each of these microorganisms the shapes of the growth curves are identical for the two compounds and the same growth maxima are attained.

However, with *S. cerevisiae* the growth curve of the oxygen analog differs somewhat from that of biotin. Different activity ratios at various portions of the curves are, therefore, obtained. Thus, at one-half maximum growth, the activity of the *dl* oxygen analog is 25 per cent, that of *d* biotin, whereas at maximum growth this compound is only 8 per cent as active. The same growth maximum is obtained with both compounds. Whether the oxygen analog is active as such or exerts activity because of its transformation into biotin remains to be elucidated.

The procedures employed in the synthesis of the oxygen analog have demonstrated the *cis* configuration of the two fused rings. Therefore, only two racemic forms differing in the spatial orientation of the side chain are possible. The *dl* oxygen analog represents one of these racemic forms. Because of its structural relationship to biotin and its comparable biological activity, the name *dl*-oxybiotin is proposed for this compound (II). Since only one of the enantiomorphs of *dl* biotin is biologically active,[5] it appears likely that a similar situation exists for *dl* oxybiotin.

Studies now in progress on the activity of oxybiotin and related compounds, both for animals and for microorganisms, will be presented in subsequent publications.

FRANCIS J. PILGRIM
A. E. AXELROD

INSTITUTE OF PATHOLOGY,
WESTERN PENNSYLVANIA HOSPITAL,
PITTSBURGH, PA.

THEODORE WINNICK
KLAUS HOFMANN

DEPARTMENT OF CHEMISTRY,
UNIVERSITY OF PITTSBURGH,
PITTSBURGH, PA.

OBSERVATIONS ON THE EFFECT OF PREFLIGHT MEALS UPON ALTITUDE TOLERANCE[1]

ALTITUDE tolerance represents only one aspect of preflight and inflight feeding of aviation personnel, but under many circumstances it represents an important consideration. Both empirical observations and carefully controlled experiments indicate the need for food intake at approximately normal meal-time intervals, in order to maintain optimal performance. Hence timing and attractiveness are important aspects of aviation feeding, in addition to provision for an optimal state of nutrition in terms of general health and the maintenance of optimal performance capacity during special stress periods.

The high protein foods, such as meat, milk, eggs and cheese should be consumed in generous quantities, from a long-time point of view, to provide proteins of high quality, minerals and vitamins, and to maintain good morale.

From the point of view of altitude tolerance, however, meals relatively high in carbohydrate afford a distinct advantage when consumed during flight or at the meal preceding altitude exposure. References to the literature and a more detailed discussion of the physiological background of this relationship have been given in an earlier publication,[2] together with experimental data illustrating the gain in altitude tolerance afforded by meals having a relatively high carbohydrate content. Among the factors that apparently contribute to better altitude tolerance after high carbohydrate meals are (a) lesser oxygen demand, (b) higher carbon dioxide production rate, (c) maintenance of glycogen reserves and (d) lessened impairment from alkalosis. In order to achieve the optimum benefits from a high carbohydrate intake, a fairly high caloric intake is necessary, and there is some indication of a slight additional gain from a normal fluid intake.

Not uncommonly a question arises regarding the risk of inter-meal hypoglycemia subsequent to high carbohydrate meals, as a possible factor that might offset the advantages gained during short exposure periods. In the tests performed thus far, however, there has been no evidence of an appreciable risk of that nature when the caloric intake has been adequate.

Because unnecessary impairment is apt to occur after an interval of 6 to 7 hours or less, irrespective of the nature of the preceding meal, there is good reason to provide a convenient reserve or emergency source of food for consumption by flight personnel when unexpected extensions of flight time are encountered.

EXPERIMENTAL

Visual Field: A section of the upper right quadrant of the visual field of the right eye is plotted for sensitivity to a 0.4 mm white test object against a dark ground. The technique was adapted from Evans's procedure for plotting "angioscotoma," using a Lloyd stereocampimeter. The recorded figure is the area of campimeter surface (square inches) within which the object is not seen.

[5] J. L. Stokes and M. Gunness, *Jour. Biol. Chem.*, 157: 121, 1945.

[1] The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development (Contract OEMcmr–224) and Columbia University, and with the aid of a grant from the Nutrition Foundation.

[2] C. G. King, Hylan A. Bickerman, Winifred Bouvet, C. J. Harrer, James R. Oyler and C. P. Seitz, *Jour. Aviation Medicine* (1945, 16: 69).

Block test: The subject's task is to place 60 cylindrical wooden blocks, 1.5 inches in diameter, into a simple pattern of holes in a board placed at a convenient height. The score is the average time (seconds) on four successive trials.

Pursuitmeter: In this test the subject observes and adjusts to alignment a horizontal white bar which is moved up and down irregularly by a hidden mechanism. The task is to compensate for the movement imposed by the mechanism, by forward or backward movement of a "stick" held in both hands by the subject. An electric clock records the total amount of time, within a two-minute trial, that the bar is kept centered between two guide lines.

Addition test: A test of mental arithmetic consisting of fifty addition problems, in which the score is the number of correct solutions within a 3 (or 2½) minute interval. Equivalent forms are used for the different trials on a given day.

Self-rating: Each subject rates himself on 10 aspects of feeling and attitude. Rating is indicated for each variable by a mark on a base line, and the score is the average distance (in mm) of the ten marks from the unfavorable end of the scale.

Experimenter's rating: Each subject is rated by the same experimenter on 10 aspects of appearance and behavior, using a numerical scale from 1 to 10. The score is the average of the ten ratings.

All subjects were given preliminary practice on the block test, pursuitmeter and addition test sufficient to carry them well beyond the initial phase of rapid learning.

TABLE 1

EFFECTS OF ANOXIA ON PERFORMANCE AND RATING IN RELATION TO THE COMPOSITION OF THE PREFLIGHT MEAL*

Type of luncheon	Visual field Per cent.	Block test Per cent.	Addition test Per cent.	Self-rating Scale units	Experimenter's rating Scale units
Protein	12.1	24.2	16.1	2.6	5.1
Carbohydrate	3.7	10.7	8.9	1.0	4.6
Difference ..	8.4	13.5	7.2	1.6	.5
Reliability† .	96	99	77	98	96

* Tests started 1–¾ hours after lunch and ½ hour after reaching a simulated altitude of 17,000 feet. Testing continued for 2 hours. Values for 8 subjects are based upon impairment relative to ground level, except in case of experimenter's rating.

† Chances in 100 that the difference is real.

Test scores and self-ratings were obtained once each day at ground level, and two or more times at altitude. Results are reported in terms of impairment or difference between ground level and altitude score. The experimenter's rating was ordinarily recorded at altitude only; hence the ratings gave an index of absolute condition measured in scale units rather than a direct measure of impairment.

Data from a typical series of tests are given in Table 1. Eight subjects were exposed at 17,000 feet on each of four afternoons, beginning about 1¾ hours after a 1,000 calorie lunch. The percentage composition on a calorie basis, of the meals served on Monday and Friday, was: carbohydrate 92, protein 5, fat 3; and of the preflight meals served on Tuesday and Thursday: carbohydrate 12, protein 47, fat 41. Lunch was eaten between 12:00 and 12:30; ground level testing was between 1:00 and 2:00; and altitude was reached at approximately 2:15. Two successive series of tests were conducted during each run, starting one-half hour after reaching altitude and continuing over a period of two hours. The addition test was done once, at the end of the first series, about one hour after ascent; the experimenter's rating was done once, at the end of the second series of tests. Scores for two tests of visual field, block test and self-rating at altitude were averaged, and average data for all measures during the two days on each type of lunch are given in Table 1. This procedure makes the individual the unit of sampling in the statistical treatment. Reliabilities, stated as chances in 100 that a real difference exists, are satisfactorily high, especially in view of the known random variation in the effect of altitude on performance. The data are typical of results obtained during two and a half years of testing, in that preflight meals relatively high in carbohydrate afford better altitude tolerance than meals high in protein and fat.

Further comparisons of preflight diets are summarized in Fig. 1, based upon a series of tests with five subjects at 15,000 feet. Four diets of equicaloric value (1000 C.) were used, having the following composition (per cent. of calories): (a) carbohydrate 70, protein 10, fat 20; (b) carbohydrate 55, protein 20, fat 25; (c) carbohydrate 25, protein 40, fat 35; (d) carbohydrate 20, protein 10, fat 70. The technique of conducting the tests and the schedule of feeding and exposure were essentially as outlined above. The results are typically favorable toward high carbohydrate preflight meals, except that the gain observed in the visual testing was less than has been observed frequently.

Because of the well-known tendency of foods high in protein and fat content to digest more slowly than foods high in available carbohydrate and their tendency to result in lesser fluctuation in blood sugar concentration, there was an obvious need to consider whether 1,000 calorie meals relatively low in protein and fat content would result in lowered efficiency of performance within a normal between-meal interval. Tests were conducted therefore through a longer interval than studied in detail previously, at an altitude of 15,000 feet, and including measurements at four

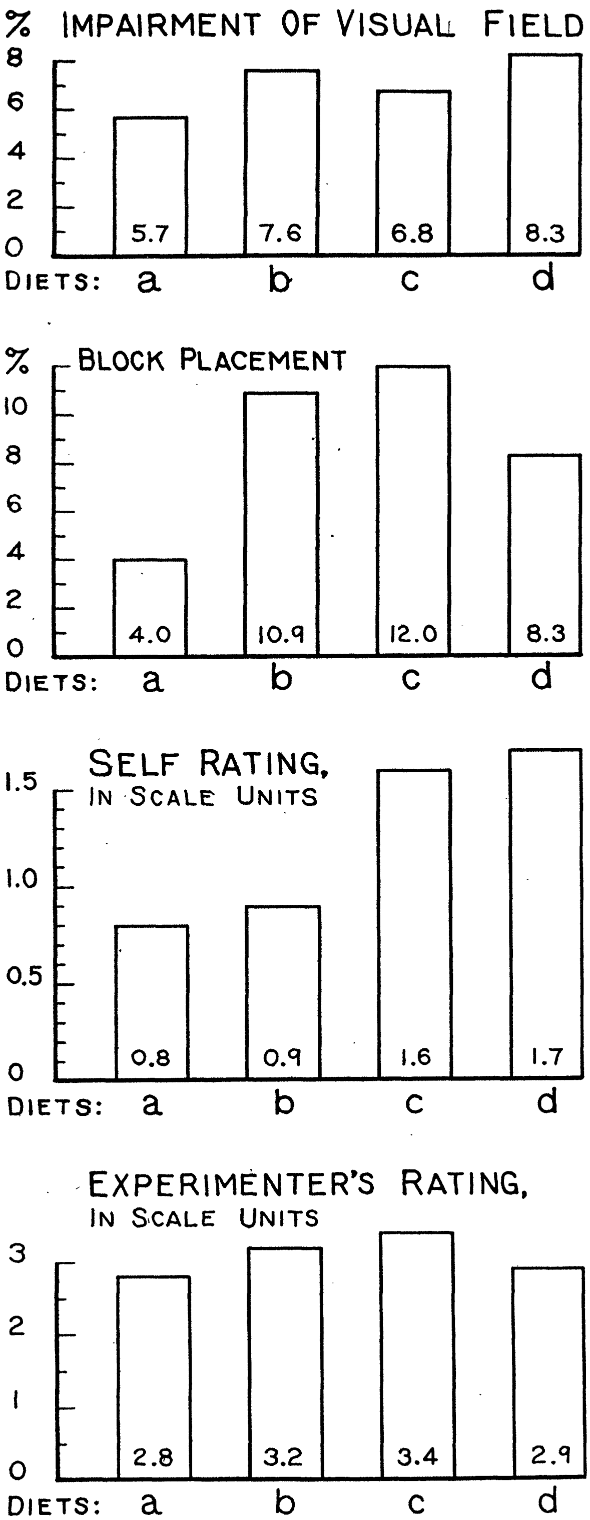

FIG. 1. Impairment during 2 hr. exposure of five subjects at 15,000 ft. Height of column in each case represents degree of impairment. Composition of test meals, in per cent. of total (1000) calories: *a*, carbohydrate 70, protein 10, fat 20; *b*, carbohydrate 55, protein 20, fat 25; *c*, carbohydrate 25, protein 40, fat 35; *d*, carbohydrate 20, protein 10, fat 70.

intervals, the last set beginning at 6 hours after lunch and ending within the ensuing hour.

Eight subjects were divided into two equal groups and exposed on four different days. On each of the experimental days one group consumed a high carbohydrate lunch (carbohydrate 92, protein 6, fat 2) and another group received an equicaloric (total—1,000 C.) low carbohydrate lunch (carbohydrate 21, protein 43, fat 36). By reversing the groups on two of the days, more consistent data were obtained than when the entire squad was given the same type of lunch.

The high carbohydrate meals held their advantage for approximately 6 hours, covering the normal interval between successive meals. Some of the tests showed slightly more and others less impairment during the 6- to 7-hour period of testing, in comparing the two types of meals, but none of the eight subjects showed a distinct tendency toward impairment as a result of the preceding meal being low in protein and fat. The average results from tests of visual field, block placement, pursuitmeter, addition, self-rating and experimenter's rating were nearly equal for the two test meals at the last period of testing.

It has been our experience and it has been demonstrated in tests conducted by the armed services that it is practical, when maximal altitude tolerance is desired, to provide attractive and satisfactory meals from regular food supplies, such as the "B" ration, having a protein content in the range of 8 to 12 per cent. of the total calories.

Preflight and inflight meals relatively high in carbohydrates, which afford increased altitude tolerance, can be followed by meals correspondingly high in protein, to provide an over-all food intake of high nutritive quality and excellent acceptability.

CHARLES GLEN KING
WINIFRED BOUVET
MASON N. CROOK
CARTER J. HARRER
JAMES R. OYLER
DAVID SCHWIMMER

DEPARTMENT OF CHEMISTRY,
COLUMBIA UNIVERSITY

STUDIES IN MECHANISMS OF PENICILLIN ACTION. I. PENICILLIN EFFECTS ON BLOOD COAGULATION

IN the course of studies on the blood levels attainable with varying dosages of penicillin given both by the oral[1] and intra-muscular routes, it was ob-

[1] L. F. Moldavsky and Wm. B. Hesselbrock, "Oral Penicillin" (in press).