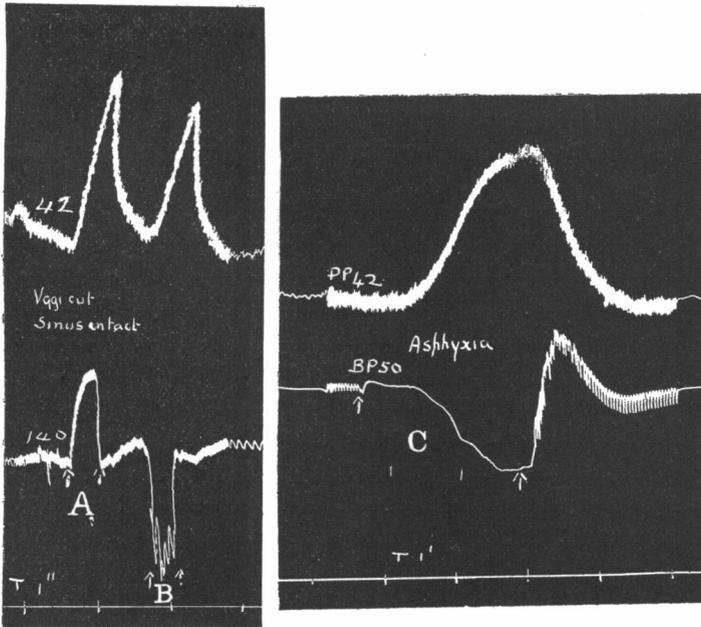


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A convenient method of studying the reactions of the vaso-motor centre. By R. J. S. McDOWALL. (*Dept. of Physiology, King's College, London.*)

The method consists of a combination of that used by Bartlett and that demonstrated by me to the Society in 1923 and subsequently described by Hemingway. It consists essentially of recording the perfusion resistance of a part of the body, the blood vessels of which



have been tied off for the most part from the general circulation. The apparatus can be made to give magnification several times that of the blood-pressure variations, and all the ordinary reactions of the vaso-motor centre may be shown with complete readiness and uncomplicated by the cardiac or peripheral vascular effect. The figures indicate typical

records obtained by the method. The upper tracing in each instance indicates perfusion resistance in the hind limbs of a cat, the lower, blood-pressure in the left carotid artery, the vagi being cut in each case. At *A* the right carotid artery was clamped, *i.e.* the carotid sinus clipped off, temporarily between the arrows, at *B* the heart was held. These records show the reaction of the centre to fall of arterial pressure. In *C* the animal was asphyxiated between the arrows. The stimulation of the vaso-motor centre due to the asphyxia is seen in the perfusion record, although it is completely masked in the record of arterial pressure. That the two circulations are sufficiently separate to warrant the results being ascribed to the vaso-motor centre is shown by the fact that these reactions disappear after denervation or loss of reaction of the vessels of the part. The method for many investigations is an excellent substitute for the plethysmograph.

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The rate of diffusion into erythrocytes. By MONTAGUE MAIZELS.

In re-investigating the permeability of erythrocytes to phosphates [Maizels and Hampson, 1927] it was found necessary to determine the rate at which the anion diffuses. As the rate of phosphate diffusion varies with temperature, the temperature coefficient of phosphate diffusion was first studied. Heparinized blood was centrifuged and the cells mixed with one hundred times their volume of potassium phosphate solution of constant *pH* at various temperatures. After 5 minutes the suspensions were centrifuged in a series of tubes drawn out into sealed graduated capillaries. The tubes were then washed without disturbing the red cells in the capillaries. The volume of red cells was read and their phosphorus content estimated. At *pH* 8.4 and *pH* 5.4 the temperature coefficient between 10° and 20° C. was 1.7; between 20° and 30° C., 2.4; and between 30° and 40° C., 1.15.

Rate of Diffusion. If cells are suspended in mixtures of H_3PO_4 , K_2HPO_4 and KH_2PO_4 , $\Delta = 0.42^\circ \text{C.}$, the maximum phosphorus content after 1 hour at 24° C. is at *pH* 5.3. But if the phosphorus content is measured after only 5 minutes' exposure it will be found that this is maximal at *pH* 5.7. This indicates that phosphate permeates most easily at *pH* 5.7 (Table I).

If KCl ($\Delta = 0.42^\circ \text{C.}$) is added to the phosphate it is found that the permeation of phosphate is greatly depressed; but the entry is most rapid at pH 6.

TABLE I.

pH	Cells in pure phosphate solutions			Cells in mixtures of potassium phosphate and chloride ($\Delta = 0.42^\circ \text{C.}$)	
	External P mg./100 cc.	Cell P		External P	Cell P at 60 min.
		5 min.	60 min.		
3.6	402	78	275	—	—
5.1	396	160	340	198	32
5.3	390	180	352	195	35
6.0	367	192	325	183	68
6.2	358	155	290	179	60
6.7	337	105	230	168	45

When 0.05 c.c. of cells is suspended in a mixture of equal parts of KCl, and KH_2PO_4 , the resulting pH is about 5.1, and the cell chloride is 112 millimoles, compared with 62 mm. in the external fluid. It appears that excess of chloride enters the red cell to balance the osmotic pressure of the external chloride and phosphate, and to satisfy the anion requirements of the red cell at pH 5.1. If cells are placed in a mixture of KCl (1 part) and KH_2PO_4 (5 parts), the external chloride is 21 mm. and the internal Cl 102 mm. This preponderance of cell chloride is brought about by an excess of any relatively indiffusible anion or non-electrolyte in the external solution.

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Impulses in the giant nerve fibres of earthworms. By J. C. ECCLES, R. GRANIT and J. Z. YOUNG.

In the ventral nerve cord of the earthworm there lie three very large non-medullated nerve fibres, and it has recently been shown that in the living worm the middle of these conducts antero-posteriorly and the two lateral fibres postero-anteriorly [Stough, 1926, 1930]. The fibres are not continuous throughout their length, but are divided into segments by membranes which apparently resemble the surface membranes of the fibres. The surfaces of contact are usually not flat, but curved in various ways so that the concave end of one segment fits over the convex end of its neighbour.

Impulses in the nerve cord can be recorded by a Matthews' oscillograph when the head or tail of the earthworm is stroked with a feather.

The conduction of such impulses has been studied in the isolated nerve cord stimulated by induction shocks. Two impulses are set up by a sufficiently strong shock applied to either the head or tail end of the nerve, the conduction rate of the faster impulse varying in different experiments from 17 to 25 metres a second and that of the slower from 7 to 12 metres a second (temp. 10° to 12° C.).

By altering the strength of the stimulus it can be shown that the impulses have an all or nothing relationship to this stimulus, even the finest adjustment of the threshold failing to show that either impulse is made up of two separable impulses. Stough has described transverse connections between the lateral fibres, so it would appear that the presence of only two impulses is due to these two fibres forming a single conducting unit. By stimulating the nerve trunk first at one end and then at the other end a few sigma later and leading from the centre of the nerve to the oscillograph, it has been shown that the fast impulse in one direction travels in the same fibre as the fast impulse in the other direction, and similarly with the slow impulse. Thus, in spite of the transverse membrane, the impulses can pass in either direction. The unidirectional conduction found by Stough is not, as he suggested, due to the transverse membranes; it must be due to the connections of the nerve fibres.

At the head end the threshold stimulus for setting up the fast impulse is much lower than that for the slow impulse, while at the tail end the difference is always less. Also the action potential of the fast impulse at the head end is much greater than that of the slow impulse, but at the tail end the potential of the latter may even exceed that of the former. Since at this end the diameters of the lateral fibres are relatively to the median fibre, greater than anteriorly it seems certain that the slow impulse travels in the lateral fibres and the fast impulse in the median fibre. Experiments on the nerve impulse indicate that the rate of conduction is approximately proportional to the diameter of the fibre, and the action potential to the cross-sectional area. In our experiments the relative velocities of conduction of the fast and slow impulses are in accordance with the relative diameters of these fibres, but the action potential of the slow impulse is relatively about twice the size that would be expected from a single lateral fibre. This doubtless is due to the summed potential resulting from the two lateral fibres conducting as one.

The refractory period and recovery curve have been determined in three experiments, and are approximately the same for the median and lateral fibres. An impulse is conducted more slowly in the relatively refractory period and it has a lower potential. In fact the impulses in the

earthworm nerve have been very similar to the A group of impulses in frog nerve. In such respects, therefore, the transverse membranes have no influence on the conduction of impulses, although the separation of the segments by means of these transverse membranes appears to be as complete as that existing at vertebrate synaptic junctions. However, investigation into the polarization of these nerves by galvanic currents, though still in its preliminary stages, seems to bring out certain differences from vertebrate nerve which may be ascribable to the polarization of these membranes.

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The action of veratrine on frog's nerve. By H. FROMHERZ
 and A. V. HILL.

In muscle the prolonged veratrine contraction is associated [Hartree and Hill, 1922] with a prolonged liberation of heat, the ratio (at any moment) of tension to rate of heat production being the same as in an ordinary tetanus.

Nerves soaked in 1/50,000 veratrine and subjected to a short tetanus show a somewhat prolonged heat production: they also give a slight after-potential. In order, however, to obtain the characteristic veratrine effect we have first poisoned our nerves, then asphyxiated them in pure N₂ or H₂, then allowed them to recover in O₂. Graham and Gasser [1931] found this treatment to yield a prolonged after-potential. We have observed veratrine after-potentials lasting for minutes following a single shock to a nerve fully recovered from asphyxia. Presumably the drug is unable to penetrate and produce its characteristic effect until the nerve surface is somehow disorganized by oxygen want.

In a nerve veratrinized in this way the heat produced in response to a single condenser discharge may be 100 to 1000 times as great as in a normal nerve. In a succession of shocks at regular intervals the heat per shock is less, depending on the interval, but still far more than normally. The "veratrine ratio" is greatest after prolonged rest and grows less as the period since previous activity diminishes. The second of two shocks, e.g. at 5 sec. interval, may give half as much heat as the first, at 10 sec. interval two-thirds, at 30 sec. interval three-quarters.

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The effect on the body temperature of animals of injections of an extract of parathyroid glands. By M. H. B. ROBINSON and J. H. THOMPSON. (*Research Laboratories of the University of London, King's College and the Royal College of Surgeons, London.*)

It has been shown that extirpation of the parathyroid glands in rats and rabbits results in a disturbance of the heat-regulating mechanism; the injection of parathyroid preparations somewhat compensates for this loss of regulatory function [Ogawa, 1925].

A series of readings has been taken in rabbits and rats which have been injected with an extract of parathyroid glands, free from the factor which raises the blood calcium [Collip]. The preparation of the extract is described by Robinson and Thompson. The temperature readings were taken under standard conditions with regard to room temperature (65° F. thermostat controlled), diet, and time relation to injection. The thermometer was inserted per rectum sufficiently far to cover a fixed mark on the bulb. Daily observations were made. The results are tabulated as follows:

Range of temperature: average of 12 rabbits.

<i>Rabbits.</i>		Weeks		
		1st	3rd	5th
Experimental	Average maximum	100	100.1	100.2
	Average minimum	99	99.2	99.3
Controls	Average maximum	101.5	101.2	102
	Average minimum	101	100.4	100.8

The average range of temperature during the experimental period was:

Experimental rabbits	99.1 to 100.1
Control rabbits	100.7 to 101.5

The experimental rabbits maintained their body temperature at a lower level than that of the control rabbits throughout the experiment.

Range of temperature.

<i>Rats.</i>		Weeks				
		1st	2nd	3rd	4th	5th
Experimental	Average maximum	97.3	97.5	98	98.6	98.6
	Average minimum	97.2	97.1	97.2	98.0	98.0
Controls	Average maximum	98.2	98.9	98.6	98.9	98.7
	Average minimum	98.0	98.0	98.1	98.3	98.4

The average range of temperature during the period in which injections were made was:

Experimental rats	97.2 to 97.6
Control rats	98.0 to 98.6

Injections were discontinued after the end of the third week, and the

temperature of the experimental animals began to rise three days after cessation of injection. From that time up till the last readings the temperature of the experimental rats has closely approximated that of the control animals.

A preliminary experiment indicates that injection of extract of anterior lobe of pituitary gland can raise the temperature of animals in which it has been lowered by injection of a parathyroid extract as described.

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The effect of veratrine on the electrical response of crab's nerve.

By S. L. COWAN. (*Marine Biological Laboratory, Plymouth.*)

With a Cambridge Instrument Company's A and M galvanometer (sensitivity 1 mm. = $4 \cdot 10^{-10}$ amp. at 3 metres, and period 3.8 sec.) a spider crab's (*Maia squinado*) leg nerve gives an action current deflection of about 30 mm. in response to a single just maximal shock [A. V. Hill, 1932, and Beresina and Feng, 1932], provided by a condenser discharge.

Usually, after dissection, the nerve is allowed to rest for an hour in aerated sea water to avoid the onset of reversible inexcitability; in the present experiments it was transferred at the end of the first half hour to sea water to which had been added previously the required amount of veratrine hydrochloride solution, any carbon dioxide liberated being blown off by passing air through. With such dilute veratrine solutions as were used, 1 in 10 millions to 1 in 100 millions, the pH of the sea water need never be altered by more than 0.1 unit, and control experiments showed that nerves soaked in sea water, which had been acidified with hydrochloric acid and the carbon dioxide removed by blowing in air, gave responses which did not differ from those given by nerves soaked in untreated sea water. At the end of the second half hour the nerve was mounted, the peripheral end crushed and galvanometer connections were made *via* non-polarizable electrodes. After oxygen had been passed through the chamber for fifteen minutes to allow the nerve to recover from the crushing, readings were taken to get a base line and then the nerve was stimulated at the central end. The initial action current response of a nerve so treated with veratrine was very large, as much as

650 mm., and the area of the deflection time curve was increased more than a hundredfold. The "retention" of action current described by Levin [1927] and by Furusawa [1929] lasted for nearly half an hour.

The optimum concentration of veratrine, for autumn crabs, lies in the region of 1 in 25 millions to 1 in 50 millions. A definite fall in the response can be noticed with concentrations of 1 in 10 millions on the one side or 1 in 100 millions on the other; in the latter case the response of these non-medullated nerves is still about fifty times larger than normal. Asphyxiation after soaking in veratrine sea water and previous to stimulation in oxygen does not affect the response.

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Loss of heat at high altitudes. By BRYAN H. C. MATTHEWS. (*Physiological Laboratory, Cambridge.*)

At sea level, in dry cold air, 15–25 p.c. of the total heat production of the human body is dissipated through the lungs and respiratory passages, in vaporizing water, setting CO₂ free from solution, and warming air. At high altitudes a much higher percentage of the total heat produced must inevitably be lost from the lungs, etc., for the heat loss per litre of respired air remains about the same while the potential heat gain in the form of oxygen becomes less and less. The rapid respiration necessary to obtain adequate oxygen may dissipate heat as fast as it can be gained by utilizing that oxygen.

If these effects are considered quantitatively some surprising results come to light. The heat loss per litre of air at -10° C. respired (whether dry or saturated makes little difference) is approximately 27.5 cal. in water vapour, 2.5 cal. in CO₂ and warming air. *Thus total heat lost per litre of air respired is 30 cal.* From 1 c.c. of oxygen absorbed about 5 cal. can be produced. For each millimetre by which the tensions of oxygen in inspired and expired air differ, approximately 1.3 c.c. of oxygen are absorbed from each litre respired, and 6.5 cal. are available. *Total heat gained per litre respired and per mm. difference in oxygen tension in inspired and expired air, 6.5 cal.*

As the barometric pressure falls the oxygen tension in inspired air falls, that in alveolar air also falls, that of the expired air will always be a little above that of the alveolar sample owing to dead space, etc. With fall of barometric pressure the difference between the oxygen tensions in inspired and expired air becomes smaller and smaller.

It will be seen from the above figures that unless the inspired and expired air differ in oxygen tension by about 5 mm., even if clothing is so perfect that it prevents any heat loss from the skin, the body temperature cannot be maintained. By extrapolation from figures for alveolar air up to 23,000 ft. [Barcroft, 1925; Somervell, 1925] it appears that these conditions will be realized somewhere round about 30,000 ft. Human life above the point where this occurs will be impossible without respiratory aids or artificial heating, for the body temperature must fall.

I have constructed several forms of respirator to recover the heat and water vapour from air expired and return it to the inspired air; these are at present undergoing tests. It is hoped it may be possible to prevent 40–80 p.c. of the total heat loss at high altitudes, and to eliminate the throat irritation resulting from desiccation.

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Decreased urinary flow in rats on high fat diet. By CASIMIR FUNK and P. P. ZEFIROW. (*Casa Biochemica, Rueil-Malmaison, France.*)

In connection with the work on the hormones appearing in urine [Casimir Funk and P. P. Zefirow, 1932] an interesting observation was made, which apparently so far has escaped the attention of investigators and clinicians. A series of rats were kept on a practically fat-free diet on one hand, and on a high-fat diet on the other. Without any noticeable difference in the water consumption in the two series of animals, and with the food consumption lowered only by 40 p.c. in average, the urine excretion was much lower in the high-fat series. In a few instances an addition of 125 g. of butter to the usual (but not controlled) diet in human beings caused a diminution of urine volume by about 20 p.c. No explanation can be offered at present, but it seems possible that a high-fat diet may influence the pituitary gland.

The animals used were rats, two males and one female kept together

in a metabolism cage. Altogether 48 young growing animals were used. Water and food were given *ad libitum*. The diets used consisted of 24 g. caseinogen, 62 g. starch, 10 g. dried yeast, 4 g. salt mixture, and 2 c.c. of cod-liver oil. In the high-fat diet 48 g. of starch were replaced by butter. In the last recorded experiment the fat content was increased to 73 p.c. and lard used instead of butter, without change in the results obtained. The first two experiments were performed during the heat of the summer, the last two in autumn and winter. In summer the urine volume was lower, due to increased loss through the skin. The results are summarized in the table below:

Exp.	Duration of experiment, days	Fat-poor diet: daily variations	Average	High-fat diet: daily variations	Average
		c.c.	c.c.	c.c.	c.c.
I	8	22-30	26.2	1-6	3.3
II	14	20-53	32	1-11	3.7
III	10	14-34	26.1	11-24	14.2
IV	41	12-44	28.7	1.5-11	6.0

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Action of ether on the sympathetic system. By B. B. BHATIA and J. H. BURN.

Elliott [1912] showed that ether, chloroform and urethane caused a discharge of adrenaline from the suprarenals, which occurred so long as the splanchnic nerves were intact. We have investigated the action of ether on other parts of the sympathetic system, making our observations on cats from which the suprarenals were removed and using the decerebrate preparation with vagi cut, and also the spinal preparation.

When ether vapour is mixed with the air used for artificial respiration, there is a powerful contraction of the spleen, inhibition of intestinal movements and tone, inhibition of uterine movements and rise of heart rate. These effects are reversed as soon as the ether is discontinued. In animals in which the spinal cord is destroyed, these effects are not seen, except that a gradual paralysis of intestinal movements occurs which persists long after removal of the ether. The contraction of the spleen in the decerebrate cat is abolished when the sympathetic ganglia are paralysed by nicotine.

As shown by heart-lung experiments, ether weakens the heart more than is commonly supposed, but this is not obvious in the intact animal

because of a simultaneous vaso-constriction, presumably due to sympathetic impulses. Thus an amount of ether which has no effect on the blood-pressure of a decerebrate cat causes a profound fall of blood-pressure after paralysis of the sympathetic ganglia by nicotine. Since ether has no appreciable action on the blood vessels themselves, as shown by perfusion experiments, this fall represents the uncomplicated effect on the heart. It is concluded that ether causes a discharge of impulses along all sympathetic nerves.

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Electric symmetry of the thorax. By W. A. OSBORNE (*Melbourne*).

When the two hands are led off to the string galvanometer, as in the conventional lead I, and when the string is adjusted to give the sensitivity required for standard electrocardiograms, it will be found that normally a deep breath produces either a very small deflection or none at all. As is well known a slight movement of either arm or hand develops a current of several millivolts. Lack of symmetrical expansion of the thorax in deep breathing can be readily detected in this way, and it is rather curious that, though the diaphragm is not bilaterally symmetrical in the normal human being, no potential difference of any magnitude is produced. A remarkable fact is that all the left-handed students I have examined, both male and female, show on taking a deep breath a string deflection of several millivolts amplitude pointing to some disturbance of the normal balance of effort in the right and left halves of the thorax.