Reports of the Air Medical Investigation Committee. 8, The effects of diminished tension of oxygen, with especial reference to the activity of the adrenal glands. 9, The ear in relation to certain disabilities in flying.

NATIONAL HEALTH INSURANCE

MEDICAL RESEARCH COMMITTEE

Reports of the Air Medical Investigation Committee

VIII. The Effects of Diminished Tension of Oxygen, with especial reference to the Activity of the Adrenal Glands

IX. The Ear in relation to certain Disabilities in Flying

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REPORTS OF THE AIR MEDICAL INVESTIGATION COMMITTEE

VIII. THE EFFECTS OF DIMINISHED TENSION OF OXYGEN, WITH ESPECIAL REFERENCE TO THE ACTIVITY OF THE ADRENAL GLANDS

BY

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1. Introduction.

The development of aerial warfare has been associated with the recognition in flying officers of certain symptom-complexes which follow prolonged service flying, or may result from 'crashes' or other incidents accompanied by nervous stress. The best defined examples of these conditions are 'flying stress' and 'cardio-vascular debility'. In both the outstanding feature is a degree of instability, in the one case of the nervous, and in the other of the cardio-vascular system. Since these conditions occur in men flying at low as well as at high altitudes, and even in those engaged in war service other than flying, it is evident that nervous excitement must play an

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important part in their production. Evidence has, however, been accumulating to show that in airmen repeated exposure to want of oxygen, as suggested by Flack (1918), is a powerful adjuvant to nervous excitement. In men suffering from these forms of 'flying sickness' it was conceivable that this 'instability' might extend to the mechanism governing the activity of the suprarenal glands and that stimuli below the threshold of effectiveness in the normal individual might cause in them an increased output of adrenalin.

Hitherto there have been no direct observations upon the effect of anoxaemia in causing increased output of adrenalin. The work of Cannon and his co-workers (1916) established the fact that emotional excitement is one form of stimulus which operates in this way, though this has been recently denied by Stewart and Rogoff (1917 b); Cannon and Hoskins (1911), Elliot (1912) and Anrep (1912) showed that asphyxia also causes such an increased output, though this again has been called in question by Stewart and Rogoff (1917 a) and by Gley and Quinquaud (1918). Cannon has suggested a relation between the hyperglycaemia which results from emotional excitement and the increased output of adrenalin which occurs at the same time, and a similar relation has been supposed by some to exist in the case of asphyxia. According to Stewart and Rogoff (1917 b) no such relationship exists.

In all these investigations into the effect of asphyxia upon adrenalin output no attempt has been made to graduate the severity of the asphyxia, and for the most part the negative observations have been vitiated by the complicating effects of severe operative procedure under anaesthesia. It seemed desirable, therefore, to take up this question again, and, since there is no known satisfactory method of determining the presence of adrenalin in the peripheral blood of man, the observations have been made upon unanaesthetized cats, in which the preferential dilatation of the pupil, sensitized by previous removal of the corresponding superior cervical ganglion, has been used as an index of the output of adrenalin. This proved to be perfectly satisfactory as an index of the suprarenal activity in the milder degrees of anoxaemia and asphyxia, when produced in unanaesthetized animals.

Given this convenient method of detecting acceleration of the output of adrenalin under these conditions, it was now possible to put to the test the following questions concerning acceleration of adrenalin output and the appearance of hyperglycaemia.

(1) Does asphyxia cause an increase in the output of adrenalin? The production of hyperglycaemia in asphyxia was already well established.

(2) Given that both these effects can be demonstrated as a result of asphyxia, can they be produced by anoxaemia alone?

(3) If anoxaemia can act in this way, does it do so when of the kind and degree encountered in high flying?

It will be seen that all these questions were answered in the positive sense by my experiments. There remained, therefore, for investigation the nature of the mechanism by which anoxaemia caused both these effects, and the further question as to how

far the hyperglycaemia was a result of the accelerated output of adrenalin, and how far it was a more direct result of anoxaemia.

In addition to the experiments which bear directly on the central problem above stated, some incidental observations were made on other more general physiological changes in animals exposed to degrees of anoxaemia, comparable in duration and severity with those to which airmen are subjected.

In flying the ascent and descent are rapid, and the duration of the anoxaemia so produced does not extend beyond an hour or two. The adaptation of man to lack of oxygen in mountain climbing has been described by Haldane (1917), Barcroft (1914), and other workers. It occurs somewhat slowly and is not fully developed for several days. It is unlikely, therefore, that any of the various accommodating mechanisms discussed by them come seriously into operation during high flights, with the possible exception of increase in the corpuscular content of the blood, as indicated by the work of Dreyer and Walker (1913), which the recent work of Bazett and Corbett (1918) seems to confirm. This change, when it appears rapidly during a short period of anoxaemia, must presumably be attributed to loss of plasma from the vessels.

Recently a great deal of attention has been paid to changes in the capacity of the plasma for combining with carbon-dioxide in shock, gas gangrene, and other conditions. It seemed likely that the production of fixed acids in anoxaemia (Araki (1891, 1894)) would cause a fall in the alkali reserve. I have investigated the changes in the alkali reserve in anoxaemia in order to discover if they were of such magnitude as to play any serious part in producing the recognizable symptoms accompanying want of oxygen. Some observations have also been made on the volume of the blood in anoxaemia, with a view to ascertaining whether any alteration, by loss of plasma or otherwise, occurs in the volume of blood in effective circulation.

2. Methods.

Atmospheres containing reduced proportions of oxygen were prepared by the method described by Dreyer (1918), in which air and nitrogen pass through separate meters at accurately adjustable rates, into a mixing chamber from which the mixture is delivered to the subject of experiment.

As a mixing chamber I used for small animals a glass bell-jar holding 22 litres, fixed on a board through which the inlet and outlet pipes passed, the junction of the bell-jar and the board being made air-tight with 'plasticine'. For larger animals the bell-jar was replaced by a glazed stone-ware jar holding 36 litres. When anoxaemia uncomplicated by anaesthesia was to be produced, the mixture of air and nitrogen was administered to the animal by means of a mask. This was formed from a truncated cone of tinplate, oval in cross section. The inlet and outlet tubes were of half-inch bore and were soldered into the closed and smaller end of the mask. A piece of thin sheet rubber was cut into a suitable strip and

joined by rubber solution so as to form a short, wide, conical tube. The broader end of this tube was of considerably smaller diameter than the open end of the mask and was stretched over this latter and bound down round the margin with insulating tape. The narrow end of the tube was then invaginated into the mask and furnished an opening in an elastic diaphragm, which fitted the snout of the animal. Experience in the use of this mask showed that if the rubber was renewed as often as it showed signs of losing elasticity the contact made with the animal's face was practically air-tight, so that it breathed nothing but the mixture supplied to the mask during the time that the latter was in position. The outlet tube of the mask was fitted with an expiratory valve and the inlet tube was connected by wide-bore tubing with the mixing chamber of the Dreyer apparatus. The mask was used successfully with cats, dogs, and goats.

In certain experiments cats and rabbits were placed inside the bell-jar while the mixture of air and nitrogen was passed through it. Analysis of the air from the outlet tube of the bell-jar showed no appreciable increase in carbon dioxide, so that the flow of the mixture was sufficiently rapid to wash out the animal's expired air.

In some experiments the animal was anaesthetized while still in the bell-jar. For this purpose a three-necked Wolff's bottle, containing strips of gauze, was inserted in the path of the flow from the meters to the bell-jar. The middle neck of the bottle was fitted with a dropping funnel from which chloroform or ether could be dropped on to the gauze without opening the apparatus.

When anoxaemia was produced in animals under anaesthesia the mixture of air and nitrogen was supplied to the animal through a tracheal cannula provided with inlet and outlet valves. When a volatile anaesthetic was being administered the mixture was passed through the anaesthetic bottle of the operating table supplied by Palmer. This enabled the amount of anaesthetic administered to be regulated by means of a four-way tap, so that any required fraction of the gas mixture supplied to the animal passed through the anaesthetic bottle. Artificial respiration could be carried out if necessary with this gas mixture by putting the Brodie pump into circuit. Some experiments were made under urethane, in which case the mixture of air and nitrogen was led straight to the tracheal cannula.

The nitrogen used was of 98 per cent. purity and contained a small proportion of oxygen. The calculation of the percentages of oxygen in the mixtures from the meter readings could not, therefore, in any case give a high order of accuracy, but analyses of samples with Haldane's gas-analysis apparatus showed that the correspondence was sufficiently close for my purpose. Table I shows the kind of accuracy obtained. In later experiments the composition was calculated from meter readings only.

No. of Expt.	*TA in seconds.*	*TN in seconds.*	*Calculated* O_2 %.	*Observed* O_2 %.
1	59	60	10·57	10·52
2	56	201	16·39	16·44
3	29	28·4	10·4	10·6
4	28	17·5	8·0	7·8
5	34·5	31·5	10·0	9·9
6	39	19·5	6·99	6·80

When mixtures were administered to animals over long periods the small variations in speed of the motor which drove the gas compressor caused corresponding small alterations in the rate of flow of air. Frequent readings of the times of flow through both meters were taken and, in addition, the initial and final readings of both meters enabled an average value for the oxygen content of the mixture to be calculated.

Mixtures containing excess of carbon dioxide were obtained by the use of the same apparatus with the substitution of a container filled with this gas for the nitrogen cylinder.

Asphyxia was produced by making the animal breathe into the mask above described, which was connected by one outlet with a long piece of rubber tubing, the other being suitably closed. In other experiments the long tube was replaced by a collapsible air-tight bag connected with the mask by a short, wide tube. Samples of air for analysis could be obtained from this at the end of the period of asphyxia.

Blood samples were obtained in animals under anaesthesia from the cut end of a carotid artery. The animal was bled to the required amount into a centrifuge tube containing a few milligrams of dry powdered potassium oxalate.

In unanaesthetized animals the method used varied with the animal under experiment. In goats and cats samples were removed by a syringe, the needle of which was pushed into one or other of the external jugular veins. Rabbits were bled from the marginal vein of the ear, which was shaved at the margin and warmed to expedite the flow of blood.

The method of determining the blood sugar was a modification of the Lewis-Benedict method described by S. R. Benedict (1918). 2 c.c. of blood, which is prevented from clotting by the addition of solid dry potassium oxalate, are measured in a pipette, which is twice washed out with distilled water—the washings being added to the blood. The volume is made up to 25 c.c. with picric-picrate solution. The mixture is filtered and 8 c.c. of the filtrate are taken. To this 1 c.c. of 20 per cent. sodium carbonate solution is added. This is then placed in a water bath at 100° C. for ten minutes, removed and cooled under the tap and diluted according to strength to an appropriate dilution—12·5 c.c. or 25 c.c. for normal bloods. The mixture is then estimated against a picramic acid standard in the Du Boscq colorimeter—standard being set at 15 mm. The basic standard recommended by Benedict is a solution of 0·64 mg. of glucose dissolved in 4 c.c. of water to which 4 c.c. of picric-picrate glucose solution and 1 c.c. of sodium carbonate (20 per cent. solution) are added—heated for ten minutes in boiling water, cooled and diluted to 12·5 c.c. A solution of picramic acid made up as follows matches this basic standard with the colorimeter set at 15 mm. A stock solution of picramic acid (m.p. 198° C.) containing 100 mg. picramic acid and 200 mg. sodium carbonate per litre is first made. 146 c.c. of this stock solution is taken to which 1 c.c. of 20 per cent. sodium carbonate solution and 15 c.c. picric-picrate solution are added, and the whole made up to 300 c.c. with distilled water. It will be noted that I have found it necessary to modify slightly the standard recommended by Benedict.

An investigation was first carried out by comparing varying strengths of glucose dissolved in 4 c.c. of water to which 4 c.c. of picric-picrate solution and 1 c.c. of 20 per cent. sodium carbonate solution were added, heated at 100° C. for ten minutes, cooled and diluted as follows :

0·64 mg. of glucose treated in this way and diluted finally to 12·5 c.c. matches the picramic standard at 15 mm.

1·28	mg. of glucose—final dilution			12·5	c.c. matches at	7	mm.
1·28	,,	,,	,,	25	,,	14·8	,,
1·92	,,	,,	,,	18·5	,,	7	,,
1·92	,,	,,	,,	25	,,	9·3	,,
1·92	,,	,,	,,	37·5	,,	15	,,
2·56	,,	,,	,,	25	,,	7	,,
2·56	,,	,,	,,	50	,,	15	,,

These results indicate that the amount of reduction of the picric-picrate solution is strictly proportional to the amounts of glucose added, but that the picramic acid so produced undergoes some change on dilution. When the picramic acid is present in too concentrated a form, the readings are too low and sugar percentages calculated from them would be too high. This effect may be corrected by taking a rough reading, diluting to an appropriate degree and then taking a series of exact readings.

The method was then further tested by adding known amounts of glucose to blood of which the natural sugar percentage had been determined. Two series were put up, the blood used being taken from the ear vein of an unanaesthetized rabbit.

Series I.	*Observed B.S. %*	*Calculated B.S. %*
Blood 2 c.c. Final dilution 25 c.c.	0·187	—
Blood 2 c.c.+2·2 mg. glucose. Final dilution 37·5 c.c. Reading 14·7 m.	0·306	0·297
Blood 2 c.c., 4·4 mg. glucose. Final dilution 50 c.c. Reading 15 mm.	0·400	0·407

	Corresponding % as if 2 c.c. Blood were present.	
	Observed.	*Calculated.*
2·2 mg. glucose in 4 c.c. of water treated exactly as the blood samples above. Final dilution 25 c.c.	0·225	0·220

Series II.	*Observed B.S. %*	*Calculated B.S. %*
2 c.c. blood. Reading 17·5	0·171	—
2 c.c. blood+0·275 mg. glucose Reading 16·8.	0·179	0·184
2 c.c. blood+0·55 mg. glucose. Reading 15·0.	0·200	0·198
2 c.c. blood+0·825 mg. glucose Reading 14·5.	0·207	0·212

In making observations on the blood sugar of small animals, e. g. cats and rabbits, two complicating factors had to be considered—haemorrhage due to the taking of samples and emotional disturbance in non-anaesthetized animals. It was not possible to eliminate the second factor, and consequently the blood-sugar determinations recorded are frequently too high, *vide* Scott (1914). This, however, does not invalidate my conclusions as it is true of all the observations

on normal cats and rabbits. The haemorrhage effect of taking three or four small bleedings of 2–3 c.c. each was found in control experiments to cause no appreciable rise in the blood sugar, though more considerable haemorrhages, as Epstein and Bahr (1914) have shown, cause a marked hyperglycaemia.

It will be convenient to deal first with the observations on the general effects of anoxaemia before proceeding to those concerned with the more specific subject of inquiry in this investigation.

3. General Effects of Anoxaemia.

It became evident early in the research that most of the experimental work would have to be done under conditions uncomplicated by anaesthesia. Hill and Flack (1908) investigated the respiratory response of the dog and cat under light anaesthesia to atmospheres poor in oxygen but containing excess of CO_2. They obtained graphic records of the respiration of animals under experiment. Though it was not possible to obtain such records in non-anaesthetized animals, caused to breathe atmospheres containing diminished quantities of oxygen by placing them under the bell-jar of the Dreyer apparatus, an opportunity was afforded for observation of the respiration and other effects of anoxaemia of varying degree and duration. These observations were made in greatest detail upon the cat.

The respiration rate of a cat, under normal conditions, was somewhat irregular in rhythm, the rate varying between 25 and 30 per minute. The inhalation of an atmosphere containing 10·4 per cent. of oxygen caused an almost immediate increase in the rate of breathing to 37 and after ten minutes to 44 per minute. The depth of the respiration likewise increased. The animal breathed with its mouth open and tongue protruding. After about fifty minutes the respirations were 30 per minute and much more efficient, so that the animal appeared to be more comfortable. After eighty minutes' inhalation of this atmosphere the percentage of oxygen present was reduced to 8 per cent. The cat responded at once by becoming restless and excited. It exhibited an unusual degree of dyspnoea, for during the first ten minutes after this change of atmosphere the respirations increased to the extraordinary rate of 240 per minute, but were very shallow. The mouth remained open and the animal salivated freely. After twenty minutes the breathing was much deeper, the frequency was 64 per minute and the animal appeared to be much more comfortable. It was now removed from the bell-jar. The heart-beat was forcible and regular and the respiration rate quickly subsided to normal. The cyanosis of the mucous membranes, which had been marked throughout the period of anoxaemia, did not completely disappear for some minutes.

Another cat of 2,400 grm. weight was placed under the bell-jar of the Dreyer apparatus and there subjected for one and three-quarter hours to an atmosphere containing 10·4 per cent. of oxygen. In this case the respiratory response was not nearly so marked as in the previously recorded experiment. The normal rate of respiration was 24 per minute, and when the inhalation of the mixture poor

in oxygen was started this rose to 33 per minute. There was, however, marked increase in the depth of respiration, and though after a quarter of an hour the rate had fallen to 20 per minute, the depth had continued to increase. During this first period of anoxaemia the cat was comfortable and slept part of the time. The percentage of oxygen was now reduced to 9·2 per cent. This corresponds to that obtained at about 22,000 ft., and was maintained for one and a quarter hours. At the beginning of this period the cat exhibited some dyspnoea, but towards its end the respiration was about normal in rate, though excessive in depth. The animal salivated freely and vomited during this time.

After three hours' exposure to an atmosphere poor in oxygen, anaesthesia was commenced with ether by the method described above, the animal remaining in the bell-jar and the percentage of oxygen in the air being increased to 10·6 per cent. When the cat was thoroughly anaesthetized it was removed from the bell-jar and rapidly tracheotomized, and the administration of anaesthetic, together with the mixture of air and nitrogen, was continued. The blood-pressure was recorded and was found to be 160 mm. Hg, a height which was steadily maintained for considerably over an hour. The output of the heart remained good and the heart-beats were regular during this period.

It was evident that prolonged anoxaemia of this degree did not produce any notable change in the efficiency of the circulation.

In cats breathing mixtures containing 7 per cent. of oxygen a characteristic rapid shallow type of breathing with occasional deep sighing inspirations was frequently observed. It is probable that this phenomenon, like the rapid shallow breathing observed in men after gas poisoning by Haldane, Meakins, and Priestley (1918), is explained by a derangement of the normal relation existing between the Hering-Breuer reflex and the regulation of the breathing by chemical stimuli. The administration of atmospheres, containing 7 per cent. of oxygen and over, never caused, in my experience, any loss of consciousness, nor was the animal's sight or hearing evidently affected.

In cats with unpigmented feet, to which mixtures of air and nitrogen were administered by means of a mask, the appearance of the pads afforded useful evidence of the degree of anoxaemia produced. When this was severe the pads became cyanosed and sweated freely.

The respiratory changes observed in the goat were less, and in the rabbit more marked for corresponding degrees of anoxaemia than those observed in the cat.

Despite the fact that determinations of the percentage of oxygen saturation of the arterial blood afford the only absolute index of the degree of anoxaemia produced in an animal, I have not complicated the interpretation of the results of experiments on small animals by taking additional blood samples for this purpose. Observations of the condition of the pads and mucous membranes have been used as evidence of the fact that anoxaemia was being produced. A few observations have been made on the percentage oxygen saturation of the venous blood in the goat, in which animal blood

samples of considerable size could be removed without affecting the haemoglobin value. The observations were made by the method described by van Slyke (1918). The normal content of oxygen in saturated blood for a goat of 15 kilos was 11 volumes per cent. The venous blood normally contained 7·4 volumes, and after inhalation for fifty-five minutes of a mixture containing 8·5 per cent. of oxygen, 3·8 volumes per cent. The percentage oxygen saturation of the venous blood had fallen from 67·3 per cent. to 34·5 per cent. On another occasion the percentage oxygen saturation of the venous blood of the same animal was 62 per cent. before exposure for an hour and a half to an atmosphere containing 9 per cent. of oxygen, and fell to 31·4 per cent. at the end of this period.

4. Effects on the Alkali Reserve of the Plasma and on the Volume of the Blood in Effective Circulation.

Reference has already been made to the recent work on the alkali reserve in shock, gas gangrene, and allied conditions. Observations have been made on the cat and goat in which severe anoxaemia was produced. A few experiments sufficed to show that the diminution of the capacity of the plasma for combining with carbon dioxide was a small and generally evanescent effect, which could not be regarded as playing any serious part in the production of the symptoms following anoxaemia of the degree here in question. The estimations were carried out by the method of van Slyke (1917) on blood obtained from the jugular vein of the animal. To avoid loss of CO_2 before separation of the corpuscles, the blood was transferred, as indicated by van Slyke, directly to centrifuge tubes containing a little dry powdered oxalate covered by a layer of liquid paraffin, and immediately centrifuged.

The experiments were uncomplicated by anaesthesia, and in the cat the effect of haemorrhage (*vide* Milroy (1917)) on the values obtained was eliminated by a suitable control.

A goat weighing 15 kilos inhaled by means of a mask an atmosphere containing 11·4 per cent. O_2 for twenty-five minutes and for the ensuing fifty-five minutes one of 8·5 per cent. The blood samples were of 12 c.c. each. There was no change in the haemoglobin percentage, which was 58 per cent. throughout. The degree of anoxaemia produced is shown by the percentage oxygen saturation of the venous blood which fell from 67·3 per cent. to 34·5 per cent. Before anoxaemia the alkali reserve was 63·9 per cent., immediately after it was 62·0 per cent. and one hour later it was 57·8 per cent.

A cat of 2,300 grm. which, while in the bell-jar, inhaled for one hour and forty minutes an atmosphere containing 7 per cent. of oxygen gave the following results :

Time.	*Hb. %.*	*% CO_2 combining capacity.*
10.20 a.m.	76	34·9
10.40–12.30, cat under the bell-jar.		
12.25 p.m.	72	33·6
2.30 p.m.	62	29·0
3·30 p.m.	74	34·0

Another cat of 3,500 grm. was bled at the following time intervals

without being made anoxaemic. Four samples each of 6 c.c. were taken :

Time.	*Hb. %.*	*% CO_2 combining capacity.*
12·15 p.m.	100	48·6
12·30 p.m.	100	46·8
1·0 p.m.	97	47·8
2·5 p.m.	92	46·0

A week later its weight was 3,600 grm. ; three samples of 6 c.c. were taken and between the first and second bleedings the cat was placed in the bell-jar of the Dreyer apparatus and breathed an atmosphere containing 7·6 per cent. of oxygen.

Time.	*Hb. %*	*% CO_2 combining capacity.*
11·5 a.m.	90	45·8
11.23–11.58 a.m. anoxaemia 7·6 % oxygen.		
12·5 p.m.	90	40·0
1·5 p.m.	87·3	44·9

It is evident from these results that the reduction of the alkali reserve of the plasma due to diminished tension of oxygen in the air breathed and in the circulating arterial blood is not comparable to the severe reduction which occurs when the peripheral circulation through the capillaries is defective even though the arterial blood is saturated with oxygen (*vide* M. R. C. report, 1918). The values obtained for the haemoglobin percentage in these and other experiments did not afford any evidence of loss of volume of the circulating blood. A few direct observations were made on this point using the vital red method introduced by Keith, Rowntree, and Geraghty (1915).

In control experiments on the cat and rabbit, successive determination of the volume of the circulating plasma could be made at one or two hours' interval, with fairly concordant results. When these animals were rendered anoxaemic during the interval between the observations the volume of the plasma was not found to undergo any diminution but rather a slight increase, as the following tabulated observations show :

Animal under experiment.	*Degree of anoxaemia.*	*Initial plasma volume.*	*% corpuscular volume by haematocrit.*	*Initial blood volume.*	*Final plasma volume.*	*% corpuscular volume by haematocrit.*	*Final blood volume.*
Rabbit, 1,850 grm.	Control	60 c.c.	35	92 c.c.	65 c.c. (4 hrs. later)	32·5	96 c.c.
Rabbit, 2,600 grm.	Control	122 c.c.	30·8	177 c.c.	116 c.c. (40 min. later)	32·8	173 c.c.
Rabbit, 2,600 grm.	7 % O_2, 1 hr.	100 c.c.	30·9	145 c.c.	107 c.c.	32·6	158 c.c.
Rabbit, 3,000 grm	7 % O_2, 1 hr.	108 c.c.	29·3	150 c.c.	110 c.c.	24·9	146 c.c.
Cat, 2,500 grm.	9·5 % O_2 1 hr. 35 min.	100 c.c.	35·2	154 c.c.	109 c.c.	35	168 c.c.

In these animals it appears that any small changes in the volume of the circulating blood which may occur as a result of anoxaemia are not detectable with any certainty by this method. There is not, however, any evidence of diminution in volume of the plasma but rather the contrary.

The injection of vital red into a goat of 15 kilos weight was followed by toxic symptoms, and whereas, in the same animal, anoxaemia uncomplicated by such an injection caused no change in the haemoglobin value (*vide supra*), the inhalation of 9 per cent. oxygen for one and a half hours produced on this occasion an increase in the corpuscular content of the blood accompanied by a corresponding increase in the haemoglobin value, as determined both colorimetrically and by calculation from the oxygen-carrying capacity of the blood.

The estimation of the volume of the plasma showed, not a fall in correspondence with this rise in corpuscular content, but an apparent large increase. It is evident, therefore, that in this animal the vital red injected does not remain in the circulating plasma for any appreciable time, and that the results obtained for the volume of the plasma are not to be relied upon.

In one experiment on a dog, although no toxic symptoms were noted, the results obtained for the volume of the plasma showed a large increase as a result of inhalation of an atmosphere containing 8 per cent. oxygen for one hour. At the same time the corpuscular content of the blood was diminished, as shown by a fall in the haemoglobin percentage and directly by haematocrit, though not sufficiently to be in accord with the plasma volume determinations.

It is to be noted that any influence which makes the vital red leave the circulation at more than the normally very slow rate will increase the apparent volume of the plasma. The apparent increase shown in some cases, without a corresponding fall in the proportion of corpuscles, is probably fallacious.

5. The Effect of Anoxaemia on the Output of Adrenalin and on the Blood Sugar.

A. *The Paradoxical Pupil Reaction.*

In cats in which one pupil has been partially denervated by the removal some days before of the corresponding superior cervical ganglion, this sensitized pupil is normally, under conditions of bright illumination, slightly smaller than its fellow. The nictitating membrane is partially prolapsed and the palpebral fissure narrowed on the denervated side.

When the animal is asphyxiated by one of the methods described above, the following changes constantly occur. As soon as the mask is removed both pupils are found to be widely dilated. Half a minute later, the pupils being illuminated meanwhile, either by daylight or by means of an electric filament lamp, symmetrically placed at a fixed distance from the animal's eyes, the normal pupil is contracted down to a slit while the denervated one remains dilated for a variable period. At the end of the asphyxia the nictitating membrane on the denervated side is retracted and the palpebral

fissure wider than that on the normal side. As the denervated pupil contracts the nictitating membrane prolapses and the palpebral fissure becomes narrower.

This reaction is known as the paradoxical pupil reaction. It was first described by Budge (1855). Anderson (1903) gave an historical account of the investigations concerning it which had been carried out up to that time. He obtained the reaction in excitement, asphyxia, and in anaesthesia, and observed that it could be elicited twenty-four hours after the removal of the ganglion and for more than a year afterwards. Meltzer and Auer (1904) showed that it occurred as a result of the injection of adrenalin.

Dale and Laidlaw (1912) used the reaction in investigating the action of certain alkaloids on the adrenal glands. Elliott (1912) arrived at the conclusion that the secretion of adrenalin ' is the cause of nearly all the phenomena of paradoxical pupillodilatation '. He observed that when one superior cervical ganglion was removed in the adult cat, and when subsequently the suprarenals were removed, the dilatation of the corresponding pupil, which before the second operation had followed emotional excitement or light asphyxia, was no longer present, though deep asphyxia still gave dilatation of the denervated pupil in the terminal spasms. Stewart and Rogoff (1916 b), however, observed that in cats in which one suprarenal had been removed and the splanchnics of the opposite side divided, fright, asphyxia, and anaesthesia with ether gave reactions of the denervated pupil ' which did not differ from those reactions in cats whose suprarenals had not been interfered with '. The same workers (1916 a), using their ' pocket ' method in cats under urethane anaesthesia, observed the effects produced by asphyxia on the output of adrenalin as measured by the effect of suprarenal vein blood on the blood-pressure and on the denervated pupil. Their results in these experiments may be interpreted as indicating a slight increase in the output of adrenalin in this condition. They pointed out, however, that the effect of asphyxia in producing rise of blood-pressure and dilatation of both pupils, apart from the effect due to the suprarenals, made it difficult to use these reactions as a measure of the output of adrenalin, and that such positive results as they obtained were capable of interpretation as resulting from increased rate of filling of the caval ' pocket ' with adrenal blood, due to the rise in blood-pressure caused by asphyxia. They also referred to the possibility that the extensive operative procedures adopted in these experiments might, by diminishing the secretion of adrenalin, vitiate any negative conclusions arrived at in this way. In Stewart's experiments the use of the reaction of the denervated pupil as an index of increased output of adrenalin in asphyxia has yielded results difficult of interpretation, because no attempt was made to graduate the severity of the asphyxia used.

Reviewing the evidence I concluded that it was safe to proceed on the assumption that, in the unanaesthetized animal, the paradoxical dilatation was an index of accelerated output of adrenalin in anoxaemia and asphyxia, except in the case of the residual effects, which extreme asphyxia produces even after both suprarenal glands have been removed. The correctness of this assumption received cumula-

tive confirmation as the work proceeded and the points of evidence can most conveniently be noted in connexion with the experiments in which they arose.

Special attention was paid to the extent of the reaction. This may be gauged by (1) the size and shape of the dilated sensitized pupil relative to its fellow of the opposite side and (2) the time taken by the sensitized pupil to attain equality to its fellow. Half a minute after this equality has been attained the denervated pupil was invariably found to have become once more smaller than the normal one. If the effect produced is a maximal one the denervated pupil is circular in outline and only the narrowest margin of iris is visible at its circumference. In less marked reactions angulation is evident in the outline of the pupil at each extremity of its vertical diameter. The time during which the preferential dilatation persists, that is to say the time elapsing between the cessation of the asphyxia and the attainment of equality by the two pupils, varies from ten minutes to less than one minute, according to the severity of the asphyxia and the sensitiveness of the reaction in the particular cat under experiment.

B. *The Part played by Want of Oxygen and by Excess of CO_2 in producing Acceleration of the Output of Adrenalin and Hyperglycaemia in Asphyxia.*

The following experiments upon cats in which the right superior cervical ganglion had been previously removed[1] were made to decide the question of accelerated output of adrenalin. The full experimental details of these and other experiments will be given in another paper.

Cat 1.

1. 11. 18. Removal of the right superior cervical ganglion under ether anaesthesia with aseptic precautions.[1]

2. 12. 18. Cat tied out on the table. No anaesthetic administered. The effects on the pupils of asphyxia, anoxaemia, and excess of CO_2 respectively were observed. Mixtures containing known percentages of CO_2 and of oxygen were passed through a mask which was applied to the animal's face.

a.m.

11.32–11.37. Animal inhaling atmospheric air circulating through the mask.

11.37. No preferential dilatation observed.

11.53–11.58. Animal inhaling a mixture of air and nitrogen containing 7 per cent. O_2.

11.58. Maximal preferential dilatation of the sensitized pupil which persisted for seven minutes.

p.m.

2.38–2.54. Animal inhaling atmospheric air containing 7·4 per cent. of CO_2.

[1] All the operative procedures after which the animal was allowed to recover were kindly performed for me by Dr. H. H. Dale, F.R.S.

p.m.	
2.54.	No preferential reaction observed.
3.17–3.21.	Asphyxia. Mask in position and 6 ft. 9 in. of rubber tubing attached to it.
3.21.	Maximal preferential pupillary reaction which lasted seven minutes.
3.35–3.40.	Animal inhaling atmosphere containing 6·6 per cent. CO_2.
3.40.	No preferential reaction.
3.40–3.47.	Animal inhaling the same mixture.
3.47.	No preferential reaction.

Cat 2. In this animal the effects of the inhalation of atmospheres containing excess of CO_2 and diminished amount of oxygen were contrasted. The right superior cervical ganglion had been removed a month before. The animal was under urethane anaesthesia, and the mixtures were administered by means of a tracheal cannula with inlet and outlet valves.

The inhalation of an atmosphere containing 6·7 per cent. of CO_2 and 19·4 per cent. of oxygen caused no preferential dilatation of the sensitized pupil. The inhalation of an atmosphere containing only 6·8 per cent. of oxygen for four minutes, on the other hand, caused dilatation of both pupils, the sensitized pupil dilating more than its fellow. When air was once again flowing through the cannula the sensitized pupil went on dilating while the normal one contracted till the preferential reaction was almost maximal half a minute after the flow of pure air had commenced. The reaction persisted for seven minutes.

Cat 5. In this animal the right superior cervical ganglion had been removed aseptically under ether eight days before. The following experiments were conducted without anaesthesia. Asphyxia, produced by making the cat breathe into the mask connected with a tube 7 ft. long for four minutes, caused a maximal preferential dilatation of the sensitized pupil which lasted for five minutes. Circulation of atmospheric air through the mask as a general rule caused no reaction, though once a very small and evanescent preferential dilatation of the sensitized pupil was observed. This effect was probably due to emotional causes, as the cat was angry and excited at the time. The animal also inhaled mixtures containing 10 per cent. and 16·5 per cent. of CO_2 respectively. In the first case no reaction was observed, and in the latter the barely perceptible preferential dilatation which was observed may have been due to emotional causes, as the cat struggled a good deal and was very excited. The animal also inhaled mixtures containing 13, 11, 10, 7·5, and 6 per cent. of oxygen respectively with resulting paradoxical pupil reactions which were greater as the anoxaemia became more severe. The inhalation of an atmosphere containing 6 per cent. of oxygen for five minutes, and of pure nitrogen for one minute, both resulted in maximal preferential dilatation of the sensitized pupil which persisted for five minutes.

These and a number of similar experiments made at this time seemed to indicate that the paradoxical pupillary reaction which

occurs in asphyxia is due entirely to the diminution of oxygen and not to excess of CO_2 in the air breathed, and that its duration and extent depends very largely upon the degree of anoxaemia produced. More recent observations have shown that the inhalation of mixtures containing percentages of CO_2 of the order of 15 per cent. regularly cause small paradoxical reactions.

The following experiments upon goats and cats were made to investigate the hyperglycaemia of asphyxia.

A goat weighing 15 kilos whose initial blood sugar was 0·101 per cent. was asphyxiated for three minutes by breathing into a mask to which a bag was attached. A sample of the air from the bag at the end of three minutes contained 7·8 per cent. of CO_2 and 12·3 per cent. of oxygen. The blood sugar rose to 0·136 per cent. On another occasion the administration of an atmosphere containing 3·5 per cent. of CO_2 for half an hour caused a slight fall in the blood sugar from 0·100 per cent. to 0·097 per cent. The inhalation of a mixture containing 7·3 per cent. of CO_2 caused a further fall to 0·091 per cent.

A cat weighing 2,300 grm. whose initial blood sugar was 0·130 per cent. inhaled from a mask a mixture containing 7 per cent. of CO_2. After twelve minutes its blood sugar was 0·120 per cent. and half an hour later it was 0·125. On the same day some hours afterwards, seven minutes' asphyxia produced by re-breathing through a long tube attached to the mask caused a rise of blood sugar from 0·120 to 0·306 per cent.

Some later observations upon cats on the effect of excess of CO_2 yielded results which were difficult of interpretation, because of the large rise of blood sugar which occurred from emotional causes. One such animal which gave initial sugar values of 0·128 and 0·130 per cent., when samples were taken immediately after tying out upon the table, gave an initial blood sugar of 0·193 per cent. when tied out for seven minutes before taking the sample. When tied out for a similar period, during five minutes of which an atmosphere containing 15 per cent. CO_2 and 17 per cent. oxygen was inhaled, the blood sugar rose from 0·130 to 0·222 per cent. Now during a similar period of inhalation of the same mixture there was a fall in the oxygen content of the venous blood, which in itself was sufficient to account for the excess of rise over and above that which occurred as a result of emotional excitement.

In another cat, whose blood sugar was not so sensitive an index emotional excitement, a small rise of blood sugar was obtained with the inhalation of an atmosphere containing 5 per cent. CO_2, though no rise was noted as a result of the inhalation of air by the mask for the same period. The inhalation of a mixture containing 15 per cent. CO_2, but with the oxygen content reduced to 17 per cent., showed a rise in the blood sugar from 0·119 to 0·197 per cent.

In still another cat, which had had the right superior cervical ganglion excised aseptically under ether some days before, and in which the blood sugar was very sensitive to emotional disturbance, the inhalation of 5 per cent. CO_2 for five minutes gave a rise from 0·206 to 0·240 per cent. in the blood sugar. The inhalation of atmospheric air for the same period gave a rise which was quite comparable with this, i. e. from 0·176 to 0·206 per cent. In neither

case was there any paradoxical dilatation of the pupil. When, however, an atmosphere containing 15 per cent. of CO_2 and 17 per cent. of oxygen was inhaled for the same period, the blood sugar rose from 0·240 to 0·349 per cent. and there was at the same time a small but definite paradoxical reaction lasting for one minute.

The inhalation of a mixture containing 17 per cent. of oxygen without excess of CO_2 gave no pupil reaction, but caused a rise in the blood sugar from 0·154 to 0·209 per cent.

Of the three possible factors, emotional disturbance, anoxaemia, and excess of CO_2, which might be regarded as playing some part in the production of these effects of asphyxia, there can be no doubt about the rôle of the first two. Mathison (1910–11) has demonstrated the effectiveness of high percentages of CO_2 in stimulating the bulbo-spinal centres, and from the observation recorded above it is evident that percentages of CO_2 of the order of 15 per cent. can cause acceleration of the output of adrenalin and hyperglycaemia. The part played by excess of CO_2 in asphyxia requires further investigation.

For the present purpose it is sufficient to know that anoxaemia can by itself cause both these effects of asphyxia.

C. *Does Anoxaemia of the Degree and Duration met with in Flying at High Altitudes suffice to produce these Effects?*

The evidence submitted later in connexion with the mechanism of production of these effects cannot be adduced in answer to this question, because for this latter purpose it was found convenient to make the experimental animals inhale atmospheres deficient in oxygen to varying extent for very brief periods, e. g. five to six minutes, and the change from normal air to such atmospheres was sudden and not at all comparable to the more gradual diminution of oxygen tension during the ascent to a height. It was not to be expected that such definite pupil reactions would be obtained with gradual as with sudden development of anoxaemia.

Some experiments with *Cat* 5, before its splanchnic nerves were divided, in which the animal was rendered anoxaemic by being placed under the bell-jar of the Dreyer apparatus, pointed to this conclusion. Inhalation of 13·3 per cent. oxygen for five minutes by means of the mask gave in this cat a definite preferential pupil reaction. When the animal inhaled 9 per cent. oxygen under the bell-jar and some three or four minutes were taken in reducing the oxygen content of the air breathed to this level, though the nictitating membrane was retracted no definite pupil reaction was obtained. When the oxygen present in the mixture was further reduced to 7 per cent. a definite pupil reaction was obtained after five minutes.

This sort of result suggested that the emotional disturbance produced by tying the animal out on the table and administering mixtures deficient in oxygen by means of a mask had a distinctly adjuvant effect on the acceleration of the output of adrenalin by anoxaemia.

No difficulty was experienced in showing that anoxaemia of the degree associated with high flying is sufficient to cause hyperglycaemia, though brief, suddenly produced anoxaemia is much more potent in causing rise of blood sugar than prolonged anoxaemia with more

gradual onset. A partial explanation is to be found in this case in the fact that time is allowed for the excretion of sugar in the urine.

There is nothing new in the production of glycosuria by anoxaemia. Araki (1891) produced glycosuria in animals rendered anoxaemic to unknown degrees, and showed that at the end of such experiments their blood contained excess of sugar.

I have made experiments on rabbits, cats, and goats, which for this purpose were not anaesthetized. A rabbit weighing 2,300 grm. with an initial blood sugar of 0·189 per cent. was placed under the bell-jar of the Dreyer apparatus. The bell-jar was ventilated with atmospheric air for half an hour and at the end of this time the blood sugar had risen to 0·197 per cent. The inhalation of an atmosphere containing 8 per cent. of oxygen for an hour caused a rise in the blood sugar to 0·272 per cent. A control animal bled at corresponding time intervals gave successive blood sugar readings of 0·176, 0·176, 0·167, and 0·166 per cent. Successive haemorrhages of 2½ c.c. in this animal did not cause any rise in the blood sugar. The additional emotional disturbance caused in the experimental animal by placing it under the bell-jar caused a small rise from 0·189 to 0·197 per cent.

A cat of 2,800 grm. weight, with a normal blood sugar of 0·131 per cent., was placed under the bell-jar through which atmospheric air was circulating. After thirty-five minutes its blood sugar was found to be unchanged. The percentage of oxygen in the atmosphere breathed by the animal was then lowered to 7·3 per cent. and the cat remained under the bell-jar for over two hours at the end of which time its blood sugar was 0·156 per cent. Forty-five minutes later it had risen still further to 0·175 per cent., and two hours after the period of anoxaemia it was 0·123 per cent.

A goat of 14 kilos with an initial blood sugar of 0·077 per cent. inhaled by means of a mask a mixture containing 11·4 per cent. of oxygen. After twenty-five minutes the percentage of oxygen was further diminished to 5·5 per cent. After the inhalation of this atmosphere for rather less than an hour the blood sugar was 0·098 per cent. and an hour later, during which time the animal breathed normal air, its blood sugar had once more returned to 0·078 per cent.

There can be no doubt from the experimental evidence submitted that anoxaemia of the degree met with in high flying is capable of causing hyperglycaemia, and while the accelerated output of adrenalin under the same circumstances is more difficult to demonstrate its occurrence may reasonably be inferred.

D. *The Nature of the Mechanism by which Anoxaemia causes Accelerated Output of Adrenalin and Increase in the Blood Sugar.*

In order to investigate the manner in which anoxaemia produced these effects, experiments were made upon cats in which the right superior cervical ganglion had been removed some days previously. Two separate kinds of experiment were made. In one, such cats were anaesthetized with volatile anaesthetic and subsequently with urethane. Pure nitrogen was administered for short periods by means of a tracheal cannula provided with inlet and outlet valves

before and after removal of the suprarenal glands, or with and without occlusion of the aorta above the origin of the vessels supplying these organs. Finally, the animals were killed and observations were made on the isolated iris preparations in oxygenated Ringer's solution, by the method devised by Dale and Laidlaw (1912).

In the other type of experiment the blood-sugar change and pupil reactions were studied in cats with sensitized pupils which were not under anaesthesia when the observations were made. Various mixtures of air and nitrogen were administered by means of a mask for short periods (five minutes) and the maximal oxygen content of the mixture necessary to produce (1) rise in blood sugar, and (2) preferential dilatation of the denervated pupil was determined.

(i) In the intact animal.
(ii) In the animal in which all the splanchnic fibres had been divided proximal to the semilunar ganglion some days before, and time allowed for the cat to get back to its normal weight.
(iii) In the animal with the splanchnics divided and the adrenal glands removed. Time was allowed for the effect of the anaesthetic to pass off, but the observations were made before definite symptoms due to removal of the suprarenals had occurred.
(iv) In other cats with the splanchnic fibres intact but with the adrenals removed. Here again the observations were made before the symptoms due to decapsulation had appeared.

In this report I propose to state only the general results of these experiments. The full protocols will be published later.

(a) *Experiments under urethane anaesthesia and observations on the iris preparations in vitro.* In these experiments the administration of a volatile anaesthetic caused a preferential dilatation of the denervated pupil which was not, however, very marked under urethane, but which in some animals made it difficult to say when a paradox due to anoxaemia had passed off.

Before removal of the suprarenal glands the administration of pure nitrogen for one and a half minutes caused dilatation of both pupils. As soon as the inhalation of nitrogen was stopped the normal pupil contracted down rapidly, while the denervated one remained dilated for some minutes. This reaction was often almost maximal. After the suprarenal glands had been removed a similar administration of nitrogen gave quite a different pupil reaction. Though both pupils dilated somewhat while the nitrogen was being inhaled—the normal one now rather more than the sensitized one—as soon as air was once more passing through the cannula they contracted down quickly. The preferential dilatation of the denervated pupil was no longer present in response to this degree of anoxaemia when the suprarenal glands had been removed.

Similar results were obtained by occluding the aorta above the level at which the arterial supply to the suprarenal was given off. Anoxaemia during such occlusion did not give rise to any paradoxical pupil reaction or only to a very trivial effect, but a marked preferential reaction appeared when the vessel was released.

In order to analyse the changes in the pupils which resulted from anoxaemia in the urethanized animal use was made of isolated iris preparations. It was important to know what the direct effect of urethane was upon the normal and upon the denervated iris, and whether the paradox which occurred under urethane anaesthesia was due to the direct action of the drug on the denervated dilator of the iris, or was produced indirectly by stimulating suprarenal activity. The effect of anoxaemia upon the isolated preparations was also of interest because of its bearing upon the ' residual paradox ' which sometimes occurred in severe anoxaemia after the adrenals had been removed. These preparations were made from the excised eyeballs by cutting away the sclerotic just behind the cornea-sclerotic junction. The cornea was likewise cut away and the lens removed. Any tags of lens capsule or suspensory ligament were carefully clipped off with scissors and the iris was left supported by a stout ring of cornea-sclerotic junction tissue. The preparations were placed in a beaker containing 250 c.c. of Ringer's solution at a temperature of 36–37° C. which rested on a white tile in a constant temperature bath.

In such preparations the pupils rapidly contracted down till they were equal slits when oxygen was bubbled through the Ringer. The addition of adrenalin to the oxygenated Ringer so as to make a 1 in 2,500,000 solution caused a well-marked preferential effect in such a pair of isolated irises. The normal iris remained contracted while the denervated one dilated up to about half the size of a maximal dilatation in the living animal. Adrenalin in the strength of 1 in 25,000,000 did not give any result.

When the Ringer was changed the dilatation of the denervated pupil gradually passed off and the pupils were once more equal and contracted. The addition of 1 grain of urethane dissolved in 10 c.c. of saline so as to make a 1 in 260 solution with the fresh oxygen at Ringer also caused a preferential effect, the normal pupil remaining contracted while the denervated one dilated, not, however, to such an extent as it did with adrenalin of the strength mentioned above. When the Ringer was once again changed this inequality of the pupils gradually disappeared.

When nitrogen was bubbled through the Ringer in place of oxygen a gradual and equal dilatation of both pupils occurred. This dilatation was not a very large effect and never exceeded about one-fourth of the full dilatation of the pupil as observed in the living animal. The replacement of the nitrogen by oxygen caused the pupils to contract down to slits once more. There was no trace of any direct preferential action of anoxaemia upon the denervated dilator.

The effect of urethane and of adrenalin was also tested when nitrogen instead of oxygen was bubbled through the Ringer. It was found that the preferential effects still occurred though now the normal pupil was somewhat dilated and the denervated one more so than during the application of a similar dosage to the preparations when the Ringer was oxygenated.

(b) *Experiments on unanaesthetized cats in which the right pupil had been previously sensitized by removal of the corresponding superior cervical ganglion.*

(i) *Results in the cat with intact splanchnics and suprarenals.* It was occasionally found that when the animal was excited and when it struggled a good deal while being tied down for the experiment there was a preferential dilatation of the denervated pupil. A similar result was sometimes obtained when air was inhaled through the mask for five minutes. Such effects were by no means invariable and varied in different cats and even in the same cat at different times. For instance, when several observations were made on a cat in the course of a day, it became more excitable and more easily gave the reaction. These effects however were, when present, small in extent and short in duration compared with the reactions resulting from anoxaemia.

There was some variation in the sensitiveness of different animals to anoxaemia. Generally speaking, percentages of oxygen as high as 13 and 14 per cent. administered for five minutes gave definitely recognizable preferential reactions and the reaction obtained became more marked as the mixtures breathed contained less oxygen. Mixtures containing 5 per cent. oxygen breathed for five minutes usually produced maximal preferential dilatation of the denervated pupil and the effect lasted several minutes.

The increase in the blood sugar was found to be much more easily influenced by excitement. Mere application of the mask ventilated with pure air was found to cause a small rise in the blood sugar and mixtures containing more oxygen than those necessary to give pupil reactions gave a well marked increase in the blood sugar.

It was conceivable that changes in the blood sugar were a more sensitive index of accelerated output of adrenalin than was the paradoxical reaction. It was found that 0·1 c.c. of 1 in 200,000 adrenalin injected into the ear vein gave a well marked rise in the blood sugar without giving any pupillary paradox. It was also possible that excitement and anoxaemia alike stimulated the central nervous system and through sympathetic stimulation caused increased mobilization of sugar by the liver. There was, however, no evidence in the experiments under discussion as to which of these explanations should be invoked to explain the greater sensitiveness of the blood-sugar changes to anoxaemia and to emotional excitement. It did not appear to be possible to differentiate these two effects. That the second suggested explanation is partly responsible is indicated by the behaviour of animals in which the adrenals have been removed leaving the splanchnics intact. At all events in the normal animal the inhalation of mixtures containing, say, 10 per cent. of oxygen, which caused only a moderate pupil reaction, frequently doubled the percentage of sugar in circulation.

(ii) *Results in the cat with the splanchnics divided proximal to the semilunar ganglion but with the adrenals intact.* The splanchnics were divided in these cats through two flank incisions under ether anaesthesia with full aseptic precautions by Dr. H. H. Dale. After some days, during which the only noticeable symptom which followed the operation was diarrhoea, when the cat had regained its normal weight and its operation wounds were soundly healed, observations were made as in the normal animal before division of the splanchnics.

Section of the splanchnics was found to abolish completely the effects of emotional excitement both on the blood sugar and on the output of adrenalin. Further, the 'threshold value' of anoxaemia required to cause these effects was now more severe than in the intact animal.

In one cat it was found that only atmospheres containing percentages of oxygen sufficiently small to cause a definite pupil reaction now gave rise to increase in the blood sugar. For instance, before and after the inhalation of an atmosphere containing 10 per cent. of oxygen, the blood sugar was 0·108 per cent. and the inhalation caused no paradoxical dilatation of the pupil. An atmosphere containing 9 per cent. oxygen on the other hand, which gave a definite preferential pupil reaction when inhaled for the same time, also caused a rise of the blood sugar from 0·108 to 0·182 per cent. Repeated observations on this cat showed that for the production of both the accelerated output of adrenalin and hyperglycaemia the 'threshold value' was the same, about 9 per cent. This somewhat unexpected result, in view of the fact that amounts of adrenalin too small to cause a pupil reaction are efficient in producing a rise in the blood sugar, was not an invariable phenomenon after section of the splanchnics. In another cat the 'threshold value' for the production of hyperglycaemia was, as might be expected, a somewhat less severe grade anoxaemia than that required to produce a pupillary paradox, but a very much more severe degree of anoxaemia was required to produce both these results than in the same animal before the splanchnics were divided.

So definite is the picture presented by the animal with its splanchnics divided that in two cats in which the operation of division of these nerves was attempted it was possible to decide that some of the splanchnics had not been divided at operation. In one case this was confirmed at autopsy and in the other a second operation was successfully carried out for the division of the remaining intact fibres.

(iii) *Results in the cat with the splanchnic nerves divided and the adrenal glands removed.* The adrenals were removed under full ether anaesthesia with aseptic precautions by Dr. H. H. Dale. Great care was taken in these operations to secure absolute haemostasis. The cats usually lapped milk within a couple of hours of the end of the operation, and five hours after this time, when they had completely recovered from the anaesthetic, they were practically indistinguishable from normal animals. They walked about the laboratory of their own volition and sprang down from benches and tables when placed there.

The effect of the removal of the adrenals in animals whose splanchnics had already been divided was to make them still more insensitive to anoxaemia as far as its effect on the output of adrenalin and the blood sugar were concerned. For instance, in the cat referred to in the previous section, in which a certain parallelism had existed after the section of the splanchnics between accelerated output of adrenalin and hyperglycaemia, this parallelism appeared to persist after removal of the suprarenals. Before this latter operation the inhalation of an atmosphere containing 9 per cent. of oxygen produced both these effects, whereas after the removal of the glands the administration

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5 per cent. oxygen for five minutes gave a small residual paradox which lasted for over five minutes to equality. It was eight minutes before the normal pupil relations were again established. One hour afterwards the inhalation of pure nitrogen for one and a half minutes, at the end of which time the respiration failed, was ineffective in producing even the smallest paradox. Such a weak and prolonged adrenalin effect is very suggestive of the stimulation of extra-adrenal chromaffin tissue by severe anoxaemia, and the fact that the source of adrenalin or adrenalin-like substance is easily exhausted is also in favour of this hypothesis.

It is evident from the blood sugar results, obtained from these cats with intact splanchnics but with the suprarenals removed, that in the intact animal hyperglycaemia due to emotion or to anoxaemia is largely an effect of the stimulation of the central nervous system and the consequent passage of impulses through the splanchnics to the liver as well as to the suprarenals.

(v) *Conclusions drawn from the results of the experiments above described.* It is apparent that anoxaemia produces a rise in the blood sugar and at the same time accelerates the output of adrenalin. In the normal animal the mere excitement incidental to the observations is sufficient to produce both these effects in some degree. It cannot be doubted, therefore, that this excitement is a contributory factor to the larger effects in this direction produced by mild degrees of anoxaemia in the normal animal. In such an animal the whole of the effect produced by these degrees of anoxaemia appears to be due to stimulation of the central nervous system whether by anoxaemia or otherwise. This stimulus gives rise to the passage of nervous impulses along the splanchnics which cause a mobilization of sugar in two ways—directly by action on the liver cells of impulses reaching them through the splanchnic innervation of that organ, and indirectly by accelerating the output of adrenalin, which in turn acts on the liver. It seems, then, that the glycogenic function of the liver is under a twofold control, and in this respect the liver resembles other organs supplied by the sympathetic.

In the more severe anoxaemia which corresponds to the threshold value of stimulus in the cat with the splanchnics divided, a further factor in the effect of such degrees of anoxaemia on the intact animal is isolated. The direct action of want of oxygen of this degree on the suprarenal, apart from any stimulation of the central nervous system, causes increased output of adrenalin with its consequent effect on the blood sugar. When the anoxaemia is still more severe there appears to be a direct action of want of oxygen on the liver cells themselves causing increased mobilization of sugar.

There remains for consideration the residual paradoxical pupil reaction which occurs in some animals in extreme asphyxia or anoxaemia, even when the adrenals are removed.

Several possible explanations suggest themselves.

1. That the removal of the superior cervical ganglion makes the dilator of the iris unduly sensitive to severe degrees of anoxaemia. This suggestion is negatived by the experiments referred to above on the isolated iris preparation.
2. That the accessory chromaffin tissue may conceivably yield

enough adrenalin to the intense stimulus of severe anoxaemia to account for the occurrence of the pupil reaction after removal of the adrenals.

3. That some substance other than adrenalin, which has a similar action on the sensitized pupil, may be produced in the body as a result of intense anoxaemia.

It may be noted that Elliot (1912) sometimes observed a slight dilatation of the sensitized pupil on stimulating the splanchnics in the eviscerated and decapsulated animal. On the other hand, Cannon and Hoskins (1911) found evidence of the output in response to extreme asphyxia of a substance inhibiting the isolated intestine even after decapsulation, and ligature of the aorta and inferior vena cava at the diaphragm and of the carotids in the neck. It is difficult to suppose that sufficient accessory chromaffin tissue remains accessible to the circulation after such a procedure. Dale and Laidlaw (1912) found evidence under somewhat similar conditions of the output of a substance dilating the pupil in response to nicotine.

The only evidence in my experiments which bears upon this question is the fact that, in two animals in which the suprarenals had been removed, a moderately severe anoxaemia elicited this residual phenomenon, while subsequent attempts to produce it failed completely, despite the use of even more severe degrees of anoxaemia.

This suggests that in the causation of the residual paradox some substance is used up or the mechanism that produces it is so fatigued that it is not possible to reproduce the effect. In both of these cats the effect, though small in intensity, was extremely prolonged, and suggested a prolonged though very small output of adrenalin. The behaviour of these two animals seems to me to lend support to the view that the residual paradox is due to the output of adrenalin from accessory chromaffin tissue which is stimulated by extreme degrees of anoxaemia. and that this tissue is readily exhausted. It should be emphasized that this residual effect, whatever its cause, is a relatively trivial and inconstant element in the paradoxical dilatation of the pupil as produced by asphyxia in the normal animal, and that it cannot contribute significantly to the effect of the milder degrees of anoxaemia.

6. The Probable Value of the Blood-Sugar Changes in Anoxaemia as a Test for Flying Officers.

No experiments on the effect of anoxaemia on the sugar content of the blood of man have been made, but the results of the animal experiments described in this report offer presumptive evidence that the hyperglycaemic reaction to anoxaemia may furnish a useful test, both in the investigation of the fitness of individuals as flying officers, and in determining in doubtful cases of 'flying sickness' whether the patient is fit to resume flying.

In devising such a test there are two possible alternative methods, (1) a determination of the 'threshold' degree of anoxaemia, i. e. the percentage of oxygen in the atmosphere inhaled which just sufficed to cause a hyperglycaemia, or (2) a determination of the

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and not upon the exigencies of the moment. A much more serious objection to its use, in the case of officers who are suffering from 'flying sickness', is that a test of this nature may conceivably make the patient more nervous and militate against his improvement. Generally speaking, in these doubtful cases, if the application of the test operated in this way there would be no doubt as to the unfitness of the individual in question for flying. Lasfly, it seems important to point out that a great many observations will have to be made on normal persons and also on those who are definitely unfit for flying before any positive pronouncement concerning its value can be made.

I wish to acknowledge my indebtedness to the Medical Research Committee, who kindly allowed me to carry out the experiments here described in their Department of Biochemistry and Pharmacology, also to the Head of that Department, Dr. H. H. Dale, in whose laboratory this work has been done, for much help and advice, in addition to his kindness in performing for me the various necessary operations from which the experimental animals were allowed to recover.

REFERENCES.

Anderson, *J. Physiol.*, 1903, **30**, 290.
Anrep, *J. Physiol.*, 1912, **45**, 307.
Araki, *Ztschr. f. physiol. Chem.*, Strassb., 1891, **15**, 334.
Araki, ibid., 1894, **19**, 422.
Barcroft, *The Respiratory Function of the Blood*, 1914, Cam. Univ. Press.
Barcroft, Camis, Mathison, Roberts, and Ryffel, *Phil. Tr.*, Lond., 1914, b. **206**, 49.
Bazett and Corbett, *Reports of the Air Medical Investigation Committee*, No. 5, 1918.
Benedict, *J. Biol. Chem.*, N.Y., 1918, **34**, 203.
Budge, *Ueber die Bewegung der Iris*, Braunschweig, 1855.
Cannon, *Bodily Changes in Pain, Hunger, Fear, and Rage*, Appleton, 1916.
Cannon, *Reports of the Special Investigation Committee on Surgical Shock and Allied Conditions*, No. 2, 1917.
Cannon and Hoskins, *Am. J. Physiol.*, Bost., 1911, **29**, 274
Dale and Laidlaw, *J. Physiol.*, 1912, **45**, 1.
Douglas, Haldane, Henderson, and Schneider, *Phil. Tr.*, Lond., 1913, b. **203**, 185.
Dreyer and Ainley Walker, *Lancet*, Lond., Oct. 25, 1913.
Dreyer, *Reports of the Air Medical Investigation Committee*, No. 2, II, 1918.
Elliott, *J. Physiol.*, 1912, **44**, 399.
Epstein and Bahr, *J. Biol. Chem.*, N.Y., 1914, **18**, 18.
Flack, *Reports of the Air Medical Investigation Committee*, No. 3, pp. 39 and 40, 1918.
Gley and Quinquaud, *J. de physiol. et de path. gén.*, 1918, **17**, 807.
Haldane, *Organism and Environment as Illustrated by the Physiology of Breathing*, Yale Univ. Press, 1917.
Haldane, Meakins, and Priestley, *Reports of Chemical Warfare Medical Committee*, No. 5, pp. 6 and 7, 1918.
Hill and Flack, *J. Physiol.*, 1908, **37**, 77.
Keith, Rowntree, and Geraghty, *Arch. Int. Med.*, Chicago, Oct. 1915, p. 547.
M. R. C., *Reports of the Special Investigation Committee on Surgical Shock and Allied Conditions*, No. 7, 1918.
Mathison, *J. Physiol.*, 1910, **41**, 416, and 1911, **42**, 283.
Meltzer and Auer, *Am. J. Physiol.*, Bost., 1904, **11**, 28.
Milroy, *J. Physiol.*, 1917, **51**, 279.
Scott, *Am. J. Physiol.*, Bost., 1914, **34**, 271.
Stewart and Rogoff, *J. Pharmacol. and Exper. Therap.*, Balt., 1916, a. **8**, 517.
Stewart and Rogoff, *J. Exper. M.*, N.Y., 1916, b. **24**, 717.
Stewart and Rogoff, *J. Pharmacol. and Exper. Therap.*, Balt., 1917, a. **10**, 49.
Stewart and Rogoff, *Am. J. Physiol.*, Bost., 1917, b. **44**, 543.
Van Slyke, *J. Biol. Chem.*, N.Y., 1917, **30**, 347.
Van Slyke, ibid., 1918, **33**, 127.

IX. THE EAR IN RELATION TO CERTAIN DISABILITIES IN FLYING

BY

SYDNEY SCOTT, F.R.C.S.

(Late Temporary Major, R.A.M.C.)

CONTENTS

PRELIMINARY.

ON February 26, 1918, I received a request from the Director General A.M.S. to give up my civil duties and proceed to France 'to investigate certain questions connected with the special disorders of flying'. . . . Accordingly I rejoined the B.E.F. for about four months. While in France I examined upwards of 300 flying officers, more than half of whom were affected by one or more of the following complaints: deafness, discharge from the ear, rhinitis, pharyngitis, tonsillitis, eustachian obstruction, cerumen, tinnitus, vomiting, vertigo.

The other 150 include officers who were examined whilst on duty with their respective Air Force Units in the field. They comprise normal individuals, those who complained of headache after flying, faintness in the air, and others who had been concussed by a crash, &c. They include pilots who were making bad landings without crashing, as well as flight commanders and leaders who possessed exceptional flying and fighting ability: a number of these volunteered to serve as controls in comparing the results of rotation and other special labyrinth tests. Some flying observation officers, who were applying to be trained as pilots, were also tested.

All officers admitted to hospital were systematically examined by the medical officers attached to the Air Force before being sent to me. The majority were seen in co-operation with Lieut.-Colonel James L. Birley, the late Captain (and afterwards Lieut.-Colonel) C. Dudley H. Corbett, Captain H. C. Bazett, M.C., or Captain James Wyatt. When an ophthalmological examination was necessary, it was undertaken by Captain Foster Moore, Captain H. P. Gibb, or Captain Juler, the ophthalmic medical officers in the Administrative Area. The majority of those seen in the field were examined in conjunction with Captain Porteous, medical officer to the 11th Wing.

A routine examination was made of the ears, nose, and throat, including the eustachian tubes. Seventy-five officers were submitted

to special labyrinth tests in the rotation chair. After analysing the data from a series of sixty-two cases the rotation tests were abandoned, because the results were considered to show these tests were unnecessary for the purpose of investigating the special ailments attributable to flying. Incidentally it was inferred that the rotation tests did not serve to discriminate qualities either favourable or unfavourable to individual flying ability. (See Part 2.)

TABLE A.

A. ft.	*B.* mm. Hg.	*C.* mm. Hg.	*A.* ft.	*B.* mm. Hg.	*C.* mm. Hg.
	370	390	10,000 . .	530	230
20,000 . .	380	380	9,000 . .	550	210
19,000 . .	390	370	8,000 . .	570	190
18,000 . .	400	360	7,000 . .	590	170
17,000 . .	410	350	6,000 . .	610	150
16,000 . .	420	340	5,000 . .	630	130
15,000 . .	430	330	4,000 . .	660	100
14,000 . .	450	310	3,000 . .	680	80
13,000 . .	470	290	2,000 . .	710	50
12,000 . .	490	270	1,000 . .	740	20
11,000 . .	510	250	Sea-level .	760	0°

A. Altitude in feet.
B. General barometric pressure in mm. Hg. (Approximate.)
C. Excess of pressure; compressing the drum when the eustachian tube fails to open during descent from the altitude given in Column *A* to sea-level. (Approximate.)

1. Abnormal Appearance of the Tympanic Membrane resulting from Flying especially after Rapid Descent from High Altitudes due to Imperfect Action of the Eustachian Tubes.

Many airmen, after flying to high altitudes, are liable, under certain conditions, to be temporarily affected to some extent by deafness, discomfort or pain in the ears, headaches, dizziness, nausea, fainting or vomiting, on returning to the denser atmospheric pressure of low altitudes. In these circumstances an inspection of the airman's ear with mirror and speculum *immediately* after landing shows a marked change from the normal; the fundus is bright red, owing to distension of the blood vessels in the tympanic membrane and mucosa of the middle ear. In extreme cases the tympanic membrane is strongly invaginated[1] into the tympanum; the membrane closely embraces the neck and handle of the malleus and the short process of the incus and incudo-stapedial joint, and is evenly moulded over the edge of the fossula rotunda. Occasionally globules of mucus can be observed through the invaginated drumhead within the cavum tympani.

Reference to the accompanying table (Table A) will serve to recall that the atmospheric pressure at, say, 18,000 ft., is approximately 400 millimetres of mercury, as compared with 760 millimetres at sea-level; assuming the eustachian tubes open regularly while ascending but fail to open during the descent from 18,000 ft., there

[1] I suggested the term 'invagination' as representing the extreme displacement of the tympanic membrane, which I met with among high-flying airmen.

would be an excess of gradually increasing pressure on the outer surface of the tympanic membranes, over the pressure within the tympanic cavity which would attain a pressure equal to 360 millimetres of mercury, on returning to sea-level.

Some aviators who had not learned how to prevent discomfort and misery on returning from high patrols have actually given up flying, and others, similarly affected, have contemplated doing so. After being taught the effect of auto-inflation when *starting* to dive, and *repeating the self-inflation frequently during the descent*, many added a new lease to their flying career.

When, for the purpose of this investigation, I was making a descent from between 19,000 and 20,000 ft., I became aware of the increasing atmospheric pressure on my ear drums at about 16,000 ft. The relief from self-inflation at this height lasted down to about 13,000 ft. when self-inflation again removed all trace of discomfort. While descending below 10,000 ft., the increasing pressure on the ear-drums became noticeable more and more quickly, for swallowing did not suffice to open the eustachian tubes rapidly enough to prevent this. By repeating the inflation at every 1,500 ft. descent, and then every 1,000 ft., even the slightest discomfort and traces of deafness disappeared, and after self-inflating again while a few hundred feet up, I was able to land free from any abnormal sensations in the ears.

In an unbroken ascent we meet with auditory symptoms only occasionally. An officer with eustachian obstruction was more comfortable at between 4,000 and 5,000 ft. than near sea-level, but became affected at 11,000 ft.;[1] another with bilateral obstruction complained of ear distress at 11,000 ft. On attaining 11,000 ft. in a flight which had then taken nearly a quarter of an hour, I became suddenly and unexpectedly conscious of a desire to 'clear' my ears: the sensation resembled that experienced during the earlier stages of a descent though swallowing did not give the expected relief. I realized the sensation must be due to the tympanum being relatively too full of air owing to the expansion of the air within the middle ear, which corresponded to the falling atmospheric pressure in the external ear. My eustachian tubes did not open when swallowing to relieve this sensation, but a very carefully graduated self-inflation, just sufficient to open the tubes, caused the feeling of fullness in the ears instantly to cease, nor did it recur during flight, even when climbing nearly 9,000 ft. higher still.

Function of Eustachian Tubes while Flying.

Normally, the eustachian tubes open once only during each act of swallowing: any difference in atmospheric pressure within and without the tympanic cavity is thus equalized. Even when the tubes act normally it is necessary to swallow repeatedly and frequently to keep pace with the continuous and often rapid changes of pressure which take place during descents. When flying at great height for long, and especially if engaged in the exertions of aerial

[1] This case I described in detail in the *Proceedings of the Royal Society of Medicine*, vol. xi, Otol. Section, p. 21.

combat, airmen are liable to breathe with mouth open. The throat is then apt to get parched and swallowing becomes positively fatiguing or well-nigh impossible. If this occurs and the normal regulating mechanism for opening the eustachian tubes prove unequal to the task, the airman experiences considerable discomfort, often intense pain, and sometimes is in great distress. The symptoms may be only momentary or they last for some time after landing: one frequently sees airmen, just returned from high flights, put the fingers to the ear and press on the tragus several times, or else try to self-inflate the ears after landing; I found the drums invaginated in these cases. Swallowing is often ineffectual in opening up the lumen, probably owing to swelling from hyperaemia of the mucosa lining the eustachian tube. Sometimes this occlusion of the eustachian tubes lasts for hours, days, or weeks, during which period flying increases the deafness and discomfort or pain.

Clinical Records.

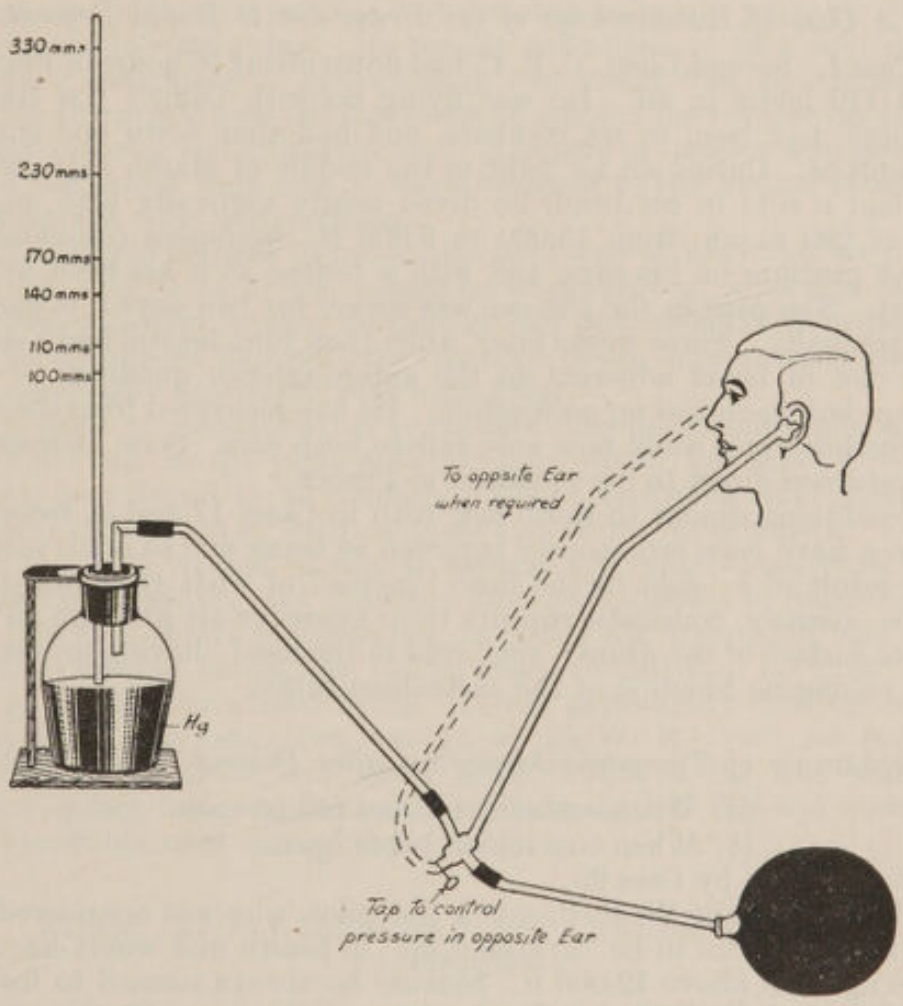
Case 17. Lieut. H. H. S. F. was a flying officer of one and three-quarter years' experience, with 200 hours flying including 150 on active service. In February 1918, when on a Sopwith Camel (Bentley Rotary 170 h.p. engine) while chasing an enemy machine, he dived with engine on, from 18,000 to 1,000 ft. He was conscious of greatly increasing pressure sensations in his head and deafness, which he failed to relieve by repeatedly swallowing as usual. The pressure caused pain in the ears which became more and more intense. He felt 'as though his head would burst', and being incapable of catching his enemy, broke off pursuit and returned to his aerodrome, in such pain that he at once went to a casualty clearing station. Unfortunately, the medical officer had no instruments to examine the ears, but he recommended him to have them syringed; however, this gave no relief. He endured the pain which lasted four or five days and there was a slight discharge, which lasted a few weeks. Subsequently, when on leave to England, it was discovered that the right tympanic membrane was ruptured. In April the rupture could be seen in the quadrant nearest the eustachian tube; I kept this officer under my care until the rupture healed and, having taught him how and when to self-inflate both ears, allowed him to return to duty with his squadron near Dunkirk. There was then no obvious deafness, and the hearing tests showed the merest defect in the right ear.

Hearing tests.	*Right.*	*Left.*	
Tone range.			
Lowest	16 d.v.	16 d.v.	Bezold-Edelmann,
Highest	0·3	0·2	Galton-Edelmann whistle.
Tone acuity.			
(Mixed sounds) Watch .	10 in.	15 in. (normal—15).	
(High pure tones). c^5 fork, 2 seconds, normal.			
Weber's test, fork on vertex heard louder in the right ear.			

I was informed by Lieut.-Colonel Birley that this officer subsequently did well after resuming flying duties and had no further trouble with his ears, which he was careful to inflate during descents.

Laboratory Tests of the Effect of Compression of Air in the External Ear.

To test the sensations of variable air pressure on the drum I adapted a mercurial sphygmomanometer and connected it by thick walled rubber tube to a nozzle which accurately fitted the external auditory meatus. With this arrangement one could compress the air in the external auditory canal on to the drum, and read the pressures attained in millimetres of the column of mercury. Having first tested the effect of compression on myself, I applied it to others and



soon found the tolerance to pressure varied among different individuals. Some could not bear more than 140 mm.[1] on the first occasion without pain, but after repeated trial the threshold was raised to 170 mm.[2] Others found 280 mm.[3] the first time quite tolerable. The first symptom of increasing pressure was deafness; as the pressure was raised the discomfort passed on to acute stabbing pain in the ear.

A few individuals noticed distinct dizziness when high pressure

[1] This would correspond with the excess of atmospheric pressure on the drum produced by a rapid descent from about 6,000 ft. to near sea-level, with eustachian tubes remaining closed

[2] Corresponding to descent from nearly 7,000 ft., eustachian tubes keeping closed.

[3] Corresponding to descent from nearly 13,000 ft,. eustachian tubes keeping closed.

was applied to one ear at a time, but no dizziness when both ears were equally compressed.

A pressure limited to 320 mm. Hg was insufficient to rupture the drum of the cadaver—(both ears were tested in ten cases to ascertain this point).

The rapid descent from 18,000 ft. which caused the drums to be ruptured in the flying officer, whose case is described above, would correspond to a pressure of about 350 mm. Hg, a pressure not applied in the laboratory.

A Case of Haemorrhage of the Drum due to Rapid Descent.

Case 4. Second Lieut. C. R. C. had flown about 50 hours in France, and 110 hours in all. He was flying Sopwith Camels (La Rhone engine), had been in six combats, and had shot down one enemy aeroplane. During an air fight in the middle of March 1918, when he had a cold in his head, he dived nearly vertically with engine on at 200 m.p.h. from 15,000 to 3,000 ft., becoming conscious of great pressure on his ears, and with a feeling as if his head would burst. The pain in the left ear was severe for two days : it passed off gradually. Three weeks later, when I saw him, he still had a small dry clot of blood adherent to the antero-inferior quadrant of the drum, but there was no perforation. He had recovered from the cold in the head and could now auto-inflate both ears. Soon afterwards he returned direct to his squadron in France.

Conditions similar to those met with in Cases 17 and 4, recorded above, have been erroneously regarded as being due to otitis media, the result of a ' cold in the head ' instead of what they primarily were—namely, traumatic rupture from excessive air pressure on the outer surface of the drum : the ' cold in the head ' having prevented the regulating function of the eustachian tubes.

Appearance of Tympanic Membrane after Descent from 17,000 *ft.*

(*a*) When eustachian tubes fail to open.
(*b*) When eustachian tubes open.

Exemplified by Case 98.

Flight Sergeant W. F. P. was a test pilot, who was considered by his fellow officers to be ' breaking up ' in health and would have to give up tests above 12,000 ft., because he always seemed to feel so ' bad ' when he landed. They supposed this was due to ' heart trouble ', but the medical officer found the heart normal.

On May 9, 1918, at 7 p.m., I saw him land a Bristol Fighter in which he had been up to 17,000 ft. for an hour. He admitted to his friends he felt ' off colour ' but to the medical officer said ' he felt alright ', except that ' his head was throbbing a bit ' and ' of course ' he was ' deafish '. This was not obvious during conversation, but he could only hear a watch when within 4 in. from the right ear and 8 in. from the left, which was one-quarter and one-half the full hearing distance for this particular watch. He was persuaded to allow me to examine the drums of the ears. I found they looked bright red : the blood vessels could be seen to be distended and the whole drum was tensely invaginated and moulded over the ossicles

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if they were plugged'. After this he had found even ordinary flying difficult, and had returned from flights unusually tired and sleepy. He had especial difficulty in co-ordinating his controls, 'always putting on too much rudder and not enough bank', and was losing self-confidence. Faulty flying had caused him to come down in a spin, though he managed to pull out in time to prevent a bad crash, staggered to his hut, and was later seen by the medical officer who sent him to the hospital. I found he had rhinitis and obstruction of the left eustachian tube. He could not auto-inflate the left ear but he could inflate the right; doing so made him feel giddy and he nearly fell off his seat.

The tympanic membrane of the left ear was then only slightly invaginated and a dusky red reflex showed the mucosa of the middle ear to be hypervascular. When a catheter was passed into the left eustachian tube and air was blown into the middle ear, he suddenly exclaimed 'I'm going off', shut his eyes tightly and gripped hold of the chair, but his lips were not pallid and his pulse was strong. At the same time forced movements of the head and neck-muscles commenced, causing the face to turn toward the left with flexion of the head to the left and backward extension. He felt 'as if he was 'falling to the right, and that the room was tilting down to the left'. All these sensations passed off in less than a minute. He recovered from the rhinitis and eustachian obstruction and was, on account of enlarged tonsils, recommended for leave to England before returning to duty.

Unilateral Eustachian Obstruction causing Vertigo with so-called Nerve Deafness.

Case 21. Vertigo, vomiting, so-called *nerve-deafness*, nystagmus, rhombergism, forced reeling gait, eustachian catarrh; complete recovery and return to active flying duties as test pilot.

Lieut. A. B. T., a Canadian; was a test pilot who had been in France about two months. He had a slight cold in the head and had merely tested the air-speed of a Sopwith Camel at between 2,000 and 3,000 ft., without rolling or spinning the machine; on landing he felt sick and giddy, and afterwards went to his quarters and lay down for a few hours. In the evening he was well enough to go into mess. After breakfast the following morning, while in an S. E. 5 warming up the engine, he again felt giddy. He switched off the engine, climbed out of the machine, staggered to his hut, and vomited. He remained in bed for twenty-four hours without food, the giddiness persisting and being worse when he moved his head or attempted to get up. Five days later he was sent to hospital, where he was overhauled by the late Lieut.-Colonel Corbett, who, finding he could not hear a watch with the left ear, asked me to examine him.

As he entered the room I noticed he walked slowly with outstretched arm, apparently apprehensive of falling. While seated he inclined the head to his left, though he said he was quite unaware of doing so. While I held his head straight he said it felt inclined to the right, and I observed both eyeballs slowly rotate about an

antero-posterior axis, clockwise, to the left to take up their original position in space. Moreover, when the eyes were deviated towards the right, fine rotary nystagmus appeared with the rapid jerk counter-clockwise, i. e. upper meridian of the eyeball, to the right. There was no nystagmus when the visual axis were directed towards the left. When released the head again slowly inclined to the left, resuming its original position of left lateral flexion.

On attempting to stand with eyes shut with feet close together the patient fell towards the left. He also lurched heavily to the left when attempting to walk straight, with eyes closed, the line followed being some forty-five degrees away from the straight line he had intended to follow. There was nothing else abnormal discovered in the general neurological survey. The *tympanic membranes were perfectly normal in appearance*, with absolutely no displacement inwards or outwards and no hyperaemia. However, he could not auto-inflate the left ear, although he could inflate the right, by Valsalva's well-known method.

Tone range.	*Right.*	*Left.*
Lowest audible . . .	16 d.v.	24 d.v. (Bezold fork).
Highest audible . . .	0·6 mm.	1·6 (Galton whistle).
Tone acuity.		
(High pitch watch) . . .	8 to 12 in.	nil (normal 12 to 15 in.).
c^1 fork	normal	— sec.
Schwabach-conduction . .	normal	Slight loss of bone conduction.

(Rinne method) air conduction better than bone on each side.
(Weber's method) bone conduction from the vertex louder in the right ear.

These tests indicated a condition often so-named ' nerve-deafness ' in the left ear.

Air was inflated through a catheter into the eustachian tube on each side, first the right, which increased the hearing acuity for the watch, but produced no effect on the giddiness ; when air was blown through the catheter into the left eustachian tube, fluid *râle* was audibly produced in the left middle ear. The blowing was continued until the *râle* was displaced by the clear sound of air entry, and the catheter was then removed. The patient immediately exclaimed that the giddiness had ceased ; as evidence of this he could stand and walk straight with eyes shut, there was no lateral flexion of the head, and it was seen as objective evidence that the nystagmus had disappeared. The hearing for lowest tones 16 d.v. was equal on the two sides, and in Weber's test the bone conduction was equalized, but the hearing for high tones at first improved hardly at all. Next morning the symptoms of giddiness, together with all other signs described above, recurred ; and again the left ear could not be inflated without the catheter, which on this occasion also put an end to the giddiness instantly. The catheter was necessary, for the same reasons, on the third day, after which the patency of both eustachian tubes came under the patient's control, for he was now able to inflate both ears equally and has ceased to be troubled with giddiness since. Instead of his being transferred to England as an invalid, I recommended that this officer be allowed to return direct to flying duties without restriction, and a few days afterwards he ferried a captured Hanover two-seater to Farnborough, bringing back a new S. E. 5 two days later, and subsequently carried out his

ordinary test-flying up to 16,000 and 20,000 ft. without any recurrence of symptoms.

Two points in his history were brought out afterwards. Firstly, he had had a cold in the head about a fortnight and for ten days had felt slightly giddy when flying without having complained. His fellow officers told me they had noticed he was not flying as well as usual for ten days, and, in fact, had told him that he would crash because he was *flying and landing with the left wing lower than the right even when direct into the wind.* After the treatment described above he flew quite level, as I saw for myself. These observations fully tally with the signs of inco-ordination and forced movements which I noticed when he came to the hospital. The importance of the foregoing case in connexion with crashes of unknown origin deserves full recognition.

Vertigo and Nystagmus, associated with Obstinate Eustachian Obstruction, reproduced by Pressure Changes in the Middle Ear.[1]

Case 129. Lieut. G. F. S. This officer was sent to me on account of deafness in the left ear, which was worse after flying and had been increasing for some months past. He had also had occasional attacks of pain especially during descents, and he had felt dizzy several times when landing. He had been in France since March 1918 with a squadron engaged principally in artillery observation and rarely flew above 9,000 or 10,000 ft.

At the time of examination, in May 1918, he had no pharyngitis or rhinitis, but the eustachian obstruction was so marked that for a week it defied all attempts to blow air into the middle ear, in spite of the use of the eustachian catheter, bougies, and the application of cocaine, adrenalin, atropine, menthol inhalations, and the administrations of iodides and aperients. The right ear was always easily self-inflated, and there was no special difficulty in introducing the catheter into either eustachian tube. Every day the drums were inspected before and after these attempts, but the left drum remained unmoved in a position of invagination; the mucosa of the middle ear could be seen to be hyperaemic through the transparent membrane.

On the eighth day, air blown through the catheter could be heard entering the tympanum by means of the auscultatory tube. At the same moment, the patient felt giddy and there were manifest forced, jerking movements of the head and nystagmus.

When the inflation was weak, the head was inclined, and face turned to the right, and the nystagmus (combined horizontal and rotatory) was to the left.

Stronger inflation—distending the tympanum—caused the forced movements of the head and eyes to be reversed.

It was over three weeks before this patient succeeded in self-inflating the left ear and he was afterwards transferred to England,

[1] By permission of the Director General, I was permitted to record this case in the *Journal of Laryngology, Rhinology, and Otology*, February 1919, vol. xxxiv, No. 2, p. 51, where a fuller account would be found.

and though he flew again, he was, I understand, eventually invalided out of the Air Force, owing to the persistent ear trouble and impossibility of self-inflating the left tympanum.

Concluding Remarks to Part I.

The foregoing clinical cases are selected from over 300 records of officers examined in France. They serve to illustrate the outstanding importance of efficient eustachian tubes, whereby an airman should be able to correctly regulate and equalize the continuous changes of atmospheric pressure experienced in flights from low to high and from high to low altitudes.

These cases also serve to show that the deafness and distress in the ears which occur through flying are the result of inefficient eustachian tubes, and that these symptoms are preventable. And lastly that vertigo and vomiting and forced movements, which interfere with the proper control of an aeroplane, are sometimes induced by the unequal pressure in the ears, resulting from unilateral eustachian obstruction, and that such symptoms are overcome by removing the cause.

How to prevent Giddiness, Deafness, and Earache due to Descents from High Altitudes.

The following rules were proposed to Lieut.-Colonel Birley as a result of my experience among airmen in France :

(1) That airmen should not fly with a cold in the head, sore throat, or when unable to inflate both eustachian tubes at will.

N.B. Airmen with large bilateral perforations of the tympanic membrane did not feel the ear symptoms experienced by those with normal drums. Contrary to the usual practice I recommended they be permitted to continue flying duty which they carried out with success.

(2) Airmen who can open the eustachian tubes at will by swallowing should use chewing gum to stimulate the flow of saliva and keep swallowing, especially while descending.

(3) Airmen who cannot rely upon swallowing, to open the eustachian tubes repeatedly and rapidly, should make a rule of self-inflating the ears by Valsalva's method and should *begin to do so at the commencement of the descent—repeating the procedure* once, say every 1,000 ft., and not wait until they land.

(4) All may practise, though few succeed, in the following procedure :

Open the mouth slightly while trying to maintain the lower incisor teeth as far in front of the upper as possible. The effort can only be strongly sustained for a minute or less : one should be conscious of tightly contracting the muscles of the palate and upper pharynx at the same time. If the procedure succeeds, one can pass through considerable changes of atmospheric pressure, without having to swallow or inflate the ears, as the walls of the eustachian tubes are

kept apart for an appreciable time by this voluntary muscular action alone.

2. Part played by the Semi-circular Canals in Aviation.

It has been assumed, but never proved, that a pilot is dependent upon the sensitiveness of the semi-circular canals to maintain equilibrium when flying. Yet a person whose semi-circular canals have all been removed on both sides, can run and ride, dance and turn, hop and jump with eyes open or shut, and presumably could learn to fly. These extreme views we shall have to reconsider in the light of investigations made on airmen in the Air Force in France during the War.

The clinical methods of investigating the semi-circular canals have been applied to airmen. The tests employed in clinical practice depend upon the fact that normal semi-circular canals can be so stimulated, artificially, that they set up certain characteristic reflex movements which differ in intensity in different individuals. Semi-circular canals destroyed by disease are of course irresponsive to even the strongest stimulating agents. We can thus ascertain whether each canal is responding to stimulus or not, and so can recognize diseased conditions.

The methods of stimulating the semi-circular canal system employed clinically are as follows :

1st. Rotation with sudden deceleration.
2nd. Thermal (hot or cold water or air).
3rd. Pressure (limited to certain conditions only).
4th. Galvanism.

Clinical methods have been applied to airmen, in order to ascertain and compare the intensity of the reactions which are so set up, and which are described later, probably in the first instance on purely hypothetical grounds.

For we must believe that the assumption was that a pilot depended largely on the semi-circular canal system to maintain his own equilibrium and that of his aeroplane.[1]

In investigating disorders of the central nervous system, and of certain diseases of the ear, it is often necessary to employ *all* these methods before an accurate diagnosis can be made. In this paper I shall confine my observations to rotation and caloric tests as applied to airmen, because these tests have been employed by other medical officers in the selection of candidates for the Flying Services and in grading flying officers according to the different reactions displayed.

Normal Phenomena produced by Rotation.

The individual is rotated in a chair or a turning stool, or a seat suspended from a beam, or, failing these appliances, simply on the feet, round and round, a certain number of times at a certain rate

[1] *Vertigo and Equilibrium*, by Major Isaac Jones, M.D., American Aviation Service (Lippincott, 1918).

and then suddenly stopped. This sudden stop after turning (i. e. *deceleration*) causes dizziness, which varies in degree and duration in different persons, and is accompanied, according to the strength of stimulus, by forced movements of eyes, head, and limbs.

The direction and character of nystagmus and other forced movements, and the kind of subjective sensations depend upon the *position of the head*, while being turned, and on its being maintained in the same constant position throughout the turning and at the moment when the head is brought to a sudden standstill.

The rate of rotation should not be less than one turn in four seconds, otherwise the stimulus is insufficient to evoke the phenomena sought for. As a rule, from five to ten turns are necessary to produce a definite effect. The same rate should be observed in making both clockwise and counter-clockwise rotation.

Three different positions of the head during turning are adopted.

First Position—Head erect. Care should be taken that the chin is depressed (the mouth being closed) and the face is not elevated ; otherwise, the superior semi-circular canals will respond in place of the external canals. For instance, a normal subject with head in position for stimulating external canals will deviate to the right after clockwise rotation, whereas if the head is too erect, so that the superior canals receive part of the stimulus, he will deviate and lean to the left after clockwise rotation. After being turned, six to ten complete revolutions, the individual attempts to walk straight, with eyes shut ; it can be seen that many individuals, when told not to resist, will tend to walk circuswise, where space permits, in the same direction as the rotations were made. Instead of attempting to walk, he may try to point, as Bárány explained, in a prearranged direction with hand or foot, when the ' normal error of deviation ' due to rotation stimulation can be observed.

The nystagmus is ' horizontal ' and greatest when the eyes are voluntarily turned opposite to the direction of rotation ; its duration varies in different persons.

Second Position—Face directly downwards. Five turns in fifteen seconds usually suffice to produce a response. On stopping the turning as before, the individual rises with head erect and is directed to try and walk straight. Some will succeed, with eyes open or shut, others will stagger to the ground, unable to rise for perhaps half a minute or longer. The nystagmus, which must be sought for quickly, will be seen to be fine and rotatory, with the more rapid jerk of the upper meridian of the eyeball away from the direction towards which the previous turnings were made. There is a considerable difference in the duration of nystagmus, in seconds of time, among different groups of individuals in health.

Instead of attempting to walk directly after being turned, the subject under examination can try to hold the head erect, with eyes shut, and extend both arms laterally level with shoulders ; he will involuntarily hold one arm more or less above, and the other below the horizontal level, the head and trunk showing a tendency, more or less marked, to incline laterally towards the lower side. The sensations to an airman somewhat resemble those associated with ' banking '.

Third Position during rotation—With the right side of the head downwards, and face forwards, the sagittal plane of the head being maintained as horizontally as possible. The turnings are made first counter-clockwise, the face travelling forwards, and then clockwise. Five or six turns in ten or twelve seconds are usually sufficient to provoke a response and reaction, for directly the head is raised into the erect position after stopping, emprosthotonus or opisthotonus is set up, according to the direction of rotation, counter-clockwise or clockwise. The nystagmus is of short duration and is upwards in the former and downwards in the latter case.

The sensations of the normal individual produced by rotations in the third or lateral position have been compared by airmen to those experienced in ' zooming ' on the one hand and ' nose diving ' on the other, as soon as the head is raised to the erect posture.

Among any considerable number of normal persons, we shall find some who experience no disagreeable sensation whatever after being turned, with head in any position. Others are intensely giddy only after being turned with face down or up.

The result of turning in the erect position is an unreliable indication of the degree of reaction likely to be produced by turning with face down or sideways ; in consideration of this point it should be remarked that it has been the custom to alter the position of the head and resume the erect position after turning in the second and third positions, whereas the head is maintained in the same position in relation to space both during and after rotation, in the first position. [In reapplying clinical tests this point will probably need further investigation.]

The above-described phenomena are the usual result of hyper-stimulation by rotation in normal persons. They do not occur after destruction of both vestibular end-organs, and they are markedly asymmetrical in patients who have unilateral destruction of the semi-circular canals.

Caloric Test.

As is well known, the application of cool or tepid water to the drum of the ear abstracts heat from the tympanic cavity and, more slowly, from the outer wall of the labyrinth : the endolymph and perilymph will condense and so convection currents are set up in the superior semi-circular canal when the head is erect (and in the external semi-circular canal if the face is either upwards or downwards).

The reactions obtained by these caloric tests with head erect are similar in character to those obtained by rotation stimuli with the head in the face-down position. (See p. 41.)

The caloric test can, however, be applied to one side at a time, and the reaction obtained can be compared with that provoked by applying the test to the opposite ear.

Normal individuals with normal drums and normal eustachian tubes react equally strongly whether the right or left ear is stimulated, provided the temperature of the water and the rate of flow is constant.

When I went to France I found some airmen who had been admitted to hospital with giddiness associated with deafness had been already

subjected to the caloric tests, even when the drums were intact; the method employed being that of irrigating the external auditory canal in the usual way with tepid water for one or more minutes until nystagmus or dizziness was induced, the head being kept erect.

It so happened, however, that in the airmen mentioned above, the reaction was unequal, being stronger in some when the test was applied to the affected ear, as compared with the normal ear and in others weaker when applied to the affected ear.

I was already aware that any person whose drum was invaginated reacted more readily to the caloric test applied to that side than to the normal side—for the simple physical reason that the drum being closer to the labyrinthine wall, the heat was abstracted more quickly by the irrigating stream than when a cushion of air intervenes.

Further, hypervascularity of the drum or lining membranes and the presence of mucus in the tympanum retard the reaction to the caloric test.

It was for these reasons that I did not employ this test as a routine in the case of airmen—although it is one of great service in the investigation of the labyrinth in diseases of the central nervous system and in some cases of suppuration in the middle ear, when we desire to ascertain simply whether there is a response or no response.

Results of Rotation. Tests in France.

In order to obtain first-hand data on the relation between rotation reactions and flying ability by the application of the clinical labyrinthine tests to flying men, I made notes of a series of sixty-two pilots and observers, among whom were twelve high-grade and experienced pilots—all of whom volunteered to submit to the examination.

I relied chiefly upon the tests to observe the activity of the forced movements, in so far as rotation-deceleration interfered with the attempt to walk straight, immediately after turning.

The sensations of disturbed equilibrium and of induced giddiness were also inquired into and noted.

It seemed unavoidable that a mathematical formula must give way to some such convention as can be expressed by the terms:

Forced Movements—Absent or Slight. Group 1.
Forced Movements—Moderate. Group 2.
Forced Movements—Strong. Group 3.

In Group 3, shown in Table I, 'strong forced movements' after rotation, cases are included in which rotation caused the individual to collapse to the floor, from which he could not rise for several seconds at least; and those who staggered so much while attempting to walk that they failed to approach a previously selected mark. It is interesting to notice that this group included some 'crack' airmen who will be further alluded to.

TABLE I.

Rotation type.	*Forced movements.*	*Giddiness.*	*Number tested.*
A.	Absent or slight	Slight	21
B.	Moderate	Slight	17
C.	Strong	Slight	8
D.	Absent or slight	Moderate	—
E.	Moderate	Moderate	6
F.	Strong	Moderate	2
G.	Slight	Intense	3
H.	Moderate	Intense	4
J.	Strong	Intense	1

First grade pilots 12. Observers and other pilots 50. Total 62.

The first group—' forced movements: absent or slight '—was designed to include those who walked rapidly to the chosen mark, without showing more than a mere waver; this also included some of the best fighting airmen of their day. (See A. D. G., Tables I and II.)

The ' moderate group ' included those who, after a definite détour, managed to gain the point sought for without an apparent struggle. (See B. E. H., Tables I and II.)

In estimating the individual's category, most reliance was placed on the result of the face-down test.

In Table I we notice that *giddiness* was not always in proportion to the ' activity of the forced movement '. It is certain that, as in Type C, there are always some individuals who are averse from admitting feeling giddy, while in Type G we meet with others who feel giddy and every motion when in the air as in the rotation-chair and are regarded as ' temperamentally unfit ', though they do not show strong ' objective ' reactions in the rotation-chair.[1]

TABLE II. (*First Grade Pilots only.*)

Rotation type.	*Forced movements.*	*Giddiness.*	*Number tested.*	
A.	Absent or slight	Slight	6	Capt. No. 1, Capt. No. 15, Capt. No. 55, Capt. No. 16, Capt. No. 64, Gen. L.
B.	Moderate	Slight	3	Capt. No. 19, Capt. No. 42, Capt. No. 43.
C.	Strong	Slight	—	
D.	Absent or slight	Moderate	—	
E.	Moderate	Moderate	—	
F.	Strong	Moderate	1	Capt. No. 25.
G.	Absent or slight	Intense[2]	—	
H.	Moderate	Intense	1	Capt. No. 14.
J.	Strong	Intense	1	Major No. 81.

[1] The chair employed was lent by the United States of America Aviation Medical Service through the courtesy of Lieut.-Colonel Isaac Jones, and was similar to that in use in America, by the medical officers for the examination of candidates for the Air Service.

[2] i.e. giddiness with shock reactions, pallor, clamminess, small pulse—headache, nausea lasting a quarter of an hour or longer.

TABLE III. [*Type A.* (See Table II.)]

Rotation test.	*Position of head.*	*Direction of rotation.*	*Number of turns.*	*Induced rhombergism.*	*Effect of gait.*	*Sensations of orientations, &c.*	*Intrinsic sensations, dizziness, nausea, &c.*
1	Erect	Clockwise	6	No	Slight curve to right	Room going round horizontally to left	Momentarily giddy—no nausea.
2	Erect	Counter-clockwise	6	No	Slight curve to left	Room going round horizontally to right	Momentarily giddy—no nausea.
3	Face down	Clockwise	6	Falling to right	Staggered slightly and leaned to right, but kept nearly straight course	Floor seemed to bank to left on facing forwards, eyes open	Momentarily felt as if spinning to left. Slightly 'giddy' for few seconds.
4	Face down	Counter-clockwise	6	Falling to left	Staggered slightly and leaned to left, but kept nearly straight course	Floor seemed to bank to right on facing forwards, eyes open	Momentarily felt as if spinning to right. Slightly 'giddy' for few seconds.
5	Right side of head down	Clockwise	6	Falling backwards	Difficult to get out of chair owing to opisthotonos.	Seemed to be nose diving (when facing forwards)	'Not exactly giddy.' Conscious of strong forced movements. No nausea.
6	Right side of head down	Counter-clockwise	6	Falling forwards	Flexed head and trunk forwards	Seemed to be tail sliding when facing forwards	'Not exactly giddy.' Conscious of strong forced movements. No nausea.

Case 1, Capt. Case 55, Capt. Case 64, Capt.

TABLE IV. [*Type A.* (See Table II.)]

Rotation test.	*Position of head.*	*Direction of rotation.*	*Number of turns.*	*Induced rhombergism.*	*Effect on gait, &c.*	*Sensations of orientation, &c.*	*Sensations of dizziness, nausea, &c.*
1	Erect	Clockwise	—	—			
2	Erect	Counter-clockwise	—	—			
3	Face down	Clockwise	6	No	Walked straight, slight lateral flexion to right	Momentarily as if floor was tilted a little down to left	Not dizzy. No pallor, &c.
4	Face down	Counter-clockwise	6	No	Walked straight, slight lateral flexion to left	Momentarily as if floor was tilted a little down to right	
5	Right side of head down	Clockwise	—	—			
6	Right side of head down	Counter-clockwise	—	—			

Case 15, Capt. Case 16, Capt. Case Gen. L.

TABLE V. [*Rotation Type A. First Grade Pilots.* (See Table II.)]

Case No.	*Hours flown.*	*Remarks.*
1. Capt. . .	480	Flies Bristol Fighters at 17,000 ft. Credited with fourteen E.A.'s. Was once shot down in flames. Always descends very fast—dives, side slips or spins. When spinning in machine avoids looking over at ground, otherwise gets 'deadly.giddy'. Not giddy if he keeps head in cock-pit.
		[Spads.]
15. Capt. . .	475	Flight Commander, fighting scouts. Great repute.
16. Capt. . .	325	Flight Commander, fighting scouts. Great repute. Very experienced horseman.
55. Capt. . .	650	Flight Commander, fighting scouts. Can spin 'camel' as many as eighteen turns to right, looking at ground whole time in drop of 6,000 ft. Once tried spinning to left and lost sense of position but managed to straighten out. Rotation tests, classified A. Pointing error normal. Good horseman.
64. Capt. . .	790	Flight Commander for fourteen months, fighting scouts. Can roll, spin, and do Immelmann's with ease, yet 'hates the sea like poison', 'always sea-sick'. Keen horseman. Rotation tests, classified A. Nystagmus and past pointing tests normal type.

TABLE VI. [*Rotation Type F.* (See Table II.)]

Rotation test.	*Position of head.*	*Direction of rotation.*	*Number of turns.*	*Induced rhombergism.*	*Effect of gait.*	*Sensations of orientation, &c.*	*Intrinsic sensations, dizziness, nausea, &c.*
1	Erect	Clockwise	7	Yes	Deviated to right	Room going round fast to left horizontally	Slightly dizzy. No nausea.
2	Erect	Counter-clockwise	7	Yes	Deviated to left	Room going round fast to right horizontally	Slightly dizzy. No nausea.
3	Face down	Clockwise	5	Strong to right	Could not walk at all for nearly one minute. Lay on ground on right side struggling to get up	Vertical bank and side slipping to left, when facing forwards after turning	Momentarily very giddy, rapid recovery. No nausea or pallor.
4	Face down	Counter-clockwise	5	Strong to left	Could not walk at all for nearly one minute. Lay on ground on left side struggling to get up	Vertical bank and side slipping to right, when facing forwards after turning	Momentarily very giddy, rapid recovery. No nausea or pallor.
5	Right side of head down	Clockwise	5	Strong backwards	Very strong opisthotonos	Nose diving (when facing forwards)	'Not exactly giddy'. No nausea.
6	Right side of head down	Counter-clockwise	5	Strong forwards	Strong emprosthotonos	Tail sliding (when facing forwards)	'Not exactly giddy'. No nausea.

Table VII. [*Rotation Type F. First Grade Pilots.* (See Table II.)]

Name.	*Hours flown*	*Remarks.*
25. Capt. . .	215	Fighting scout, Flight Commander. Has flown eight months. Credited with twenty-nine E.A.'s.[1] Is a dead shot. Aerobatics at early stage, but crashed many machines in learning to land scouts. Has flown to 22,000 ft. without oxygen. Never giddy or sick in air. Has been sea sick crossing Channel.

Table VIII. [*Rotation Type B. First Grade Pilots.* (See Table II.)]

Name.	*Hours flown.*	*Remarks.*
19. Capt. . .	900	A great and brave pilot credited with twenty-five E.A.'s. Can fly at 21,000 ft. without oxygen.
43. Capt. . .	480	Fighting scout, Flight Commander. Never giddy in air. Generally sick in boat. Began aerobatics early. Has twice collided in air, and safely landed in damaged machine.
42. Capt. . .	320	First flight as observer was sick in air—never since. Generally feels sick crossing Channel or Atlantic. Won M.C. for excellence of Corps work on R.E. 8's.

[1] Over twenty more since these notes were written.

TABLE IX. [*Rotation Type H.* (See Table II.)]

Rotation test.	*Position of head.*	*Direction of rotation.*	*Number of turns.*	*Induced rhombergism.*	*Effect of gait, &c.*	*Sensations of orientation, &c.*	*Sensations of dizziness, nausea, &c.*
1	Erect	Clockwise	6	No	Walked straight	Room going round to left horizontally	Giddy.
2	Erect	Counter-clockwise	6	No	Walked straight	Room going round to right horizontally	Giddy.
3	Face down	Clockwise	6	Slight to right	Walked almost straight	Felt as if spinning to left when facing down. Floor a little tilted down to left when looking ahead	Very giddy and nausea, slight pallor. Lasted several minutes.
4	Face down	Counter-clockwise	6	Slight to left	Walked almost straight	Felt as if spinning to right when facing down. Floor a little tilted down to right when looking ahead	Very giddy and nausea, slight pallor. Lasted several minutes.
5	Right side of head down	Clockwise	6	Falling backwards	Found it difficult to get up from chair	Felt as if nose diving	
6	Right side of head down	Counter-clockwise	6	Falling forwards	Found it difficult to prevent stooping forwards	Felt as if floor was coming up towards the face	

TABLE X. [*Rotation Type H. First Grade Pilots.* (See Table II.)]

Name.	*Hours flown.*	*Remarks.*
14. Capt.	700 at least.	Has flown since 1915. Credited with at least twelve E.A.'s. Fine pilot, but is 'not fond of spinning'. Prefers other manœuvres.

TABLE XI. [*Rotation Type J. First Grade Pilots.* (See Table II.)]

		Remarks.
81. Major.	Long experience, and a Squadron Commander of S.E. 5's in 1918.	Fine war pilot, leader and instructor of scout flying and fighting. 'Nearly always sea sick on sea: never while flying.' A keen dancer. He considered the effect in the rotation-chair *far exceeded* any induced by evolutions when flying.

Table II shows the results obtained from the First Grade Pilots only.

We find three exceptionally good scout pilots who showed strong forced movements or distressing giddiness, after slow turning. I would draw especial attention to Captain 25 [Tables VI and VII], who had already shot down twenty-nine enemy aeroplanes, and later was credited with nearly as many more. When this officer was turned five turns, even slower than was the average rate, he collapsed to the floor, after the face-down test, and struggled vainly to rise for fully half a minute. But he showed no signs of distress such as pallor, or clamminess of the skin, and had no headache.

Two other distinguished pilots with long war flying experience closely resembled Captain 25 in the reaction shown to hyperstimulation of the labyrinth by rotation, viz. Captain 14 [Table IX and X] and Major 81 [Table XI].

Both officers were absolutely normal men in their best flying form.

In contrast with the three above-mentioned officers, Nos. 25, 14, and 81, who reacted strongly, we can refer to the Groups A and B, which includes those whose responses were normal but the reactions were moderate, slight or absent.

None of these twelve pilots appears to have derived any assistance from the semi-circular canals to estimate position in space while flying, for they all admit losing the sense of position in dense clouds.

Conclusion.

Consideration of the data presented in the above Tables appears to show that the reactions to rotation may be excessive in some individuals and suppressed in others, but in neither case do the reactions of the semi-circular canals serve to indicate an airman's probable flying ability.

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