(NASA-CR-160403) SKYLAB WATER BALANCE ERROR ANALYSIS (General Electric Co.) 39 p HC A03/MF A01 CSCL 05H

N80-13771

Unclas
G3/54 46341

160403

SYSTEMS DEPARTMENT

GENERAL ELECTRIC

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TIR 782-LSP-7006

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5/4/77		NAS9-14523	

SUBJECT

Skylab Water Balance Error Analysis

The attached report is an analysis of the precision of the Skylab water balance analysis previously submitted (TIR 782-LSP-7003) and should be considered a companion report to that document. This report contains estimates of overall precision of the indirect balance method of measuring changes in body water, a propagation of error analysis whereby total error is separated into biological variability and instrument error for each quantity in the water balance, and an analysis of covariances and correlation coefficients of the terms in the water balance. The overall conclusion is that the water balance method as used in the previous report is reasonably precise and reliable. The incorporation of suitable correction factors is a unique feature that permits the balance period to be extended over long periods of time. This is accomplished without the accumulation of serious errors which have previously limited this technique. Suggestions for increasing the reliability of such studies are included. The estimates of precision may be useful for designing forthcoming Shuttle fluid balance experiments.

/db
Attachment

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SKYLAB WATER BALANCE ERROR ANALYSIS

CONTRACT NAS9-14523

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WATER BALANCE ERROR ANALYSIS

INTRODUCTION

The water balance is an indirect measurement determined by the algebraic sum of terms in the water balance equation. It is subject to the errors in the directly measured components.

Experimental errors may be classified into several convenient categories (Beers, 1957): a) determinate vs. indeterminate errors, and b) random vs. systematic errors. Errors which may be evaluated by some logical procedure, either theoretical or experimental, are called determinate, while others are called indeterminate. Random errors are errors resulting from the effects of uncontrolled variables such as fluctuating conditions, noise, small disturbances, observer error, etc. They are sometimes called experimental, accidental or sampling errors. Random error is said to be shown when repeated measurements of the same quantity give rise to differing values scattered in some distribution about a mean value. Thus, "biological variability" and lack of perfect instrument reproducibility are most often random errors. In theory, these types of errors may be diminished without limit by replication of sampling, although redesign of experimental protocol and improved instrumentation are often more logical alternatives to accomplish the same end. Random errors are determinate because they may be evaluated by statistical analysis. Statistical treatment of data reveals information regarding random errors only.

Systematic errors are constant errors which affect all measurements of a particular quantity by the same amount. They may be due to calibration errors, personal methods of observation, neglect of small residual terms in metabolic balances, etc. Systematic errors may be determinate or indeterminate. If determinate, they are evaluated by auxiliary experiments such as calibration of instruments against standards, and if indeterminate, they may be inferred only indirectly by comparison with other measurements of the same quantity. They cannot be treated statistically except to find the random errors associated with calibration. Systematic errors cannot be diminished by repetition and if indeterminate, almost always set a limit beyond which repetition is valueless. Systematic errors exist in the typical water balance study, but these have been accounted for and have been discussed in a previous report (Leonard, 1977).

In this study we are interested in the source of random errors associated with estimations of the Skylab water balance. In principle the mean water balance for all nine men over the entire course of the mission (preflight, inflight, postflight) is associated with a variance which is indicative of the difference between a single observation and the true mean value for a large population. This sampling error includes differences in observations due to: day-to-day variation for any one individual, subject-to-subject variation, variation between flight phases (i.e., zero-g vs. 1-g), variation between flights, and a variation associated with instrument errors. These components of variance (except for instrument error) can be evaluated quite readily by an analysis of variance (ANOVA) although it is not the purpose of this study to do this, Rather, we are interested in an analysis of the ultimate precision (i.e., total sampling error) and sources of imprecision in the water balance technique as it is used in Skylab. Thus, our aim is to investigate whether or not it is possible to reduce the errors in the water balance in future experiments by such techniques as reducing measurement or instrument error, make additional measurements that were omitted in Skylab or change experimental design or protocol.

The three major objectives of this study may be listed as follows: a) to determine the total variance and ultimate precision of the water balance technique that was obtained in this study and that might be expected from future studies, b) to determine the sources of error in the water balance technique by examining sampling and instrument errors of all terms in the water balance equation, and c) to identify any questionable data collected from any of the crewmembers by examining the consistency of the errors among all subjects.

METHODS OF COMPUTATION

The purpose of this section is to present the mathematical expressions used in the calculations of various quantities shown in the remainder of the report.

Propagation of Errors

The error in the water balance can be expressed as the sum of errors of each term in the balance equation. The water balance equation used in this study is given by:

$$\text{Daily Water Balance} = \Delta\text{TBW} = \Delta\text{BWgt} - \text{Food Solids} + \text{Urine Solids} + \text{Fecal Solids} + \text{IML} + \text{CF} \tag{1}$$

where Urine Solids = Urine Volume x (Sp Gr - 1)

IML = net insensible metabolic loss from metabolism of foodstuff (carbohydrate, fat and protein) with digestive efficiency, EFF

$= (H_2O + CO_2 - O_2)_{\text{metabolism}}$

$= \text{EFF}\ (1.009 \cdot \text{CHO} + 1.007 \cdot \text{FAT} + 0.563 \cdot \text{PRO})$

CF = correction factor that includes unmeasured losses due to dry skin losses plus IML of body tissue metabolism.

For simplicity, let the terms of this equation be represented by the following notation where there is a one-to-one correspondence between Equations (1) and (2):

$$\bar{X}(\Delta\text{TBW}) = \bar{X}_1 - \bar{X}_2 + \bar{X}_3 + \bar{X}_4 + \bar{X}_5 + \bar{X}_6 \tag{2}$$

The bar over each term designates that they represent the mean daily value of that quantity for the time interval under consideration. The mean value is found from the set of continuous daily measurements for a single crewman.

The variance of $\overline{X}(\Delta TBW)$ can be determined from either of two separate calculations:

a) from the N set of calculated values of $X_i(\Delta TBW)$, i.e.,

$$S^2(\Delta TBW) = \left[\sum_i^N (X_i(\Delta TBW) - \overline{X}(\Delta TBW))^2\right] / (N-1) \tag{3}$$

and b) from the "propagation of errors" (Beers, 1957); i.e., the algebraic sum of the variances (S_i) and covariances (S_{ij}) of the six terms in Equation (2):

$$S^2(\Delta TBW) = \sum_i^6 a_i S_i^2 + 2\sum_i^6 \sum_j^6 a_i a_j S_{ij} \tag{4}$$

The quantities a_i, a_j are the coefficients (-1 or +1) of each term on the right side of Equation (2).

Both of these methods will result in similar estimates of $\sigma^2(\Delta TBW)$, the first equation being the traditional approach. However, Method (b) has the virtue of allowing the relative contribution of each term to the total variance to be determined.

Expanding Equation (4) and letting $S_6 = O$*, we get:

$$\begin{aligned} S^2(\Delta TBW) &= S_1^2 + S_2^2 + S_3^2 + S_4^2 + S_5^2 \\ &\quad + 2(-S_{12} + S_{13} + S_{14} + S_{15} - S_{23} - S_{24} - S_{25} \\ &\quad + S_{34} + S_{35} + S_{45}) \end{aligned} \tag{5}$$

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* This term, a correction factor, has been assumed to be constant for each subject and, therefore, by definition, has no error. In fact, however, this term does have a day-to-day variance which is indeterminate. To the degree that the computed value of CF is in error, there will be an indeterminate systematic error in the mean water balance. The method presented here is designed to study sources of random error only, not systematic error. See the companion study "Skylab Water Balance Analysis" (Leonard, 1977) for a further discussion of the errors involved in CF.

where the variances are given by a form of Equation (3) and the covariances are given by:

$$S_{xy} = \left[\sum_{i}^{N} (X_i Y_i - N \overline{X} \, \overline{Y}) \right] / (N - 1) \tag{6}$$

The covariances can also be computed from the correlation coefficients, ρ , between two terms, as follows:

$$S_{xy} = \rho_{xy} S_x S_y \tag{7}$$

If each term in Equation (2) is statistically independent of each other the correlation coefficients will be zero and the covariances will vanish.

Cumulative Water Balance and Precision

The water balance and the standard error of the water balance have been included in this report as a function of time of flight. In those cases we can define the "updated" mean cumulative water balance through day N as:

$$\overline{\Delta TBW}_N = \frac{\sum_{i}^{N} X_i (\Delta TBW)}{N} \tag{8}$$

and the "updated" cumulative standard error of the mean on day N as:

$$SE_N (\Delta TBW) = \frac{S(\Delta TBW)}{\sqrt{N}} \tag{9}$$

where S (ΔTBW) is the standard deviation given by Equation (3). The confidence intervals (95%) for the water balance for any day can be determined by:

$$\overline{\Delta TBW}_N \pm 2 \, SE_N \tag{10}$$

If these intervals are based on the entire number of days in the balance series and if the larger perturbations at the beginning and end of the series are omitted, they may perhaps be regarded as the minimal feasible uncertainties and a measure of balance precision (Hegsted, 1975).

Pooled Variance

The best estimate of $\sigma^2(X)$ (the variance of X) is taken to be the pooled variance determined from all crewmen as follows:

$$S_p^2(x) = \frac{\sum_i^k (N_i - 1)\, S_i^2(x)}{N - k} \tag{11}$$

where S_i^2 is the variance of x for the ith crewman determined from N_i daily measurements, N is the total number of daily measurements for all crewmen and k is the number of subjects. The equation was also used to average the standard errors in the tables of this report.

RESULTS AND DISCUSSION

In each subsection of this portion of the report, the error analysis for one crewman will be presented first. The results and conclusions will then be extended to include the entire crew of nine subjects.

Precision of Water Balance

In the example to follow only the data for an extended inflight portion of a single crewman is treated. Thus, we shall be interested in examining the errors associated with daily variation in water balance rather than variation between subjects, between flights, or between flight phases. The subject was not chosen at random, but represents the individual whose total body water was most constant (i.e., water balance closest to zero) over the longest period of time. This approach was chosen in an attempt to estimate the best precision obtainable for measuring water balance indirectly under the most ideal condition during the Skylab series.

In Figure 1, this crewman's (SL4/CDR) water balance and integrated water balance (i.e., total body water change) are shown. The variability of the water balance is often greatest at the beginning and end of the flight. Thus, we have chosen to analyze this data by omitting the first two days and last four days of the inflight period, the so called "edge effects" (Hegsted, 1975).

In Figure 2, the updated cumulative mean daily water balance and cumulative standard error are plotted using Equations (8) and (9). These graphs show an initial period of oscillation for the first 2 weeks inflight and then show a smoothing effect in which the values decrease to an apparent asymptote. (The asymptote is zero for the water balance and 33 ml for the standard error; if the flight were carried out indefinitely the true asymptote of SE_k would theoretically approach zero). The qualitative appearance of these curves suggests that comparatively little new information is added by the second half of the balance period. Unfortunately, the first two weeks of the period are the least stable. This may have implications for future Shuttle experiments which are expected to last less than two weeks. These results are similar to those obtained by Hegstad (1975) for mineral balance data. He also demonstrated that the characteristic shape of these curves are due in part to the averaging process assuming the quantities accumuldated are sufficiently gaussian.

Corresponding plots of the other crewmen are similar in appearance, but are not presented. However, their final asymptotic values are given in Table I. The two cases illustrated are with and without edge effects removed. It can be seen that on the average similar standard errors are obtained for both cases.*
However, removal of edge effects does change the direction of the mean daily water balance from a net loss to a small net gain. This indicates that after the initial loss of body water (occurring primarily during the first two days of flight), the body does not lose more water, but tends to gain fluid slowly. However, there is no apparent bias toward fluid retention in cases where edge effects have been removed; four crewmen have negative balances while five have positive balances. This is in accord with the intuition that the body may require long periods of time to ready a steady-state after an initial disturbance, but that having done so will remain reasonably in equilibrium. Some of the crew appear to have approached a steady-state (zero balance) much faster than others.

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* The removal of these "edge effects" has previously been suggested by Hegsted in his analyses of SMEAT metabolic balance data. It turns out, however, that having performed the analysis with and without edge effects included, the removal of the edge effects do not always lead to improvements in precision. This is apparent when we realize precision (as measured by inverse of standard error) increases with additional number of observations, but decreases as the dispersion of these additional observations increases from the mean value.

The 95% confidence intervals for the case where edge effects have been removed are $-125 < \overline{\Delta TBW} < +153$ on the average and all the intervals computed for each individual overlap. This fact, together with the lack of bias toward net retention has been used by Hegsted as evidence lending credence to the findings of the balance technique.

The cumulative standard error of the net balance of a quantity has been used as a measure of the precision of the technique (Hegsted, 1975; Lentner, 1975). Under the most ideal conditions, the best precision for a single crewman has been shown as $\pm$ 33 ml/day (SE after 78 days for SL4/CDR). The 95% confidence intervals for this subject is, therefore, $\pm$ 66 ml/day. This particular subject had a daily total body water turnover of approximately 2600 ml (as indicated roughly by mean water intake). Thus, the relative spread of water balance error with regard to turnover can be given as $66/2600 \times 100\% = \pm 2.5\%$, which is a reasonably accurate precision for balance techniques.

The precision of the water balances for each of the crewmen during preflight and inflight periods are given in Table II for the case where edge effects are included. Two values for SE_k are given for each subject for each flight period. The first is the cumulative standard error at the end of the first 14 days, which roughly corresponds to the expected orbit time of Shuttle. The second is the standard error for the entire preflight or inflight period. While the precision decreases for the shorter interval, as expected, it is still reasonably close to the longer term precision.

The best estimate of the variance of the mean water balance can be obtained by pooling the variances (See Equation 10) for each of the nine crewmen during the entire preflight and inflight periods. These values, shown in the last row of Table A-I, result in $\sigma^2(\Delta TBW) = 390)^2$ and represent over 750 separate man-days of measuring water balance from the indirect balance technique. This value (as well as those shown in Table II) can be used to provide confidence intervals for determining water balance on future flights using the same experimental method. Thus, we might state that in 95% of any future water balance determinations the interval between $\overline{\Delta TBW} \pm 2\sigma/\sqrt{N}$ will include the true mean. In this case, $\overline{\Delta TBW}$ is the sample mean, N is the number of observations and $\sigma = 390$ ml. The minimal number of samples required to resolve a change in water balance of ΔTBW ml (at 95% level) can be found from, $N = (2\sigma/\Delta TBW)^2$. For example, 10 preflight and 10 inflight samples are needed to resolve a change of 250 ml in daily water balance.

Propagation of Error Analysis

The last section was concerned with the absolute errors in mean daily changes of body water using the indirect balance method. The discussion to follow will attempt to analyze the sources of these errors as they derive from each component or term of the water balance equation. As before, the SL4/CDR crewman's data will be used for a detailed example.

Water balance is an indirect measurement and is subject to the propagation of random errors shown by Equations (4) and (5). These errors are listed in terms of standard deviation, S_i, in Table III for each term in the water balance. The sum of these errors (actually the square root of the sum of squares) is shown at the bottom of the column as $S = 302$ ml. Covariances, as shown in Equation (5) have been omitted from the calculation. If they had been included they would change the standard deviation only slightly to $S = 296$ which represents only a small covariance contribution. Therefore, we have elected to exclude covariances from these calculations of error propagation.* The error contribution of each term can be easily found by dividing the variance of each term by the total variance as shown in Table III. Also shown are the 95% confidence limits for each term. By far, the largest error is seen to be due to those associated with measuring changes in body weight. In fact, almost all the total error in net water balance can be ascribed to this single source (96.5%).

* Accounting for the covariance error contribution in each water balance term would involve a form of factor analysis and determination of eigenvalues, a calculation which is not justified here. We shall demonstrate that the covariances play a relatively small role in total error for all other crewmen as well.

The errors just discussed are total sampling errors which include the randomness due to biological variability (the errors present even if all measurements could be made with perfect precision) as well as the random errors associated with the technique of measurement or "instrument error" (the errors present if a known calibration standard were repeatedly measured).

In general:

Total variance = biological variance + instrument variance

We have attempted to estimate the instrument errors for each quantity in the water balance equation. Details of the calculations are given in the appendix and the results of that analysis are shown in Table III (E_i) along with their relative error contribution and confidence limits. Note that since a measurement of any quantity is independent of the measurement of any other quantity the total instrument variance is exactly equal to the sum of the individual variances since the covariances vanish. It is apparent that the largest source of instrumentation error (70%) is due to the mass measuring device for determining changes in daily body mass. Nevertheless, from the last column of Table III it is also apparent that instrument error contributes only minimally (1.6%) to the uncertainty associated with the mean values observed in this study. That is, biological variability far exceeds instrument error, a conclusion which is quantitatively and qualitatively similar to the one reached by Hegsted for mineral balances.

A portion of the variance of the term "food solids" and "insensible metabolic loss" (the latter is a direct function of the food components) is due to the cyclical nature of the six day rotational diet that was used in Skylab. It is possible to remove this contribution (see Hegsted's report), but the conclusions would not be different because both of these terms only contribute several percent towards total water balance variance.

Since instrument error contributes only a fraction to the total variance little is to be gained by improvements in analytical accuracy. If improvements in instrumentation are desired, however, the analysis suggests that emphasis be placed soley on the mass measurement device. Total variance is high because of mainly one factor, the variance in daily changes in body mass. This is basically due to biological factors and little is presently known how to control this quantity. Whether more careful control of food and water intake within rigid limits would assist to control body weight changes is not known. This may warrant some attention.

One of Hegsted's principal findings was that substantial reduction in variance are not available for mineral balance studies. Unfortunately, we reach the same general conclusion with the exceptions noted below. He based his conclusions on the argument that the major source of error in balance methods is due to unmeasured skin losses which "although it cannot be proven . . . (must be) . . . higher than the conventional estimates." In Skylab this takes on additional significance where "the effects of the (zero-g) environment on dermal losses are completely unexplored." He suggests the need for independent measures of total body composition for such quantities as calcium, potassium, etc. We have shown that correction of the balance technique with total body water measurements does indeed lead to more acceptable and meaningful results, and that this in itself has drastically reduced a major source of error (Leonard, 1977). However, while separate corrections were determined for each subject, it was only possible to apply a constant correction factor for each day of flight; the actual day-to-day variability is not known and neither is the variability due to change in gravitational field. Therefore, we concur with, and extend, Hegsted's suggestion for future research: that it be directed toward a) measurement of skin losses, and b) estimation of total body composition by direct methods which should be used at frequent intervals during balance periods on earth and during weightlessness.

Covariances and Correlations

The conclusions reached in the previous section regarding the minimal contribution of covariances of one crewman can be extended to all crewmen. Table IV illustrates the errors (expressed there as SE) in each subject's water balance due to: a) all variances and covariances (column 1) and, b) variances only as obtained from the propagation of errors (column 2). The percentage difference between these two (in the last column) is an estimate of the covariance contribution which on the average is only 10%. For reasons which are not completely clear, the covariance contribution of all men on SL3 (Men #4, 5, and 6) are much higher than the other crews. Also shown in Table IV are the errors due to ΔBWgt which in all cases are similar to the errors due to ΔTBW indicating that the total water balance error is almost entirely due to errors in measuring body mass.

Although the covariances are of negligible importance to total error contribution, they are useful insofar as they provide information about correlation coefficients for water balance components as shown by Equation (7). Table V shows the variance-covariance matrix and correlation coefficients for water balance terms of subject SL4/CDR. It should be noted that covariances will have low values if either the correlation coefficient is low <u>or</u> if at least one of the variances are very small. Both of these situations can explain the low covariances seen in this study.

The most significant correlation is seen to be the one relating food solids and insensible metabolic loss. This, of course, is expected from the fact that IML is derived from dry food consumption. Other significant correlations exist between ΔBWgt-Food Solids and ΔBWgt-Urine Solids. Neither of these is unexpected since at a constant rate of metabolism the major changes in body weight are due to solid and liquid changes in the diet. The low correlation between food and fecal solids exists only as an artifact since there was not a bowel movement on each day and the fecal values for these days are zero. There was no attempt to correlate food intake or body weight with a delayed or lagged urine or fecal output. The irregularity of the fecal output precludes obtaining meaningful information from such an analysis.

Table VI shows the corresponding correlation coefficients for the entire crew of nine subjects expressed as a weighted mean value. The only significant values that appear in this table that were not discussed above is the correlation between food and urine solids. This value was unusually low for SL4/CDR compared to most of the other crewmembers. The correlation coefficients for each crewmember is given in Appendix Table A-II. From that table it may be seen that the SL3 crewmembers had as many significant correlations between factors as the other six crewmen combined. In particular the fecal-urine solids correlations were higher in part because the second crew had more frequent bowel movements. This helps to explain the previously observed high covariance contribution of these subjects shown in Table IV.

Correlation Using Water Balance as a Common Factor

Another type of correlation coefficient computed was that between the daily water balance and each term of the water balance equation. (In the previous calculations, water balance was not used as a common factor). These coefficients are shown in Table VII for subject SL4/CDR, in Table VIII as mean coefficients for the entire crew and in Table A-III (Appendix) for each of the nine crewmen. The results shown in Table VII suggest: a) that body weight changes are nearly perfectly correlated with water balance, b) that the other factors have lower, but still significant, correlations with water balance, and c) that removal of edge effects enhances the significance of several factors. This latter effect is to be expected since total body water changes dramatically the first two days of flight regardless of food eaten or excreta produced.

The mean values of coefficients shown in Table VII show no remarkable changes with regard to comparison of control with inflight phase. They are in fair agreement with corresponding values obtained for the single crewman SL4/CDR. These values represent a mean for the nine crewman and in some cases there is a considerable dispersion among the subjects as shown in Table A-III.

The boxes surrounding particular coefficients denote outlying values (greater than or less than two times the mean value). Very low or very high coefficients for particular subjects may mean true biological correlations deviant from the norm or some consistent error in data collection. Each successive crew of three subjects show increasing numbers of outlying values. However, there do not appear to be consistent trends that suggest data collection errors.

General Types of Errors in the Balance Technique

Errors in the balance technique have been reviewed by Hegsted (1975, 1976), and Forbes (1973). The major types of error they discuss include the following: a) certain losses are not measured in the usual balance study, especially nutrients lost through the skin, b) there is a consistent bias in most balance studies arising from an overestimation of intake (the subject may not eat all of the food offered, but cannot consume more than offered) and an underestimation of output (it is difficult or impossible to collect all excreta and difficult to collect more excreta than are actually produced), and c) balance studies designed to identify minimal dietary requirements are based on an assumption of achieving a true steady-state metabolic balance which may take longer periods of time than allowed in most studies. In addition, there is an additional source of error in the water balance technique used here: d) the body is capable of generating water by the catabolism of body tissue and this quantity cannot normally be measured accurately.

The errors due to (a) and (d) will tend to underestimate water balance and those associated with (b) will make the balances falsely high. The errors of (c) do not really apply to this study because there was no assumption of the existence of a steady-state. Furthermore, long term changes in water intake, if they were present at all, are reflected very rapidly by corresponding changes in total body water composition.

Dermal losses and body tissue losses were accounted for in the present study by correcting the balance with total body water direct measurements at various intervals throughout the long study period, thereby minimizing the errors (a) and (d). Ultimately, however, the precision of balance studies are limited by the precision with which the intake and output can be determined. Collection of excreta and measurement of food and water intake were carefully performed and corrections were included for food not eaten at each meal. It was more the responsibility of the crewmen than the principal investigators to perform the actual collection and reporting tasks. However, the crews were highly trained and well motivated and it is not likely that consistent errors were introduced. It is more likely that occasional lapses in reporting occurred due to rigid scheduling of other tasks. This source of error would tend to be minimal when averaged over the entire 900 man-days of observation.

SUMMARY

Estimates of the precision of the net water balance have been obtained for the entire preflight and inflight phases as well as for the first two weeks of flight. After two weeks the confidence intervals are approximately $\pm$ 250 ml/day. These intervals were shown to decrease rapidly after the first two weeks of flight. The smallest 95% confidence interval obtained for any one crewman was $\pm$ 66 ml/day and $\pm$ 124 ml/day for the mean of all nine crewmen. The overall "best" Skylab estimate of water balance variance was found to be $\sigma^2 = (390)^2\ ml^2$. These values can be used as guidelines in making inferences about design and analysis of Shuttle experiments.

Quantitative estimates of both total sampling errors and instrumentation errors were obtained. It was shown that measurement error is minimal in comparison to biological variability and little can be gained from improvement in analytical accuracy. In addition, a propagation of error analysis demonstrated that total water balance error could be accounted for almost entirely by the errors associated with body mass changes. Errors due to interaction between terms in the water balance equation (covariances) represented less than 10% of the total error. A correlation analysis between terms in the water balance equation did not produce any notable or unexpected results.

Overall, this analysis provided evidence that daily measurements of body water changes obtained from the indirect balance technique are reasonable, precise, and reliable. The method is not biased toward net retention or loss as has been shown in balances previously reported because a correction factor (representing unmeasured skin and tissue losses) was employed based on direct total body water measurements. It is suggested that improvements in the present water balance mehtod should be directed toward obtaining better estimates of the correction factor and its errors. This can be accomplished by direct measurements of skin losses, body tissue changes and more frequent measurements of total body water.

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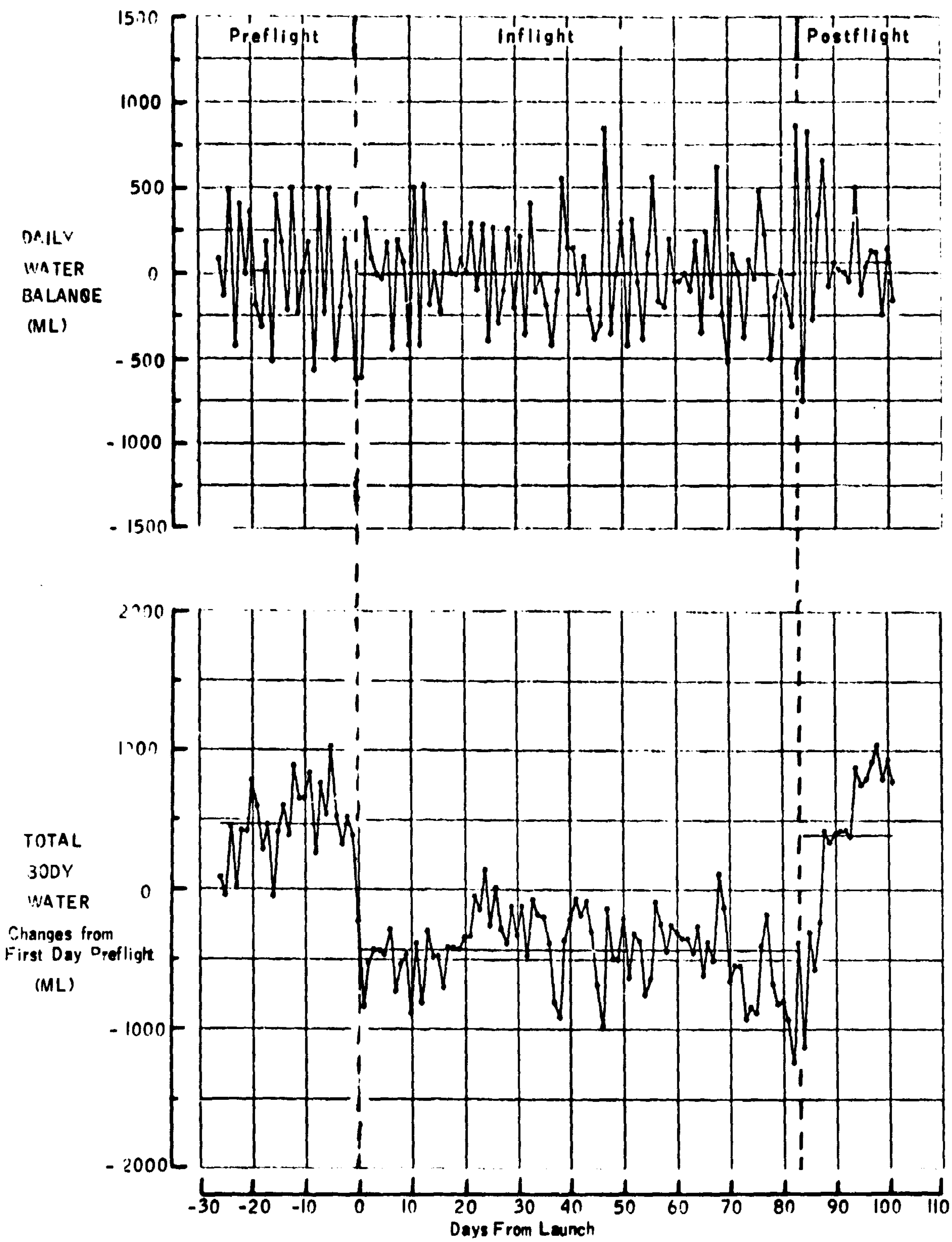
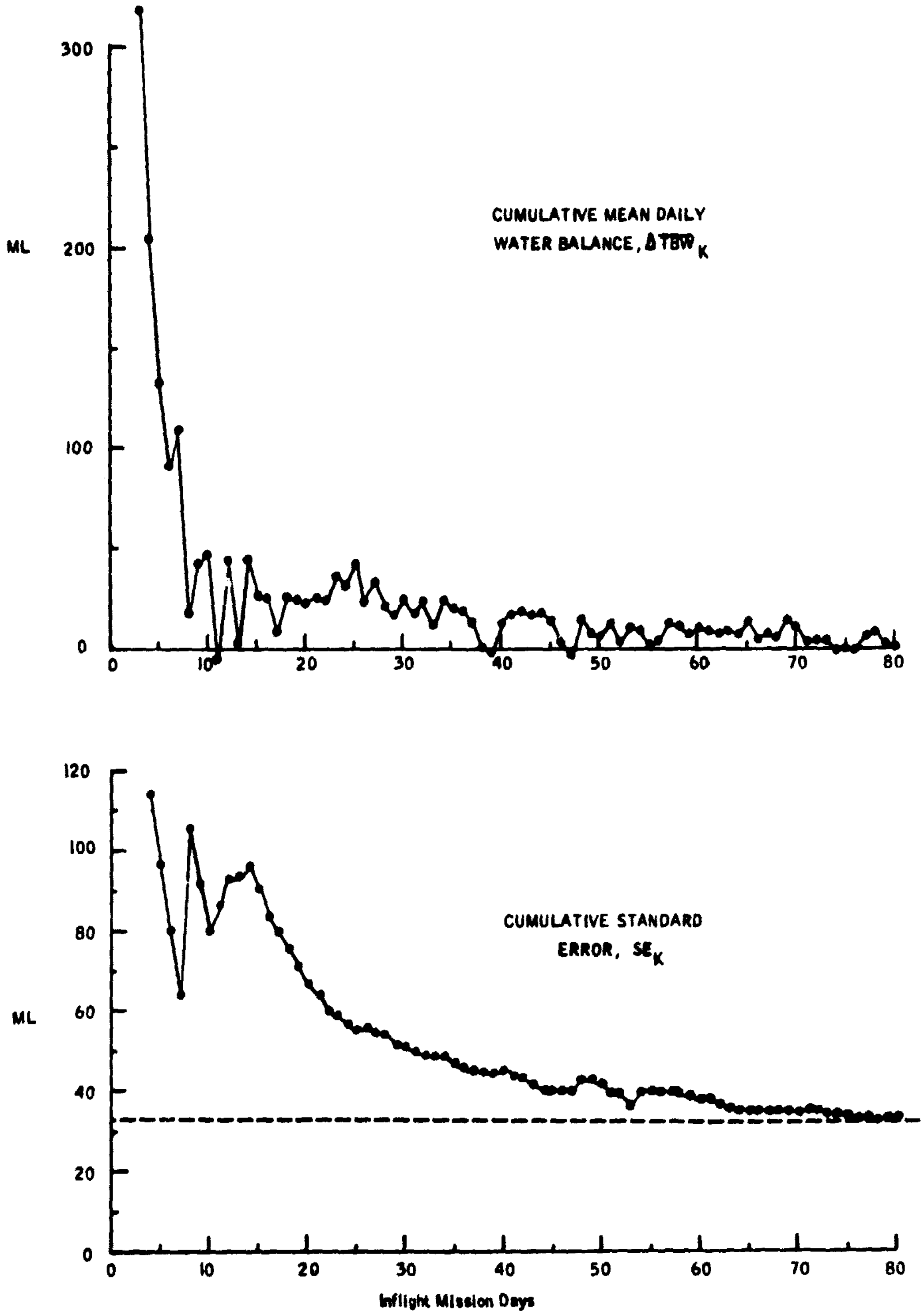


DAILY WATER BALANCE AND TOTAL BODY WATER COMPUTED FROM WATER BALANCE EQUATION FOR A SINGLE SKYLAB CREWMAN (SL4/CDR)

FIGURE I



CUMULATIVE MEAN AND STANDARD ERROR OF WATER BALANCE
DURING 78 CONSECUTIVE INFLIGHT DAYS OF ONE CREWMEMBER (SL4/CDR)
(EDGE EFFECTS REMOVED)

FIGURE 2

TABLE I

Comparison of Inflight Standard Errors in ΔTBW and ΔBWgt for All Skylab Crewmen

MAN	Edge Effects Included*			Edge Effects Removed**		
	N	$\overline{\Delta TBW}$	ΔTBW SE	N	$\overline{\Delta TBW}$	ΔTBW SE
1	28	-14.5	86	22	- 3.1	107
2	28	- 6.4	90	22	-61.0	107
3	28	-74.7	78	22	-49.8	95
4	59	-23.1	43	53	19.5	39
5	59	+ 2.1	47	53	52.2	41
6	59	-56.7	68	53	31.3	51
7	84	- 9.2	34	78	0.3	33
8	84	- 7.35	46	78	- 4.1	48
9	84	-19.0	36	78	7.12	35
Means		-23.2	62		+12.7	69

* All inflight days included, N = 84

** 1st 2 inflight days and last 4 inflight days removed, N = 78

TABLE II

Precision of Water Balance During Preflight and Inflight Periods

MAN	PREFLIGHT			INFLIGHT		
	Total Days in Period N_T	Cumulative SE_k		Total Days in Period N_T	Cumulative SE_k	
		k=14 days*	$k=N_T$		k=14 days	$k=N_T$
1	30	113	67	28	149	86
2	30	93	64	28	137	90
3	30	67	58	28	98	78
4	20	10[illegible]	32	59	123	43
5	20	127	116	59	126	47
6	20	156	121	59	157	68
7	26	89	68	84	104	34
8	26	118	78	84	58	46
9	26	54	56	84	141	36
Mean		106 ml	82 ml		125 ml	62 ml
SD		± 81	± 66		± 82	± 52

* SE_k = standard error for 1st 14 days of period

TABLE III

Propagation of Error Analysis for Computing Daily Changes in Body Water From Water Balance Equation

Inflight Measurements for SL-4/CDR (N=78)

			TOTAL ERROR			INSTRUMENT ERROR			RATIO
i	QUANTITY	DAILY MEAN $\overline{X}_i$	STANDARD DEVIATION S_i	ERROR CONTRIBUTION $S_i^2/S^2 \times 100$	95% CONFIDENCE LIMITS $\pm 2 \times S_i/\sqrt{N}$	STANDARD DEVIATION E_i	ERROR CONTRIBUTION $E_i^2/E^2 \times 100$	95% CONFIDENCE LIMITS $\pm 2 \times E_i/\sqrt{N}$	INSTRUMENT: TOTAL ERROR $E_i^2/S_i^2 \times 100$
1	Δ Body Weight	10	297	96.5%	± 67	32	70.0%	± 7	1.2 %
2	Food Solids	641	38	1.5%	± 9	10	6.0%	± 2	6.9 %
3	Urine Solids	34	9	0.1%	± 2	5	1.7%	± 1	31.0 %
4	Fecal Solids	28	22	0.5%	± 5	1	0.1%	± 0	0.2 %
5	Insensible Metabolic Loss	543	35	1.4%	± 8	13	11.6%	± 3	13.0 %
6	Correction Factor	26	0	0	0	12	9.0%	± 3	—
	Water Balance, ΔTBW	$\overline{X}=0$	S=302	100%	± 68	E=38	100 %	± 9	1.6 %

Water Balance Equation : $\overline{X}$ (Water Balance) $= X_1 - X_2 + X_3 + X_4 + X_5 + X_6$

Propagation of all Sampling Errors : S^2 (Water Balance) $= \sum_{i=1}^{6} S_i^2$

Propagation of Instrument Errors : E^2 (Water Balance) $= \sum_{i=1}^{6} E_i^2$

* N = number of consecutive daily observations = 78

Unless otherwise noted units are in gms.

TABLE IV

Estimates of Covariance Contribution to Total Variance

(Comparison of Standard Errors of Water Balance With Propagation of Standard Error Terms)

Man	ΔTBW SE*	Propagation of SE of Water Balance Terms**	BWgt. SE	Covariance Contribution(%)***
1	86	89	88	7%
2	90	93	92	7%
3	78	80	78	5%
4	43	47	45	19%
5	47	51	48	18%
6	68	73	69	15%
7	34	35	34	6%
8	46	47	46	4%
9	36	39	38	17%
Mean	62	65	63	10%

* Includes covariance contribution

$SE^2 = SD^2(\Delta TBW)/N$ N= total inflight days

** Does not include covariance contribution

$SE = SE^2(\Delta BWgt) + SE^2(Food) + SE^2(Urine) + SE^2(Feces) + SE^2(IML)$

*** $\% = \frac{(Column\ 1)^2 - (Column\ 2)^2}{(Column\ 1)^2} \times 100$

TABLE V

Error Matrices for Inflight Water Balance of SL-4/CDR **

A) Correlation Coefficients

	ΔBWgt	Food Solids	Urine Solids	Fecal Solids	Metabolic Loss
ΔBWgt	1.00				
Food Solids	0.32*	1.00			
Urine Solids	-0.37*	0.05	1.00		
Fecal Solids	0.10	0.12	-0.09	1.00	
Metabolic Loss	0.29*	0.99*	0.09	0.12	1.00

B) Variance - Covariance Matrix ***

	ΔBWgt.	Food Solids	Urine Solids	Fecal Solids	Metabolic Loss
ΔBWgt.	87.95				
Food Solids	3.58	1.41			
Urine Solids	-0.94	0.02	0.07		
Fecal Solids	0.63	0.10	-0.02	0.49	
Metabolic Loss	3.05	1.31	0.03	0.09	1.25

* $p < 0.05$

** Edge effects removed, N=78

*** Each element has been divided by 10^3

TABLE VI

Mean Correlation Coefficients for Terms in Inflight Water Balance for Entire Skylab Crew (n=9) +

	ΔBWgt	Food Solids	Urine Solids	Fecal Solids	Metabolic Loss
ΔBWgt	1.00				
Food Solids	0.20*	1.00			
Urine Solids	-0.15*	0.29*	1.00		
Fecal Solids	-0.16*	0.03	0.07	1.00	
Metabolic Loss	0.19*	0.99*	0.29*	0.03	1.00

+ Weighted average accounting for unequal inflight days for each subject; total number of inflight man-days = 513

* $p < 0.05$, based on N_{inf} = 513 days

TABLE VII

Correlation Coefficients Between ΔTBW and Each Term Inflight Water Balance for SL-4/CDR*

Variables		Edge Effects Removed	Edge Effects Included
ΔTBW –	ΔBWgt	1.00*	1.00
ΔTBW –	Food Solids	0.32*	.16
ΔTBW –	IML	0.30*	.15
ΔTBW –	Urine Solids	0.34*	–.26 *
ΔTBW –	Fecal Solids	0.17	.21*

* $p < .05$, N = 78 column (1)

N = 84 column (2)

TABLE VIII

Skylab Mean Correlation Coefficients (n=9) Between ΔTBW
and Each Term in Water Balance Equation
for Preflight and Inflight Phases**

Variable	Preflight	Inflight
ΔTBW – BWgt.	0.997*	0.997*
ΔTBW – Food Solids	0.239*	0.192*
ΔTBW – IML	0.241*	0.180*
ΔTBW – Urine Solids	-0.234*	-0.133*
ΔTBW – Fecal Solids	-0.146*	-0.097

* $p < .05$ based on N_{pre} = 228 days, N_{inf} = 513 days

** Weighted average accounting for unequal number of days in each flight phase and without removing edge effects

APPENDIX I

ESTIMATES OF INSTRUMENT AND MEASUREMENT ERRORS

Instrument errors have not, unfortunately, been established precisely and are not available from any single source. They have been estimated in this study from several documents (Hegsted, 1975; Arnold, 1972; Thornton, 1974), from discussions with principal investigators and from reasonable estimates if no other information was available.

Body Weight Changes

The best available information regarding errors associated with the body mass measuring device was found in the Skylab Life Sciences Symposium. Thornton states the "repeatability of body mass measurements was $\pm$ 0.1 pounds, and absolute accuracy was.... probably nearer + 1/4 pounds." In the water balance equation, the term ΔBWgt refers to a change in weight between consecutive morning weighings. Thus, the measure of error we are interested in is repeatability (or reproducibility), assuming the absolute accuracy were constant. In this case, as well as others to follow, we shall assume that reproducibility implies a statement such as "95% of the measurements of all samples were within $\pm 2\,\sigma$ of the true mean." Thus, if repeatability of the mass measurement was $\pm$ 0.1 pound or $\pm$ 45 gms = $2\,\sigma$(BWgt), then σ(BWgt) = 22.5 gm. For a change in weight between day 1 and day 2:

$$\Delta \text{BWgt} = \text{BWgt}_2 - \text{BWgt}_1$$

and

$$\sigma^2(\Delta\text{BWgt}) = \sigma^2(\text{BWgt}_2) + \sigma^2(\text{BWgt}_1)$$
$$= 22.5^2 + 22.5^2$$

or

$$\sigma(\Delta\text{BWgt}) = \pm 32 \text{ gm}$$

Food Solids

From Hegsted's analysis of errors we learn that food weight was measured within $\pm$ 2 to $\pm$ 2.5%. Increasing this estimate slightly to account for food that was not removed from the container or entirely ingested (some of these errors have already been included in verified food data) we obtain $2\sigma = \pm 3\% = \pm 20$ gms (based on an average daily dry food value of 630 gm x .03 ≅ 20) or σ (food solids) = $\pm$ 10 gms.

Urine Solids

Urine solids are obtained from the product "urine volume · (specific gravity - 1)." The errors for a product of two independent random variables, ($Z = X \cdot Y$), can be taken as (Beers, 1957):

$$\sigma^2(Z) = \overline{X}^2 \sigma^2(Y) + \overline{Y}^2 \sigma^2(X)$$

or in the case at hand:

$$\sigma^2(\text{urine solids}) = (\text{urine volume})^2 \sigma^2(\text{sg}) + (\text{sg} - 1)^2 \sigma^2 (\text{urine volume})$$

Mean Skylab inflight values for urine volume and specific gravity of urine are 1630 ml and 1.022, respectively. We will use Hegsted's estimate of σ(urine volume) = 3 ml and assume that specific gravity can be measured quite precisely at 0.5% or 2σ (sg) = 0.005 x 1.022 = 0.005 or σ (sg) = 0.0025. Substituting these into the above equation results in σ(urine solids) = $\pm$ 5 gm.

Fecal Solids

We shall accept Hegsted's estimate of the standard deviation of fecal solid measurement as $\pm$ 0.4 gm and increase it to allow for incomplete collection, so that σ(fecal solids) = $\pm$ 1 gm.

Insensible Metabolic Loss

Net insensible metabolic losses (IML) were obtained from the expression: IML = EFF (A_1 · Diet Protein + A_2 · Diet Fat + A_3 · Diet Carbohydrates). A_i are stoichiometric constrants whose errors are not known to us, but are based on precise estimates of the water, CO_2, O_2 and urinary nitrogen produced or consumed during metabolism. We shall assume no errors in these quantities. The term EFF represents the calculation (food solids - fecal solids)/food solids. The mean $\pm$ pooled standard deviation for EFF for all subjects was approximately 0.954 ± 0.04 and we shall assume that half of the total error is due to measurement error, so that $\sigma(\text{EFF}) = 0.02$. If each of the dietary constituents can be measured with the same accuracy as the total food weight (i.e., within $\pm$ 3% or σ = 1.5%) than using average inflight values for dietary protein, fat and carbohydrates as 111 gm, 83 gm, and 412 gm, respectively, we calculate that σ(protein) = 1.7 gm, σ(fat) = 1.3 gm, and σ(carbohydrates) = 6.2 gm. An expression for the variance in insensible metabolic losses can be taken from combining the formulations for total errors of products and sums of independent random variables (Beers, 1957):

$$\sigma^2(\text{IML}) = \overline{\text{EFF}}^2\,\sigma^2(X) + \overline{X}^2\,\sigma^2(\text{EFF})$$

where X = diet carbohydrate + diet fat + 0.563 diet protein

and $\sigma^2(X) = \sigma^2(\text{diet carbohydrate}) + \sigma^2(\text{diet fat}) + 0.563^2\,\sigma^2(\text{diet protein})$

Substituting the above values into these equations results in:

$\overline{X}$ = 557 gm, $\sigma(X)$ = 6.4 gm and $\sigma(\text{IML}) = \pm$ 13 gm.

Correction Factor

As previously discussed, it is not possible to determine the random errors associated with the day-to-day variation of the correction factor. However, it may be possible to estimate lower limits of its measurement error. The value of CF is based heavily on differences in two consecutive measurements of total body water which are usually considered to be no more accurate than $\pm$ 5 %. Using a typical value of 40 liters for TBW we can calculate, using the above procedure for body weight, that the standard deviation associated with a difference in two measurements of TBW is about 1400 gm. The standard error of the mean for nine subjects would then be $\sigma_m(\Delta TBW) = 1400/\sqrt{9} = 470$ gm. However, this represents measurements over an interval of up to 28 days in the shortest flight and 84 days in the longest flight. Thus, a daily estimate of error of ΔTBW may be found by dividing by this interval which gives $\sigma_i(\Delta TBW) = 17$ gm to 50 gm for each crewman and $\sigma_m(\Delta TBW) = 6$ to 17 gm for the entire crew. The actual standard error of the mean for the inflight correction factor for all nine crewmen has been shown to be about 12 gm which gives credence to these calculations.

Other Errors Due to Insensible Metabolic Loss

Some mention should be made regarding the indirect calculation of IML based on food consumption. In the typical water balance where a correction factor is not used, the use of this equation is justified only when there is no net tissue storage or loss, that is, all of the energy required by the body is derived from food metabolism. If all foods are metabolized and more energy is still required, the body may draw on its own tissue stores in which case values for IML will be too low. On the other hand, if all foods are not metabolized and are not excreted they will be stored by the body and values for IML will be falsely high.

The use of the correction factor was incorporated into the present water balance to account for, in part, the failure to compute IML precisely correct each day. However, the correction factor was applied as a constant value for each day of the mission which undoubtedly leads to some errors. These errors tend to be reduced and are not accumulative due to certain self-regulatory features of the water balance equation.

First, in computing daily water balances, it is assumed that all of the food consumed is converted to water, carbon dioxide and urinary nitrogen on that same day. This is not strictly true and would be inappropriate if the total length of the experiment were only several days. However, over extended periods of time, this type of error will be self-compensating. Thus, if all the food consumed in a 24-hour period take parts of two days to be fully metabolized, the

IML for the first day will be too high and will be equally low on the second day. The average over this two-day period will be essentially correct.

Secondly, the expression for IML shows that the total error in IML due to body tissue catabolism is less than the weight of the tissue lost. For example, it has been estimated that the average daily loss of body fat and protein during Skylab flights were roughly 20-40 gm/day. Assume the higher figure and equal proportions of fat and protein loss; i.e., 20 gm protein and 20 gm fat loss. The coefficients pertaining to protein and fat in the IML equation are $A_1 = 0.563$ and $A_2 = 1.0$ respectively, which lead to an underestimation of IML (food + tissue) of 0.563×20 gm $+ 21.0 \times 20 = 31$ gm which is about 80% of the total assumed loss. This, in turn, will lead to underestimations of water balance by this amount. This is not a very serious error when considering the large losses of 700 ml/day during the first two days of flight or similar gains upon recovery. However, it does become more serious during the extended portion of the flight when the crew appear on the average to be in water balance. The correction factor that was applied ensures that these errors due to underestimation of IML do not accumulate.

TABLE A-II

Correlation Coefficients for Covariance Terms in Inflight Water Balance for Each Skylab Crewman

SUBJECT

Correlation Variables	1	2	3	4	5	6	7	8	9
ΔBWgt. – Food	.01	-.03	.24	.22*	.44*	.34*	.16	.02	.23*
ΔBWgt. – Urine	-.18	-.21	-.21	-.43*	.13	.00	-.28*	-.18*	-.07
ΔBWgt. – Feces	-.33*	-.20	.17	-.59*	-.19	-.17	.14	-.03	-.30*
ΔBWgt. – IML	-.01	-.02	.27	.21*	.45*	.34*	.15	.04	.20*
Food-Urine	.35*	.26	.54*	.16	.42*	.55*	.03	.03	.47*
Food-Feces	.13	.03	-.25	.04	.10	.19	.04	0.0	-.05
Food-IML	1.0*	1.0*	1.0*	1.0*	1.0*	1.0*	.99*	1.0*	.99*
Urine-Feces	-.07	.13	-.31	.26*	.27*	.34*	-.10	.05	-.04
Urine-IML	.30	.24	.53*	.15	.40*	.53*	.12	.03	.48*
Feces-IML	.17	.01	-.26	.04	.10	.18	.04	.01	-.07
No. days	28	28	28	59	59	59	84	84	84

* $p < .05$

TABLE A-III

Correlation Coefficients Between ΔTBW and Each Term in Preflight and Inflight Water Balance for Skylab Crew **

Man	Flight Phase	ΔBWgt	Food Solids	Insensible Met. Loss	Urine Solids	Fecal Solids	N(days)
1	Pre	1.00*	0.16	0.14	(-0.02)	-0.28	30
	Inf	1.00*	(0.02)	(0.00)	-0.17	(-0.29)	28
2	Pre	1.00*	0.15	0.18	-0.27	-0.19	30
	Inf	1.00*	(-0.03)	(-0.02)	-0.19	-0.15	28
3	Pre	0.99*	0.20	0.17	0.19	-0.22	30
	Inf	1.00*	0.23	0.25	-0.21	(0.20)	28
4	Pre	1.00*	0.16	0.15	(-0.78*)	-0.08	20
	Inf	1.00*	0.22*	0.21	(-0.42*)	(-0.54*)	59
5	Pre	1.00*	0.47*	0.46*	(-0.57*)	(-0.42*)	20
	Inf	1.00*	(0.43)	(0.44*)	0.15	-0.13	59
6	Pre	1.00*	0.43*	0.44*	-0.40*	(-0.03)	20
	Inf	1.00*	0.32*	0.32*	(0.00)	-0.14	59
7	Pre	1.00*	0.22	0.27	-0.21	(0.41*)	26
	Inf	1.00*	0.16	0.15	(-0.26*)	(0.21*)	84
8	Pre	1.00*	(-0.05)	(-0.06)	-0.18	(-0.39*)	26
	Inf	1.00*	(0.02)	(0.04)	-0.15	(0.031)	84
9	Pre	0.99*	(0.53*)	(0.53*)	-0.19	-0.09	26
	Inf	1.00*	0.24*	0.21	(-0.04)	(-0.22)	84
Mean	Pre	1.00*	0.24*	0.24*	-0.23*	-0.15*	228
	Inf	1.00*	0.19*	0.18*	-0.13*	-0.10	513

* $p < .05$

** Edge Effects Included

( ) Denotes $1/2\ \bar{\rho} \leq \rho \geq 2\ \bar{\rho}$