

The Psychological and Physiological Effects of Acute Occupational Stress in New Anesthesiology Residents

A Pilot Trial

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ABSTRACT

Background: Occupational stress in resident physicians has profound implications for wellness, professionalism, and patient care. This observational pilot trial measured psychological and physiological stress biomarkers before, during, and after the start of anesthesia residency.

Methods: Eighteen physician interns scheduled to begin anesthesia residency were recruited for evaluation at three time points: baseline (collected remotely before residency in June 2013); first-month visit 1 (July); and follow-up visit 2 (residency months 3 to 5, September–November). Validated scales were used to measure stress, anxiety, resilience, and wellness at all three time points. During visits 1 and 2, the authors measured resting heart-rate variability, responses to laboratory mental stress (hemodynamic, catecholamine, cortisol, and interleukin-6), and chronic stress indices (C-reactive protein, 24-h ambulatory heart rate and blood pressure, 24-h urinary cortisol and catecholamines, overnight heart-rate variability).

Results: Thirteen interns agreed to participate (72% enrollment). There were seven men and six women, aged 27 to 33 yr. The mean \pm SD of all study variables are reported.

Conclusion: The novelty of this report is the prospective design in a defined cohort of residents newly exposed to the similar occupational stress of the operating environment. Because of the paucity of literature specific to the measures and stress conditions in this investigation, no data were available to generate *a priori* definition of primary outcomes and a data analytic plan. These findings will allow power analysis for future design of trials examining occupational stress and stress-reducing interventions. Given the importance of physician burnout in our country, the impact of chronic stress on resident wellness requires further study. (*ANESTHESIOLOGY* 2014; 121:878-93)

THE health and well-being of physicians and other healthcare providers is critical to our nation's healthcare system. Unfortunately, increasing evidence suggests that the nation's physicians and nurses are experiencing epidemic levels of burnout, dissatisfaction, and work-related stress.¹⁻³ These factors appear to be a particular concern for resident physicians where burnout and distress have been shown to impact patient safety^{4,5} and be related to medical knowledge as assessed by standardized tests.⁶ Stress encompasses a wide range of psychological and physical perturbations that negatively affect health, relationships, quality of life, and well-being. Recent surveys have shown increasing levels of stress and burnout in physicians³ and also a connection between burnout and patient outcomes.¹ Given this association, an intense area of new empirical interest is occupational stress in the context of professionalism among healthcare workers.

What We Already Know about This Topic

- Occupational stress in physicians in training has been reported to be high in surveys, but has not been prospectively quantified in terms of psychology and physiology

What This Article Tells Us That Is New

- In a pilot study of 18 individuals recruited to assess stress at the beginning of residency, 72% consented and participated in assessments of stress, anxiety, resilience, and wellness in addition to physiological biomarkers for stress
- The results provide a detailed image of stress conditions during the first months of residency as well as variability data for power analyses for hypothesis testing investigations

This is particularly important in perioperative resident physicians who have the least experience in the operating room organizational hierarchy. Furthermore, compared with other

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healthcare providers, residents are most affected in health, personal support, professional support, and outside activities.⁷

To identify the impact of stress on well-being, one strategy is to select a cohort of residents who will encounter an anticipated training stressor. The first month of anesthesiology residency represents an extreme degree of psychological, intellectual, procedural, technical, managerial, and logistical stress. In addition to the factors just described, the start of anesthesiology residency may also impact health behaviors, including a stress component that can be considered “deprivation stress,” which may involve less sleep, an irregular sleeping schedule, a reduction in physical activity level, a reduction in pleasurable activities or hobbies, poor nutrition, and a reduction in personal or family time.⁸

The emotional stress and burnout risk in residency training has been well documented, but the method of data collection has primarily been through psychological surveys that evaluate stress level, burnout, or mood. Similarly, for physiological measures, although some variables have been recorded in simulator training modules,⁹ nothing has been collected during real-time “in the field” patient-care activities. Thus, there is a major knowledge gap in the quantifiable psychological and physiological effects of the profound occupational stress associated with novice medical residents transitioning to residency training. Reliable markers of stress would be considered essential repeated measures in interventional trials aimed at reducing stress and optimizing the training experience, with implications for resident wellness, professionalism, and patient care.

With this information as background, the purpose of this pilot and feasibility trial was to prospectively collect high-resolution psychological and physiological data in new clinical anesthesia year-1 trainees. Therefore, the study goals were to (1) quantify the acute psychological stress of starting anesthesia residency by measuring physical activity level, perceived stress, state anxiety, resilience, and perceptions of well-being; (2) record heart-rate variability (HRV) as a marker of cardiac autonomic modulation; (3) measure chronic markers of stress including 24-h urinary catecholamines (epinephrine and norepinephrine), 24-h urinary cortisol, and C-reactive protein; and (4) administer an acute mental stress protocol in our laboratory to generate a data base of acute cardiovascular and biomarker responses during the first month of anesthesiology residency and a follow-up visit.

Materials and Methods

Subjects

This study received approval from the Department of Anesthesiology and the Mayo Clinic Institutional Review Board, Rochester, Minnesota. Eighteen incoming clinical anesthesia year-1 residents, scheduled to begin anesthesia training on July 1, 2013, were recruited in June 2013. All individuals were completing postgraduate year-1 at the time of recruitment. An Institutional Review Board–approved written informed consent form and health screening questionnaire were sent to each incoming resident by mail. Upon return of the signed consent form, the health screen was reviewed by the research nurses to ensure that

no medical, psychiatric, or physical conditions would preclude participation in this study. Personal details such as marital status, children, or personal conflicts were not obtained. To ensure confidentiality, no investigator had access to the participants’ health screen or medical records. Even though this was considered a minimal risk protocol, pregnant women were excluded. Under the principles of protection of human subjects, no information was gathered on individuals who declined participation.

Preanesthesia Residency “Baseline” Condition

As shown in figure 1, participants were evaluated during three time conditions: prestress baseline (collected remotely prereidency in June 2013); first-month visit 1, between 5 and 14 working days after starting residency (July 8 to 19, 2013); and follow-up visit 2 (any working day during an operating room or pain service rotation 3 to 5 months after starting residency between September 18 and November 21, 2013). During the prestress baseline, subjects completed the following survey instruments, which are provided in appendices 1 to 4:

Minnesota Leisure-Time Physical Activity Questionnaire.

Minnesota Leisure-Time Physical Activity Questionnaire was used to determine the amount of energy expended during the previous 12 months (appendix 1). The questionnaire recorded information on frequency and duration of activities, providing an estimate of the amount of energy expended per activity, averaged per day in metabolic equivalents.¹⁰

Cohen’s Perceived Stress Scale. Cohen’s Perceived Stress Scale is a 14-item scale designed to measure the degree to which situations in one’s life are appraised as stressful (appendix 2).¹¹ The Perceived Stress Scale has been shown to be a predictor of psychological symptoms, physical symptoms, and utilization of health services. The mean Cohen’s Perceived Stress Scale score for working adult men and women aged 26 to 35 yrs is 25.0 ± 8.2 .¹² The mean Cohen’s Perceived Stress Scale scores for college-age men is 22.4 ± 6.8 , and for college-age women is 23.6 ± 7.6 .¹³ Cronbach’s alpha coefficient for the internal reliability of the scale is 0.78.¹⁴

Spielberger State Anxiety Index. Spielberger State Anxiety Index is a scale for measuring anxiety and has been used in simulated trauma scenarios for resident trainees (appendix 3).¹⁵ It includes 20 questions with a scale (20 to 80 points, higher score indicates higher anxiety) to describe how the respondent feels at a particular moment in time (state anxiety) using subjective feelings of apprehension, tension, nervousness, worry, and activation/arousal of the autonomic nervous system.¹⁶ In a population of working adults ($n = 1,387/451$ men/women), the mean Spielberger State Anxiety Index is 35.7 ± 10.4 , and in college students ($n = 296/481$ men/women), the mean is 38.8 ± 12 .¹⁷ The internal consistency of the state anxiety scale has an alpha of 0.92.¹⁵

Resiliency and Daily Well-being Surveys. Two questions provided an abbreviated index of the Connor-Davidson Resilience Scale (appendix 4).¹⁸ The mean Connor-Davidson Resilience Scale score is 6.91 ± 1.5 in a general adult population.¹⁸ Four questions provided a fast and simple assessment of daily well-being as used in employee wellness trials at our

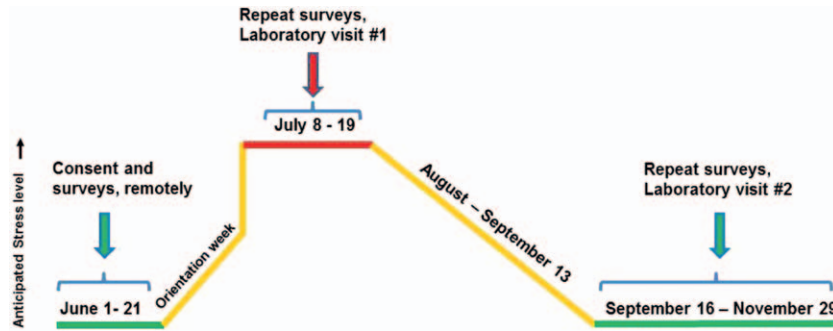


Fig. 1. Study timeline. Incoming clinical anesthesia year-1 trainees were evaluated in 2013 during three conditions. The month before starting anesthesia was considered baseline and psychological data were collected remotely. In-person visit 1 occurred in weeks 2 and 3 of the first month of clinical anesthesia year-1 training. Follow-up visit 2 was identical to visit 1 and occurred during an operating room or pain rotation in the fall.

institution.¹⁹ For the stress level (scale 0 to 10), a report at our institution on a cohort of 104 employees undergoing a stress reduction program found a mean stress level of 4.2 ± 2.25 at baseline, and 5.6 ± 2.07 after the 12-week program.¹⁹

First-month Visit 1

Three days before this visit, subjects were fitted with a Body Media Sensewear (BodyMedia, Inc., Pittsburgh, PA) physical activity monitor.²⁰ This is an elastic band worn on the upper arm that measures activity, energy expenditure, sleep, and sleep efficiency. Subjects wore the band for 3 days and nights until arriving for their study visit. The Daily Well-being and Resiliency Surveys were also completed at this time. To control for daytime variations, all study visits were conducted between noon and 4 PM in the Clinical Research Unit. Upon arrival, vital signs were obtained; the Daily Well-being and Resiliency Surveys were completed by the subjects. To measure dietary habits, an Automated Self-Administered 24-h Dietary Recall was administered.²¹ Subjects were placed supine in a quiet room. An 18 to 20 gauge intravenous catheter was placed in the antecubital fossa for blood draws. Heart rate (HR) was measured by 3-lead electrocardiogram and recorded at 1,000 Hz on LabChart (AD Instruments, Colorado Springs, CO). Respiratory rate was measured by capnography with a nasal cannula, and blood pressure was measured continuously by finger plethysmography (Nexfin; Edwards Lifesciences, Irvine, CA) and confirmed periodically with an automated brachial oscillometric cuff. Stroke volume, cardiac output, and systemic vascular resistance were derived from pulse contour analysis of the finger plethysmography waveform according to Nexfin algorithms.²² A Polar chest belt was fitted that transmits HR to a proprietary HRV application on a smart phone (@-life; Mikropis Holding, Inc., Zalec, Slovenia).²³

After resting in the supine position for 20 min, HR was recorded for HRV analysis. The electrocardiogram signal was imported into the Nevrokard Advanced HRV Analyses software (version 13.2.1; Nevrokard Kiauta k.d., Izola, Slovenia) for time and frequency domain analyses as described recently.²⁴ After this, venous blood draws were collected for the following assays. Serum C-reactive protein was determined as a generalized measure of systemic inflammation, elevated in chronic

job strain and caregiver strain.^{25,26} Serum cortisol, serum epinephrine, and serum norepinephrine were determined to measure the degree of sympathoexcitation at rest and during mental stress.²⁷ Salivary cortisol was also collected for comparison with serum cortisol. Serum interleukin-6 was collected as a biomarker shown to respond to mental stress to a greater extent than C-reactive protein.²⁸ Interassay variability and coefficients of variation are described in detail in appendix 5.

Once resting blood samples were drawn, subjects were moved to a semirecumbent chair for a computerized mental stress protocol, described in detail in appendix 5.²⁹ After 2 min of baseline HR and blood pressure recording and 30 s of instructions, a mathematical subtraction test commenced for 5 min, followed by the Stroop colored word conflict test for 5 min, and concluding with 4.5 min of a second mathematical subtraction test, for a total stress duration of 15 min. At the end of the 15 min, blood sampling was repeated for serum cortisol, serum epinephrine and norepinephrine, and serum interleukin-6. Saliva was collected for salivary cortisol. After a 5-min recovery period, subjects were deinstrumented and completed a psychological distress survey modified from a mental arithmetic stress survey by Reims *et al.*³⁰

As detailed in the appendix 5, before discharge, subjects were fitted with a 24-h ambulatory blood pressure monitor. Blood pressure and HR were measured using the Spacelabs 90202 recorder (Spacelabs Inc., Snoqualmie, WA) as described by our laboratory.³¹ Subjects were also instructed to wear the Polar chest belt from bedtime to awakening the next morning, and HR was recorded by the proprietary application on a mobile smartphone (@-life; Mikropis Holding, Inc.). Finally, subjects received containers for 24-h urine collection and were instructed to return all devices 24 h later. Urine was analyzed for cortisol, epinephrine, and norepinephrine as indicators of stress over 24 h and controls for circadian variability.³²⁻³⁴

Follow-up Visit 2

Subjects were not scheduled after a call night or during a critical care rotation. All procedures were identical to first-month visit 1 as described above.

Measurements and Statistical Analysis

Data are summarized using mean \pm SD for continuous variables. Daily Well-being and Resiliency scores were averaged for the 3 preceding days and the visit day, on the day of study visits 1 and 2.

Results

Demographics

Thirteen of 18 (72%) incoming anesthesia residents were consented and enrolled. Enrolled subjects consisted of seven men and six women. No health issues or medications were detected by the screen nurses that precluded participation. The mean age of enrollees was 29.2 ± 1.9 yr, and the mean body mass index was 22.6 ± 2.8 kg/m². All 13 subjects completed the screen questionnaires and the first-month visit 1, while one subject was automatically excluded from follow-up visit 2 because of pregnancy.

Psychological Variables

Table 1 displays the psychological and estimated daily physical activity variables that were collected at all three time points. Reference values are listed for each survey where applicable.

Table 1. Psychological Variables and Activity at Screen, First Month, and Follow-up Visit

Variable	Screen	First-month Visit 1	Follow-up Visit 2	Reference Values
Cohen's PSS (0–56: low–high)	17.8 ± 6.5	23.6 ± 5.3	19.1 ± 6.1	25.0 ± 8.2^{12}
Spielberger SAI (20–80: low–high)	34.5 ± 9.4	38.7 ± 10.7	32.7 ± 6.3	35.7 ± 10.4^{17}
CD-RISC2 (0–8: low–high)	6.9 ± 1.0	6.6 ± 0.8	6.5 ± 0.9	6.9 ± 1.5^{18}
Stress level (0–10: low–high)	3.5 ± 1.8	5.9 ± 2.0	4.4 ± 1.7	4.2 ± 2.25^{19}
Energy level (0–10: low–high)	6.8 ± 2.2	5.4 ± 2.1	6.2 ± 1.5	
Concentration (0–10: poor–good)	7.1 ± 2.1	6.2 ± 1.2	6.5 ± 1.4	
Quality of sleep (0–10: poor–good)	7.2 ± 2.5	5.8 ± 2.4	6.8 ± 1.5	
Est. daily physical activity (METs)	7.3 ± 4.9	7.2 ± 4.2	6.3 ± 6.7	

Data are presented as mean \pm SD. Data for the screen condition was collected by mail-in questionnaires before the start of residency, including estimated daily physical activity that was determined by the Minnesota Leisure-Time Physical Activity Questionnaire. As described in the Materials and Methods, reference values are published means from similar populations where available.

CD-RISC = Connor-Davidson Resiliency Scale abbreviated; METs = metabolic equivalents; PSS = perceived stress scale; SAI = state anxiety index.

Table 2. Measured Health Behaviors and Chronic Stress Biomarkers during Study Visits

Variable	First-month Visit 1	Follow-up Visit 2
Daily energy expenditure (Cal)	$3,021 \pm 691$	$3,111 \pm 663$
Daily physical activity >3 METs (h)	3.8 ± 1.4	4.1 ± 1.2
Daily sleep (h)	6.5 ± 1.1	6.7 ± 1.2
Daily sleep efficiency (%)	83.8 ± 4.7	85.4 ± 5.4
Caloric intake, 24 h (Cal)	$2,349 \pm 1,282$	$2,189 \pm 871$
Fat intake, 24 h (g)	97.7 ± 57.9	81.5 ± 41.9
Saturated fat intake, 24 h (g)	36.7 ± 23.4	30.8 ± 21.3
Carbohydrate intake, 24 h (g)	244.2 ± 148.5	244.7 ± 116.1
Sodium intake, 24 h (mg)	$4,088 \pm 1,953$	$4,287 \pm 1,523$
Urine cortisol, 24 h (μ g/dl)	30.23 ± 14.02	29.42 ± 9.20
Urine epinephrine, 24 h (μ g/dl)	8.85 ± 6.01	8.46 ± 5.11
Urine norepinephrine, 24 h (μ g/dl)	36.62 ± 16.23	35.67 ± 10.04
Serum C-reactive protein (mg/dl)	0.066 ± 0.086	0.074 ± 0.077

Data are presented as mean \pm SD. Data for the screen condition was collected by mail-in questionnaires before the start of residency, including estimated daily physical activity that was determined by the Minnesota Leisure-Time Physical Activity Questionnaire.

CD-RISC = Connor-Davidson Resiliency Scale abbreviated; METs = metabolic equivalents; SAI = state anxiety index.

Measured Health Behaviors and Chronic Stress Biomarkers during First-month Visit 1 and Follow-up Visit 2

Table 2 displays energy expenditure, physical activity, sleep, and sleep efficiency measured by the arm accelerometer band. Dietary caloric intake and caloric components from the Automated Self-Administered 24-h Dietary Recall online service are shown. Finally, the 24-h urinary cortisol, catecholamines, and C-reactive protein are also depicted.

Cardiac Autonomic Modulation at Rest and during Acute Mental Stress

Table 3 lists the HRV measures during 10 min supine rest and 15 min mental stress, and the Reims perceived stress scores that were collected immediately after completion of the mental stressor.

Cardiovascular Hemodynamics and Acute Stress Biomarkers at Rest, during, and after Acute Mental Stress

Hemodynamic variables in the mental stress trials are listed for both visits in table 4. The acute stress biomarkers collected at the conclusion of the resting HRV

and immediately following mental stress are displayed in table 5. To compare the two methods of obtaining cortisol (serum and saliva), a linear regression was performed on the absolute values of serum *versus* salivary cortisol at rest and during mental stress in both visits. The serum and saliva samples were collected in separate tubes and processed in different laboratories (serum cortisol: Immunochemical lab in the Mayo Clinical Research Unit; salivary cortisol: Endocrinology laboratory at Mayo). As shown in figure 2, the correlation coefficients in all four conditions were significant ($P < 0.01$ for all).

Ambulatory Hemodynamics and Nighttime Cardiac Autonomic Modulation

Table 6 displays the 24-h ambulatory blood pressure monitor variables from the ambulatory cuff and nighttime HRV from the chest belt.

Discussion

The overall goal of this pilot study was to determine the feasibility of enrolling and collecting high-resolution psychological and physiological variables in incoming resident physicians.

Table 3. Heart Rate Variability during Supine Rest and during Mental Stress

Variable	First-month Visit 1		Follow-up Visit 2	
	Rest	Mental Stress	Rest	Mental Stress
Mean NN	1,044.5 ± 177.1	811.1 ± 180.2	1,062.9 ± 209.9	825.0 ± 151.1
SDNN (ms)	71.1 ± 38.9	77.0 ± 27.2	66.9 ± 27.7	75.6 ± 24.4
RMSSD (ms)	68.0 ± 56.9	42.1 ± 25.2	57.5 ± 27.2	42.1 ± 19.9
LF (ms ²)	750.1 ± 1,212.6	330.1 ± 272.0	574.3 ± 881.6	329.0 ± 224.6
HF (ms ²)	567.1 ± 917.7	164.8 ± 127.2	455.1 ± 507.8	152.7 ± 80.6
LFnu	51.3 ± 14.1	62.3 ± 12.4	47.8 ± 16.4	60.9 ± 12.6
HFnu	44.8 ± 12.9	30.1 ± 12.4	48.3 ± 16.1	30.1 ± 10.3
LF/HF	1.37 ± 0.9	2.6 ± 1.6	1.3 ± 1.0	2.5 ± 1.7
Perceived stress score	24.1 ± 4.3		22.9 ± 3.4	

Data presented as mean ± SD. Perceived stress scores acquired immediately after stress trial as described in text.

HF = high frequency; HFnu = high-frequency normalized units; LF = low frequency; LFnu = low-frequency normalized units; LF/HF = LF-to-HF ratio; MAP = mean arterial pressure; Mean NN = mean normal-to-normal interval; RMSSD = square root of the mean squared differences of successive N-N intervals; SDNN = SD of the N-N intervals.

Table 4. Hemodynamics before, during, and Recovery from Mental Stress

Variable	First-month Visit 1			Follow-up Visit 2		
	Rest	Mental Stress	Recovery	Rest	Mental Stress	Recovery
HR (beats/min)	64.0 ± 12.4	78.2 ± 16.1	63.6 ± 12.9	58.4 ± 21.1	69.9 ± 24.9	57.0 ± 19.8
SBP (mmHg)	129.9 ± 9.1	143.3 ± 12.4	136.9 ± 14.1	117.6 ± 36.8	132.1 ± 40.9	124.0 ± 38.8
DBP (mmHg)	75.0 ± 5.7	83.2 ± 7.8	77.8 ± 8.4	68.0 ± 21.2	75.6 ± 24.1	69.4 ± 21.8
MAP (mmHg)	95.5 ± 5.4	107.2 ± 9.3	100.2 ± 9.1	87.0 ± 27.0	97.9 ± 30.9	89.9 ± 28.1
Cardiac output (l/min)	6.8 ± 1.4	8.3 ± 1.7	7.0 ± 1.4	6.3 ± 2.1	7.6 ± 2.5	6.5 ± 2.2
Stroke volume (ml)	108.7 ± 21.3	108.3 ± 19.7	111.9 ± 21.0	102.6 ± 36.6	104.0 ± 36.4	107.5 ± 37.5
SVR (dyn•s/cm ⁵)	1,172.8 ± 268.3	1,079.6 ± 241.2	1,180.5 ± 226.6	1,122.2 ± 158.2	1,036.5 ± 141.8	1,126.3 ± 154.5

Data presented as mean ± SD.

DBP = diastolic blood pressure; HR = heart rate; MAP = mean arterial pressure; SBP = systolic blood pressure; SVR = systemic vascular resistance.

Table 5. Stress Biomarkers before and after Mental Stress

Variable	First-month Visit 1		Follow-up Visit 2	
	Rest	Mental Stress	Rest	Mental Stress
Serum cortisol (μg/dl)	7.01 ± 1.66	8.36 ± 2.46	7.0 ± 1.80	6.53 ± 1.96
Salivary cortisol (ng/dl)	76.7 ± 31.9	99.4 ± 63.5	84.3 ± 34.5	62.8 ± 28.8
Serum Epi (pg/ml)	13.7 ± 9.4	25.4 ± 16.1	17.3 ± 11.7	27.8 ± 12.3
Serum NE (pg/ml)	155.4 ± 53.0	203.7 ± 58.9	171.2 ± 52.4	212.1 ± 62.5
Serum IL-6 (pg/ml)	0.81 ± 0.69	0.83 ± 0.69	0.84 ± 0.71	0.85 ± 0.70

Data are presented as mean ± SD. Due to the counter-intuitive nature of cortisol decreasing in response to mental stress during visit 2, a linear regression analysis was highly significant for serum vs. salivary cortisol in all four conditions (rest, mental stress, visit 1, and visit 2) as described in the Results and displayed in figure 2. Epi = epinephrine; IL-6 = interleukin-6; NE = norepinephrine.

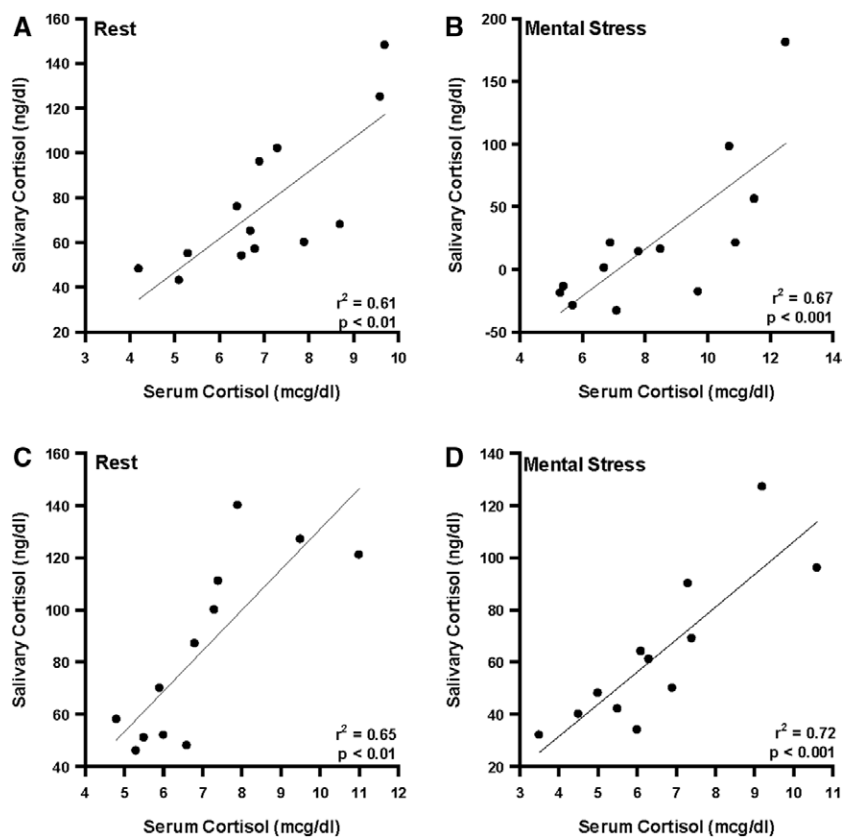


Fig. 2. Linear regression analysis of serum *versus* salivary cortisol. (A) Displays the correlation between serum and salivary cortisol at rest during visit 1; (B) displays the correlation between serum and salivary cortisol during mental stress in visit 1. (C) Displays the correlation between serum and salivary cortisol at rest during visit 2; (D) displays the correlation between serum and salivary cortisol during mental stress in visit 2.

The exploratory study objective was to measure stress variables and related health behaviors that have direct implications for professionalism, quality of health care, and well-being of residents. The novel nature of our report is the prospective design in a defined cohort of new residents newly exposed to the similar occupational stress of the operating environment. Because of the paucity of literature specific to the repeated measures and stress conditions in this investigation, no data were available to generate *a priori* definition of primary outcomes and a data analytic plan. The sample size was dependent on the number of incoming residents that were available, with a 72% enrollment rate. Although the sample size was underpowered to make statistical inferences from our findings, the findings instead will allow power analysis for future study design of trials examining occupational stress and stress-reducing interventions.

Well-being in residents is associated with their capacity for empathy and patient care,^{35,36} and it has been postulated that the stressors of residency may counter the goals of training to promote professionalism and high-quality patient care.^{37,38} Scores indicative of burnout have been associated with lower medical student empathy scores and with lower professionalism climate scores observed in medical students, residents, and faculty.^{39,40} Specific to anesthesiology, perioperative patient safety and efficiency requires high performance by a

health care team that absolutely depends on professionalism among anesthesia providers.⁷ Early in training, anesthesia residents are likely to perceive a low degree of latitude in the setting of high expectations or demand.

Additional measures of well-being such as health behaviors were gathered to gain insight into factors that would potentially influence perceived stress. Resilience is a measure of coping ability, hardiness, and the ability to thrive in the face of adversity.¹⁸ Based on the resiliency scores, our subjects appeared to adapt their schedules and health behaviors to combat the sudden disruption in work-life balance, an idea that has been described as a “time for temporary imbalance,” when professional effort gives way to other life domains.⁸ It is cautionary that residents may have already become accustomed to intermittent work-life imbalances, as a variety of internship rotations were likely filled with novel professional and personal challenges. Residents may also be particularly optimistic about the onset of training in their field of choice, and welcomed the onset of anesthesiology as a stressful yet engaging stressor.

Decreased HRV indicates a sympathetic dominance and/or reduced vagal activity, which occurs in normal aging and many pathological conditions including hypertension, diabetes, and heart failure.⁴¹ Detrimental effects of job strain are partly mediated through increased HR reactivity to a stressful

Table 6. Twenty-four Hour Ambulatory Hemodynamics and Nighttime Heart Rate Variability

	First-month Visit 1	Follow-up Visit 2
Variable		
HR (beats/min)		
24 h	67.3 ± 10.6	70.1 ± 10.3
Day	70.6 ± 11.7	73.3 ± 10.5
Night	58.6 ± 8.8	60.3 ± 9.8
SBP (mmHg)		
24 h	118.8 ± 11.7	119.4 ± 8.7
Day	121.7 ± 11.3	121.2 ± 7.6
Night	110.0 ± 13.5	109.4 ± 12.3
DBP (mmHg)		
24 h	71.3 ± 8.6	71.3 ± 8.0
Day	75.1 ± 8.9	75.6 ± 8.4
Night	60.4 ± 8.9	59.1 ± 6.8
MAP (mmHg)		
24 h	86.7 ± 8.7	86.4 ± 7.0
Day	90.1 ± 8.5	91.1 ± 8.1
Night	76.8 ± 9.3	75.4 ± 7.4
Night-time HRV		
Mean NN	1,114.3 ± 179.8	1,009.1 ± 158.5
SDNN (ms)	131.0 ± 24.8	150.0 ± 85.5
RMSSD (ms)	66.6 ± 22.8	70.3 ± 59.6
LF (ms ²)	869.5 ± 695.2	906.3 ± 972.4
HF (ms ²)	721.0 ± 585.9	976.4 ± 1,705.3
LFnu%	54.4 ± 10.1	58.2 ± 10.5
HFnu%	45.6 ± 10.1	41.8 ± 10.5
LF:HF ratio	1.31 ± 0.62	1.53 ± 0.59

Data are presented as mean ± SD. LFnu% is derived from LF/LF + HF and HFnu% is derived from HF/LF + HF as described in the text.

DBP = diastolic blood pressure; HF = high frequency; HFnu = high-frequency normalized units; HR = heart rate; HRV = heart rate variability; LF = low frequency; LFnu = low-frequency normalized units; MAP = mean arterial pressure; RMSSD = square root of the mean squared differences of successive N-N intervals; SBP = systolic blood pressure; SDNN = SD of the N-N intervals.

workday, increased systolic blood pressure, and lower vagal tone.⁴² A recent study using 24-h Holter monitors on 54 residents in multiple specialties found that those who reported high job strain (high-demand, low-latitude) had decreased HRV compared with low-strain residents.⁴³ This is consistent with an earlier study in nonphysician middle-age males that showed job strain and low-decision latitude were associated with a reduction in cardiac vagal control (high frequency) and elevations in sympathetic control (low frequency).⁴⁴ Thus, we measured both daytime resting and nighttime HRV in the first month and follow-up visit. We were also interested in the HRV response to laboratory mental stress during the stress encountered in starting residency, as we have previously shown that dietary sodium affects HRV at rest and during mental stress in healthy nonphysician men and women.²⁴ One drawback of this methodology is the detection of HRV alterations in subjects who are healthy, physically-fit trainees with little change in their lifestyle habits (including sleep). Additionally, although some authors have reported that vagal control (high frequency) is reduced with stress,^{42,45,46} other studies have shown no relationship,^{47,48} and the overall utility of HRV in sleep deprivation

is mixed.⁴⁹ Finally, perceived control is highly predictive of stress, and because residents select their training site, they may have a high level of perceived control over the challenges they encounter as new residents.⁵⁰

Two endocrine response systems are particularly reactive to psychological stress: the hypothalamic–pituitary–adrenocortical axis and the sympathoadrenal system.⁵¹ Cortisol, the primary effector of hypothalamic–pituitary–adrenocortical activation in humans, is a common biomarker in stress research. Catecholamines, which are released in response to sympathoadrenal activation, work in concert with the autonomic nervous system to exert regulatory effects on the cardiovascular and immune system among others. Prolonged or repeated activation of the hypothalamic–pituitary–adrenocortical axis and sympathoadrenal systems can interfere with their control of other physiological systems, resulting in increased risk for physical and psychiatric disorders.^{11,52} It is noteworthy that in healthy volunteers, the search for a consistent and reliable chronic stress biomarker remains a major challenge as recently reviewed in a metaanalysis of 31 studies on 38 biomarkers.⁵³

A limitation of measuring serum and salivary cortisol levels is the wide range of interindividual variance. The kinetics of cortisol production and metabolism is dependent on circadian rhythm, menstrual cycle, oral contraceptives, and cortisol binding globulin, which, aside from circadian rhythm, were not controlled for in this study cohort.^{32,54} Additionally, an interpretive challenge arises when the change in cortisol values from rest to stress falls within the assay's coefficient of variation, as it did for several of our subjects. For example, the finding that cortisol values decreased in response to mental stress during the follow-up visit seemed counterintuitive. To address this, we found that serum cortisol strongly correlated with salivary cortisol, which reinforced the integrity of the cortisol values.

Additional limitations of this report deserve mention. Despite the strength that every participant in this cohort was subjected to a similar occupational stressor (the operating room environment at one institution as opposed to a multitude of rotations), the delicate nature of studying new-resident trainees within the ethical boundaries of confidentiality and coercion limited the number of participants. We acknowledge the potential for selection bias, as the degree of resiliency in our participants may be such that many of the psychological and physiological variables explored were not affected by the stress of starting residency, but might be affected in a broader population of trainees. Finally, protocols of this nature are limited by the logistical challenge of prospective data collection in resident volunteers across convenient time points.

Preservation of health behaviors with respect to diet, physical activity level, and quality of sleep confer resiliency during periods of acute stress. Strategies to preserve or enhance these health behaviors merit further evaluation. The overall implication for resident education and occupational wellness is that subjective surveys quantifying psychological stress remain an important tool for prospective, longitudinal cohort studies. The development of objective, high-resolution physiological

variables remains a significant challenge in identifying useful variables in a cohort of physician trainees. Given the importance of physician burnout in our country, the impact of chronic stress on resident wellness requires further study. Future protocols with larger samples capable of detecting psychological and physiological effects of occupational stress will require multiple time points to appreciate the full nature of chronic job strain and its relevance to interventions designed to optimize the training experience. This report demonstrates the feasibility of studies of this nature, and provides the preliminary data necessary to generate *a priori* definition of primary outcomes and a data analytic plan.

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Competing Interests

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Appendix 1. Minnesota Leisure Time Activity Questionnaire

To be completed by participant Activity	Did you perform the activity?	Do not write in this space	Number of times since July 1	Time per occasion	
				Hour	Min

Section A:

Walking and misc.

N Y

010	Walking for pleasure							
020	Walking to work							
030	Using stairs when elevator is available							
040	Cross country hiking							
050	Back packing							
060	Mountain climbing							
115	Bicycling to work and/or for pleasure							
125	Dancing ballroom, square and/or disco							
135	Dancing, aerobic, ballet							
140	Horseback riding							

Section B:

Conditioning Exercise

150	Home Exercise							
160	Health Club Exercise							
180	Jog/walk combination							
200	Running							
210	Weight lifting							

Section C:

Water Activities

220	Water Skiing						
235	Sailing in Competition						
250	Canoeing or Rowing for Pleasure						
260	Canoeing or Rowing in Competition						
270	Canoeing on a Camping Trip						
280	Swimmin (at least 50ft) at a pool						
295	Swimming at the Beach						
310	Scuba Diving						
320	Snorkeling						

To be completed by participant Activity	Did you perform the activity?	Do not write in this space	Ave. Number of times per month	Time per occasion	
				Hour	Min

Section E.

Sports

N Y

390	Bowling						
400	Volley Ball						
410	Table Tennis						
420	Tennis, Singles						
430	Tennis, Doubles						
440	Softball						
450	Badminton						
460	Paddle Ball						
470	Racket Ball						
480	Basketball: non-game						
490	Basketball: game play						
500	Basketball: officiating						
510	Touch Football						
520	Handball						
530	Squash						
540	Soccer						
	Golf						
070	Riding a Power Cart						
080	Walking, Pulling Clubs on Cart						
090	Walking and Carrying Clubs						

Section F.

Lawn and Garden
Activities

550	Mowing Lawn with Riding Mower							
560	Mowing Lawn Walking behind a Power Mower							
570	Mowing Lawn Pushing Hand Mower							
580	Weeding and Cultivating Garden							
590	Spading, Digging, Filling in Garden							
600	Raking Lawn							

Section G.

Home Repair Activities

620	Carpentry in Wokkshop							
630	Painting Inside of House includes Paper Hanging							
640	Carpentry Outside							
650	Painting Outside of House							

Section H.

Fishing and Hunting

N Y

660	Fishing from River Bank							
670	Fishing in Stream with Wading boots							
680	Hunting Pheasant or Grouse							
690	Hunting Rabbits, Praire Chickens, Squirrels, Racoon							
710	Hunting Large Game: Deer, Elk, Bear							

Section I.

Other Activities

Appendix 2. Cohen's Perceived Stress Scale-14

INSTRUCTIONS:

The questions in this scale ask you about your feelings and thoughts during **THE LAST WEEK**. In each case, you will be asked to indicate your response by placing an "X" over the circle representing **HOW OFTEN** you felt or thought a certain way. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer fairly quickly. That is, don't try to count up the number of times you felt a particular way, but rather indicate the alternative that seems like a reasonable estimate.

	Never	Almost Never	Sometimes	Fairly Often	Very Often
	0	1	2	3	4
1. In the last week, how often have you been upset because of something that happened unexpectedly?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. In the last week, how often have you felt that you were unable to control the important things in your life?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. In the last week, how often have you felt nervous and "stressed"?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. In the last week, how often have you dealt successfully with day to day problems and annoyances?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. In the last week, how often have you felt that you were effectively coping with important changes that were occurring in your life?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. In the last week, how often have you felt confident about your ability to handle your personal problems?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. In the last week, how often have you felt that things were going your way?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. In the last week, how often have you found that you could not cope with all the things that you had to do?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. In the last week, how often have you been able to control irritations in your life?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. In the last week, how often have you felt that you were on top of things?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

PSS-14

	Never	Almost Never	Sometimes	Fairly Often	Very Often
	0	1	2	3	4
11. In the last week, how often have you been angered because of things that happened that were outside of your control?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. In the last week, how often have you found yourself thinking about things that you have to accomplish?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
13. In the last week, how often have you been able to control the way you spend your time?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
14. In the last week, how often have you felt difficulties were piling up so high that you could not overcome them?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Appendix 3. Spielberger State Anxiety Index

Please answer the following questions for how you feel now.

1. I feel calm.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

2. I feel secure.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

3. I am tense.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

4. I feel strained.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

5. I feel at ease.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

6. I feel upset.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

7. I am presently worrying over possible misfortunes.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

8. I feel satisfied.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

9. I feel frightened.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

10. I feel comfortable.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

11. I feel self-confident.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

12. I feel nervous.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

13. I feel jittery.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

14. I feel indecisive.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

15. I feel relaxed.

Not at all	Somewhat	Moderately so	Very much so
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

16. I feel content.

Not at all ☐ Somewhat ☐ Moderately so ☐ Very much so ☐

17. I feel worried.

Not at all ☐ Somewhat ☐ Moderately so ☐ Very much so ☐

18. I feel confused.

Not at all ☐ Somewhat ☐ Moderately so ☐ Very much so ☐

19. I feel steady.

Not at all ☐ Somewhat ☐ Moderately so ☐ Very much so ☐

20. I feel pleasant.

Not at all ☐ Somewhat ☐ Moderately so ☐ Very much so ☐

Appendix 4. Resiliency and Daily Well-being Surveys

1. I am able to adapt to change.

0	Not true at all
1	Rarely true
2	Sometimes true
3	Often true
4	True nearly all of the time

2. I tend to bounce back after illness or hardship.

0	Not true at all
1	Rarely true
2	Sometimes true
3	Often true
4	True nearly all of the time

3. My current stress level:

As bad as it can be. ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ As good as it can be.

0 1 2 3 4 5 6 7 8 9 10

4. My current energy level:

As bad as it can be. ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ As good as it can be.

0 1 2 3 4 5 6 7 8 9 10

5. My concentration:

As bad as it can be. ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ As good as it can be.

0 1 2 3 4 5 6 7 8 9 10

6. How well I slept last night:

As bad as it can be. ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ As good as it can be.

0 1 2 3 4 5 6 7 8 9 10

Appendix 5. Supplemental Methods

Heart Rate Variability

Components of heart-rate variability included mean heart rate (HR), mean NN interval, SD of normalized RR intervals, square root of the mean squared difference of successive normalized RR intervals, low frequency, high frequency, low-frequency normalized units, high-frequency normalized units, and low frequency/high frequency ratio.

Mental Stress

The computerized mental stress protocol was conducted in a semi-recumbent study chair with the legs elevated to the approximate level of the heart. Headphones were placed for automated audio input. After 2 min of baseline HR and blood pressure recording, a voiced recording of the printed instructions was played for each subject lasting 30 s. The instructions reminded subjects that their best effort was required and that their performance on the test would be compared with the other subjects. A computerized mathematical subtraction test for 4.5 min was administered as described in detail elsewhere.²⁴ To maximize the stress induced, the standard recording (*via* headphones) used vocally consistent monologue urging each subject to respond faster and to concentrate fully throughout the test. This was followed by 30 s instructions for a Stroop colored word test, then a 4.5 min computerized version of the Stroop colored word conflict test used previously in our laboratory was given.²⁹ When this portion was completed, a second 5-min mental stress test immediately commenced, for a total stress duration of 15 min.

After a 5-min recovery period, subjects were de-instrumented and completed a psychological distress survey modified from a mental arithmetic stress survey by Reims *et al.*, consisting of three questions: (1) Did you feel stressed while performing the color word task? (*i.e.*, “perceived stress”); (2) Was it important for you to obtain a good result on the color word task? (3) How did you experience the task altogether? In response to each question, subjects marked one of ten unnumbered boxes between extremes of least to highest degrees of perceived stress, effort, and overall discomfort, respectively.

Ambulatory Blood Pressure Monitoring

After discharge from our laboratory, subjects were outfitted with an ambulatory blood pressure monitor Spacelabs 90202 recorder (Spacelabs Inc., Issaquah, WA) as described by our laboratory.³¹ The participants were asked to continue their regular activities and to go to bed no later than 11 PM, but were not allowed to exercise during the 24-h recording period. Systolic blood pressure, diastolic blood pressure, and HR were measured every 15 min from 6 AM to 10 PM, and every 20 min from 10 PM to 6 AM. The daytime period was defined as the interval from 8 AM to 10 PM; nighttime, from midnight to 6 AM.^{40,41} The SD and coefficient of variation (CV) of the 24-h recordings were used as an index of HR, systolic blood pressure, and mean arterial pressure variability. Nocturnal dipping was expressed as the nocturnal fall in blood pressure calculated as the difference between daytime and nighttime blood pressure adjusted for the daytime blood pressure level and expressed in percentages.

Overnight HR Variability

Subjects were also instructed to wear the Polar chest belt from bedtime to awakening the next morning, and HR was recorded by the proprietary application on a mobile smartphone (@-life; Mikropis Holding, Inc. Zalec, Slovenia).

Biomarker Measurements and Assays

Serum Cortisol. Serum cortisol was measured by a competitive-binding immunoassay on the DxI automated immunoassay system (Beckman Instruments, Chaska, MN). Intraassay CVs are 13.1, 9.4, and 6.6% at 1.56, 2.85, and 30.2 µg/dl, respectively. Interassay CVs are 9.0, 8.1, and 9.3% at 2.47, 17.3, and 27.5 µg/dl, respectively. The lower limit of the CRR is 0.4 µg/dl.

Salivary Cortisol. Salivary cortisol was measured by liquid chromatography-tandem mass spectrometry (Thermo Fisher Scientific, Franklin, MA, and Applied Biosystems-MDS Sciex, Foster City, CA). Saliva intraassay CVs are 5.6, 4.5, and 2.6% at 53.5, 292.5, and 1,611.5 ng/dl, respectively. Interassay CVs are 15.2, 7.5, and 8.1% at 49.6, 293.3, and 1,560.5 ng/dl, respectively.

Urinary Cortisol. Urinary cortisol was measured by liquid chromatography-tandem mass spectrometry (Thermo Fisher Scientific and Applied Biosystems-MDS Sciex). Intraassay CVs are 6.8, 6.9, and 5.0% at 0.84, 4.88, and 13.57 µg/dl, respectively. Urine interassay CVs are 10.3, 6.7, and 6.8% at 0.88, 4.6, and 13.0 µg/dl, respectively.

Serum Catecholamines. Serum catecholamines were measured by reverse-phase high performance liquid chromatography with electrochemical detection after extraction with activated alumina. Serum intraassay CVs are norepinephrine 4.5 and 3.3% at 224 and 429 pg/ml; epinephrine 12.2 and 3.6% at 13.8 and 242 pg/ml; interassay CVs are norepinephrine 4.6 and 8.6% at 235 and 1,096 pg/ml; epinephrine 6.4 and 8.2% at 61 and 917 pg/ml.

Urine Catecholamines. Urine catecholamines were measured by reverse-phase high performance liquid chromatography with electrochemical detection after extraction with activated alumina. Urine intraassay CVs are norepinephrine 2.1 at 6.0 ng/ml; epinephrine 3.9% at 2.3 ng/ml; urine interassay CVs are norepinephrine 13.8, 9.0, and 11.9% at 1.3, 22, and 156 ng/ml, respectively; epinephrine 11.0, 7.3, and 8.7% at 0.96, 8.9, and 34 ng/ml, respectively.

Serum C-Reactive Protein, High Sensitivity. Serum C-Reactive Protein, High Sensitivity was measured on the Roche Cobas c311 chemistry analyzer (Roche Diagnostics, Indianapolis, IN) by a latex particle enhanced immunoturbidimetric assay from Roche Diagnostics. Intraassay CVs are 1.9, 1.0, and 0.2% at 0.107, 0.179, and 1.227 mg/dl, respectively. Interassay CVs are 2.4, 1.7, and 3.4% at 0.107, 0.171, and 1.226 mg/dl, respectively.

Interleukin 6, High Sensitivity. Interleukin 6, high sensitivity was measured by a quantitative two-site enzyme immunoassay from R & D Systems (Minneapolis, MN). Intraassay CVs are 8.4, 3.6, and 4.0% at 0.42, 3.88, and 9.77 pg/ml, respectively. Interassay CVs are 9.7, 7.6, and 7.7% at 0.52, 2.91, and 5.53 pg/ml, respectively.

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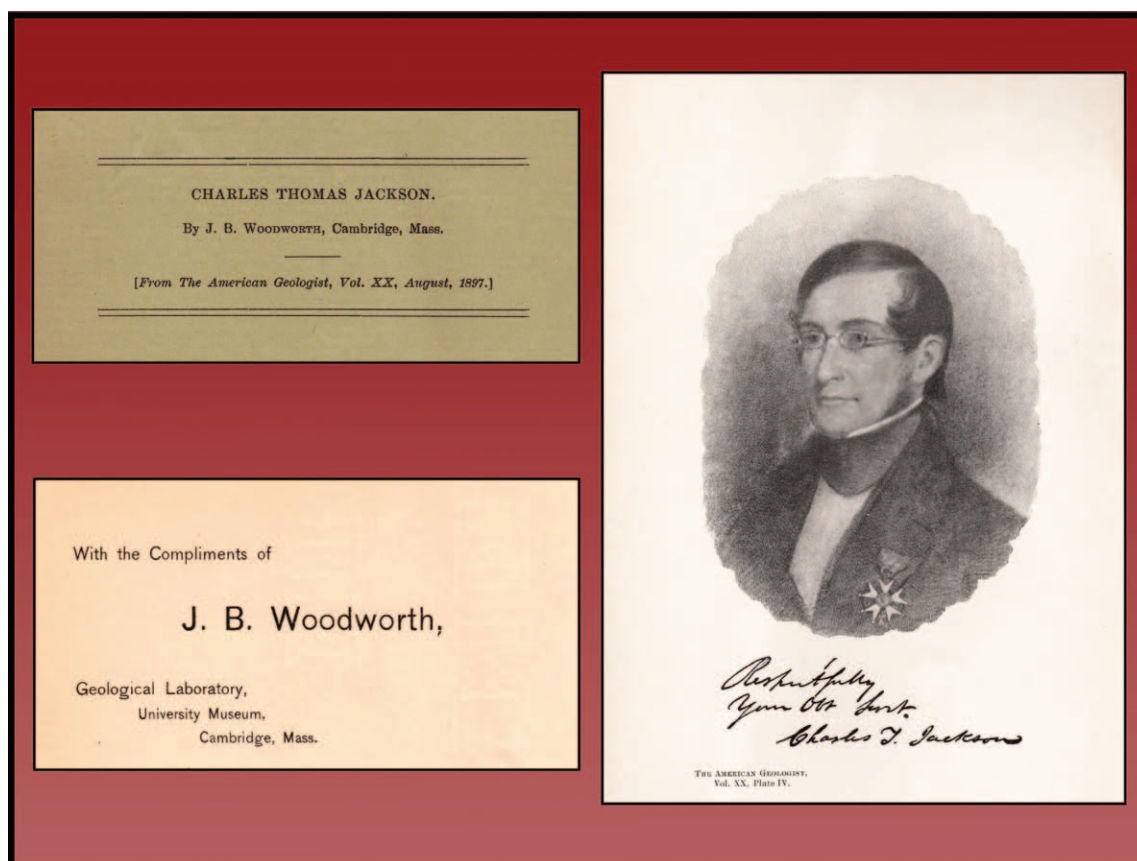
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“Charles Thomas Jackson”—Compliments of J. B. Woodworth



An instructor in Geology at Harvard, Jay Backus Woodworth (1865–1925) published an article (*upper left*) titled “Charles Thomas Jackson” in *The American Geologist* about the life and works of that geological surveyor and ether pioneer. This publication included Jackson’s portrait (*right*) above a copy of his handwritten “Respectfully / Your Obedt. Servt. / Charles T. Jackson.” Of great interest to the Wood Library-Museum of Anesthesiology, this particular printing was discovered with the author’s compliments card (*lower left*) still tucked inside. (Copyright © the American Society of Anesthesiologists, Inc.)

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