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### Perceived Stress, Psychosocial Stressors, and Behavioral Factors: Association With Inflammatory, Immune, and Neuroendocrine Biomarkers in a Cohort of Healthy Very Elderly Men and Women

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**Introduction:** By 2030, it is estimated that 20% of the US population will be over 65 years of age, and that 75% of adults will have one or more severe disabilities by age 80. Determining preventive models for age-related diseases, frailty, and functional decline is critical. Dysregulation of inflammatory pathways and desynchronization of hormonal axes have been identified in age-related diseases including cardiovascular disease, dementia, and mood disorders.

**Methodology:** In this 12-month prospective study, 28 healthy elderly and very elderly (> 85 years of age) subjects who met strict inclusion/exclusion criteria were enrolled. Twenty-one psychosocial, cognitive-behavioral, and nutritional factors that were associated with eight immunologic and neuroendocrine/endocrine biomarkers at different times of the day and at different levels of physiologic stress were measured at baseline and at 6, 9, and 12 months. Mean age of participants was 85 years with 79% female and 21% male.

**Results:** Perceived stress as determined by Holmes-Rahe revealed a mean of  $304.46 \pm 156.33$ , with 26% of subjects reporting high financial stress. In addition, 29.62% of subjects had experienced childhood health issues and 18.51% experienced a traumatic home environment. Assessment of quality of life with the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) revealed mean values of 46.43 for the mental component (MC), and 36.15 for the physical component (PC) at baseline, and 37.12 for MC 41.65 for PC at follow-up. Social interactions

averaged 24.47 activities per month and 85% of subjects reported active spiritual beliefs. Completed educational level completion was high school or higher. Nutritional assessments showed that 89% consumed prudent diet selections with no significant change over time, mean body mass index (BMI) was 25.98 (SD, 4.30), and 89% took dietary supplements. Behavioral findings revealed that 3.5% used tobacco; 28.5% drank alcohol at least once weekly, 28.57% exercised daily, and 71.43% exercised at least twice weekly with no significant change over 12 months. Neuroendocrine measures revealed mean Folstein Mini-Mental Status Exam score, 28; mean insulin-like growth factor-1, 36.98 ng/mL; mean cortisol/dehydroepiandrosterone sulfate ratio 3.2; mean tumor necrosis factor- $\alpha$ , 1.73 pg/mL; mean interleukin-6, 0.34 pg/mL; mean C-reactive protein (CRP), 3.25 mg/L; mean fibrinogen, 9.66 mg/dL; mean dehydroepiandrosterone sulfate, 3.06 ng/mL; mean testosterone, 22.69 pg/mL in women, 81.93 pg/mL in men; mean estrogen 1.94 pg/mL in women. Recursive partitioning (RP) was used to “grow trees” for each biologic marker at both the morning and evening as well as the high and low cortisol-collecting intervals. Each tree identified multiple combinations of the 21 factors/stressors (predictor variables) that led to each of the biologic markers (target variables), referred to as pathways. Two at-risk target variables were identified: CRP from the immune system and testosterone from the endocrine system at both time intervals and at the low- and high-risk cortisol levels. Predictor variables that showed the greatest frequency of both target variables were BMI, education level, socialization/activities, nutrition, marital status, and whether or not they lived alone.

**Conclusion:** It is plausible that proadaptive psychosocial and lifestyle choices, despite high perceived stress, may influence neuroendocrine and immune regulatory processes, and thus, may protect against age-related changes in proinflammatory pathways. Preventive counseling models in younger adults may be expanded to assess nontraditional clinical markers of neuroendocrine/immune function that are associated with psychosocial/behavioral/nutritional factors in efforts to prevent later age-related diseases, frailty, and functional decline.