FOREWORD

This study was performed by the Laboratories of Aviation and Naval Medicine, Karolinska Institutet, Stockholm, Sweden, with Dr. H. Bjurstedt as the principal investigator. The work was sponsored by Aerospace Medical Research Laboratories under Contract AF61(052)-153 through the European Office, Office of Aerospace Research, in support of AFSC Project 7220, "Biophysics Research." The contract was initiated in August 1958 by Dr. E. P. Hiatt, Chief, Biophysics Branch and subsequently transferred to Dr. Alvin S. Hyde, Chief, Acceleration Section, Biophysics Branch of the Biomedical Laboratory. The research reported herein was completed in July 1961.

ABSTRACT

Changes in the arterial oxygen saturation were recorded in healthy subjects on the human centrifuge by continuous cuvette oximetry before, during and after prolonged exposures to positive acceleration. With the subjects breathing air and wearing an automatically inflated anti-G suit, an immediate fall in the arterial O_2 saturation was observed upon exposure to + 4.5-5.0 G_z. After one minute of the first exposure the O_2 saturation ranged between 95 and 81 per cent, the arterial pH remaining essentially unchanged. At the same time the respiratory minute volume had increased, indicating gross deterioration in the efficiency of pulmonary function. Repeated exposures caused the arterial O_2 saturation to fall at a faster rate and to a lower level with each consecutive run. The rate of resaturation on returning to normal gravity was usually slow, and markedly so after several exposures. The last-mentioned observations are interpreted as being mainly the result of residual atelectasis in dependent regions of the lungs. The potential dangers of acceleration-induced hypoxemia in high performance flight missions are discussed.

PUBLICATION REVIEW

This technical documentary report has been reviewed and is approved.

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HYPOXEMIA IN MAN INDUCED BY PROLONGED $+G_z$ ACCELERATION *

P. O. Barr

INTRODUCTION

When exposed to long-lasting accelerative forces in high performance aircraft aviators may be affected by functional disturbances ranging from slight deterioration in intellectual capabilities to more dramatic derangements, such as blackout and loss of consciousness. Most of these disturbances have in the past been ascribed to adverse effects on the systemic circulation (for reviews see Wood et al. 1946, Gauer 1950) with reduction of the flow of blood, and consequently the supply of oxygen, to the eyes and the brain.

Barr, Bjurstedt and Coleridge (1959), starting out from the hypothesis that the pulmonary circulation would be especially susceptible to changes in accelerative vectors, demonstrated that prolonged, positive acceleration could produce marked arterial hypoxemia in anesthetized dogs even when the animals were hyperventilating on 100 per cent oxygen. This clearly pointed to greatly increased venous admixture to the arterialized blood, the obvious inference being that such acceleration-induced unsaturation would add to any adverse effects resulting from reduced blood flow to, e. g., the brain.

In the present investigation the animal studies have been extended to man. Special techniques were developed for the continuous and simultaneous recording of blood gas changes and pulmonary ventilation while the subjects were exposed to accelerative stress in the human centrifuge. The results demonstrated that prolonged exposures to positive G-loadings induce arterial hypoxemia also in man, and often to a degree that indicates gross deterioration of pulmonary function. Further investigations aimed at elucidating the complex mechanisms involved will be reported in a subsequent paper.

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* The symbol and terms "G," "positive G," and "acceleration" used throughout this report refer to $+G_z$ axis acceleration, as defined in reference 26.

SUBJECTS, METHODS AND PROCEDURE

Subjects

The experiments were performed on 8 healthy, male subjects. The vital statistics for these individuals are given in Table I and in the text of Fig. 2.

Centrifuge

All subjects were run in the human centrifuge at the Karolinska Institutet, seated in a gondola that was suspended at one end of the double-arm superstructure, 24 ft from the center of rotation. On starting the centrifuge the gondola swings out so that when a constant speed has been attained, its floor remains perpendicular to the direction of the resultant vector.

Recordings

Inspired gas volumes were recorded quantitatively by connecting the subject (wearing an aviator's oxygen mask with a leak-proof facepiece) with a rotary-type, "dry" gas meter, which was provided with a photoelectric transducer giving one impulse for every 20 ml of inspired gas. The transducer fed an electronic cumulative pulse recorder having two output channels, one for tidal volume, the other for respiratory minute volume or subdivisions thereof (Bjurstedt and Lönn 1960).

The arterial oxygen saturation was recorded using an oximeter cuvette (Wood, Geracy and Groom 1948), connected to a logarithmic amplifier according to Wiederhielm (1956). Blood was continuously collected from the left radial artery via an indwelling Teflon catheter (Barr 1961) and introduced into the cuvette, the rate of flow being kept constant at 8 ml/min by means of a roller pump. The Teflon catheter (length: 5 cm; inside diameter: 0.9 mm) was introduced percutaneously under local anesthesia. By employing this device any subjective inconvenience that would normally occur with an indwelling hypodermic needle could be avoided, even if the subject inadvertently moved his wrist under high G-loadings. The arterial O_2 saturation could thus be continuously monitored and recorded before, during and after the centrifuge runs. The oximeter assembly yielded a linear response to changes in the arterial O_2 saturation and was calibrated by means of Van Slyke analyses of blood sampled from the test subject during the experiment. Over the recording periods used in the experiments the drift of the instrument was negligible.

The pH of the arterial blood was continuously monitored using a technique earlier described by Barr and Bjurstedt (1959). For this purpose a glass-reference-electrode assembly, with an incorporated thermistor unit for checking the temperature of the blood, was interposed between the radial catheter and the oximeter cuvette. The time for 90 per cent of full deflection following a "square-wave" change in the composition of the blood entering the pH unit was adjusted to approximately 8 sec for both the pH and O_2 saturation readings.

The heart rate was obtained by means of an instantaneous cardiotachometer (Sturm and Wood 1947).

The G-level (resultant acceleration) was recorded by using a strain-gage accelerometer, positioned in the gondola at approximately the level of the heart (for nomenclature of accelerative forces, see Dixon and Patterson 1953).

Electrical outputs from the pickup units in the gondola were led via low-noise slip-rings to amplifiers and galvanometers outside the centrifuge hall for photokymographic recording.

Procedure

In order to acquaint the subjects with the experimental conditions they had several trial runs in the centrifuge at least on one occasion before the day of the actual experiment.

Prior to the experiment the Teflon catheter was introduced into the left radial artery. After flushing the catheter with heparinsaline solution, its stop cock was closed and 150 mg heparin injected intravenously in the right antecubital vein. The subject then entered the centrifuge gondola where he was connected to the different pickup units, the junction between the radial artery and the pH-oximeter sensors being opened just prior to the first experimental run. The backrest of the seat was inclined backwards 15° from the vertical.

All subjects were exposed to positive acceleration, breathing air, and wearing a standard, G-activated anti-G suit. The pressure in the suit at 4.0 - 5.0 G was 250 - 300 mm Hg. The onset of the first run was gradual in order not to risk loss of consciousness, a plateau of 4.0 - 4.5 G being attained with 25 sec (except in subject F H where the plateau was reached after 40 sec). The subject was asked to report immediately over the intercom system if greyout or blackout occurred. His face was watched continuously by means of a closed-circuit television monitor.

In addition, a number of experiments, mostly of a preliminary character, were run under conditions that differed from those mentioned above. Thus, several experiments were run at lower G levels, with the subjects breathing 100 per cent oxygen and wearing no anti-G suit.

RESULTS

Single Runs

Prolonged exposures to 4.5 - 5.0 g positive acceleration, with the subjects wearing a G-activated anti-G suit and breathing air, consistently caused a drop in the arterial O_2 saturation and an increase in the respiratory minute volume. If, in the first centrifuge run of any one experiment, the G-loading was kept at a constant level over a minute or longer, the arterial unsaturation usually progressed at a rapid pace during the first half-minute and thereafter gradually slowed down (Fig. 1). The maximum

Table I. Positive acceleration, air breathing, anti-G suit.

Subjects Age, Yrs Length, cm Weight, kg	Acceleration, G Duration of run, sec	Cond.	$\dot{V}_I$ L/min ATPS	Art. O_2 satur. %	Art. pH	Minimum O_2 saturation during run %
WL 17 175 71	+4.5 163	A	11.8	97.3	7.41	89.6
		B	20.4	90.7	7.42	
		B-A	+8.6	-6.6	+0.01	
ÖA 28 176 72	+4.5 153	A	7.3	97.0	7.44	89.0
		B	16.1	90.0	7.44	
		B-A	+10.2	-7.0	0	
FH 22 166 64	+4.5 122	A	11.9	97.8	7.36	90.5
		B	25.9	94.8	7.37	
		B-A	+14.0	-3.0	+0.01	
BJ 24 182 70	+4.5 97	A	11.5	98.6	7.43	94.5
		B	29.8	95.0	7.44	
		B-A	+18.3	-3.6	+0.01	
NG 21 175 72	+4.5 71	A	12.2	96.2	7.43	87.2
		B	19.3	88.0	7.44	
		B-A	+7.1	-8.2	+0.01	
BO 21 175 65	+5.0 74	A	8.4	96.2	7.38	90.4
		B	13.8	91.0	7.39	
		B-A	+5.4	-5.2	+0.01	
NO 24 173 73	+5.0 82	A	11.0	97.0	7.45	79.0
		B	20.0	81.0	7.46	
		B-A	+9.0	-16.0	+0.01	

Condition A = control values during 60 sec immediately prior to run (means for arterial O_2 saturation and pH);

Condition B = values after 60 sec had elapsed from onset of run (V_I refers to the first 60 sec after onset of run);

N. B.: Arterial O_2 saturation and pH values refer to the time when the arterialized blood left the lungs (corrections made for time lags in the readings);

degree of unsaturation was attained before 90 sec had elapsed. This pattern of response differed from that obtaining if the run was repeated after a short interval (see below). Respiration, sometimes after an initial apnea, regularly increased during the first half-minute, but showed no further augmentation during the remainder of a prolonged run, although irregularities in amplitude and frequency of breaths could sometimes be observed. In contrast to the O_2 saturation, the arterial pH showed only insignificant changes during the exposures. However, short-lasting deviations often occurred at the beginning and at the end of a run. That there were quite large inter-individual variations in the response of the arterial O_2 saturation is evident from the values given in Table 1, which also shows the responses of the arterial pH (corrected to 37° C) and the respiratory minute volume.

In several runs the subjects breathed 100 per cent oxygen or did not wear an anti-G suit. In all these instances a limited, but nevertheless noticeable, fall in the O_2 saturation occurred. The arterial pH and respiratory minute volume, however, followed a pattern that was similar to that observed with the subjects using an anti-G suit and breathing air.

Repeated Runs

The changes described above refer to the first run in any one experiment. When a second and third run followed, with intervals of up to 2 min, the fall in the arterial O_2 saturation regularly became steeper, this tendency becoming more accentuated with each consecutive run. Furthermore, the final level of unsaturation became progressively lower (Fig. 3). The hyperventilation occurring during the runs sometimes became more marked, sometimes declined somewhat with repeated exposures. The arterial pH remained essentially unchanged during consecutive runs.

Post-Run Period

On returning to normal gravity after a run by stopping the centrifuge, the arterial O_2 saturation immediately started to rise. The final return towards the pre-run level was, however, usually sluggish despite the fact that some degree of hyperventilation persisted for a short period after the run. The time required for complete resaturation varied: in some cases the pre-run level was reattained within the first minute, while in others, and especially after repeated exposures, complete resaturation occurred only after several minutes (Fig. 1 and 2). In some instances the subject was asked to make a few deep inhalations; this yielded only a temporary rise in the arterial O_2 saturation.

DISCUSSION

In view of the fact that even normal gravity has been shown to change the ventilation/perfusion relationships within the subdivisions of the lungs in man (for review see Bjurstedt et al. 1961), one might surmise that increased gravitational stress, as is present during positive acceleration in the centrifuge, would greatly exaggerate such changes. That this is the case for anesthetized dogs was borne out by the experiments of Barr,

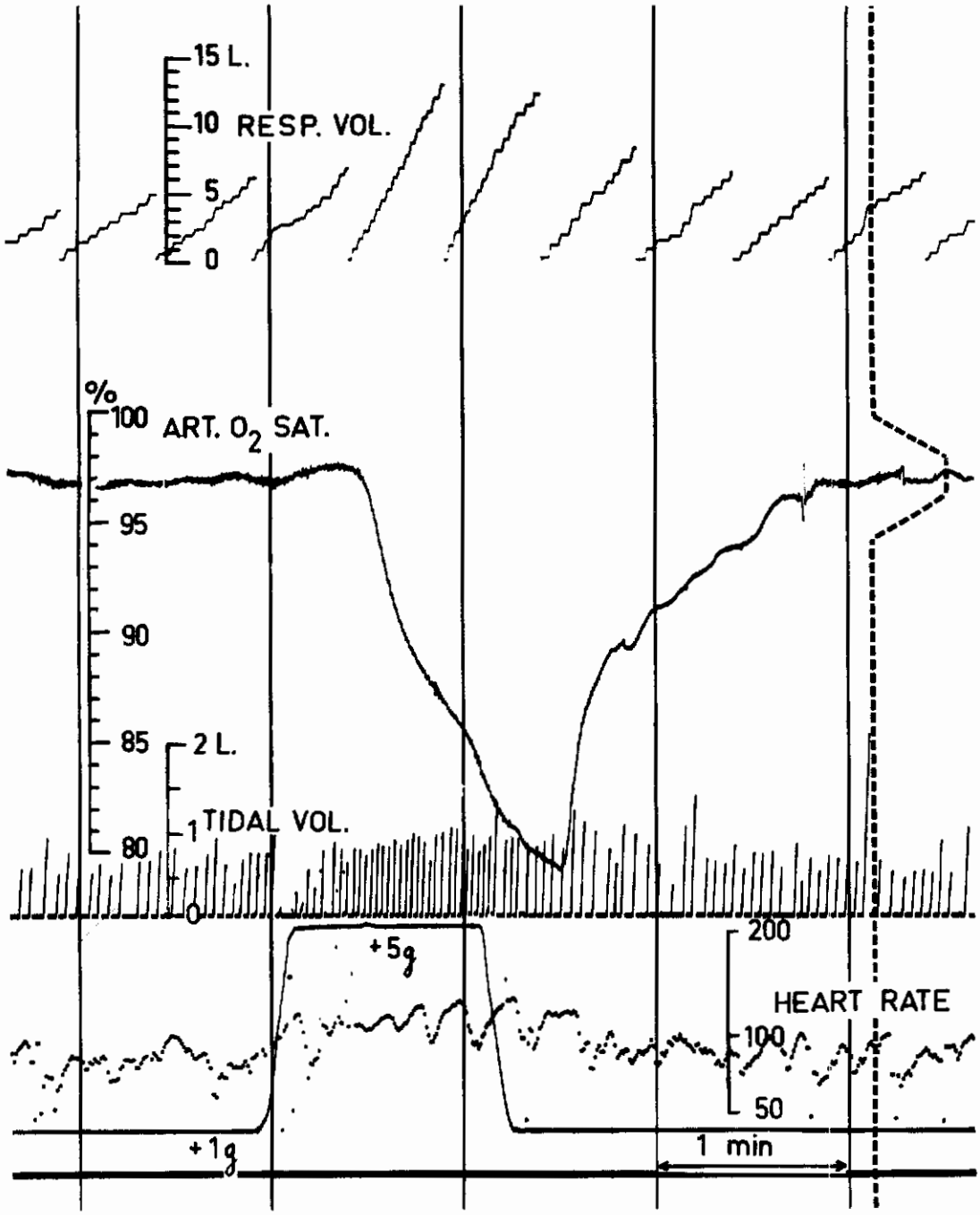

Fig. 1. Effects of prolonged positive acceleration with automatically inflated anti-G suit, air breathing. Subject N O (fighter-aircraft navigator). From above downwards: inspired gas volumes added together during half-minute periods; arterial O_2 saturation; tidal volumes (inspirations); heart rate (beats/min); accelerogram showing duration and magnitude of positive acceleration; base line. Time: 1 min between solid vertical lines. Time lag of O_2 saturation tracing indicated by vertical dashed line.

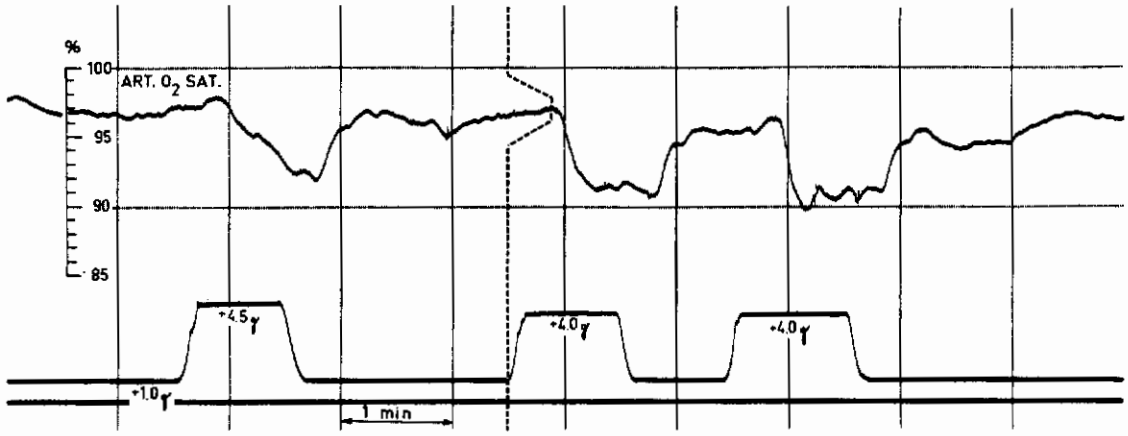

Fig. 2. Time course of changes in arterial oxygen saturation induced by consecutive exposures to positive acceleration (4.5, 4.0 and 4.0 G) in subject M E (age 20 years, length 179 cm, weight 68 kg), breathing air and wearing automatically inflated anti-G suit.

Note increasing rate and degree of unsaturation in consecutive runs, also impairment of resaturation in the post-run periods.

Bjurstedt and Coleridge (1959), in which the pulmonary gas exchange was studied by recording the changes in blood gases and respiration while the animals were subjected to positive acceleration in the centrifuge. With prolonged exposures, hypoxemia developed even when 100 per cent O_2 was breathed, indicating a great alveolar-arterial O_2 difference, and accordingly, a considerable degree of venous admixture to the arterialized blood.

In the present experiments on man the essential observations were (1) that a rather marked arterial unsaturation could develop during prolonged exposures to positive acceleration despite that the respiratory minute volume showed a considerable increase, (2) that the rate and degree of unsaturation increased if the subjects were exposed to several consecutive runs during one and the same experiment, and (3) that the arterial pH remained relatively unchanged.

Although other mechanisms might have contributed to the arterial unsaturation during the exposures (cf below), admixture in the pulmonary circulation must be assumed to have been a major component in the over-all picture. Thus, it is unlikely that any other factor would alone be effective in producing arterial hypoxemia in subjects who were hyperventilating on 100 per cent oxygen. That the arterial pH remained relatively unchanged during the exposures, irrespective of whether the degree of concomitant arterial

unsaturation was more or less marked (cf Table 1), is not incompatible with the assumption of a shunt-like effect, since some of the mixed arterial blood can be assumed to have passed through lung regions with an increased effective alveolar ventilation, and thus to have become "superarterialized" with respect to CO_2. In this way the arterial pH may be kept near its normal level by compensatory hyperventilation effected through the respiratory centers, whereas a normalization of mixed arterial O_2 saturation through a similar mechanism would not be possible because of the shape of the oxygen dissociation curve.

Normally, an alveolar-arterial O_2 difference can arise from (1) resistance to diffusion of O_2 between alveolar air and capillary blood (diffusion component), (2) admixture of venous blood to the arterialized blood (shunt component) and (3) uneven distribution of alveolar ventilation to pulmonary blood flow (distribution component) (cf Farhi and Rahn 1955, Piiper and Rahn 1960). It may be assumed, that the increased effective weight of the blood perfusing the lungs during high G-loadings can put all these components into play through (1) raised intracapillary pressure and formation of edema in dependent regions of the lungs, (2) congestion of such regions with passage of blood through non-ventilated alveoli, and (3) defective perfusion of ventilated alveoli, especially in apical regions, respectively. Since the cardiac output has been shown to decrease during positive acceleration (Wood et al. 1961), this effect may presumably in itself act to exaggerate the importance of both the shunt and distribution components. Thus, a lowering of the oxygen content of the mixed venous blood that would accompany the reduction of cardiac output must cause a further reduction of the arterial O_2 saturation for a given ratio of shunted blood/total blood flow. Likewise, a diminution of the total blood flow through the lungs would give rise to an alveolar dead space, similar to what has been observed by Gerst et al. (1959) after hemorrhage.

It is well known that changes in gravitational vectors normally produce alterations in the respiratory activity in man, so that e.g. a change from the supine to the upright body position calls forth an increase in the respiratory minute volume (for reviews, see Brogdon Franseen and Hellebrandt 1943, Bjurstedt et al. 1961). An increase in the respiratory activity in man has also been shown to occur during short-lasting exposures to positive acceleration (Gauer 1938, Lombard, Rooth and Drury 1948, Browne 1948). The present experiments demonstrate that such hyperventilation can become quite marked and usually persists throughout prolonged periods of positive G-loadings.

A remarkable feature was that the arterial pH remained relatively unchanged even though arterial unsaturation and hyperventilation were present. This brings into focus the interrelationships of different factors in the control of respiration under positive G-loadings. The fall in the arterial blood pressure that occurs in the upper part of the body (cf Wood et al. 1946) may stimulate respiration by direct influence on the medullary center via changes in the local blood flow (for review, see Schmidt 1941, p. 366). Also, hypotension at the level of the carotid sinus region may give rise to respiratory reflexes of chemoceptive or baroceptive origin (cf Euler and Liljestrand 1937, Heymans and Neil 1958). The acceleration-induced arterial hypoxemia would be expected to produce chemoreflex stimulation of respiration. Furthermore, such stimulation might become greater through ischemic

excitation of carotid chemoceptors secondary to reduced blood flow to these structures (Landgren and Neil 1951).

Any hyperventilation that would result solely from one or several of the above-mentioned disturbances in the systemic circulation would lead to respiratory alkalosis. One must then ask what prevented the arterial pH from showing greater deviations than were actually observed and what factors were responsible for the maintained hyperventilation during prolonged exposures. It is believed that part of the explanation is to be found in gross deterioration in the efficiency of pulmonary function. Thus, admixture of venous blood with a high CO_2 content to the arterialized blood, as well as enlargement of the physiological dead space (cf above), would impair the elimination of CO_2 from the lungs and so tend to increase the arterial P_{CO_2}. In addition, any increment in the acidity of the mixed venous blood secondary to increased CO_2 production and/or formation of acid metabolites in the tissues (from e.g. increased work load under high G-loadings) would be potentially capable of shifting the arterial pH in the acid direction. Thus we have during positive acceleration a peculiar state of balance where (1) the efficiency of pulmonary function is impaired, and (2) pulmonary ventilation increases to an extent that leaves the arterial pH relatively well regulated.

COMMENT

The data given in Table I were obtained in experiments where the procedure and recordings were standardized. In these experiments the degree of arterial unsaturation was in many cases not serious from the point of view of safety in high performance flight missions. However, in a number of centrifuge experiments that fell outside the standard design, the arterial O_2 saturation fairly often fell below 80 per cent at 4.5 - 5.0 G before 90 sec had elapsed (subjects breathing air and wearing a standard anti-G suit). Clearly, such levels of arterial unsaturation are not compatible with intact performance of the brain.

That the arterial O_2 saturation may fall markedly and progressively in man during positive acceleration, and that the fall occurs at a faster rate and to a lower level with consecutive exposures, should be of interest in the determination of man's resistance to such stresses. Classically, tolerance to positive acceleration has been judged by the occurrence of blackout. In view of the results reported in the present communication the adequacy of this end-point is questioned, since the effects of general hypoxemia on cerebral functions are insidious: blackout may thus occur when higher functions are already seriously affected, or loss of consciousness may ensue without such end-point or other subjective warning.

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