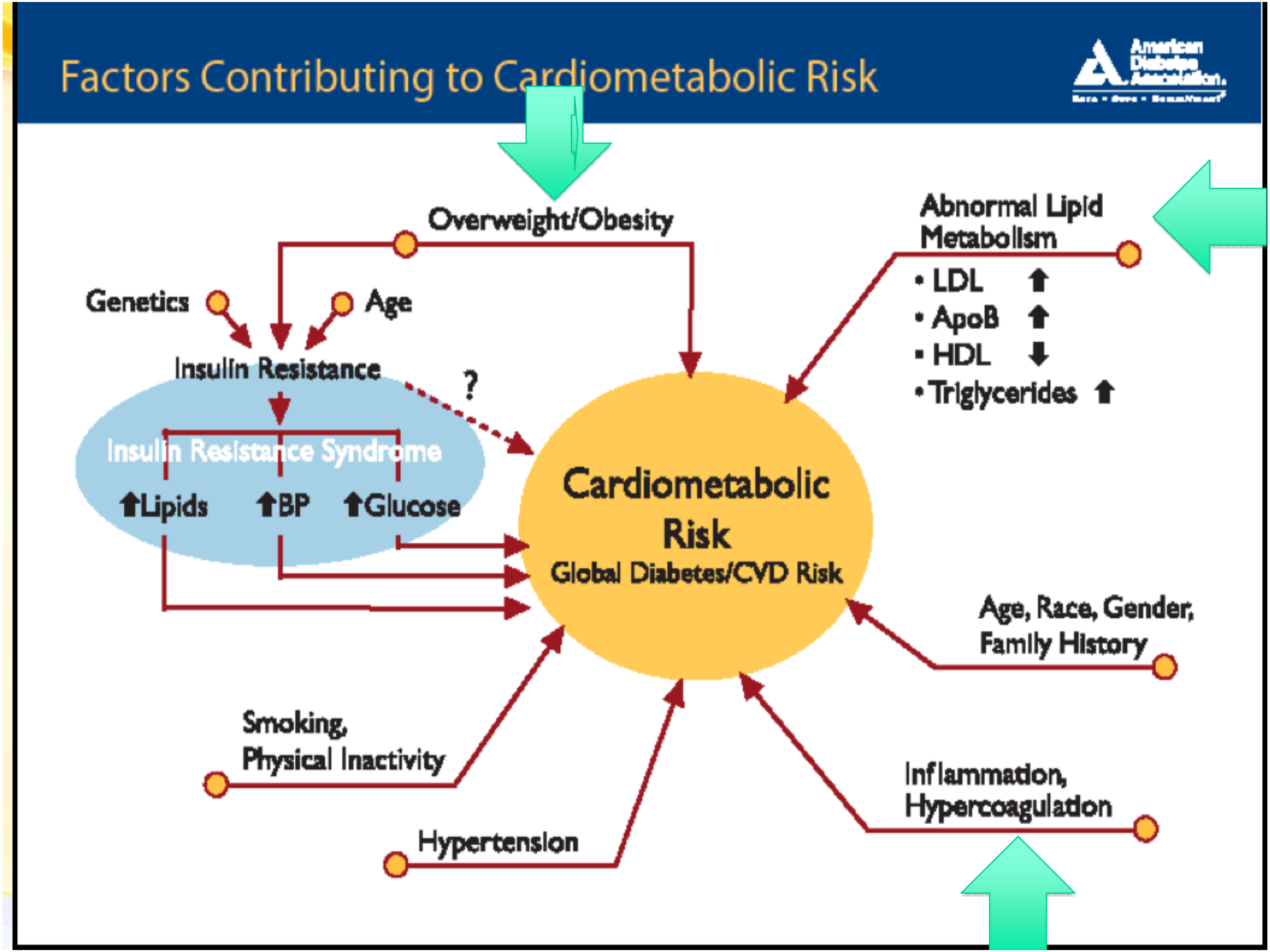
McNeill, 2005; Fried, 1998; Smith, 2007; Bauman & Spungen, 2008; Nash, 2009)

Longitudinal Aging Evidence

- CVD is the leading cause of death in long-term SCI (30+ years)
- 35% of all deaths in those with SCI 60 and older
- After excluding deaths during the first year post-injury, CVD is the most common cause of death
- 41% of all deaths in the Boston Cohort Study

DeVivo, 1999; Whiteneck, 1992; Hartkopp, 1997; Yekutiel, 1989

Factors Contributing to Cardiometabolic Risk



Atherogenic Lipid Profile After SCI

- Normal total cholesterol
- Normal or elevated LDL
- Normal or elevated triglycerides
- **Consistently low HDL**
- Significantly elevated TC:HDL ratio

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Bauman & Spungen, 2008; Nash & Mendez, 2007

Insulin Resistance

- 1/3 – 1/2 of people with SCI live in a state of insulin resistance
  - Tetra > Para
- Physical inactivity, **obesity**, sympathetic dysfunction may be causes
- Often missed with routine testing

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Duckworth, 1980 and 1983; Nash 2006; Nash & Gater, 2007; Bauman, 1994; Bauman, 1999; Groah & Nash, 2010

UNITED STATES OBESITY TRENDS

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Obesity After SCI

- Obesity is at epidemic proportions
- Obesity is due to
  - Obligatory lean muscle loss
  - Blunted sympathetic NS
  - Positive energy balance
- Obesity is UNDERestimated by BMI in people with SCI
- Central adiposity is most strongly associated with cardiometabolic syndrome

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Nash & Gater, 2007; Maruyama, 2008; Myers, 2007

Metabolic Syndrome after SCI

- Castillo, JSCM, 2007
  - N=487 veterans with SCI
  - Mean age 55.2 yrs, 48.7% tetraplegic
  - 56.5% BMI > 25 kg/m^2
  - 37% dyslipidemia
  - 63.4% HDL < 40
  - 56.5 % hypertension
  - 44.8% metabolic syndrome
- Defined as central obesity + any 2 of the following:
  - TG >= 150 md/dl
  - Low HDL-C
  - High BP
  - Fasting glucose >= 100 md/dl

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Attack of the Fat!

- Insulin resistance
- Hypertension
- Dyslipidemia
- Thromboembolism
- Inflammation

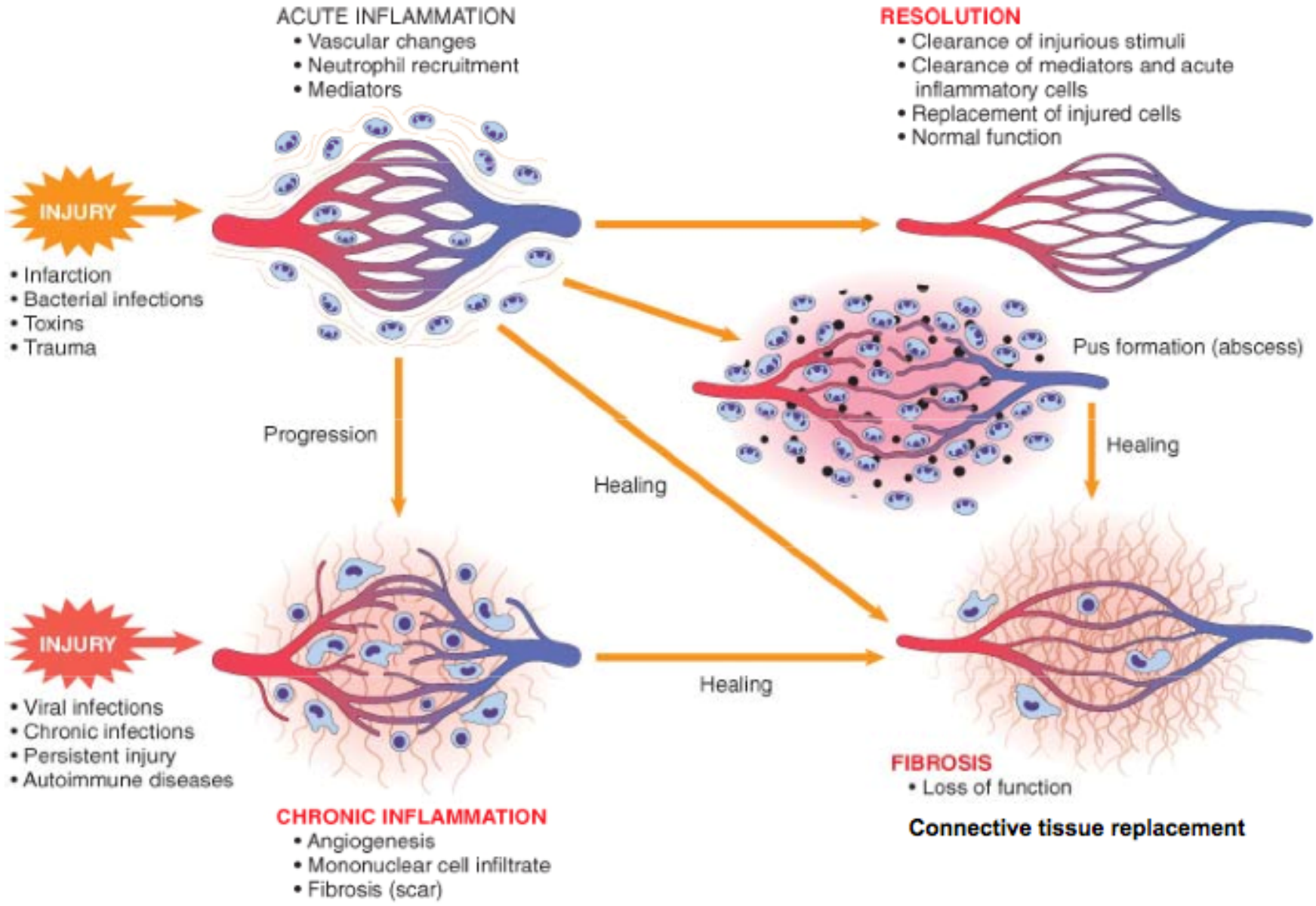
Inflammation

- Process by which body responds to injury or infection
- Important in the pathophysiology of atherosclerosis
  - CRP, hs-CRP
- Systemic inflammatory biomarkers predict cardiovascular events
- Atherosclerosis is accelerated in various inflammatory rheumatic diseases

Inflammation and Obesity

- Individuals genetically predisposed to high BMI have elevated CRP
- Adipose releases certain cytokines (IL-6) that stimulate the release of CRP
- CRP increases blood levels of cellular adhesion molecules, endothelin-1, and decreases NO
- Hence, atherosclerosis is a chronic inflammatory vascular condition

Acute Inflammation: Outcome



SCI and the Pro-Inflammatory State

- Added risk of systemic inflammation due to skin breakdown and infections
- Accelerates vascular wall stress and atherogenesis
- Recent attention on blood levels of pro-inflammatory cytokines as triggers for CVD
  - Several exceed cut-off scores for elevated CVD risk

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Frost, 2005; Lee, 2006; Liang, 2008; Manns, 2005; Morse, 2008; Wang, 2007

Homocysteine and C-Reactive Protein Summary

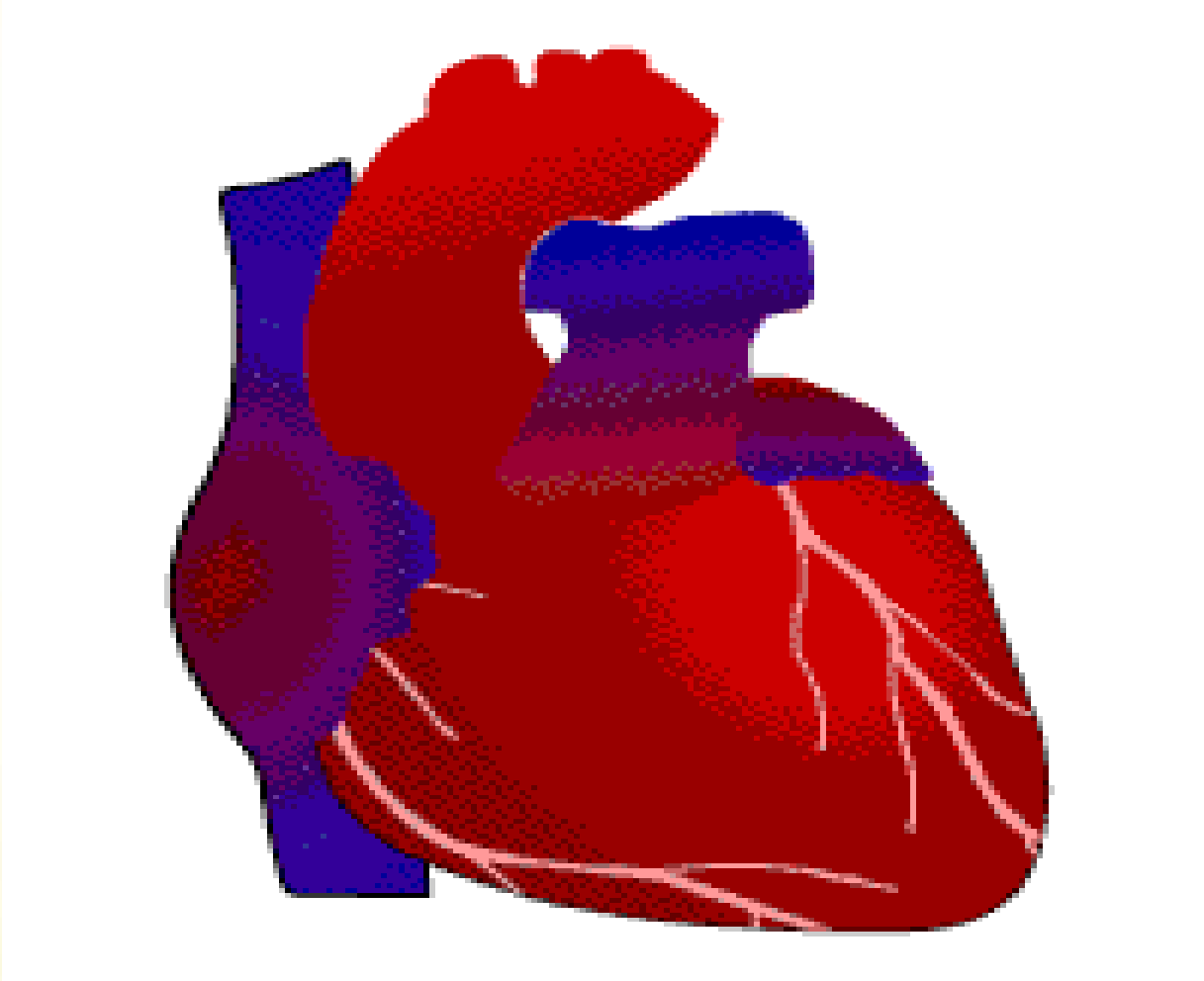
- 44% of SCI patients studied in a large sample had a homocysteine level associated with an increased mortality ratio
- 62% of SCI patients studied had moderate to high CRP levels

KNOWLEDGE BASED ON RISK FACTORS AND NOT DISEASE STATUS

Importance of Prevention

- Obesity pandemic (SCI at greater risk)
  - Primary trigger for cardiometabolic risk clustering
- ATPIII guidelines identify obesity as the primary target for intervention in cardiometabolic syndrome
- Sensory deficits may mask acute cardiovascular symptoms and obscure disease progression
- More profound impact on the health, well-being, and function of persons with SCI than those without SCI

Questions



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