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FRANK J. SEILER RESEARCH LABORATORY

FJSRL TECHNICAL REPORT -78-0015

NOVEMBER 1978

COMPARISON OF STRESS RESPONSES IN MALE AND FEMALE CADETS AT THE UNITED STATES AIR FORCE ACADEMY

ORWYN SAMPSON

HUGH T. BAINTER

JOHN B. BOMAR, JR

PROJECT 2303

AIR FORCE SYSTEMS COMMAND

UNITED STATES AIR FORCE

FJSRL-TR-78-0015

This document was prepared by the Faculty Research Division, Directorate of Chemical Sciences, Frank J. Seiler Research Laboratory, United States Air Force Academy, Colorado. The research was conducted under Project Work Unit Number 2303-F1-12, Comparison of Stress Responses in Male and Femal Cadets at the United States Air Force Academy. Lt Colonel Orwyn Sampson was the Project Scientist in charge of the work.

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This report has been reviewed by the Chief Scientist and is releasable to the National Technical Information Service (NTIS). At NTIS it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

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Cholesterol	Hematology Variables

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Forty-eight women cadets in the Class of 1980 were studied during their initial training period at the United States Air Force Academy. Hematological and serological parameters were examined over the 43-day period. The analyses were carried out using least squares first and second order curve fits. This computational procedure is described. All but 8 of the 24 variables exhibited significant change over the study period. Implications of these changes are discussed in terms of potential causal factors. The study provides valuable baseline data for future analyses.

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Block 19. Continued.

Hemoglobin
Inorganic Phosphate
Lactate Dehydrogenase
Red Blood Cell
Stress
Serology Variables
Total Protein

FJSRL TR-78-0015

COMPARISON OF STRESS RESPONSES IN MALE AND FEMALE CADETS AT THE UNITED STATES AIR FORCE ACADEMY

A PILOT PROJECT

By

Lt Col Orwyn Sampson
Lt Col Hugh T. Bainter
Major John B. Bomar, Jr

November 1978

Department of Chemistry and Biological Sciences
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INTRODUCTION

There has been a growing interest in recent years in the physiological response of women to altitude as well as to physical and other stresses. The admission of the first women cadets to the Air Force Academy in 1976 presented a unique opportunity to attempt a quantification of this response. Successful quantification would be of significant benefit not only to the scientific community in general but would be mission oriented for the Air Force in light of the increasing number of women officers and enlisted personnel.

This report provides information obtained from a pilot study conducted on female members of the Class of 1980 during their Basic Cadet Training (BCT), June-August 1976. It focuses on changes in a variety of stress indicators found in blood.

MATERIALS AND METHODS

The subjects for the study were women basic cadets from the Class of 1980. The subjects all came from hometowns with elevations below 500 meters. Initially, 50 subjects were identified and 48 consented to volunteer for the study. This sample represented 31 percent of the entering woman cadet population. On the day of inprocessing (28 June 1976), blood specimens were drawn from all 48 volunteers. The cadets were then divided into five groups and on subsequent mornings, blood samples were collected from a subgroup of approximately 10 women. Thus, a sample was drawn from each cadet every five days. Samples were drawn from an antecubital vein with a single puncture into evacuated tubes for hematological and serological analysis. A total of 15 milliliters of blood was drawn. After day 1, the samples were drawn

at approximately 0545 hours before the morning meal. Sampling was terminated on 19 July (day 21) when the cadets entered field training exercises. A final sample was drawn on 10 August (day 43) after BCT had been completed. Forty-one cadets completed the study. All cadets included in the analysis had at least five blood samples taken.

The samples for hematology were analyzed the morning of the collection day. The serum samples were frozen and held at -20°C for the entire study period before analysis.

Six hematology and 18 serology variables were measured in each sample. The analyses were carried out on automated clinical screening analyzers. The hematologies were done on a Hemac hematocytometer and the serologies were done on a Hycel-17 autoanalyzer. Table 1 lists the variables measured.

For each of the 6 hematology and the 18 serology variables, a least squares second order fit was computed for each of the individual subjects. The coefficients thus obtained for each subject represent independent estimates of the coefficients for the true curve fit to the data. These coefficients were averaged for each variable to give average coefficients, that is, an average second order fit across all subjects. A student's "t" test was employed to determine if the averaged coefficients of the second order terms were significantly different from zero. Where there was no significance, the procedure was repeated employing a first order fit to test the first order coefficients. Appendix A presents a complete description of the computational procedure employed to calculate the curve fits as well as the mathematical definitions for the averaged coefficients.

TABLE 1. VARIABLES MEASURED

Measurement	Units
Hematology (Hemac 630L)	
Red Blood Cell Count (RBC)	Millions of cells/mm^3
Hemoglobin (HGB)	g/100 ml blood
Hematocrit (HCT)	% by volume
Mean Corpuscular Volume (MCV)	μ^3
Mean Corpuscular Hemoglobin (MCH)	$\mu\mu$g/cell
Mean Corpuscular Hemoglobin Concentration (MCHC)	g/100 ml packed cells
Serology (Hycel 17)	
Creatinine (CREAT)	mg/dl
Total Calcium (Ca)	mg/dl
Lactate Dehydrogenase (LDH)	u/l
Inorganic Phosphate (I-PHOS)	mg/dl
Creatinine Phosphokinase (CPK)	u/l
Glutamate - Pyruvate Transaminase (SGPT)	u/l
Glutamate - Oxaloacetate Transaminase (SGOT)	u/l
Alkaline Phosphatase (ALK PHOS)	u/l
Total Billirubin (T BILLI)	mg/dl
Sodium Ion (Na^+)	meg/dl
Potassium Ion (K^+)	meg/dl
Cholesterol (CHOL)	mg/dl
Uric Acid (U-AC)	mg/dl
Total Protein (T PR)	g/dl
Globulins (GLOB)	g/dl
Blood Urea Nitrogen (BUN)	mg/dl
Glucose (GLUC)	mg/dl
Albumin (ALB)	g/dl

RESULTS AND DISCUSSION

Hematology

Tables 2 and 3 present the results of the curve fit analysis. For those variables which showed significant change over the measurement period, the level of significance is indicated in the last column of the table. Using the analysis techniques described, five of the six hematology variables showed significant change during the measurement period. The raw data and curve fits for these variables are presented in Figures 1 through 5. Average hematological changes were consistent with the altitude and physical stress imposed during BCT (4,7).

HGB remained relatively constant during the first two weeks of the study period and then began a slow increase (Figure 1). Although the mean of the final HGB data was below that predicted by the average curve fit, the mean value on day 43 showed an increase over that on day 0. The RBC profile, as illustrated in Figure 2, depicts a slight decrease in RBC count followed by a gradual increase toward the end of the measurement period. Hematocrit (Figure 3) showed a steady linear increase over the study period. The derived parameters, MCV (Figure 4), MCH (Figure 5), and MCHC were analyzed as if they were independent variables. The average curves for these variables were consistent with the observed changes in HGB, RBC, and HCT. Both MCV and MCH showed first order increases over the measurement period while MCHC showed no significant change. Thus, it would appear that the initial decrease in RBC was compensated by an increase in MCV and MCH so that total HGB remained relatively constant until the latter part of the study period. The increase in HCT is consistent with increased MCV and/or

TABLE 2. SUMMARIZED RESULTS FOR HEMATOLOGY PROFILES
SECOND ORDER CURVE FITS

Variable	$\bar{C}_{20}$ *	$\bar{C}_{21}$	$\bar{C}_{22}$	Level of Significance †
HGB	$1.36X10^{1}$	$-3.5X10^{-2}$	$2.0X10^{-3}$	0.05
RBC	4.77	$-2.0X10^{-2}$	$4.7X10^{-4}$	0.01
HCT	$3.97X10^{1}$	$-7.9X10^{-3}$	$2.8X10^{-3}$	NS
MCV	$8.30X10^{1}$	$3.6X10^{-1}$	$-2.8X10^{-3}$	NS
MCH	$2.86X10^{1}$	$6.4X10^{-2}$	$1.1X10^{-3}$	NS
MCHC	$3.42X10^{1}$	$-7.0X10^{-2}$	$2.5X10^{-3}$	NS

* $\bar{C}_{20}$, $\bar{C}_{21}$, $\bar{C}_{22}$ are the average intercept, first and second order coefficients respectively.

† Ho: $\bar{C}_{22} = 0$.

TABLE 3. SUMMARIZED RESULTS FOR HEMATOLOGY PROFILES
FIRST ORDER CURVE FITS

Variable	$\bar{C}_{10}$ *	$\bar{C}_{11}$	Level of Significance †
HCT	$3.94X10^{1}$	$4.5X10^{-2}$	0.01
MCV	$8.38X10^{1}$	$1.9X10^{-1}$	0.01
MCH	$2.88X10^{1}$	$4.9X10^{-2}$	0.01
MCHC	$3.41X10^{1}$	$-1.56X10^{-2}$	NS

* $\bar{C}_{10}$ and $\bar{C}_{11}$ are the average intercept and first order coefficient.

† Ho: $\bar{C}_{11} = 0$.

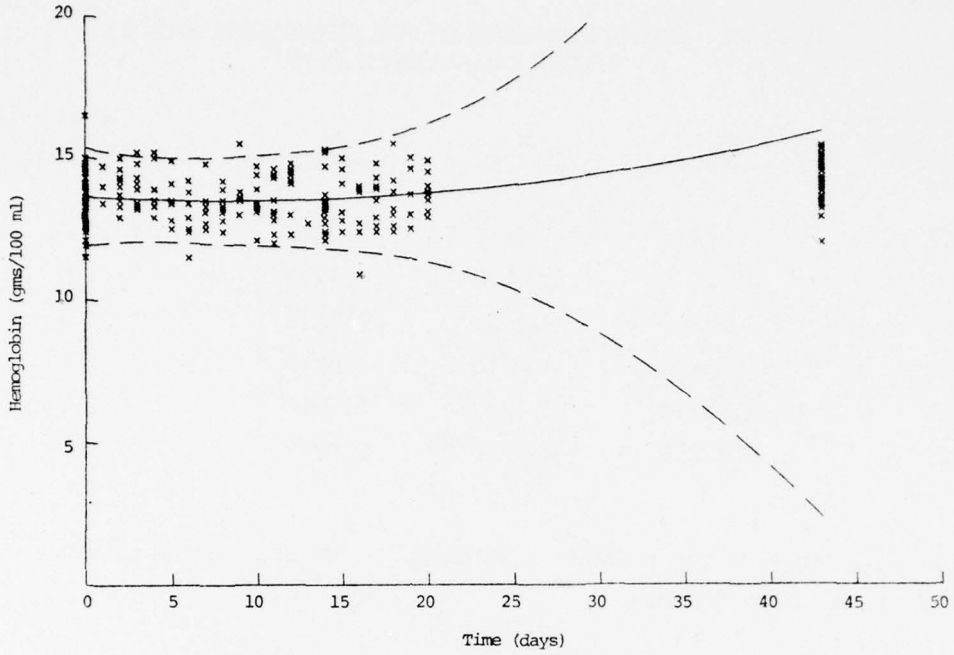

FIGURE 1. HEMOGLOBIN PROFILE. The solid line is the averaged least squares curve fit and the dashed lines are the 95% confidence limits for the curve.

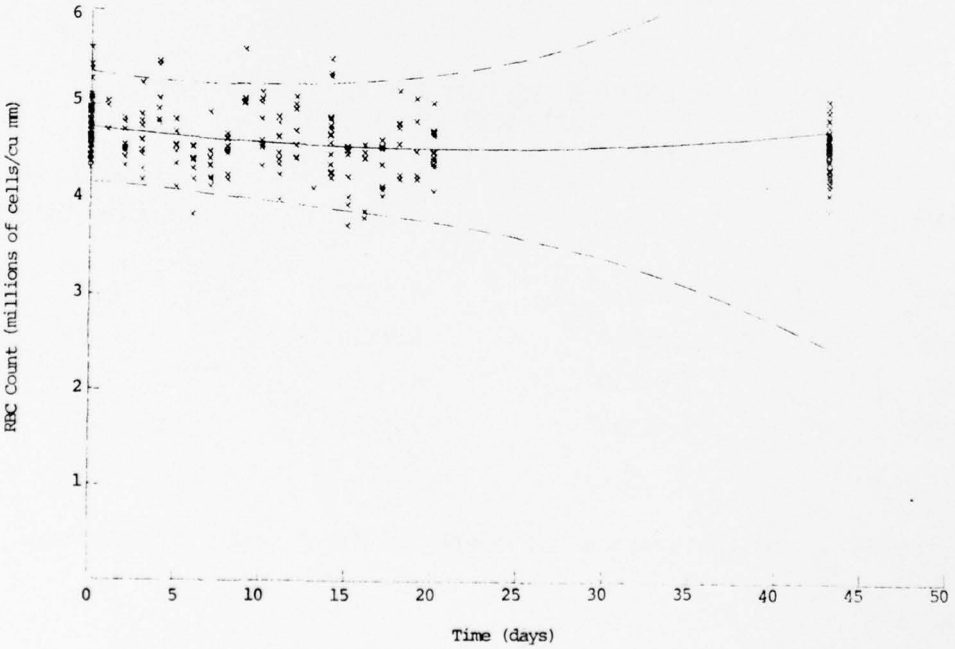

FIGURE 2. RED BLOOD CELL PROFILE. The solid line is the averaged least squares curve fit and the dashed lines are the 95% confidence limits for the curve.

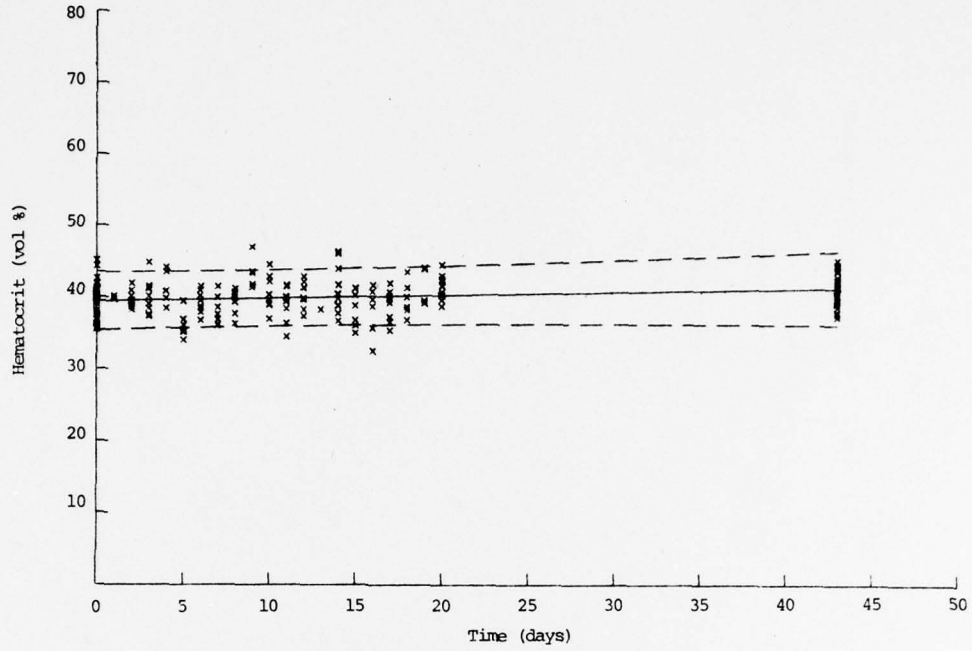

FIGURE 3. HEMATOCRIT PROFILE. The solid line is the averaged least squares fit and the dashed lines are the 95% confidence limits for the fit.

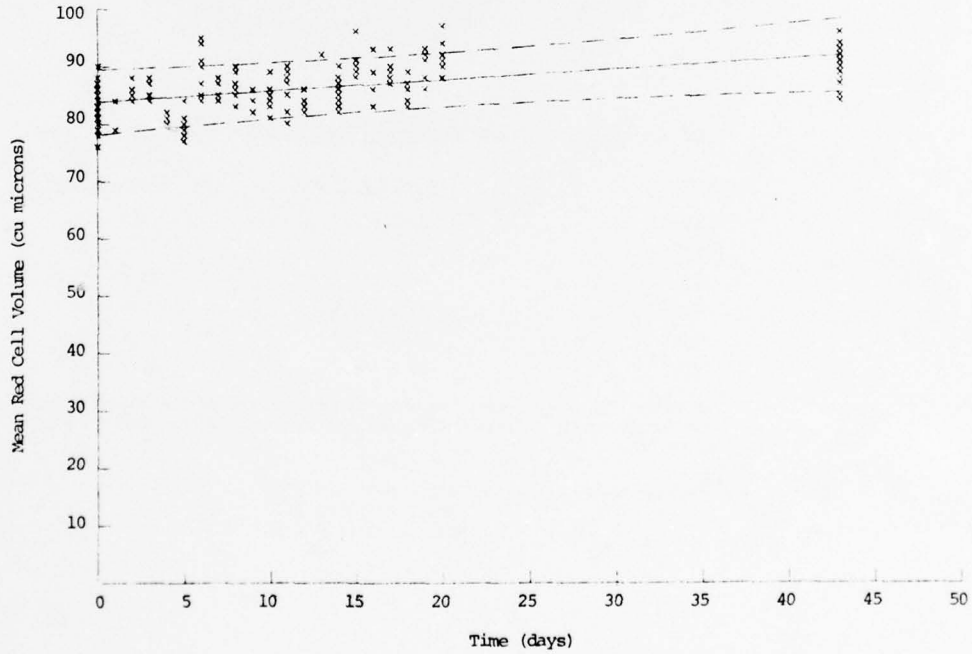

FIGURE 4. MEAN RED CELL VOLUME PROFILE. The solid line is the averaged least squares fit and the dashed lines are the 95% confidence limits for the fit.

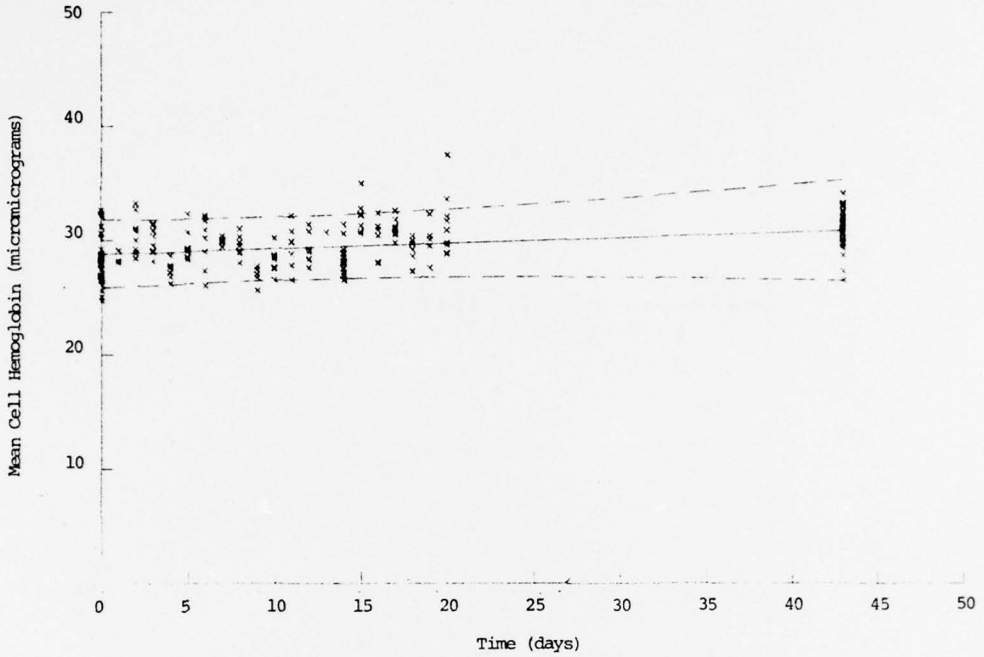

FIGURE 5. MEAN CELL HEMOGLOBIN PROFILE. The solid line is the averaged least squares fit and the dashed lines are the 95% confidence limits for the fit.

TABLE 4. ESTIMATED POPULATION MEANS ON DAY ZERO FOR HEMATOLOGY VARIABLES

Variable	Intercept* ± S.E.	Range of Normal Values (1)
HGB	13.6 ± 0.1	10 - 18
RBC	4.77 ± 0.05	3.6 - 6.0
HCT	39.7 ± 0.3	35.8 - 45.4
MCV**	83.0 ± 0.6	78 - 94
MCH**	28.6 ± 0.3	27.4 - 35.0
MCHC**	34.2 ± 0.3	31.3 - 36.9

*Intercept for second order fit when the coefficient of the second order term was significantly different from zero; otherwise intercept for the first order fit.

**Derived Values, that is: MCV = (HCT/RBC) X 10
MCH = (HGB/RBC) X 10
MCHC = (HGB/HCT) X 100

increases in both MCV and RBC. Table 4 gives values of the day zero intercept for each of the hematology variables along with ranges of "normal" values for young adult females. The intercept of the average fit was used as the best estimate of the mean value of each variable on day zero. These statistical values are important in establishing clinical baselines for women cadet basic trainees. In all cases, the confidence intervals on these intercept values are quite narrow. This is reflected in the standard error values reported in Table 4.

Serology

Tables 5 and 6 present the average coefficient results for serum chemistry variables. Again, where significant changes were found, the level of significance is given in the last column of the table. Eleven of the 18 serology variables showed significant change during the measurement period. Two of the variables, LDH and CHOL, are presented for discussion (Figures 6 and 7). The serology profiles for the remainder of the variables are presented in Appendix B.

The average curve fit for LDH (Figure 6) depicts an increase in serum LDH early in the measurement period followed by a tendency to plateau toward the latter part of the study. Previous studies in animals (6) and in humans (5) have shown that serum LDH levels increase after strenuous exercise. Moreover, these studies have indicated that the increase is greater in untrained individuals than in trained individuals. However, the post-exercise levels of serum LDH in these previous studies were measured shortly after exercise, that is, the elevated serum LDH was an acute response. In the present study, increases in serum LDH represent a chronic response to

TABLE 5. SUMMARIZED RESULTS FOR SEROLOGY PROFILES
SECOND ORDER CURVE FITS

Variable	$\bar{C}_{20}$ *	$\bar{C}_{21}$	$\bar{C}_{22}$	Level of Significance †
CREAT	1.2	$5.5X10^{-3}$	$3.8X10^{-5}$	NS
Ca	9.9	$-2.3X10^{-2}$	$9.8X10^{-4}$	0.02
LDH	$1.1X10^{2}$	2.4	$-3.9X10^{-2}$	0.02
I-PHOS	3.5	$6.8X10^{-2}$	$-1.5X10^{-3}$	0.01
CPK	$2.5X10^{1}$	1.1	$-4.9X10^{-2}$	NS
SGPT	$2.1X10^{1}$	$4.8X10^{-1}$	$-2.0X10^{-3}$	NS
SGOT	$1.7X10^{1}$	1.5	$-3.1X10^{-2}$	0.05
ALK PHOS	$1.9X10^{1}$	$-5.4X10^{-2}$	$9.2X10^{-3}$	0.01
T BILLI	$8.4X10^{-1}$	$2.7X10^{-3}$	$2.7X10^{-4}$	NS
Na^{+}	$1.4X10^{2}$	$-2.2X10^{-2}$	$2.0X10^{-3}$	NS
K^{+}	4.1	$-9.2X10^{-3}$	$2.4X10^{-4}$	NS
CHOL	$2.0X10^{2}$	-2.3	$6.8X10^{-2}$	0.01
U-AC	3.9	$1.7X10^{-2}$	$-1.2X10^{-4}$	NS
T PR	7.3	$-4.6X10^{-2}$	$1.5X10^{-3}$	0.01
GLOB	3.0	$-1.0X10^{-2}$	$3.6X10^{-4}$	NS
BUN	$1.5X10^{1}$	$2.2X10^{-1}$	$-3.5X10^{-3}$	0.05
GLUC	$8.8X10^{1}$	-1.1	$4.5X10^{-2}$	0.01
ALB	4.4	$-3.4X10^{-2}$	$1.1X10^{-3}$	NS

*,† Same as Table 2.

TABLE 6. SUMMARIZED RESULTS FOR SEROLOGY PROFILES
FIRST ORDER CURVE FITS

Variable	$\bar{C}_{10}$ *	$\bar{C}_{11}$	Level of Significance †
CREAT	1.3	$1.8X10^{-3}$	NS
CPK	$2.8X10^{1}$	$-8.6X10^{-1}$	NS
SGPT	$2.2X10^{1}$	$3.0X10^{-1}$	0.01
T BILLI	$8.4X10^{-1}$	$5.6X10^{-3}$	0.01
Na^{+}	$1.42X10^{2}$	$7.7X10^{-3}$	NS
K^{+}	4.1	$2.8X10^{-3}$	NS
U-AC	4.0	$-2.6X10^{-3}$	NS
GLOB	2.9	$-1.6X10^{-3}$	NS
ALB	4.2	$3.5X10^{-3}$	NS

*,† Same as Table 3.

intermittent physical stress along with continuous psychological pressures. It may be speculated that the observed initial increase in serum LDH followed by a tendency to level off reflects the conditioning effect of the Academy's BCT program.

The serum cholesterol profile is presented in Figure 7. The average curve shows a net increase in serum cholesterol over the study period, although the initial trend in the data was downward. The net increase over the summer is consistent with the findings of Clark, et al (2,3) who showed an increase in serum cholesterol in male AFA cadets over the basic training period July-August 1972. Clark suggested the increase was due to psychological stress induced by cadet anxiety during the period immediately preceeding the beginning of the academic school year. On the other hand, our data suggest that the increase begins at approximately day 13 following the onset of training. The causes for the initial reduction in serum cholesterol as well as its subsequent increase remain obscure. Perhaps dietary factors as well as physical and psychological stress contributed to our findings.

Table 7 presents the values of the day zero intercept for each of the serology variables along with ranges of "normal" values. Again, the confidence intervals are quite narrow. These data are presented as preliminary clinical baselines for women cadets.

CONCLUSIONS

The study has shown conclusively that some hematology and serology variables changed during BCT. Since the training consisted of both physiological and psychological stresses, it is not possible to delineate the

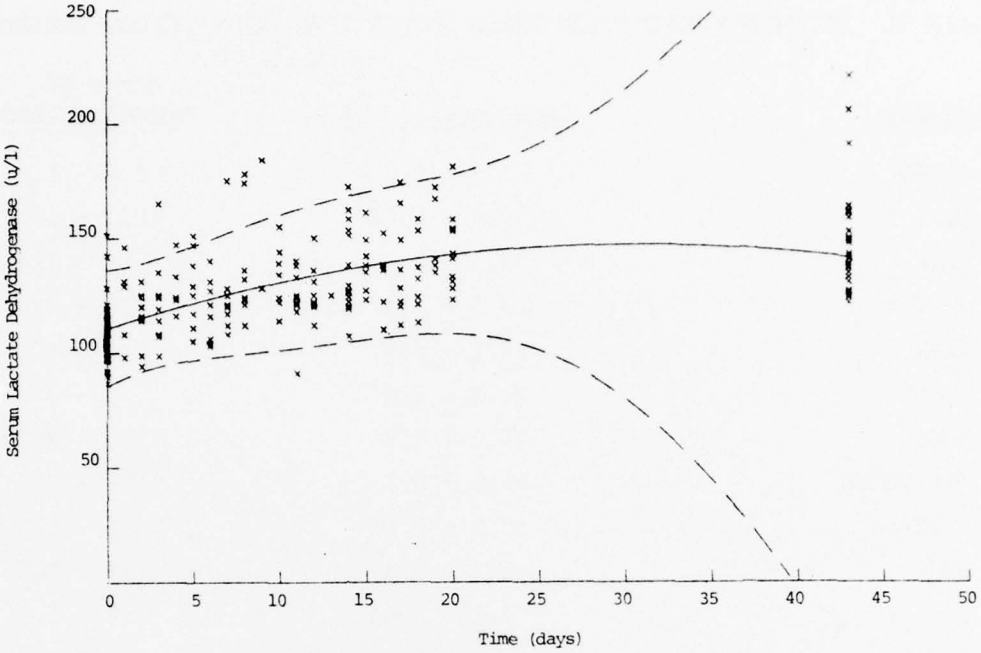

FIGURE 6. SERUM LACTATE DEHYDROGENASE PROFILE. The solid line is the averaged least squares curve fit and the dashed lines are the 95% confidence limits for the curve.

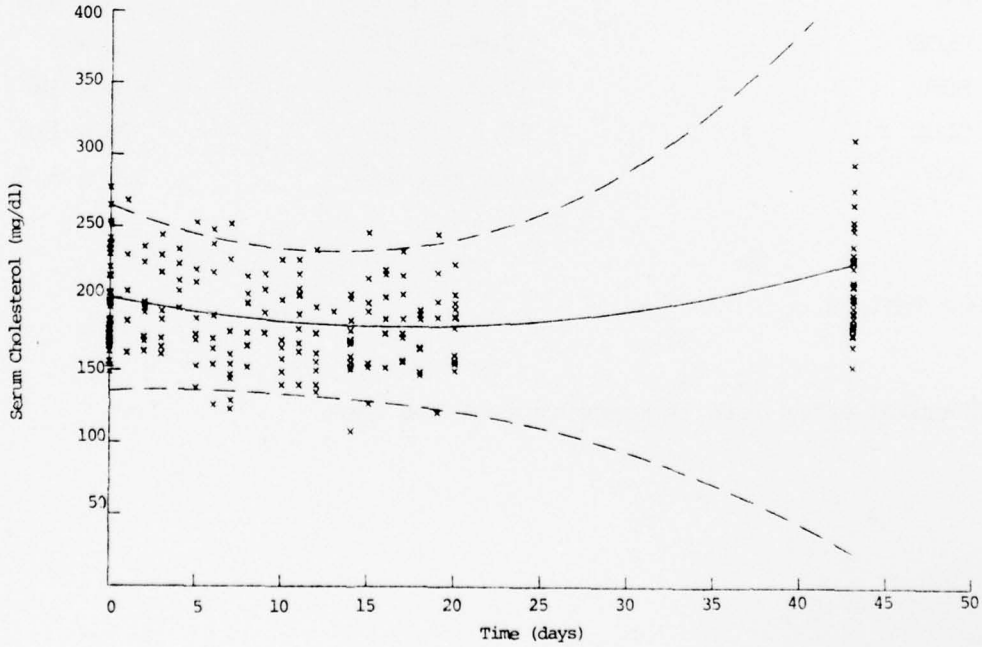

FIGURE 7. SERUM CHOLESTEROL PROFILE. The solid line is the averaged least squares curve fit and the dashed lines are the 95% confidence limits for the curve.

TABLE 7. ESTIMATED POPULATION MEANS ON DAY ZERO FOR SEROLOGY VARIABLES

Variable	Intercept* ± S.E.	Range of Normal Values (8)
CREAT	1.3 ± 0.02	0.8 - 1.6
Ca	9.9 ± 0.06†	8.7 - 10.7
LDH	111 ± 2	46 - 124
I-PHOS	3.5 ± 0.1	2.5 - 4.5
CPK	28.1 ± 1.9	0 - 52
SGPT	22.3 ± 1.0	0 - 47
SGOT	17.0 ± 0.9	11.0 - 38.0
ALK PHOS	19.0 ± 0.7	9 - 35
T BILLI	0.8 ± 0.03†	0.0 - 1.2
Na^+	142 ± 0.4†	135 - 148
K^+	4.1 ± 0.04†	3.5 - 5.3
CHOL	200 ± 5	150 - 250
U-AC	4.0 ± 0.1	2.0 - 6.0
T PR	7.3 ± 0.06†	5.5 - 8.0
GLOB	2.9 ± 0.03†	2 - 4
BUN	15.2 ± 0.4	8.0 - 18
GLUC	88.3 ± 1.5	70 - 110
ALB	4.2 ± 0.04†	3.8 - 5.2

*See Table 4.

†Standard error less than accuracy of the test.

cause-effect relationship for these variables. Moreover, altitude and diet may have contributed significantly to some of the observed changes. For future investigations of stress induced changes in blood variables during BCT, more sophisticated sampling and analysis are most certainly in order. This could possibly eliminate to a great degree the speculative nature of the explanation of the response of blood variables to stress.

Although some of the variables studied showed no change, the implication is not that these particular variables should be eliminated from consideration in future studies. On the contrary, these variables should be included in that they do contribute to baseline data and they may be valuable as reference points for studies done later in the Air Force careers of the study subjects.

For those variables which were observed to change, further investigations are definitely warranted. In most cases, changes could have been seen even without the aid of statistical methods. With the use of more sophisticated sampling, it may be possible to establish some very fundamental relationships between these blood variables and both physiological and psychological stress.

RECOMMENDATION

A continuation of this project to include a longitudinal comparison of cadet male and female stress responses was envisioned. However, this has been determined to be impractical at this time for the following reasons:

1. The phenomenon of stress is extremely complex. It not only involves physical and physiological parameters but psychological and sociological ones as well, not to mention subtle interactions between each of

these. To address the issue in a meaningful way would require a large team of experts and technicians from each of these areas, as well as an overall director capable of orchestrating the entire effort.

2. Research at the Air Force Academy is important in terms of supporting the overall mission, especially as it assists the instructor in keeping up in his specific field of knowledge and as it provides a motivational vehicle for faculty and cadets alike; all this aside from the value it provides in solving real Air Force problems. Nevertheless, research at the Academy is not a full-time job for any faculty member. Consequently, participation in a project the size of the stress investigation must be accomplished on a part-time basis. This necessitates a vast number of such participants in order to adequately explore the problem and is virtually impossible with the other demands and schedule requirements faced by each investigator.

The obvious solution to this dilemma is for the project to be carried out by an outside agency (e.g., AMD, USAFSAM, or civilian contractor) with assistance provided by Academy faculty and staff.

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APPENDIX A. MATHEMATICAL DESCRIPTION

The following derivations are presented to illustrate the method of deriving estimates of trends in sequential data. The method is applicable to repeated measures collected sequentially in time when using a subject as his own control. Any variable measured repeatedly in time is dependent on the past and future history of the variable. However, a least squares curve fit to an individual's data is an independent estimate of the true trend over time of the variable. By describing the distribution of the coefficients of the individual curve fits, one can produce an "average" curve fit with its associated confidence limits as described below.

Given

$$y(t) = f(t) + \varepsilon_r \text{ is random error} \tag{1}$$

where ε_r is random error, then let

$$f(t) = \sum_{m=0}^{\infty} C_m t^m \tag{2}$$

and

$$y(t) = \sum_{m=0}^{\infty} C_m t^m + \varepsilon_r \tag{3}$$

for a truncated p^{th} order series with $p + 1$ terms

$$y_p(t) = \sum_{m=0}^{p} C_m t^m + \varepsilon_r + \varepsilon_{fp} \tag{4}$$

where ε_{fp} is error due to truncation of the infinite series representation of $f(t)$.

For the i^{th} set of $y(t)$ vs t data a p^{th} order least squares curve fit will yield $p + 1$ coeffcients $C_{po_i}, C_{pl_i}, \ldots, C_{pp_i}$

and

$$\hat{y}_{p_i}(t) = \sum_{m=0}^{P} C_{pm_i} t^m + \varepsilon_{fp_i} + \varepsilon_{r_i} \tag{5}$$

where $\hat{y}_{p_i}(t)$ is an estimate of y(t) from the i^{th} data set and ε_{fp_i} is error due to imperfect fit which has been minimized by the least squares method.

Also,

$$\varepsilon_{r_i} + \varepsilon_{fp_i} = \sqrt{\frac{1}{K_i - 2} \sum_{j=1}^{K_i} [y_i(t_j) - \hat{y}_{p_i}(t)]^2} \tag{6}$$

where K_i is the number of data pairs in the i^{th} data set.

Now define $\bar{C}_{pm}$ as follows:

$$C_{pm} = \frac{1}{N} \sum_{i=1}^{N} C_{pm_i} \tag{7}$$

where N is the number of independent sets of y(t) vs t data.

Assuming that $\bar{C}_{pm}$ is the expected value of C_m then define

$$\hat{y}_p(t) = \sum_{m=0}^{p} \bar{C}_{pm} t^m + \varepsilon_r + \varepsilon_{fp} \tag{8}$$

where ε_{fp} is error due to imperfect fit for all y(t) vs t values, and

$$\varepsilon_r + \varepsilon_{fp} = \sqrt{\frac{\sum_{i=1}^{N} \sum_{j=1}^{K} [y_i(t_j) - \hat{y}_p(t_j)]^2}{\sum_{i=1}^{N} K_i - (p+1)}} \tag{9}$$

To compute the confidence limits on $\hat{y}_p(t)$, the following procedure is employed.

Given a function of p + 1 variables,

$$y(x_0, x_1, x_2, \ldots, x_p),$$

then

$$dy = \frac{\partial y}{\partial x_o} dx_o + \frac{\partial y}{\partial x_1} dx_1 + \frac{\partial y}{\partial x_2} dx_2 + \ldots + \frac{\partial y}{\partial x_p} dx_p \quad (10)$$

now, let

$$\hat{y}_p(t) = \sum_{m=0}^{p} \bar{C}_{pm} t^m + \varepsilon_r + \varepsilon_{fp} \quad (11)$$

at any t_j

$$\hat{dy}_p(t_j) = \sum_{m=0}^{p} \frac{\partial \hat{yp}}{\partial \bar{C}_{pm}} d\bar{C}_{pm} \quad (12)$$

since

$$\frac{\partial \hat{yp}}{\partial \bar{C}} = t^m \quad (13)$$

$$\hat{dy}_p(t_j) = \sum_{m=0}^{p} t_j^m \, d\bar{C}_{pm}, \quad (14)$$

and

$$[\hat{dy}_p(t_j)]^2 = \sum_{m=0}^{p} \sum_{n=0}^{p} t^{(m+n)} \, d\bar{C}_{pm} \, d\bar{C}_{pn} \quad (15)$$

letting differentials be equivalent to standard errors or standard deviations, then $(dx)^2 = \mathrm{Var}(x)$ and $dx\,dy = \mathrm{Cov}(xy)$.

So that,

$$[dy_p(t_j)]^2 = \mathrm{Var}[y_p(t_j)] \tag{16}$$

and

$$d\bar{C}_{pm}\, d\bar{C}_{p\ell} = \mathrm{Cov}(\bar{C}_{pm}, \bar{C}_{p\ell}) \tag{17}$$

Thus given a $\hat{y}_p(t)$, the parameters $\bar{C}_{pm}$, $\mathrm{Var}(\bar{C}_{pm})$, and $\mathrm{Cov}(C_{pm}, C_{p\ell})$ $\ell \neq m$, one can compute the variance of $\hat{y}_p(t)$ at any point t_j. From

$$\mathrm{Var}[\hat{y}_p(t_j)] = \sum_{m=0}^{p} \sum_{n=0}^{p} t_j^{m+n}\, d\bar{C}_{pm}\, d\bar{C}_{pm} \tag{18}$$

one can compute the 2s (95%) confidence limits on $\hat{y}_p(t)$.

APPENDIX B. VARIABLE PROFILES

This appendix contains the data for those variables which proved to change significantly, but were not discussed in the main part of the report. Although there does not appear to be any consistent trend in the observed changes, in the interest of completeness these data are made available to the reader. Perhaps the reader will recognize a change in one of the variables which has important implications that have eluded the authors. In all of the figures, the solid line is the least squares curve and the dashed lines are the 95% confidence limits for the curve.

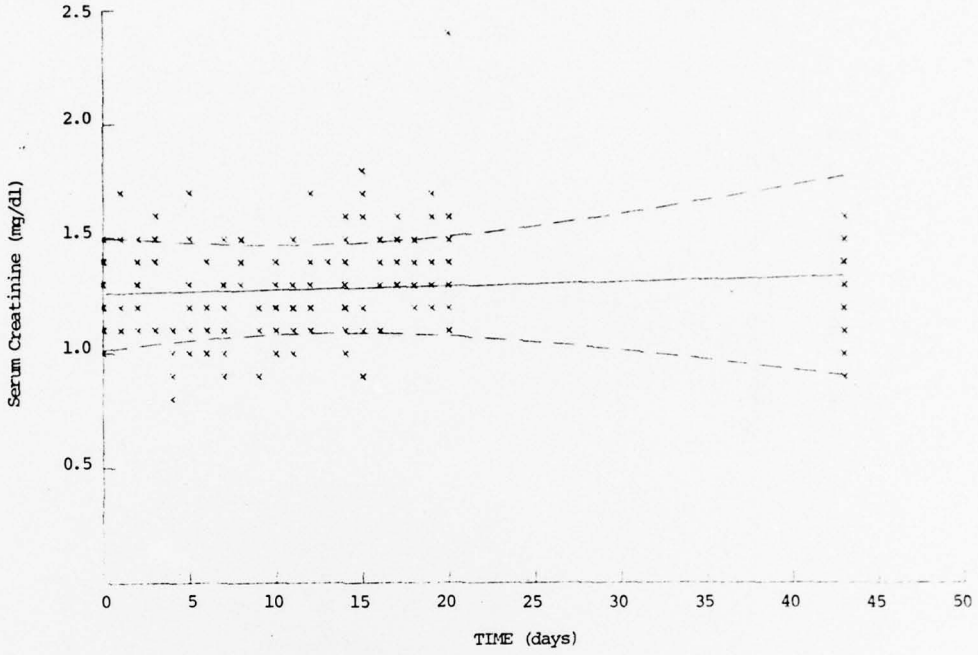

FIGURE B1. SERUM CREATININE PROFILE.

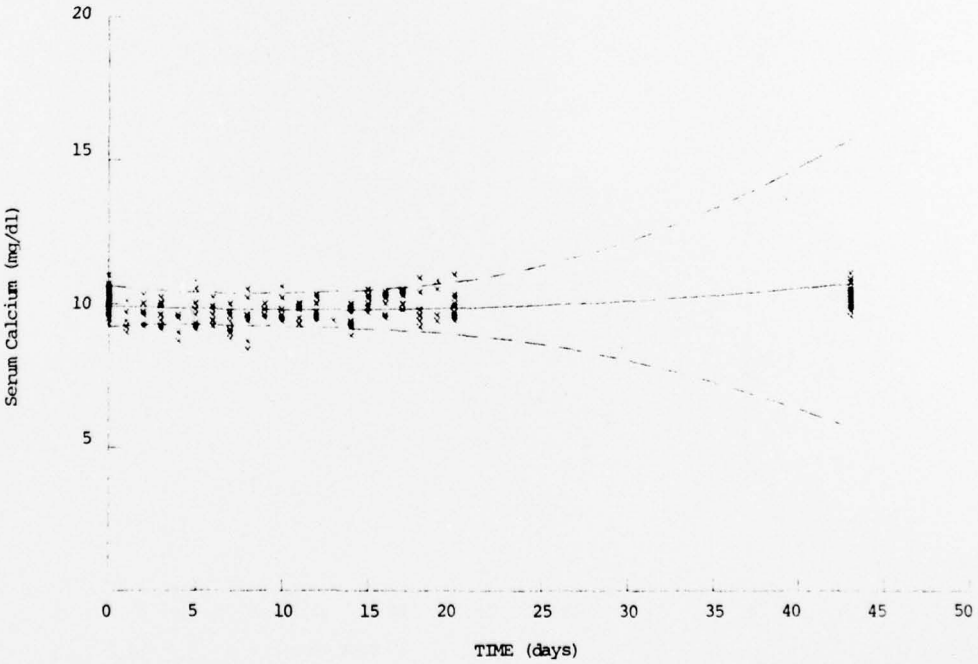

FIGURE B2. SERUM CALCIUM PROFILE.

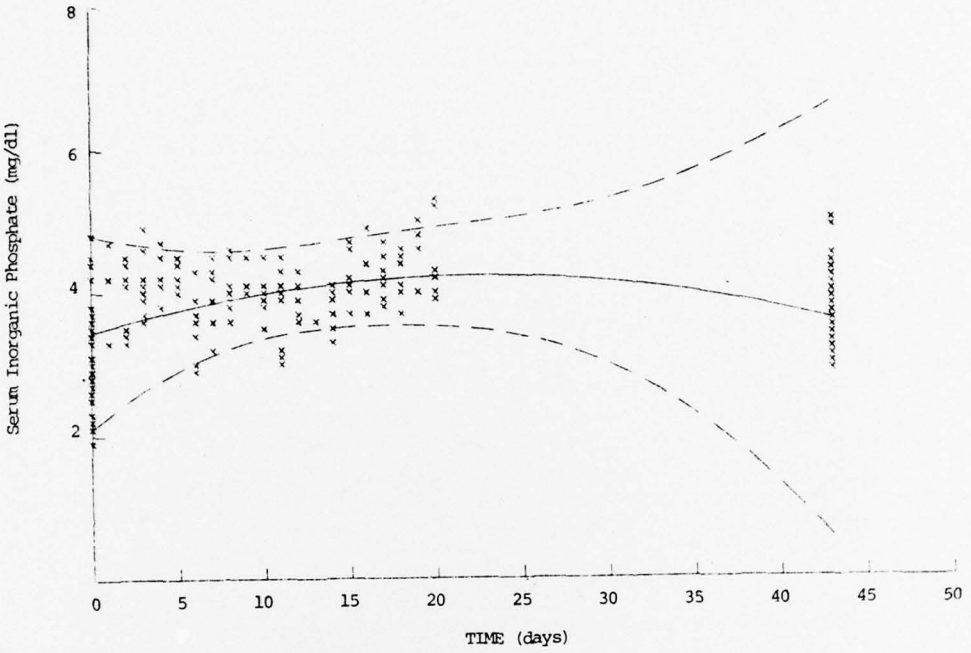

FIGURE B3. SERUM INORGANIC PHOSPHATE PROFILE.

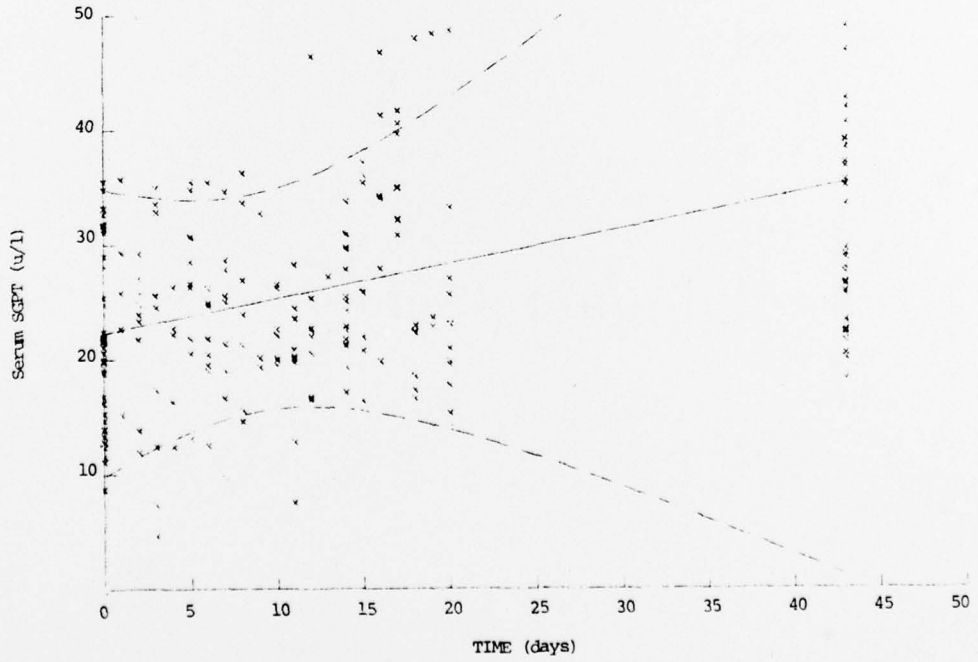

FIGURE B4. SERUM SGPT PROFILE.

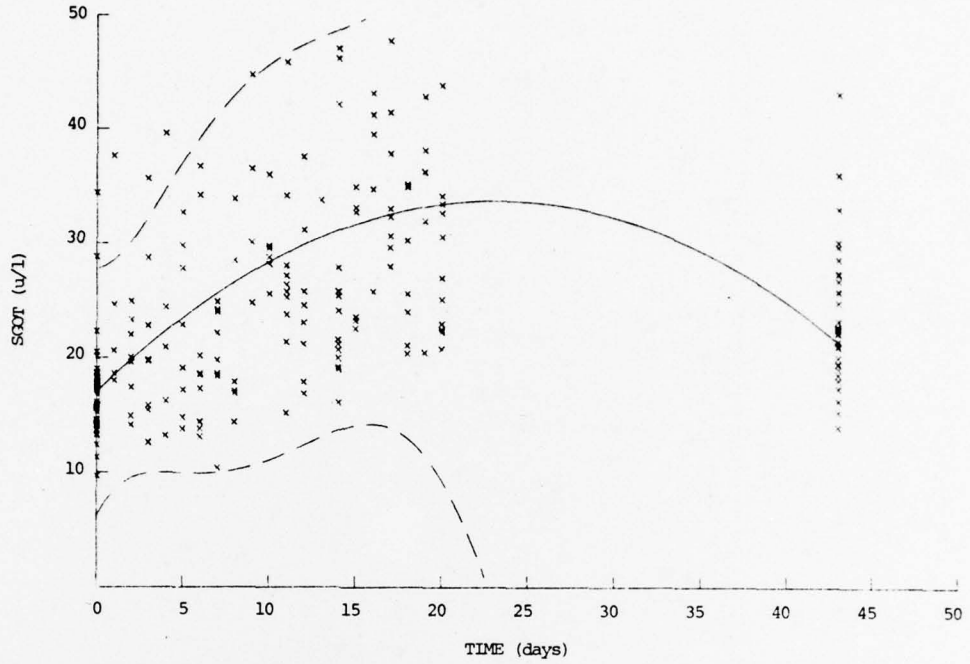

FIGURE B5. SERUM SGOT PROFILE.

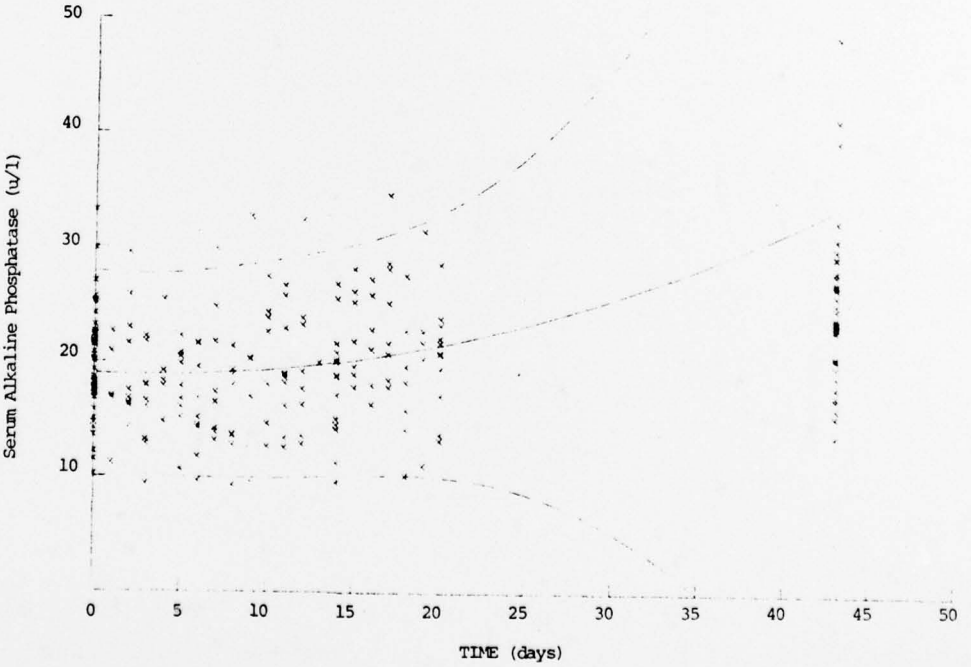

FIGURE B6. SERUM ALKALINE PHOSPHATASE PROFILE.

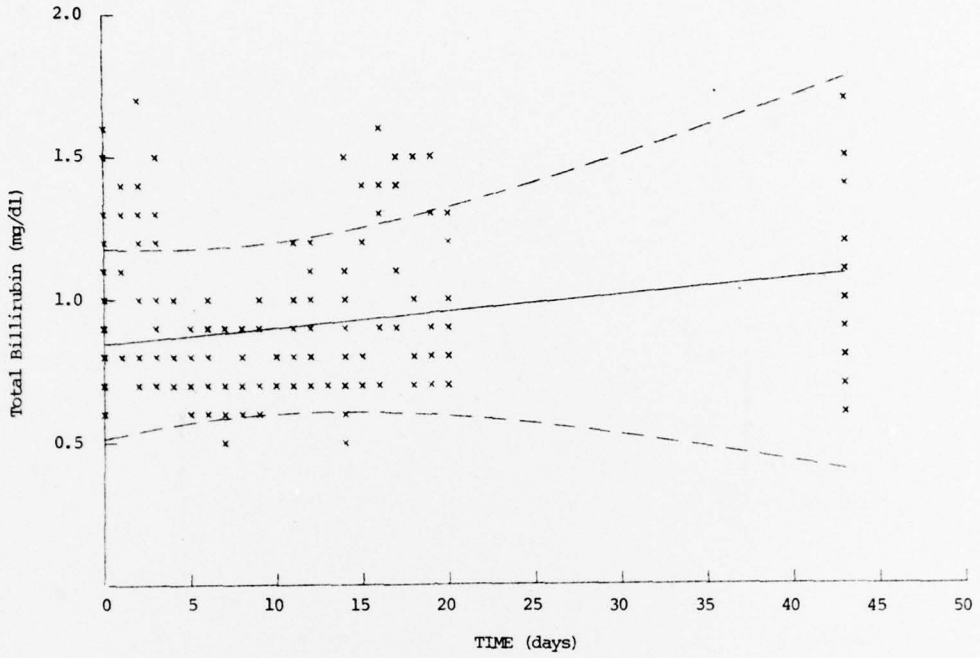

FIGURE B7. SERUM TOTAL BILLIRUBIN PROFILE.

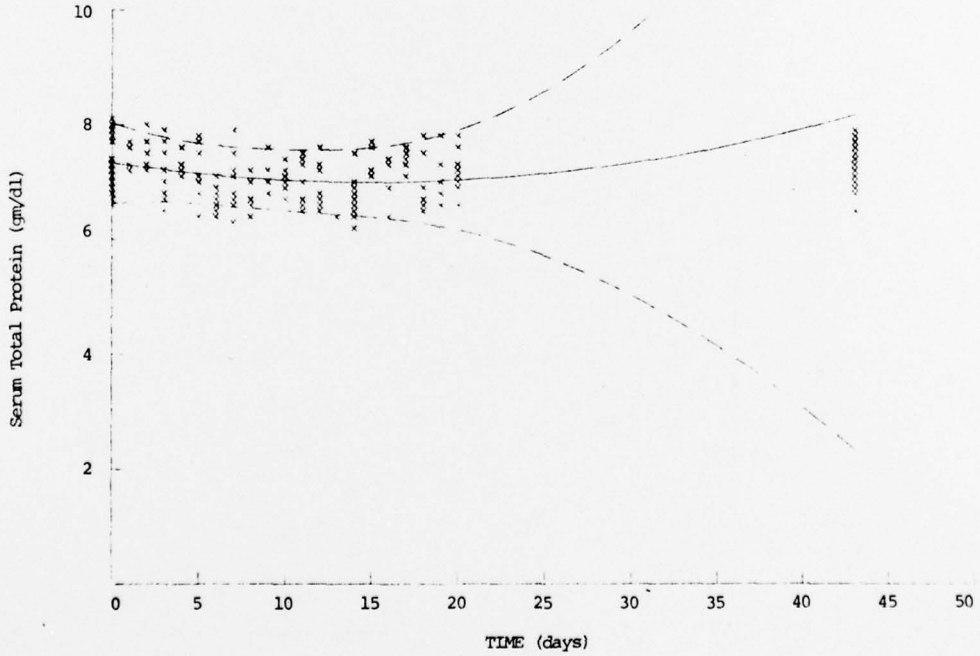

FIGURE B8. SERUM TOTAL PROTEIN PROFILE.

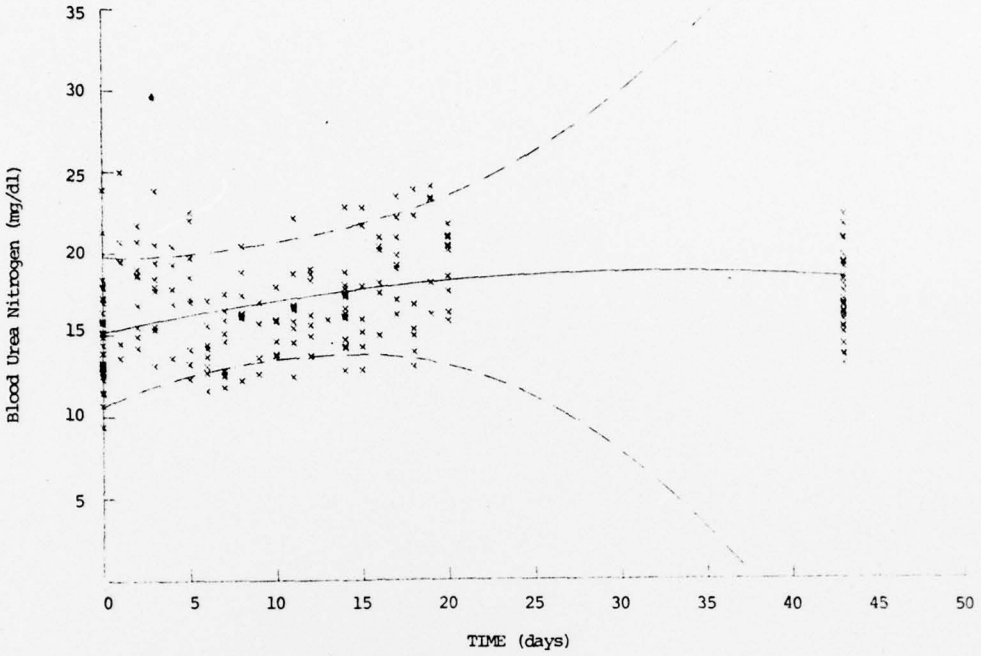

FIGURE B9. SERUM BLOOD UREA NITROGEN PROFILE.

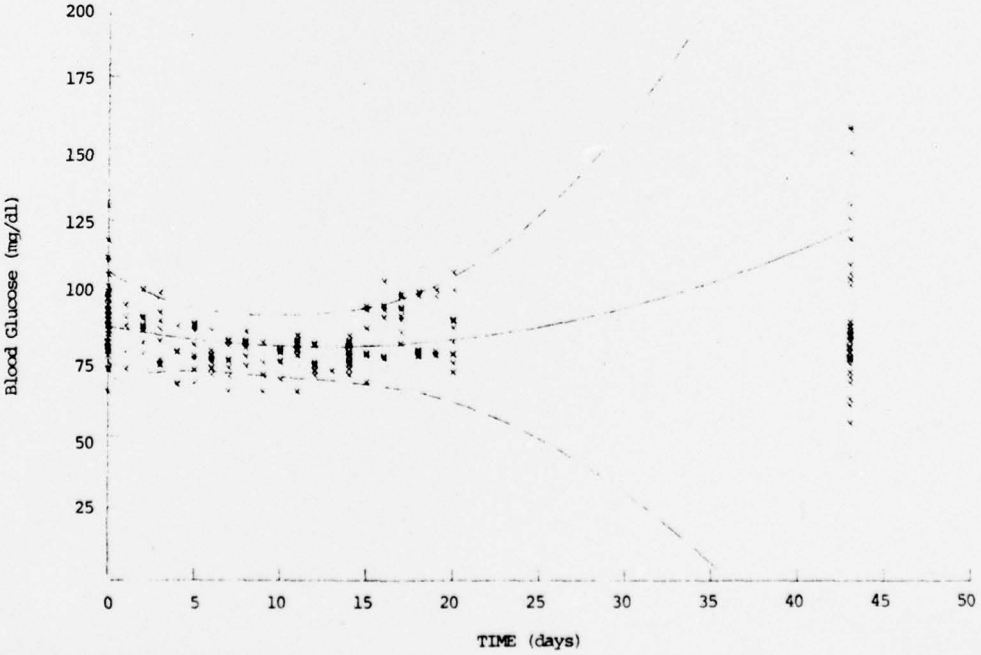

FIGURE B10. SERUM BLOOD GLUCOSE PROFILE.