Health Psychology
1997, Vol. 16, No. 4, 341-348

0278-6133/97/$3.00

Lymphocyte Subset Redistribution During Acute Laboratory Stress in Young Adults: Mediating Effects of Hemoconcentration

Anna L. Marsland
University of Pittsburgh

Tracy B. Herbert
Carnegie Mellon University

Matthew F. Muldoon
University of Pittsburgh School of Medicine

Elizabeth A. Bachen and Stephen Patterson
University of Pittsburgh

Sheldon Cohen
Carnegie Mellon University

Bruce Rabin
University of Pittsburgh School of Medicine

Stephen B. Manuck
University of Pittsburgh

Acute psychological stress is known to alter the distribution of circulating lymphocyte subsets and also to cause a reduction of plasma volume. Data were reanalyzed from 4 previously reported studies (E. A. Bachen et al., 1995; T. B. Herbert et al., 1994; A. L. Marsland, S. B. Manuck, T. V. Fazzari, C. J. Stewart, & B. S. Rabin, 1995; A. L. Marsland, S. B. Manuck, P. Wood, et al., 1995) to determine the extent to which changes in the concentration of lymphocyte subsets are attributable to such hemoconcentration. Meta-analytic procedures showed circulating concentrations of T-suppressor/cytotoxic (CD8) and natural killer (NK) cells to increase following acute laboratory challenge, whereas T-helper (CD4) and B- (CD19) cell populations did not change. Adjustments for concomitant hemoconcentration reduced the magnitude of stress-related increases in CD8 and NK cells significantly and revealed a decrease in CD4 and CD19 cell concentrations from baseline to stress measurements. These data provide evidence (a) that increases in circulating numbers of CD8 and NK cells following acute stress are partially attributable to hemoconcentration and (b) that CD4 and CD19 cell concentrations decrease during acute stress when hemoconcentration is taken into account.

Key words: stress, immunity, lymphocyte, reactivity, hemoconcentration

Acute psychological stress is known to alter components of cellular immunity in human beings (Bachen et al., 1992; Kiecolt-Glaser, Cacioppo, Malarkey, & Glaser, 1992; Manuck, Cohen, Rabin, Muldoon, & Bachen, 1991; Naliboff et al., 1991; Zakowski, McAllister, Deal, & Baum, 1992). For instance, T-suppressor/cytotoxic (CD8) and natural killer (NK) cells in the peripheral circulation typically increase in concentration within minutes of the onset of common laboratory stressors (Herbert et al., 1994). These changes are often attributed to processes such as lymphocyte migration from lymphoid organs to circulating blood or demargination of endothelium-adherent lymphocytes (e.g., Benshop, Oostveen, Heijnen, & Ballieux, 1993; van Tits et al., 1990). It is also possible, however, that lymphocyte populations do not expand under stress but instead rise only in their relative blood concentration due to a concomitant reduction in plasma volume (termed *hemoconcentration*). Under stress, an increase in arterial (hydrostatic) pressure causes fluid to filter out of the circulation into extravascular spaces, which necessarily increases the concentration of all large and nondiffusible constituents of blood (e.g., plasma proteins and blood cells, including lymphocytes; Jern, Wadenvik, Mark, Hallgren, & Jern, 1989; Patterson, Krantz, & Jochum, 1995; Patterson, Matthews, Allen, & Owens, 1995). Such hemoconcentration is typically assessed by measurement of changes in two blood indexes: (a) concentration of hemoglobin (a protein molecule within red blood cells) and (b) hematocrit (the percentage of blood that is composed of cells). An estimate of change in plasma volume can be derived from these variables and used to determine

Anna L. Marsland, Elizabeth A. Bachen, Stephen Patterson, and Stephen B. Manuck, Department of Psychology, University of Pittsburgh; Tracy B. Herbert and Sheldon Cohen, Department of Psychology, Carnegie Mellon University; Matthew F. Muldoon, Center for Clinical Pharmacology, University of Pittsburgh School of Medicine; Bruce Rabin, Department of Pathology, University of Pittsburgh School of Medicine.

Elizabeth A. Bachen is now at the Department of Psychology, University of California, San Francisco; Stephen Patterson is now at the Department of Pediatrics, University of Tennessee, Memphis.

This research was supported by National Institutes of Health (National Heart, Lung, and Blood Institute) Grant HL40962.

Correspondence concerning this article should be addressed to Anna L. Marsland, University of Pittsburgh Medical Center, 405 Iroquois Building, 3600 Forbes Avenue, Pittsburgh, Pennsylvania 15213-3412.

whether observed changes in the measured concentrations of other large (nondiffusible) compounds or cells are attributable, in whole or in part, to hemoconcentration. It has been demonstrated previously, for instance, that reductions in plasma volume can account for the acute physiological effects of stress on plasma cholesterol and triglycerides and can partially account for the stress-related increase in white blood cell count (Muldoon et al., 1992, 1995; Patterson et al., 1995). It is therefore important to determine whether any observed changes in lymphocyte subset concentrations induced by laboratory stressors (as frequently reported in the acute stress literature; e.g., Bachen et al., 1992; Manuck et al., 1991; Herbert et al., 1994) are similarly mediated by stress-induced hemoconcentration.

Of course, lymphocyte populations may change under stress by both active and passive processes, in which case hemoconcentration may account for only a portion of the rise in CD8 and NK cell numbers typically reported in this literature. It is also conceivable that certain lymphocyte subsets that do not typically respond to acute stressors, such as T-helper (CD4) and B (CD19) cells, actually decline under these conditions but appear unchanged because of the opposing effects of reduced plasma volume. In this article we seek to determine, by a reanalysis of data from four previously published studies (Bachen et al., 1995; Herbert et al., 1994; Marsland, Manuck, Fazzari, Stewart, & Rabin, 1995; Marsland, Manuck, Wood, et al., 1995) the degree to which circulating lymphocyte subsets may be altered by changes in hemoconcentration resulting from participants' exposure to acute mental stress.

Method

Participants

Participants were derived from four prior studies evaluating immune responsivity to acute laboratory stress (Bachen et al., 1995; Herbert et al., 1994; Marsland, Manuck, Fazzari, et al., 1995; Marsland, Manuck, Wood, et al., 1995). In each investigation, participants were healthy young adults (aged 18–30) recruited from the university population. Individuals were ineligible for participation if they smoked or had a history or symptoms of systemic disease known to affect the immune system. Participants were randomly assigned to either experimental or control conditions. In the experimental conditions, measurements of cell subtype distribution were obtained before and during participants' performance of a laboratory challenge of 5–21-min duration. Identical measurements were obtained in the control conditions, although these participants were not exposed to a stressor. All participants gave informed consent to participate in the investigations, which were approved by the Biomedical Institutional Review Board of the University of Pittsburgh. Participants were paid for their involvement.

Procedures

Experimental procedures for the four studies were similar. In each study, participants abstained from food, caffeine, and exercise for 12 hr before attending a laboratory session held in the morning. On arrival at the laboratory, an intravenous catheter was inserted into the antecubital fossa of one arm for collection of blood samples, and an occluding cuff was placed on the other arm for automated measurement of heart rate (HR) and blood pressure (BP; Critikon Dinamap 8100 vital signs monitor, Tampa, FL). Each participant then rested for 30 min to achieve baseline conditions. During the last 6–10 min of this period, HR and BP (four or five readings) were recorded, and blood was drawn for the determination of lymphocyte subpopulations (CD4, CD8, CD19, and NK cells). At this point, control participants were asked to continue to sit quietly, and experimental participants were instructed to perform a challenging laboratory task. In each study, HR and BP were recorded during task performance, and additional blood samples for evaluation of lymphocyte subsets were obtained during the last 2–3 min of the stressor. The same measurements were taken at corresponding times among unstressed controls. Study-specific features of the four investigations are summarized below.

Features of the Four Studies

Study 1. Study 1 (Marsland, Manuck, Fazzari, et al., 1995) included 40 male (30 experimental and 10 control) participants in a two-session protocol examining immune responses to simulated public speaking. The task consisted of 2 min of preparation for a speech in which the participant was to defend himself against an alleged transgression (shoplifting or traffic violation) followed by 3 min of videotaped speech delivery. In the first situation, participants were wrongfully accused of stealing a wallet by a department store security guard, and in the second situation they were detained by a police officer for driving through a stop sign. Experimental participants were randomly allocated one of these two transgression scenarios; only results from the first session are used in the current analysis as it provided the more analogous comparison to the other studies.

Study 2. Study 2 (Herbert et al., 1994) included 41 participants, 20 (10 men and 10 women) assigned to the experimental condition and 21 (12 men and 9 women) to the control condition. Here, the experimental group was administered a 21-min computerized version of the Stroop Color and Word Interference Test (Frankenhauser, Mellis, Rissler, Bjorksell, & Patkai, 1968; Olsson, Hjemdahl, & Rehnqvist, 1986). This task was performed under pressure of time and against a distractor (random test responses) generated by computerized voice synthesis. One male control participant was dropped from the current analyses because complete blood count (CBC) results were not available.

Study 3. Study 3 (Bachen et al., 1995) was designed to evaluate sympathoadrenal mediation of behaviorally evoked immune responses by administration of a nonselective adrenoceptor antagonist (labetolol). Fifty-two men were assigned to a labetolol or saline condition and, within each condition, were assigned to either an experimental or control group. The experimental group performed an 18-min task, consisting of (a) an 8-min version of the Stroop Color and Word Interference Test (as in Study 2), (b) mental arithmetic (5 min of consecutive one-to-three digit addition and subtraction problems), and (c) a 5-min simulated public speaking task (as in Study 1, except only the shoplifting scenario was used). Only participants in the saline condition are included in the current analysis (experimental group: $n = 14$; control group: $n = 12$).

Study 4. In Study 4 (Marsland, Manuck, Wood, et al., 1995), experimental participants performed the same laboratory challenge as in Study 2: a 21-min computerized version of the Stroop Color and Word Interference Test. CBC results were available on 17 of 22 experimental participants and on all 11 control participants. All participants were men.

Blood Measures

Blood samples for the determination of cell subtypes and hematocrit and hemoglobin were drawn into EDTA Vacutainer

tubes (Becton Dickinson, Franklin Lakes, NJ). Circulating populations of CD4, CD8, CD19, and NK cells were assessed in whole blood by using dual-color fluorescence analysis with a FACSCAN flow cytometer (Becton Dickinson, San Jose, CA). Lymphocyte subsets were analyzed using monoclonal antibodies labeled with either fluorescein or phycoerythrin to quantify CD3+ CD4+ (CD4), CD3+ CD8+ (CD8), CD3− CD19+ (CD19), and CD3− CD16+ CD56+ (NK) cells.

Absolute numbers of cells and hematocrit and hemoglobin concentrations were determined with an automatic cell counter (STKR Coulter Counter, Coulter Electroniks Inc., Hialeah, FL). Hematocrit was calculated from the red blood cell concentration and the impedance-determined mean corpuscular volume; hemoglobin concentrations were measured by the cyanomethemoglobin method. Baseline plasma volume was calculated as one minus hematocrit; change in plasma volume was calculated from changes in hemoglobin and hematocrit according to the method of Dill and Costill (1974).

Results

Principal analyses addressed two primary questions: (a) Did exposure to laboratory stressors cause significant hemoconcentration (i.e., rises in hematocrit and hemoglobin among participants exposed to laboratory stressors)? and (b) if so, does adjustment for changes in plasma volume alter the magnitude or direction of concomitant lymphocyte subset concentration responses to stress? Because the data to be analyzed were derived from several investigations that differed in aspects of procedural detail (e.g., task duration), outcomes across the four independent studies were combined by using a strategy derived from established meta-analytic procedure. The final N on which these analyses are based is 134 (81 experimental and 53 control participants.) Tests for homogeneity of variance were conducted for experimental and control conditions on each dependent variable (hematocrit; hemoconcentration; plasma volume; and CD4, CD8, CD19, and NK cell subtype numbers); for no variable did this analysis yield a significant chi-square value.

Effect of Experimental Stress on Indexes of Hemoconcentration

To address the first question, measures of hematocrit, hemoglobin concentration, and plasma volume (calculated from hematocrit and hemoglobin) were first subjected to 2 × 2 Group (experimental or control) × Period (baseline or task) repeated measures analyses of variance (ANOVAs) for each study. Adopting a fixed effects model, effect sizes were then computed from the Group × Period interaction F statistic. An effect size indicates how large an association exists between two variables without regard to sample size (Rosenthal, 1984, 1991). We used the Pearson product–moment correlation coefficient (r) as the effect size estimate and present the effect sizes to allow for comparison across the different studies (see Table 1). Interpreting the effect size is equivalent to interpreting a correlation; the range is −1 to 1, with higher absolute values indicating a stronger effect. Combined, or mean, effect sizes were then computed by transforming each r into a Fisher's z coefficient, summing these zs, dividing the sum by 4 (the number of studies), and transforming the resulting z back into an r (Rosenthal, 1984, 1991). We used weighted mean effect sizes in each analysis, assigning more weight to studies with larger numbers of participants. Finally, to determine whether the weighted mean effect size differed reliably from zero, we tested for significance of the z statistic.

This meta-analytic procedure revealed significant Group × Period interaction terms for all indexes of hemoconcentration ($ps < .001$; see Table 1), indicating that across the four studies, exposure to laboratory stressors differentially affected baseline-to-task measures of hematocrit, hemoglobin concentration, and plasma volume among experimental and control participants. To interpret these effects, we then compared baseline-to-task changes in hemoconcentration separately among experimental and control participants. Here, effect sizes in each condition (experimental, control) and for each study were computed from t statistics derived from paired t tests comparing baseline and task values. The weighted mean effect size across studies showed that hemoglobin concentration and hematocrit increased significantly and that plasma volume decreased from baseline to task measurements among the participants exposed to laboratory stressors ($ps < .001$); corresponding measurements did not differ among unstressed controls. The ANOVA conducted on each study similarly showed a significant rise in hematocrit and hemoglobin and a decrease in plasma volume between baseline and task measurements in experimental, but not in control, participants.

Magnitude and Pattern of Quantitative Immune Responses Before and After Adjustment for Change in Plasma Volume

The second set of analyses sought to determine whether adjustment of task measurements for changes in hemoconcentration (as demonstrated above) alters the magnitude of participants' immune responses to the same stimuli. As there was no change in plasma volume to adjust for among control participants, the following analyses were performed only on data from stressed participants.

Baseline-to-task changes in each lymphocyte population were evaluated prior to adjustment for hemoconcentration. To determine the statistical significance of task-evoked changes in quantitative immune measures, we performed paired t tests on the unadjusted cell subtype numbers for each study comparing corresponding baseline and task measurements. Once again, the t statistic for each study was transformed into an effect size and a weighted mean effect across studies was calculated as in the section above (see Table 2). As expected, the mean effect across studies showed a significant rise in circulating numbers of CD8 and NK cells from baseline to task measurements (M effect = .29, $p < .005$; M effect = .59, $p < .001$, respectively). In contrast, analysis of CD4 and CD19 lymphocyte subsets revealed no significant change from baseline (M effects = −.06 and −.13, respectively).

Next, task values for each immune measure were adjusted for changes in hemoconcentration, and the statistical significance of participants' immune responses to stress was

Table 1
Mean Values and Standard Deviations for Hemoconcentration Parameters During Baseline and Stress Periods, ANOVA Group × Period F Statistic, and Meta-Analysis of the Effect

Hemoconcentration indexes and study	Experimental group						Control group						Interaction		
	Baseline		Task		Effect size	*M* effect[a]	Baseline		Task		Effect size	*M* effect[a]	*F*	*dfs*	*M* effect[a]
	M	*SD*	*M*	*SD*			*M*	*SD*	*M*	*SD*					
Hematocrit (%)						.528** (5.07)						−.040 (.29)			.789** (11.31)
1	41.3	2.6	42.4	2.58	.54		41.0	1.81	41.0	1.83	.00		13.86***	1, 38	
2	40.1	4.32	41.2	4.18	.49		40.5	3.83	40.5	3.72	.03		21.45***	1, 38	
3	39.1	2.98	40.8	3.00	.73		40.6	4.01	40.5	3.68	−.08		40.31***	1, 24	
4	43.6	1.52	44.2	1.58	.34		43.1	2.00	43.0	1.93	−.16		7.38*	1, 26	
Hemoglobin (g/L)						31** (6.32)						.092 (.65)			.809** (11.81)
1	14.4	0.97	14.8	0.98	.57		14.1	0.67	14.2	0.65	.11		14.25***	1, 38	
2	14.0	1.46	14.3	1.43	.60		14.1	1.36	14.1	1.33	.06		28.24***	1, 38	
3	13.6	1.08	14.2	1.04	.79		14.1	1.43	14.2	1.40	.16		28.03***	1, 24	
4	15.2	0.63	15.4	0.64	.61		15.0	0.76	15.0	0.73	.06		14.23***	1, 26	
Plasma volume (%)						.602** (5.94)						−.044 (.31)			.816** (11.99)
1	58.7	2.61	56.4	2.77	−.58		59.0	1.81	58.9	1.78	−.07		16.27***	1, 38	
2	59.9	4.32	57.6	3.99	−.57		59.5	3.83	59.4	3.60	−.06		28.19***	1, 38	
3	60.9	2.98	56.6	2.85	−.77		59.4	4.01	59.1	3.71	−.07		34.60***	1, 24	
4	56.4	1.52	55.0	1.70	−.49		56.9	2.00	56.9	1.91	.05		12.23**	1, 26	

Note. Study 1 (Marsland, Manuck, Fazzari, Stewart, & Rabin, 1995); Study 2 (Herbert et al., 1994); Study 3 (Bachen et al., 1995); Study 4 (Marsland, Manuck, Wood, et al., 1995). ANOVA = Analysis of variance.
[a]Weighted mean effect sizes, with corresponding *z* scores in parentheses.
*$p < .01$. **$p < .001$. ***$p < .0001$.

Table 2
Mean Cell Subtype Numbers and Standard Deviations Before and After Adjustment for Hemoconcentration Among Experimental Participants, and Meta-Analysis of the Comparison Before and After Adjustment

	Before adjustment							After adjustment				
	Baseline		Task					Task				
Cell subtype and study	*M*	*SD*	*M*	*SD*	Effect size	*M* effect size	*z* score	*M*	*SD*	Effect size	*M* effect size	*z* score
CD4 (cells/mm³)						−.059	.53				−.194	1.73**
1	722	214	703	198	−.08			676	193	−.22		
2	917	412	918	546	.00			881	526	−.09		
3	614	125	572	138	−.19			532	130	−.38		
4	740	225	743	259	.02			724	249	−.11		
CD8 (cells/mm³)						.289	2.61***				.217	1.95*
1	441	151	479	199	.19			458	187	.10		
2	589	247	703	411	.28			676	399	.23		
3	454	241	524	383	.21			486	356	.12		
4	518	132	615	193	.51			600	187	.47		
CD19 (cells/mm³)						−.135	1.20				−.267	2.41**
1	275	114	259	105	−.14			250	102	−.23		
2	292	120	278	105	−.14			267	126	−.24		
3	275	153	267	159	−.14			249	151	−.45		
4	247	76	240	71	−.11			234	69	−.20		
NK (cells/mm³)						.585	5.74***				.576	5.63***
1	160	162	300	170	.48			286	286	.48		
2	173	96	288	125	.68			277	116	.65		
3	187	91	457	238	.63			424	217	.62		
4	177	98	294	159	.60			286	153	.60		

Note. CD4 = T-helper cells; CD8 = T-suppressor/cytotoxic cells; CD19 = B cells; NK = natural killer cells. Study 1 (Marsland, Manuck, Fazzari, Stewart, & Rabin, 1995); Study 2 (Herbert et al., 1994); Study 3 (Bachen et al., 1995); Study 4 (Marsland, Manuck, Wood, et al., 1995).
*$p < .05$. **$p < .01$. ***$p < .005$.

reevaluated. For this analysis, estimated percentage change in plasma volume during each task (%dPV) was calculated from changes in hemoglobin level and hematocrit (Dill & Costill, 1974). Then, adjusted task values (Xt-c) for each immune measure were calculated from simple task values (Xt) using the following formula: $Xt - c = Xt/[1 - (\%dPV/100)]$. Adjusted cell subtype concentrations were then subjected to paired *t* tests against baseline values, and weighted mean effect sizes were calculated. As in analyses of unadjusted values, circulating CD8 and NK cells increased from baseline to task measures after correction for changes in plasma volume (*M* effect = .22, $p < .03$; *M* effect = .58, $p < .001$); however, the magnitude of the effect was now much reduced (see Figure 1). To determine whether the decline in CD8 and NK cell responses attributable to hemoconcentration differed significantly from unadjusted values, we then subtracted adjusted from unadjusted task values and compared this difference against an expected change of 0 by *t* test. Weighted mean effect size across studies indicated that adjustment for hemoconcentration did significantly reduce the magnitude of stress-related increases in both CD8 and NK cells (CD8: *M* effect = .49, $z = 4.64, p < .001$; NK: *M* effect = .44, $z = 4.11, p < .001$).

After similar adjustment for hemoconcentration, CD4 and CD19 lymphocytes were found to decrease significantly between baseline and task periods (CD4: *M* effect = −.19, $p < .04$; CD19: *M* effect = −.27, $p < .008$; see Figure 1). As in the case of CD8 and NK cells, the changes (i.e., declines) in CD4 and CD19 concentrations seen after adjustment for hemoconcentration differed significantly from the corresponding unadjusted values (CD4: *M* effect = .53, $z = 5.06$, $p < .001$; CD19: *M* effect = .52, $z = 5.01, p < .001$). These findings suggest that CD4 and CD19 cell subtypes are actively removed from circulation on participants' exposure to laboratory stressors but that such changes are masked by opposing effects of hemoconcentration.

Discussion

In this combination of data from four previously reported studies, we first demonstrated that acute psychological stress causes an increase in the number of CD8 and NK cells in circulation (but does not alter CD4 and CD19 subsets), as other investigators have also reported (e.g., Kiecolt-Glaser et al., 1992; Naliboff et al., 1991). Additionally, we found evidence that hemoconcentration occurred in all four studies, with small but reliable decreases in plasma volume in response to the same stimuli, corroborating prior observations (Jern et al., 1989; Muldoon et al., 1992; Patterson, Krantz, & Jochum, 1995; Patterson, Matthews, et al., 1995). When viewed in conjunction with prior similar findings, it seems reasonable to conclude that hemoconcentration is consistently elicited by acute laboratory stress paradigms. This concentration of blood-borne constituents modifies the interpretation of acute stress experiments (Jern et al., 1989; Muldoon et al., 1992; Patterson, Krantz, & Jochum, 1995)

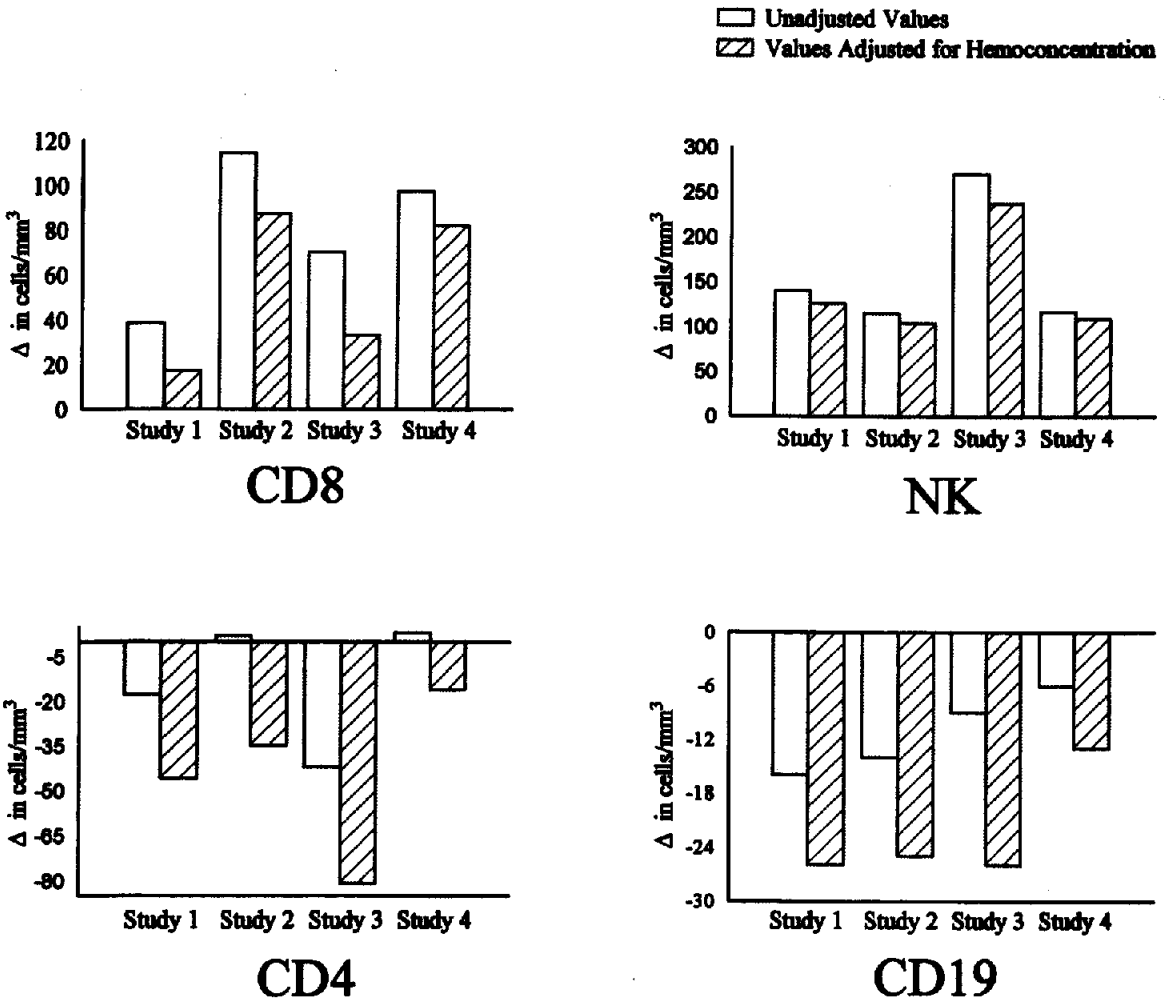

Figure 1. Mean cell subtype changes in experimental participants before and after adjustment for hemoconcentration. CD8 = T-suppressor/cytotoxic cells; CD4 = T-helper cells; NK = natural killer cells; CD19 = B cells. Study 1 (Marsland, Manuck, Fazzari, Stewart, & Rabin, 1995); Study 2 (Herbert et al., 1994); Study 3 (Bachen et al., 1995); Study 4 (Marsland, Manuck, Wood, et al., 1995).

that have observed changes in the blood concentration of any nondiffusible elements, such as stress-induced increases in cholesterol, blood viscosity, and any proteins, including those involved in hemostasis.

The principal purpose of the present analyses, however, was to extend the general issue of induced reductions in plasma volume to specific features of immunologic responsivity to acute psychological stress. Specifically, we sought to determine the extent to which this concentration of blood constituents under stress influences, or accounts for, concurrent changes in lymphocyte subtype concentrations. Our results demonstrate that the increases in CD8 and NK cells (per mm^3 of blood) seen here following stress were partly attributable to decreases in plasma volume, thus identifying hemoconcentration as one mechanism of stress-induced immune alteration. Whereas the current analyses reveal an association between lymphocyte subset changes and hemoconcentration without establishing causation, it is almost certainly the case that the plasma volume reduction produced by acute stress affects circulating lymphocytes in the same manner and to the same degree that it affects concentrations of red cells (Jern et al., 1989; Patterson, Krantz, & Jochum, 1995). Arithmetic adjustment of posttask lymphocyte values for hemoconcentration reduced by half the magnitude of change in circulating CD8 cells associated with participants' exposure to laboratory stressors. On the other hand, the same adjustment for hemoconcentration diminished NK cell responses by only 10%, although this more modest effect was still statistically significant.

Moreover, whereas unadjusted CD4 and CD19 cell counts were unaffected by stress, both of these measures decreased significantly from baseline values after hemoconcentration was taken into account. This indicates that the reactions of certain immune parameters may be governed by opponent processes, one actively removing lymphocytes from circulation and the other obscuring such changes by simultaneously reducing plasma volume.

Whatever the mechanism, there is evidence that the initial

cellular immune reactions to acute mental stress are regulated by activity of the sympathetic-adrenomedullary system. For instance, immune responses to common laboratory stressors (a) covary with the magnitude of sympathetic activation elicited under the same stimulus conditions (Herbert et al., 1994; Manuck et al., 1991; Zakowski et al., 1992) and (b) may be prevented by administration of an adrenergic inhibitor (Bachen et al., 1995; Benshop et al., 1994). Furthermore, infusion of epinephrine elicits the same pattern of immune responses as that seen during mental stress (Crary et al., 1983). Our findings suggest that sympathetic influences on immunologic reactivity to stress may act through both passive and active physiologic processes. Regarding the former, an increased concentration of nondiffusible blood constituents results from the transient loss of fluid into extravascular spaces, presumably because of the increased arterial (hydrostatic) pressure that is elicited by mental stress. In this regard, it has been demonstrated that stress-related reductions in calculated plasma volume are related to concomitant increases in systolic BP, HR, and plasma catecholamines (Muldoon et al., 1995; Patterson et al., 1995). That more active mechanisms of immune response must also be implicated is indicated in our data by the persistence of elevated CD8 and NK cell numbers following stress, after adjustment for concomitant hemoconcentration. In this regard, it is thought that alterations in adhesion molecules on cell surfaces may enable these cell populations to be mobilized into circulation from the endothelium of blood vessels. Recent studies indicate, for example, that catecholamines prevent the adherence of human NK cells to endothelial tissue in vitro (Benshop et al., 1993). It has also been speculated that, by changing the expression of surface adhesion molecules on lymphocytes and the endothelium, catecholamines alter migration of peripheral lymphocytes into or out of lymphoid organs (Ottaway & Husband, 1992).

Finally, the fact that other cell subtypes may decrease, rather than increase, in number in response to experimental stressors indicates a further complexity of acute immunologic reactivity, in which directionality of effect is modulated as well. Here, evidence indicates that lymphocyte subtypes differ in both adrenergic receptor density and in the generation of cyclic adenosine monophosphate following activation by the sympathetic nervous system (Maisel et al., 1989). Hence, it is possible that differential responses of the various lymphocyte subsets to sympathetic activation could alter patterns of cell trafficking.

In conclusion, we have demonstrated that for healthy college students hemoconcentration is one proximate mechanism responsible for lymphocyte redistribution following acute mental stress, partially accounting for increases in some cell types (CD8 and NK cells) and masking decreases in others (CD4 and CD19 cells). Although these findings are of interest in clarifying the mechanisms of stress-induced immune changes, the circulating lymphocyte concentrations reflected in measured (unadjusted) values are, of course, still of potential importance; this would be the case, for instance, when studying the physiologic implications of lymphocyte redistribution per se.

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