PHYSIOLOGICAL STUDIES OF FAINTNESS AND SYNCOPE

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During experiments to determine the relationship of the ethyl iodide content of alveolar air and arterial blood in the upright position a number of subjects experienced faintness and two collapsed. Such an incident, occurring during a time when measurements of respiration and circulation were in progress, provided unusual opportunity for complete observation of the phenomena of faintness and syncope. Our study of the six cases which form the subject of this report represents an effort to improve such opportunities. Our attempts to enlarge the series met with failure. It seemed to us that, as soon as the danger of fainting became known to the subjects, syncope no longer occurred. Those who collapsed were taken by surprise.

Studies of fainting attacks in soldiers with irritable hearts have been made by Cotton and Lewis (1). A case of syncope following short periods of cardiac arrest has been carefully studied by Laslett (2). In both of these vagal stimulation was identified as the chief factor; in our cases this appears to have been of secondary importance only.

METHODS

The apparatus and methods used for the determination of cardiac output (3) were employed. The subject, standing, inhaled from a spirometer containing about 1 cc. of ethyl iodide in 300 liters of air. One hand was placed in water at 43° to 45°C.; and late in the experiment blood, equivalent to arterial blood in gas content (4) was obtained from a vein on the back of this hand. Respiration was recorded by a pointer, attached to the spirometer bell, writing on kymograph paper. Blood pressure and pulse rate were determined frequently. In the last experiments an electrocardiograph was used, recording from lead II. The subjects were instructed to tap with the foot whenever unusual sensations were noted, the time was then recorded on the record, and the signals interpreted after the experiment.

The subjects were healthy young men between the ages of 27 and 35. Three were doctors of medicine, one a physiologist. All were accustomed to the proceedings involved in this study. Subjects J. H. and H. H. had had syncopal attacks before, the others could not recall any.

After a brief period of adaptation, holding the hand in hot water caused no discomfort to the subjects. In all the entire skin became warm and moist. Some noted increased axillary perspiration. In one, who did not faint, there was generalized perspiration throughout the experiment.

RESULTS

Control experiments without faintness. In the experiments in which faintness did not occur no significant changes of blood pressure, pulse and respiration took place. Hence these records have not been given.

Experiments in which faintness occurred. Data collected in the six experiments are presented in the figures and described below.

I. Subjective sensations. Among the sensations of faintness experienced by the subjects were tinnitus, light headedness, vertigo, nausea, a sinking feeling in the abdomen similar to that produced by rapid descent in an elevator, and finally a feeling that near objects were becoming distant and indistinct. A feeling of apprehension often preceded and always accompanied more definite sensations. For convenience of expression these sensations will be referred to as faintness in the remainder of this paper.

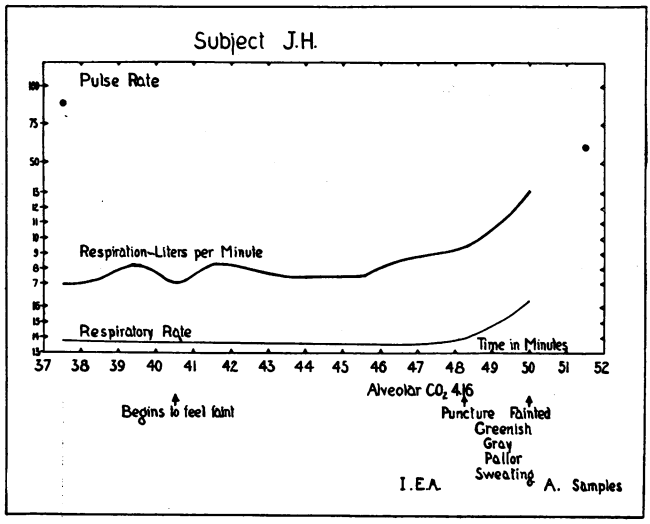
The arrows, placed on the figures under the supervision of the subjects, indicate gradual rather than sharp changes of sensation.

II. The circulation. The first estimations of cardiac output in experiments 3 and 4 were made after or during the preliminary rise of pulse rate but before the sensations of faintness, and changes in respiration and blood pressure had developed. In both cases the cardiac output was well within the normal range, much above the average normal basal level.

Unfortunately the data which could be secured during the actual period of faintness are insufficient to permit accurate calculation of cardiac output at that time, as recovery or collapse supervened too quickly to allow all requisite samples to be taken. Nevertheless, it

seems proper to assess the significance of such data as were obtained.

The samples of expired and of alveolar air secured during faintness in experiments 1, 3 and 4, together with knowledge of the concentration inhaled and of the respiration, permit the cardiac output



General explanation of figures. The results of pulse and blood pressure estimations have been placed at the time the determinations were begun. The scale for pulse and respiratory rates indicates the rate per minute; for volume of respiration liters per minute; for blood pressure the same scale is employed as for pulse rate, but it should be read as mm. of Hg. The samples of inspired, expired, alveolar, and rebreathed air, analyzed for ethyl iodide to estimate cardiac output, have been recorded under their initial letters at the time the sample was trapped. The content of alveolar samples represents the condition of alveolar air somewhat before trapping (3). The alveolar CO_2 has been recorded at the approximate time the percentage found was present.

FIG. 1. Experiment 1. At the end of the record the subject fell, was caught and carried to a nearby couch. He was unconscious for about a minute, recovered promptly, felt entirely well in about fifteen minutes.

to be calculated according to the method of Henderson and Haggard (5). The results are much above the average found in normal persons standing by Rosen and White (6), and are at or above the average calculated from our data in eighteen similar experiments (7). Also these results in experiments 2 and 3 are much above those calculated

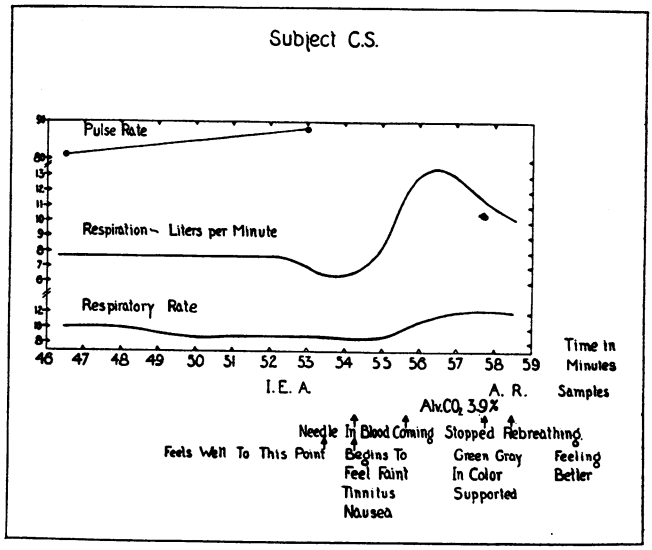


FIG. 2. Experiment 2. The cardiac output estimation was lost because of leakage around the mouthpiece at the height of symptoms.

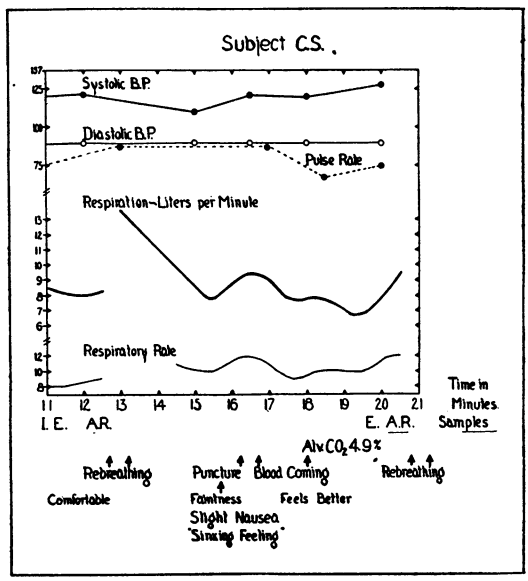


FIG. 3. Experiment 3. The subject, having become faint before, was apprehensive and excited. The pulse rose steadily from 66 to 88, the blood pressure changed from 118/80 to 120/90 during the 14 minutes preceding the period given in the figure. The first estimation of cardiac output indicated 6.9 liters per minute, the second 5.5 liters per minute. The unusually large increase in respiration following the first rebreathing was probably due to rapid accumulation of CO_2 from the high metabolism from excitement.

from experiments in which the same subjects stood without faintness (7). No similar control experiments on H. H. were performed. While we have little confidence in the figures for cardiac output thus obtained, it is obvious that the ethyl iodide in expired and in alveolar air during faintness bore the same relation to that inspired as occurs in persons

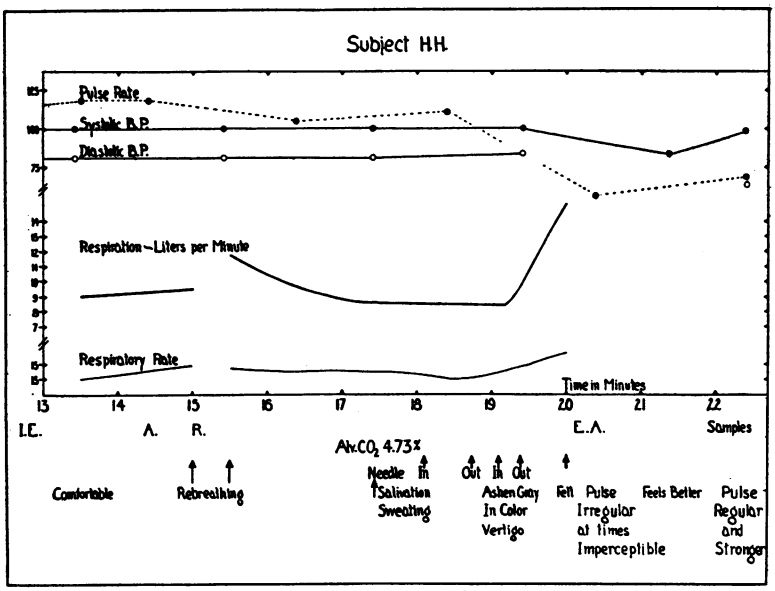


FIG. 4. Experiment 4. The pulse rose from 88 to 118, the blood pressure changed from 106/80 to 100/84 during the 16 minutes preceding the period given in the figure. The first cardiac output estimations indicated 5.1 liters per minute. The skin was punctured twice, no blood being obtained. At the end of the record the subject fell, was caught and laid flat on the couch. Some of the observers believed that he became unconscious, the subject thought not. He was fully conscious within a minute and continued to lie down for about 20 minutes.

with normal circulations. This suggests that the cardiac output during faintness was normal. But as the possibility of diminution of ethyl iodide in venous blood during faintness cannot be denied, we prefer to regard our evidence on the state of the cardiac output during these sensations as inconclusive.

Any speculation regarding the size of the cardiac output depends

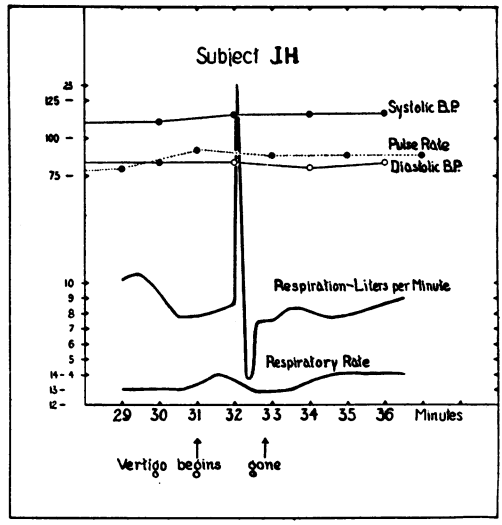


FIG. 5. Experiment 5. The respiratory change here recorded consisted of two very long deep sighing respirations, followed by severa shallow breaths.

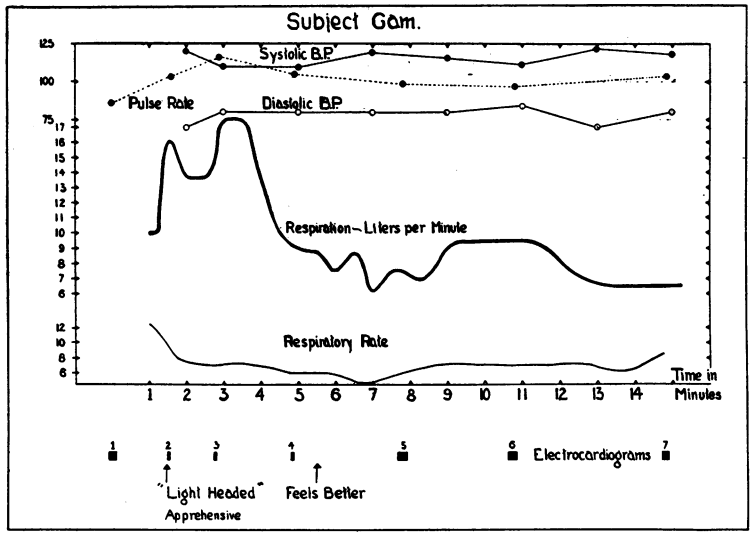


FIG. 6. Experiment 6. Electrocardiograms indicated, were taken by Dr. F. C. Wood and interpreted as follows: No. 1, normal, T wave upright 2.5 mm.; no. 2, T wave 1 mm.; no. 3, T wave less than 0.5 mm. isoelectric in one place; no. 4, T wave 0.5 mm.; no. 5, T wave 1 mm. at start rises to 2 mm. by end of record. No. 6 and no. 7, T wave 2 mm. No other changes except those of T wave.

The pulse rates recorded were obtained from the electrocardiograms.

on the assumption that the equilibrium of ethyl iodide between alveolar air and blood is not disturbed during faintness. In experiment 3 the agreement of the ethyl iodide content of "arterial" blood with that calculated from alveolar concentration and average normal distribution coefficient (6.1) demonstrates the existence of a normal equilibrium. The attempt to demonstrate it in experiment 2 failed because the fainting subject did not grasp the mouthpiece sufficiently to prevent leakage.

TABLE 1

Data bearing on cardiac output before or during faintness

Experiment number	Ethyl iodide concentration				Respiration		Temperature correction	Cardiac output
	Inspired	Expired	Alveolar	Rebreathed	Last 5 minutes	Last minute		
	mgm. per liter	*mgm. per liter*	*mgm. per liter*	*mgm. per liter*	*liters per minute*	*liters per minute*		*liters per minute*
1 a	5.34	2.82	1.58		7.5		0.92	
1 b			2.11			12.5		
2	5.77	2.50	1.84		7.7			
3 a	5.33	2.35	1.59	1.03	7.3		0.92	6.9
3 b		2.82	1.73	1.09	7.8	8.0		
4 a	5.34	2.79	1.93	1.14	8.85		0.917	5.1
4 b		3.10	2.08			11.0		

In calculating cardiac output the average normal distribution coefficient, 6.1 has been employed. The small correction for delay in taking the R sample (3) has been omitted as its value cannot be determined from the data.

Therefore we have obtained no evidence of a diminished cardiac output before or early in the process of fainting. Later when pulse rate and blood pressure had fallen markedly, a diminished cardiac output seems highly probable. We have obtained no evidence on this point.

In the five experiments in which enough counts were made, the pulse rate always increased before or early in the sensations of faintness, while the control experiments showed no similar changes. Later in the experiments the pulse rate always fell after recovery (experiments 3, 5, and 6) or after syncope (experiments 1 and 4). In ex-

periment 4 the rate during syncope was one-half that recorded before it and the pulse was irregular and at times almost imperceptible. In experiment 1 the pulse during syncope was slow but regular and strong.

The changes of blood pressure noted before syncope were so small that we are not confident of their significance. After syncope a profound fall in both systolic and diastolic pressure occurred. In experiment 4 the latter fell so far that the observer, eager to get another systolic reading, did not wait for the cuff to deflate far enough to determine the diastolic level. Recovery was accompanied by a return towards normal.

The marked cadaveric pallor, observed in experiments 1, 2, and 4 at the height of the symptoms, should be attributed to peripheral vaso-constriction. It appeared late in the process, immediately before collapse. In other experiments the symptoms were milder and pallor did not appear.

Blueness of the lips was noted just before collapse in experiment I. In other experiments the greenish color was doubtless due to the combination of cyanosis and pallor.

In experiments 2 and 3 samples of blood, obtained from a vein on the back of the hand in hot water during the sensations of faintness, were the color of arterial blood. In experiment 3 this blood contained 18.5 volumes per cent of oxygen, and was 90.4 per cent saturated. The analyses were performed in duplicate in the apparatus of Van Slyke and Neill (8). No blood was secured from the other subjects.[1]

III. Changes of respiration. A great increase in minute volume during faintness was characteristic of all our observations. In three experiments the increase started coincidentally with the beginning of the sensations, while in two the sensations preceded the increase. In Experiments 2 and 3, minute volume is recorded as diminishing before the sensations passed away, although in experiment 2 this may

[1] With the assistance of Dr. Francis C. Wood frequent electrocardiograms were made in two cases. In one subject (experiment 6) the T wave, 2 mm. high before faintness, diminished during the sensations till it was less than 0.5 mm. high and returned to its previous level as recovery occurred. However, later in the same experiment a similar diminution of the T wave took place without any faintness or other change in our records to account for it. Therefore these observations throw no light on the physiology of fainting.

be an artifact because the subject was so weak that his cheeks ballooned on each expiration and leakage of air around the mouthpiece took place.

When syncope occurred and the subject released the mouthpiece the respiratory record ceased. The violent movements of the chest, visible during the hyperpnea, were not seen after the subject was horizontal.

The rate usually changed in the same direction as the minute volume but the change often began later. In experiment 5 the rate fell as minute volume increased, but this continued only for a very brief period. In no experiment did the increase in rate account for the increased minute volume, which was primarily caused by the great increase in depth. During syncope no accurate counts were made, but the rate appeared to become slower.

As the alveolar air was collected by the repeated addition of small amounts to a large sampling tube, the gases found by analysis represented the content of the alveoli about two and a half minutes before the collection was completed. Therefore, if the respiration was increasing, the percentage of CO_2 in the alveolar air when the sampling tube was closed must have been less than that found by analysis of the sample. The alveolar CO_2 at syncope must have been lower than the figures here reported.

It is obvious that the alveolar CO_2 found was abnormally low in all cases in which syncope occurred. Identical experiments without faintness showed alveolar CO_2 contents over 1 per cent higher for C. S. and H. H., from 0.1 to 0.7 per cent higher for J. H. It is interesting that C. S., so faint that he had to be supported, recovered during a rebreathing period of 1 minute, 25 seconds duration, though he continued to stand upright.

While hyperventilation with blowing off of CO_2 will cause low blood pressure in animals (9, 10), increasing hyperventilation of the grade recorded in our subjects is not sufficient to cause much change of blood pressure, or to produce symptoms in normal subjects (11). On the other hand subjects who complain of "light headedness" when breathing deeply are occasionally encountered (12). Therefore the lowering of blood CO_2, though not the cause of syncope, may well be a factor in the production of the symptoms.

DISCUSSION

Relation of venipuncture to the production of symptoms. Only in the case of C. S. (experiments 2 and 3) did the puncture of the vein precipitate the symptoms. In experiment 1 the symptoms preceded the puncture by eight minutes and the subject was so faint that he felt no pain and hardly realized the puncture was being performed. In experiment 4 the symptoms began about one-half minute before puncture, during preparations to perform it. In the other experiments the faintness appeared and passed off so long before the puncture that the latter is not shown in the figures. Obviously the symptoms were not caused by a reflex from the discomfort of venipuncture in most of our experiments, although in two, such an explanation is possible.

Picture obtained by combining our results. The initial physiological changes of our experiments were so similar that they suggest a uniform response to similar pathological conditions. The differences of response found later may be attributed to differences in intensity of this condition, as in some cases it soon terminated in recovery, in others it progressed to collapse. Therefore it seems proper to combine our observations and so obtain a description of the process of fainting more complete than in the best single experiment (experiment 4). This description is as follows.

After a period of several minutes in which the pulse rate slowly rises the sensations of faintness appear, soon followed by a steadily increasing volume of respiration with increased respiratory rate. Changes of blood pressure are small and the cardiac output is not reduced at this stage. Recovery may follow or increasing severity of sensations, hyperpnea, greenish pallor, sweating, and perhaps cyanosis appear, soon followed by loss of consciousness and collapse. Decreased respiration, and a profound fall in blood pressure and pulse rate are now observed.

Similarity of our observations to effects of cerebral anemia. It has long been known that faintness and unconsciousness follow surgical ligation of carotids in unanesthetized patients, that these symptoms may be produced by compression of the carotid arteries (13), and that their relief promptly follows lowering of the head. It has been universally agreed that faintness and syncope are due to cerebral anemia.

It is proper to examine our data and ask whether the physiological changes found are those known to follow cerebral anemia in animal experiments. In figure 7 are shown the changes following cerebral anemia produced by elevation of the head or constriction of the carotids in anesthetized cats prepared by Dr. Carl F. Schmidt. The hyperventilation followed by apnea, the initial slight changes of blood pressure without change in pulse rate, later followed by great slowing of the heart and a fall in blood pressure, are all consistent with the observations on our subjects. Other investigators (14) have reported similar results and have also shown that the cardiac slowing disappears after section of the vagi (15). The similarity of these responses following cerebral anemia to the changes we observed during faintness is obvious. Therefore we agree that cerebral anemia is the probable cause of faintness and syncope. However, it should be pointed out that the results pictured in figure 7 are by no means always obtained and in many experiments cerebral anemia causes a rise of blood pressure followed by cardiac slowing with fall of blood pressure in animal experiments (16).

Possible causes of cerebral anemia in our experiments and in other reported cases. Concerning the cause of the cerebral anemia there is difference of opinion and without doubt difference of physiological mechanism is to be expected in different cases.

In our experiments cardiac slowing followed both an increase of pulse rate and the onset of sensations of faintness. Therefore reflex vagus stimulation, demonstrated to be the cause of syncope in Laslett's case (2) and suggested by Cotton and Lewis (1) as the explanation of fainting attacks in soldiers with irritable hearts, was not the primary cause of symptoms in our subjects.

We have obtained no evidence of diminished cardiac output or fall of blood pressure before the development of sensations. The conception of Field and Bock (17) and Turner (18, 19) that faintness on prolonged standing is due to cerebral anemia secondary to decreased cardiac output from diminished venous return does not apply to all our subjects. But undoubtedly a low cardiac output must be considered a predisposing cause of cerebral anemia as it must greatly increase the difficulty of maintaining an adequate circulation to the brain. This should be considered a factor in subject J. H., whose

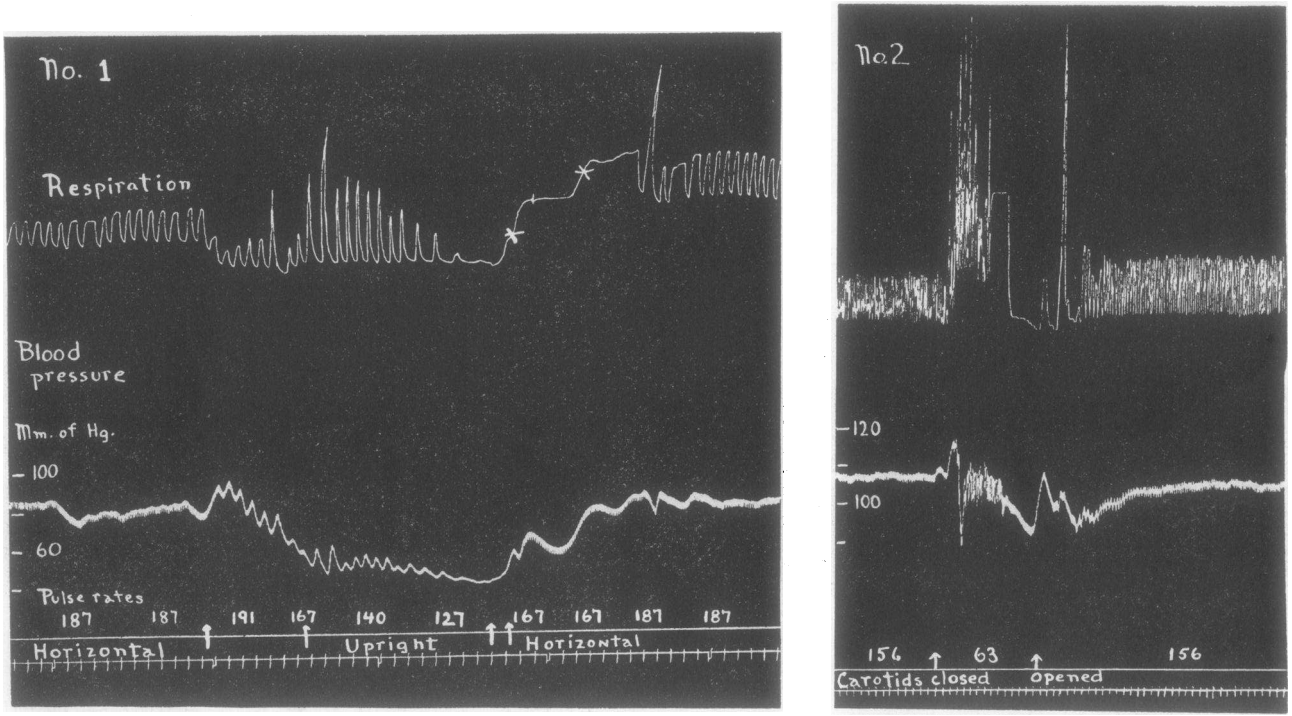


FIG. 7. Experiments on three cats anesthetized with 0.4 gram of sodium barbital per kilogram. Tracheal cannulae. Blood pressure recorded from carotid cannula in nos. 2 and 4, femoral cannula in nos. 1 and 3. Respiration recorded from an inflated bag around chest and tambour in nos. 1, 3, and 4; from Cushny plethysmograph in no. 2. The time records show five second intervals.

No. 1. Right vagus and both cervical sympathetics cut in a previous experiment. Vertebrals open. Cerebral anemia caused by raising animal's head to upright position. The change of level in the respiratory tracing is an artefact.

No. 2. Vertebral arteries tied previously. Cerebral anemia from simultaneous closure of carotids.

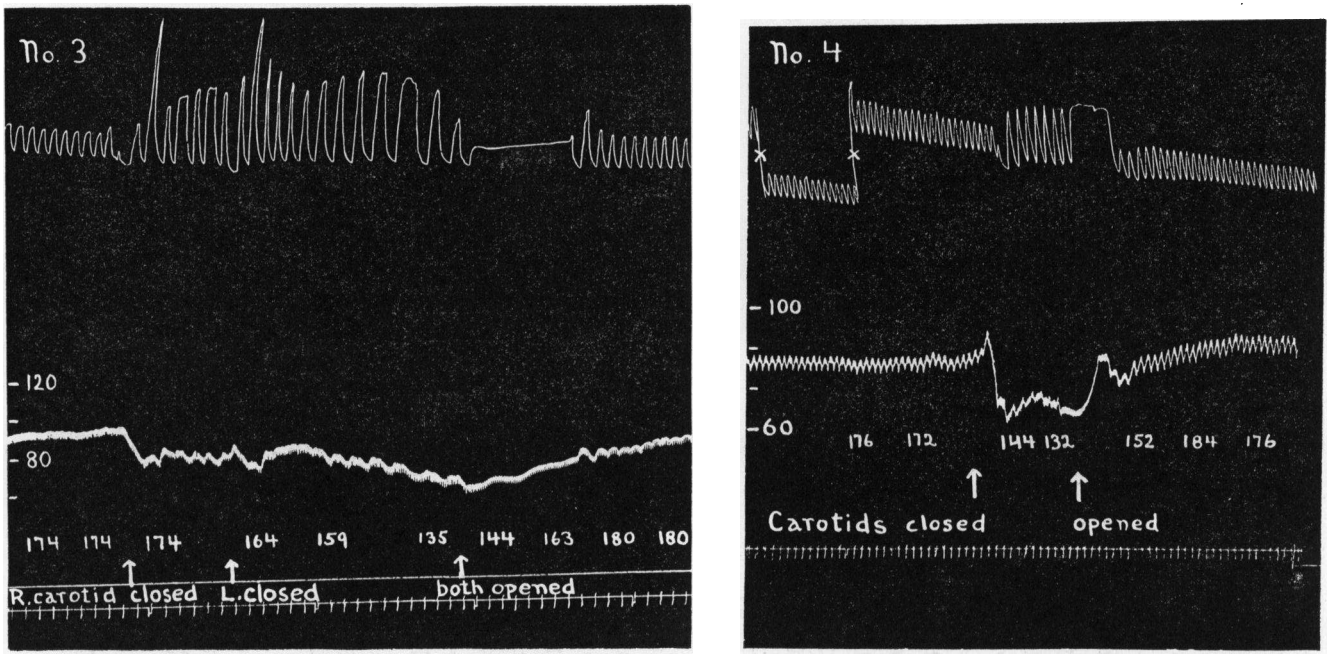


FIG. 7. See page 572 for explanation.

No. 3. Same animal as no. 1. Carotids closed separately, released together.

No. 4. Vertebrals open. Nerves intact. Cerebral anemia from closure of both carotids.

After experiments illustrated in 1 and 3 the remaining vagus was cut. After this cerebral anemia caused no slowing of pulse and usually a rise of blood pressure. Stimulation of central end of sciatic still caused a good rise of blood pressure.

cardiac output standing is constantly lower than when lying (7). This subject gave a history of occasional fainting after trivial causes. Several other subjects whose cardiac output standing resembled that lying (7) had no such history.

The three observations that faintness occurred when the blood pressure was normal deserve emphasis. This indicates the presence of sufficient energy to raise the blood to the brain if the cerebral vessels had been normal. Therefore, if the conception that cerebral anemia caused the symptoms is correct, this anemia cannot be wholly attributed to changes in the circulation outside of the vessels supplying the brain, and cerebral vasoconstriction is suggested. The old explanation (20) that cerebral vessels are largely passive and that cerebral anemia is precipitated by failure of vasomotor adjustment in the rest of the circulation cannot be applied to our experiments. Active contraction of cerebral vessels has been demonstrated (21) but knowledge of this subject has not advanced far enough to warrant discussion of cerebral vasoconstriction as a cause of syncope.

SUMMARY

Physiological changes preceding and coincident with sensations of faintness have been studied in six experiments in four healthy male subjects. Observations made included the subject's appearance, his cardiac output, pulse, blood pressure, respiration (graphic record), alveolar CO_2 and blood oxygen content. In one experiment an electrocardiograph was employed.

The records obtained are sufficiently detailed to demonstrate the order in which the symptoms developed and to permit correlation of physiological changes with sensations.

Before the sensations of faintness the pulse rate rose, but the respiration, blood pressure and cardiac output remained normal. At or soon after the beginning of faintness the volume of respiration began to increase and the alveolar carbon dioxide tension diminished, but at this stage normal blood pressure was found. Later, during syncope, a profound fall of pulse rate and blood pressure occurred.

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