

CORRESPONDENCE

ANEMIA OF SPACE FLIGHT

To the Editor:

In the recent review of the "anemia of space flight"¹ several issues are raised that have been addressed in the scientific literature²⁻⁷ but which were not included in the article.

First, the conclusion that "recovery" of the red blood cell mass (RCM) occurs during space flight seems incorrect. The only evidence of which we are aware that might be interpreted in this way are the Skylab data showing a smaller decrease in RCM the longer the crew was in orbit. Since no inflight RCM determinations were made, it is not possible to draw any firm conclusions as to whether a decrease followed by a recovery occurred during the two longer flights or whether the anemia was prevented from developing. Our analyses suggest that the data are best explained not by a recovery but by differences between missions (q.v.) which prevented the initial decrease in RCM. The Russian data obtained in flights twice as long as the longest Skylab mission are consistent with this concept, since a decrease in RCM is invariably reported.⁸ Further, there is no tenable hypothesis to explain a "recovery."

It is an oversimplification to disregard changes in diet and exercise during space flight as possible contributing factors to the anemia. Relatively minor and acute alterations in diet⁹ and exercise¹⁰ can lead to a reduction in the RCM. In addition, our multivariate correlation⁷ indicates that the greater the *change* (reduction) in caloric intake and the lower the exercise level inflight compared to preflight, the greater the degree of anemia. However, the most significant factor in this correlation was the loss of lean body mass (LBM). A decrease in the LBM coupled with changes in diet and exercise would be expected, even in a terrestrial environment, to produce a decrease in RCM.¹¹

It may also be premature to completely exclude oxygen as a causative agent in the anemia. As Tavassoli indicates, it seems unlikely that hyperoxia was of a sufficient level during the Apollo and Skylab (and Russian) missions to cause the hemolysis apparently observed during the Gemini flights. However, an increased hemoglobin-oxygen saturation capable of suppressing RBC production may have been caused by operational procedures designed to prevent the bends. All of the crews in the Apollo and Skylab programs were exposed to 100% oxygen at 1 atmosphere for at least 3 hr prior to and during launch.

Changes in red blood cell shape distributions are of interest but probably of little relevance to the anemia of space flight. There is no significant correlation (in the Skylab and Russian data) between the increased proportion of nondiscoid red blood cells (RBC) and the subsequent anemia. However, we have recently shown changes in the RBC shape distribution as a consequence of altered diet at least in squirrel monkeys.¹²

As is evident from Table 4 in Tavassoli's review, he has been very selective with the data to obtain a correlation between the change in RCM and the duration of the space flight (his Fig. 2). Rather, the results from the Apollo, Skylab, and Russian missions suggest a decrease in RCM with time, which then possibly reaches a new steady state at a 15%–20% loss of RCM. However, data from long-term flights (>3 mo) are limited and the factors that might influence this new steady state are unknown.

In addition, there are a variety of other issues that Tavassoli has touched upon but which require further elaboration.¹³⁻¹⁶ Splenic sequestration of ⁵¹Cr-labeled RBC *injected preflight* and monitored

postflight was investigated by surface counting and found to be an unlikely cause of the anemia. Likewise, no evidence for the loss of ⁵¹Cr-labeled RBC by capillary "oozing" was observed after the Gemini missions in which the largest RCM decreases were found. Radiation exposure levels have been relatively small and do not correlate with the postflight RCM deficit. Contrary to Tavassoli's statement, small but statistically significant decreases (average 2.5%) in RCM were observed in the participants of the SMEAT study. Similar to the Skylab missions, the atmospheric air during SMEAT was recirculated and reused—in neither was it "stored." It should be noted that normal ambulatory subjects showed an average decrease in RCM of 5.1% when maintained for 1 wk on the Apollo flight diet.¹⁷ Serum iron has not been measured during space flight, and some elevation of serum haptoglobin levels has been observed postflight.

We also have come to the conclusion that the suppression of erythropoiesis appears to be the primary cause of the anemia and is more likely to be mediated by direct, local effects on the marrow rather than through peripheral events secondary to the decreased plasma volume. However, the evidence for this is scant and will not even begin to be addressed until experiments are undertaken during the Spacelab-IV mission (the first dedicated life sciences flight) currently scheduled for late 1985. As Tavassoli¹ (and Johnson⁸) has noted, it is quite likely that the unique microgravity of space will uncover some previously unrecognized factors that modulate erythropoiesis.

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To the Editor:

The segment of Dr. Dunn's comments relating to the "recovery" of red cell mass (RCM) is a clear misinterpretation of my review. Even a cursory reading of my article is sufficient to indicate that I have spoken of *postflight* recovery of *reticulocytes* and not *inflight* recovery of *red cell mass*. The postflight reticulocyte recovery has, of course, been repeatedly demonstrated in both American and Soviet flights, whenever it was studied, and I have adequately referenced this finding.

With regard to the RCM deficit, a positive correlation with the duration of flight has been observed for short missions of less than 3 wk. This is evident from my Table 4 and Fig. 2, which, contrary to Dr. Dunn's statement, are not selective and contain all the American flights in which hematologic data were obtained. For missions of longer duration, as in the Skylab and the Soviet Salyut 6, there appears to be a negative correlation, so that as the duration of flight increases, a lesser magnitude of deficit is observed. For Skylab missions, 13%, 12%, and 7% deficits have been reported, respectively, for missions of 28, 59, and 84 days.¹ Similarly, in the Salyut missions, 24% deficit was reported in a 96-day mission but only 15%–17% in a 140-day flight.²

Last August, an international symposium was held in conjunction with the International Society of Hematology in Budapest wherein many Soviet and American investigators analyzed and synthesized their results. There seems to be a consensus that the deficit in red cell mass (and perhaps other red cell changes) may be adaptive in nature so that in flights of long duration, a new homeostatic setting is reached. This conclusion was particularly evident in the works of Tokarev³ and Ushakov.⁴ Soviet scientists have suggested decreased muscular loading and consequent reduced oxygen requirement as the basis for this adaptive phenomenon (primary suppression or erythropoiesis followed by homeostatic resetting).^{2,5}

Dr. Dunn has also discussed several factors that in ground-based

experimental settings can lead to the deficit in red cell mass and/or the erythropoietic suppression. I have also alluded to some of these and other possible factors in my review. My article, however, was an attempt to analyze actual data from space flights with a control data base taken from SMEAT. SMEAT was an experiment which simulated, on the ground, a full 56-day Skylab mission. A red cell mass deficit of the magnitude observed in space was not observed in SMEAT, indicating that we are probably dealing with a problem of space flight. If we take the SMEAT as our baseline control, such miscellaneous factors as discussed by Dr. Dunn may not necessarily have a bearing on the problem. But, of course, the realm of speculation and imagination is wide open. After all, space biology is only a nascent field.

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GOVERNMENT REGULATIONS AND SICKLE CELL TRAIT

To the Editor:

Several recent developments in the area of government regulations with respect to sickle cell disease would seem to be of sufficient importance to bring to the attention of the medical community. It is generally accepted that there is little firm evidence for morbidity associated with sickle cell trait¹ (except for an increased incidence of hematuria). However, individuals with sickle cell trait have been

Table 1. Proportion of Hemoglobin S in Individuals With Sickle Cell Trait

	Percent Hemoglobin S		Fraction of Subjects With HbS \leq 41%
	Mean	Median	
Percent of total hemoglobin	38.8	39.1	0.77
Percent of major hemoglobin (A + S)	39.9	40.2	0.61