

13792 P

**Reactions of Monkeys to Experimental Respiratory Infections.
V. Hematologic Observations in Nutritional Deficiency States.***

H. E. WILSON, C. A. DOAN, S. SASLAW AND J. L. SCHWAB.

*From the Departments of Medicine and Bacteriology, Ohio State University,
Columbus, Ohio.*

Earlier workers have reported studies on the hematology of vitamin B deficient monkeys.^{1, 2} The current observations were undertaken in an attempt to determine which, if any, of the presently recognized components of the vitamin B complex will maintain or restore specific blood cell and nutritional equilibria.

Methods. Healthy *Macaca mulatta*, receiving a normal diet, were isolated in individual cages and observed clinically and hematologically for a control period of 2 to 3 weeks. The animals showing satisfactory equilibria were then divided into 3 groups and placed on experimental diets: (1) No. 600¹ (modified Goldberger), (2) No. 1 and (3) No. 2 (Table I). The controls have included observations on each experimental animal before it was placed on diet and on a number of monkeys of the same species and approximate age maintained on stock diet. These animals showed no hematologic changes comparable to those to be described.

Results. All of the monkeys on the experimental diets developed leucopenia. In the 4 animals on diet 600, this appeared between the 42nd and 77th days. In the 6 animals receiving diet 1 and in the 5 receiving diet 2, the time of appearance of the initial leucopenia varied between the 30th and 103rd days.

One interesting feature of the response to these diets was a "plateau" period of remarkably stabilized total white cell counts preceding the first appearance of leucopenia. The relative constancy of the total white cell counts between the 14th and 45th diet days seen in monkey No. 4 (Fig. 1) is representative. Similar well-defined periods of stability varying in duration from 24 to 100 days were seen in 3 of the 4 monkeys on diet 600, 4 of the 6 on diet 1, and 2 of the 5 on diet 2.

* This work has been aided by a grant from the International Health Division of the Rockefeller Foundation. Constituents of the special diets were generously furnished by the S.M.A. Corporation.

¹ Langston, W. C., Darby, W. J., Shukers, C. F., and Day, P. L., *J. Exp. Med.*, 1938, **68**, 923.

² Day, P. L., Langston, W. C., Darby, W. J., Wohlin, J. G., and Nims, V., *J. Exp. Med.*, 1940, **72**, 463.

TABLE I.
Diet No. 1.

Basic Diet*		Vitamin Supplements† ‡	
	%		Daily dosage, mg
Sucrose	68	Thiamine Hydrochloride	1
Vitamin-Free Casein	18	Riboflavin	1
Vegetable Oil	8	Pyridoxin Hydrochloride	1
Salt Mixture U.S.P. No. 2	4	Nicotinic Acid Amide	25
Cod Liver Oil U.S.P.	2	Calcium Pantothenate	3
	—	Ascorbic Acid	25
	100		

Diet No. 2.	
Diet No. 1 with addition of:†	Daily dosage, mg
Choline Chloride	50
Pimelic Acid	1
Glutamine	1
Inositol	1
Sodium paraminobenzoate	50

*Liberal amounts of the basic diet and water were available to the animals at all times.

†Double doses of supplements suspended in water and fed by stomach tube every second day.

‡Biotin assays were done on feces of some of these animals with and without addition of Biotin to the diet. Since these assays indicated synthesis of large amounts in the intestine of the monkey Biotin supplements were discontinued.

Characteristic of the development of the leucopenia was an initial transitory decrease in circulating white cells, followed by one or more periods of temporary recovery, alternating with progressively more severe leucopenic depressions. The profound terminal cytopenia involved all of the white cell elements. Thus, on the 49th diet day, monkey No. 4 showed a fall to 7000 white cells from the lowest control level of 13,500, while the lymphocytes were reduced from 5300 to 3700 and the neutrophils from 4500 to 1800. Following this initial leucopenia there was a period of recovery to normal levels until the 70th day of diet, when the lymphocytes were reduced to the previous leucopenic level and the neutrophils and monocytes fell to still lower levels. Another brief period of partial recovery preceded the final precipitous fall of all the white cell elements (2000 W.B.C.) with death on the 91st diet day (Fig. 1).

The leucopenia was more consistent than, and independent of, the anemia. Three of the 4 monkeys receiving diet 600 exhibited moderate degrees of anemia. There was no significant anemia prior to the terminal state in 3 of the 6 monkeys receiving diet 1 (Nos. 22, 26, 27) nor in 3 of the 5 receiving diet 2 (Nos. 16, 40, 42). Monkey No. 23 (diet 1) and monkey No. 136 (diet 2) both showed moderate degrees of normocytic anemia appearing between the 76th

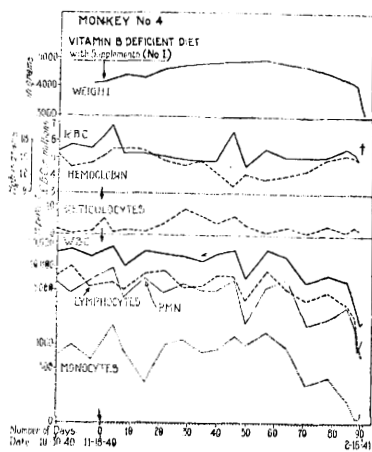


Fig 1

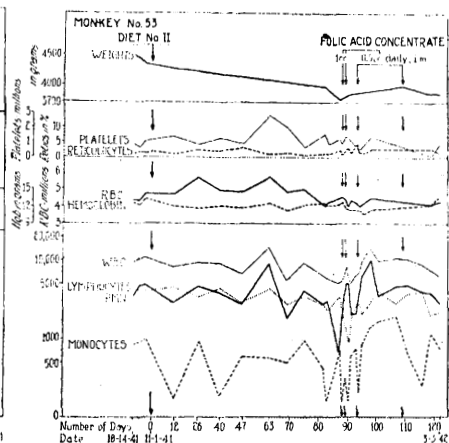


Fig 2

and 82nd diet days. Two of the monkeys on diet 600 (Nos. 8, 14) and 2 of those on diet 1 (Nos. 4, 11) exhibited slight microcytic anemia, appearing in each case on the 33rd or 34th diet day and lasting for 38 to 40 days.

Two monkeys, exhibiting leucopenia while on diet,² with specific vitamin supplements as indicated were given intramuscular injections of folic acid concentrate (S.M.A.) prepared from yeast autolysate.³ Preliminary observations (*e. g.*, monkey No. 53, Fig. 2) suggest that some factor in this preparation is effective in reestablishing a normal white cell equilibrium. In striking contrast (in the following paper,⁴ Fig. 1) there was prompt exhaustion of a transitory abortive leucocytic response to infection during a similar period of nutritional leucopenia.

³ Hutchings, B. L., Bohonos, N., Peterson, W. H., *J. Biol. Chem.*, 1941, **141**, 521.

⁴ Saslaw, S., Schwab, J. L., Woolpert, O. C., Wilson, H. E., in press.