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Involuntary activity in biceps following the sudden application of velocity to the abducted forearm.

By P. H. HAMMOND. *Radar Research Establishment, Ministry of Supply, Malvern, Worcs.*

Recent work (Eldred, Granit & Merton, 1953) has indicated that the sensory endings in skeletal muscle are length detectors in a closed loop control system which positions the limb. The apparatus shown diagrammatically in Fig. 1 was designed to test the closed-loop hypothesis on the intact human subject. A pull of constant velocity can be applied without warning to the abducted arm; arrangements are made to measure the force exerted at the wrist and the e.m.g. activity from skin electrodes over the biceps.

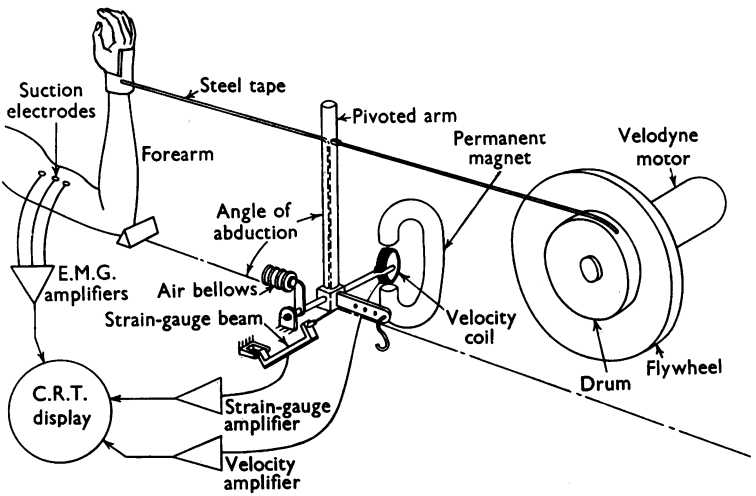

Fig. 1. Diagram of apparatus.

Initially the arm is abducted at about 80° and the subject exerts a constant force against a stop, by reference to a meter deflexion derived from strain gauges. A constant-velocity pull is then applied to the wrist by clutching in a speed controlled motor; the subject being previously instructed either to

let go or to resist when pulled. Typical recordings of force and e.m.g. are shown in Fig. 2. Three subjects have been studied and give results which are remarkably consistent.

According to the closed-loop hypothesis the initial spike in the force record due to the sudden acceleration of the forearm should be followed by a period during which the force is due to extension of the muscles whilst in a state of steady excitation corresponding to the initial conditions. Sensory endings in the muscles begin to stretch when the pull is applied though their rate of stretch is reduced by series elastic elements. After delay due to nerve transmission action potentials appear reflexly at the muscle and active force builds up until voluntary control is established from higher centres and force build up is accelerated or stopped.

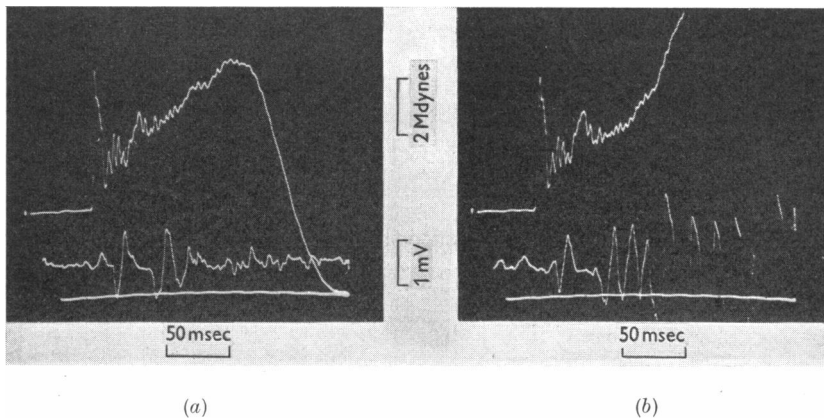

Fig. 2. Force (uppermost) and e.m.g. recordings with a pull velocity of 40 cm/sec. (*a*) Subject instructed to let go when pulled. (*b*) Subject instructed to resist when pulled.

The force records obtained show a slow rise after the initial inertia spike and a rapid rise or fall when voluntary control is established about 100 msec after the beginning of the pull. E.m.g. records have a diphasic wave occurring about 18 msec after the pull, a latency according well with reflex arc transmission time. Following this wave is a 'silent period' possibly caused by a transient slackening of the muscle spindles (Merton, 1951). Associated with the diphasic wave is a twitch on the force record which, however, may be due to a fluctuation in motor speed. Activity following the silent period is interrupted abruptly if the subject is instructed to let go when pulled, otherwise it is continuously maintained.

The evidence so far obtained to support the closed-loop hypothesis is not decisive. The records show that only about 4 Mdyn of resisting force are turned on before voluntary control supervenes. Maximal effort at the wrist is about 30 Mdyn so that the involuntary mechanism plays a minor part in resisting

forcible extension of the forearm. Its failure in this respect may be due to the buffer action of the elastic elements between external events and their detection by the sensory endings in muscle.

Acknowledgement is made to the Chief Scientist, the Ministry of Supply, and to the Controller of H.M. Stationery Office for permission to publish this paper. Crown copyright reserved.

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A respiratory anemometer. By B. M. Wright. *Medical Research Council, Pneumoconiosis Research Unit, Llandough Hospital, near Penarth, Glam.*

The anemometer was designed as a form of portable gas meter for measuring the respiratory volume of ambulant subjects. It weighs only 17 g and can be fitted in place of an inspiratory valve in a respirator face-piece. It consists of a hollow cylinder 3 cm in diameter and 2 cm long, one end of which is inserted in the respirator, the other being closed.

Air enters the cylinder through a number of tangential jets and drives a very light two-bladed rotor which is connected to a counting train. The latter, which is made from a wrist-watch movement, is mounted on the closed end of the cylinder and has a dial and hands to indicate the revolutions of the rotor. Details of its performance and characteristics will be given at the demonstration.

A full account of the instrument will be published elsewhere.

An apparatus for the analysis of film records. By D. A. McDonald. *Department of Physiology, St Bartholomew's Hospital Medical College, London, E.C.* 1

The cine-camera is an excellent medium for recording and studying movements in a qualitative way. Deriving precise measurements from these records has proved more difficult. Where the movement is in a straight line a good method is to project the film on to a moving drum and derive a curve relating the linear movement against time. This raises one practical problem in the necessity of aligning the movement projected at right angles to the movement of the drum. The apparatus to be demonstrated is an adjustable stand for a drum kymograph that allows the drum to be tilted accurately in relation to a projected picture.

It has been used for the analysis of high-speed films of arterial blood flow. The movement of a bubble of oxygen injected into the blood stream is filmed

at 1500 frames/sec. The film is then projected at 16, or 2, frames/sec on to the drum and a curve of distance travelled against time is traced. The velocity curve is then derived from the slope of this curve at successive points. The details of the method have been previously described (McDonald, 1952).

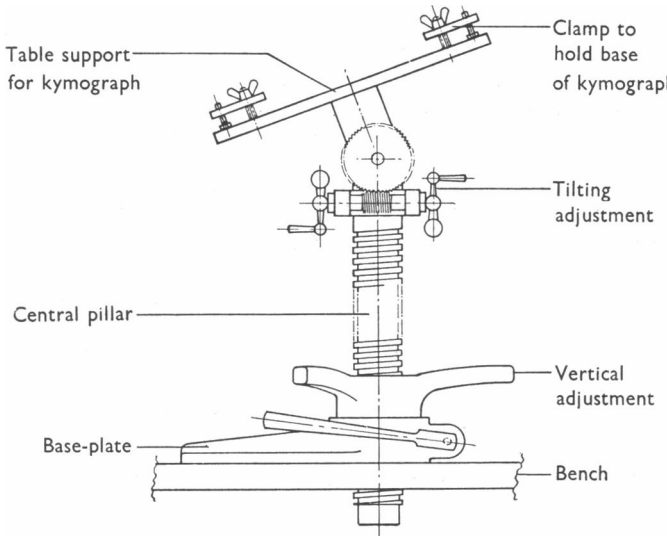

Fig. 1. The tilting table is designed to hold a standard Palmer electric drum kymograph. The degree of tilt is controlled by the worm-gear. The vertical height is varied by the screw on the central pillar. The base-plate is screwed to the bench.

The construction of the tilting table is shown in Fig. 1. The drum can be tilted to 60° from the vertical on either side, and is controlled by a worm-gear. The central pillar has a vertical movement of 24 cm. Apart from its specialized use it is thought that the table may find other uses as a versatile type of drum support.

The apparatus was designed and built by Mr E. W. Ellis and C. F. Palmer Ltd. The cost was defrayed by a grant from the Medical Research Council.

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The cytology of pancreatic secretion. By D. Lacy. *Department of Zoology and Comparative Anatomy, St Bartholomew's Medical College, London, E.C.* 1

Pancreatic secretion has been studied in cells which have not been stimulated by artificial means. Under natural conditions it has been shown that there exists a *secretion cycle* which consists of three main phases: (1) *Recovery* phase,

during which zymogen synthesis is maximal; (2) *Resting* phase, during which zymogen synthesis is minimal; and (3) *Discharge* phase, in which zymogen granules are lost from the cells. Zymogen synthesis is brought about by certain lipoidal prozymogen bodies which originate from mitochondria in the form of small granules. These pass towards the Golgi apparatus, probably receive some contribution from it, and become vacuolated. Each vacuolated prozymogen body consists of an outer lipoidal coat enveloping an immature zymogen granule. Eventually the lipoidal coat is shed and a mature zymogen granule is produced. Zymogen discharge is brought about in a similar way. Amongst the zymogen granules there appear small secretion bodies which gradually increase in size. Each secretion body consists of an outer lipoidal coat and an inner substance which is probably formed by the liquefaction and absorption of zymogen granules. Eventually the secretion bodies are extruded into intercellular secretion canaliculi. It appears that both the synthesis of zymogen granules and their absorption is brought about by the activity of an intracellular lipoidal cycle.

Secretion in cells has also been studied with the electron microscope in collaboration with Dr C. E. Challice of the Wright-Fleming Institute. It is suggested that the area presented by the cytoplasmic reticulum to the interreticular substance alters during the phases of the secretion cycle. Further, after the previous use of pilocarpine hydrochloride most of the reticulum breaks down during the discharge phase to form a second secretory product of pancreas cells.

The application of interference contrast microscopy to the study of living muscle fibres. By F. J. Aumonier. *Department of Physiology, St Bartholomew's Medical College, London, E.C.* 1

The interference contrast microscope, devised by F. H. Smith of Chas. Baker Ltd., is an instrument which enables small differences of refractive index in an object to be rendered visible to an observer and to be measured. A beam of polarized light is focused by a substage condenser upon the specimen. The condenser is of conventional type except for the fact that a calcite plate is cemented to the plane surface of the front lens. This system enables a sharply focused image of the light source to impinge upon the specimen and a second image to be focused above the specimen. The objective has a similar calcite plate cemented to its front. The result of this arrangement is that in the back focal plane of the objective there are two series of wave trains, one, the image-forming beam, consists of rays which have passed through the object; the other, the reference beam, has passed round the object, but not through it. Both wave trains have arisen

from identical points in the light source, and so are capable of interfering. The planes of polarization of the reference and imaging beams are at right angles to each other. A quarter wave plate with its optic axis at 45° to the reference beam is placed just behind the objective. After traversing this plate the two beams are circularly polarized in opposite directions. Behind the quarter wave plate is a rotating analyser. The effect of rotating the analyser is to change the phase relationship between the two beams. The rotation of the analyser can be read off on a scale divided in degrees of angle.

In order to determine the refractive index of a given object the following data must be available: (1) the wavelength of the light used, (2) the refractive index of the mounting medium, and (3) the thickness of the object.

The instrument is first adjusted for Köhler or critical illumination with the polarizer, quarter wave plate and analyser out of the optical train. These accessories are then placed in their working positions, the eyepiece is removed, and the back lens of the objective is examined. A series of interference bands can be seen crossing it. The condenser adjusting screws are then turned till one band covers the whole of the back lens. The eyepiece is replaced, the specimen is focused, and a suitable object found. The analyser is now rotated till the background is at its darkest, and the reading of the analyser scale is noted. The analyser is again rotated till the object becomes dark, and the new reading is recorded. The difference between these readings D can then be used to determine the refractive index N of the object from the equation: $N=\frac{2D\lambda}{360t}+n$, where λ = the wavelength of the light used, t = the thickness of the specimen (both λ and t must be in the same units), and n = the refractive index of the mounting medium.

This method only applies to specimens which produce a phase shift of less than one wavelength. When the object is thin but of very high refractive index, or thick but of lower index, then a change of more than one wavelength may occur. In this case a number of interference fringes will be seen crossing the object, and the number of fringes will be equal to the number of wavelengths of retardation produced by the object.

The following demonstrations will be given:

(1) The determination of the refractive index of a test object (a glass fibre in canada balsam).

(2) The determination of the refractive index of a muscle fibre mounted in serum.

(3) The determination of the refractive index of a muscle fibre damaged by the action of a Coxsackie virus.

Measurement of ultrasonic absorption in tissue. By H. S. HATFIELD

Rahere rabbits and Merion rats. By W. H. Woodcock

A simple method of recording repeated histamine-induced bronchospasm in the anaesthetized guinea-pig. By J. P. D. Thomas and C. Todd. *Department of Physiology, St Bartholomew's Hospital Medical College, London, E.C.* 1

Guinea-pigs were anaesthetized with 1–1·5 ml./kg intraperitoneal paraldehyde, the later ones with inhaled cyclopropane. With a tracheal cannula inserted, tidal air was recorded using a 'circle-type' closed circuit incorporating two small Perspex uniflow valves, a low-resistance soda-lime chamber, and a re-breathing bag connected to a float recorder. Oxygen flow was adjusted to give a steady horizontal record. Intrapleural pressure was recorded via a cannula, with lateral holes, that was inserted through the right chest wall and connected to a mercury manometer or tambour, the pneumothorax being reduced to a minimum of about 1 ml. air and tracings obtained on a kymograph with smoked paper. Latterly intrathoracic pressure has been recorded in the oesophagus using a capacitance manometer.

Intravenous injections of 1–20 μg histamine acid phosphate, calculated as base, produced characteristic changes in records of tidal air and intrapleural pressure. The sensitivity of the individual animals varied, but normally pronounced effects were obtained with 4–8 μg. A marked reduction of tidal air and a simultaneous increased variation of intrapleural pressure, lasting about 30 sec, denoted a satisfactory bronchospasm. This could be reproduced in identical form, with the given dose of histamine, provided an interval of up to 5 min was allowed between injections.

The effects of antispasmodic drugs such as mepyramine maleate, adrenaline HCl, and aminophylline HCl were studied in three ways.

(*a*) After repeating a given dose of histamine three times the antispasmodic drug was given, and repeated increasing injections of histamine given until a response was obtained similar to the first three, thus showing the degree of protection.

(*b*) After the initial three doses of histamine the antispasmodic drug was given, and the initial dose of histamine was repeated at set intervals until the original response was repeated. In this way the length of time was obtained during which the antispasmodic drug was effective.

(*c*) In a few experiments a slow constant infusion of histamine was given, producing a definite degree of bronchospasm; the effectiveness of antispasmodics was then studied on an already induced spasm.

Using the complete animal physiological responses can be studied, although other methods using isolated organs may be preferable for assay purposes.

Fifteen million volt linear accelerator for radiobiological research. By J. ROTBLAT

Muscle metabolism and the regulation of breathing. By A. G. RAMSAY. *The Institute of Physiology, University of Glasgow*

In the regulation of breathing two components may be distinguished, a blood-borne chemical component, and a component known as the 'exercise stimulus' whose nature is obscure (Grodins, 1950). It is thought that this 'exercise stimulus' may originate in receptors in the region of the working muscles, and some regard these receptors as being proprioceptors sensitive to tension or movement. The present experiments investigate the possibility that an increase in the metabolic activity of the muscle cells stimulates nerve receptors and leads to an increase in pulmonary ventilation.

The hind limb of one anaesthetized dog, the recipient, was perfused via its femoral vessels with blood from a second anaesthetized dog, the donor (both dogs anaesthetized with barbitone, 200 mg/kg). All vascular channels between the hind limb of the recipient and its parent body were occluded. Pulmonary ventilation and oxygen consumption were continuously recorded by spirometer in both dogs. Muscle temperatures in both limbs of the recipient dog were also continuously recorded by thermocouple. Into the arterial side of the perfusion system was injected 5 mg/kg of 2:4-dinitrophenol. The metabolic rate of the donor dog, together with that of the perfused limb, rapidly rose to from two to four times the resting value. As soon as oxygen consumption of the donor began to rise, the ventilation of the recipient also rose, although the oxygen consumption of the recipient did not change. The increase in ventilation occurred before any change in muscle temperature could be detected. No change in ventilation of the recipient occurred on injection of saline. After the sciatic and femoral nerves of the perfused limb had been cut, injection of DNP caused no change in the ventilation of the recipient.

It thus appears that an increase in the metabolism of the limb caused the increase in pulmonary ventilation; this effect was mediated by nerves. It is suggested that there are receptors sensitive to changes in metabolic activity; these may be the site of origin of the 'exercise stimulus'.

This work was done in the Physiology Department, Northwestern University, Chicago, U.S.A., under the direction of Dr F. S. Grodins, to whom grateful acknowledgement is made. The investigation was supported in part by a research grant from the National Institutes of Health, U.S. Public Health Service.

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Further observations on the rostral portion of the vagina in the rabbit. By F. J. AUMONIER, K. J. FRANKLIN and N. E. WINSTONE

The effect of intravenous infusions upon the heart rate of the anaesthetized dog. By J. C. G. COLERIDGE and R. J. LINDEN. *Department of Physiology, School of Medicine, Leeds*

Experiments were carried out to determine the conditions necessary for the elicitation of the Bainbridge reflex. The majority of experiments were performed on dogs anaesthetized with a combination of morphia, Dial-urethane (Ciba) and sodium pentobarbital. Infusions of blood or saline were made into the femoral vein; small volumes were infused rapidly, e.g. 50 ml. in 10 sec; larger volumes were infused more slowly, e.g. 200–400 ml. were given over periods of up to 4 min (Bainbridge, 1915).

Variable changes in heart rate following infusion were produced which appeared to be related chiefly to two factors: the volume of the infusion and the initial heart rate. Alterations in rate occurred more frequently after large infusions. If an alteration in rate was produced its direction and extent appeared to be determined by the initial heart rate in that acceleration occurred when the initial rate was low (acceleration always occurred if the initial rate was less than 110/min), whereas slowing took place when the initial rate was high (more than 150/min in most cases). In some experiments the initial rate changed during the course of successive observations, i.e. a low initial heart rate gradually changed to a higher rate. In these circumstances it was sometimes possible to show that an infusion which had caused cardiac acceleration in the earlier observations later brought about a slowing. On the other hand, if the trend was from a high initial heart rate to a low one the reverse occurred.

As far as could be determined the different changes in rate were not related to particular changes in arterial blood pressure or respiration caused by the infusion, or to the character of the fluid infused.

The infusion always caused an increase in mean right atrial pressure (measured with reference to atmospheric pressure), but a striking feature of the majority of experiments was that the greatest change in heart rate did not occur at the same time as the peak atrial pressure. In several experiments the maximum heart rate occurred over a minute after the end of the infusion when right atrial pressure had fallen almost to the pre-infusion level.

The expenses of this research were partly defrayed by grants from the Medical Research Council.

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Calcium and muscle sodium. By R. CREESE and H. E. ROBERTS.
Department of Physiology, The London Hospital Medical College, E. 1

Diaphragm muscles exposed to an environment deficient in calcium show, after the rapid development of neuromuscular block, a slower and progressive diminution in the contractions obtained by direct stimulation of the muscle. This functional failure is accompanied by a considerable gain in the sodium content of the tissue, and a fall in potassium.

An exercise experiment under field conditions. By J. V. G. A. DURNIN.
Institute of Physiology, University of Glasgow

Several well-controlled exercise experiments under laboratory conditions have been described in the literature (Taylor, 1944; Erickson, Simonson, Taylor, Alexander & Keys, 1946; and others). In recent years there have been few similar experiments under field conditions. Also, especially in a form of exercise such as grade-walking, there are reasons why climbing on a treadmill may not reflect accurately the effects experienced by a subject under more natural conditions.

An experiment is described where the oxygen consumption and energy expenditure of two subjects climbing a hillside were determined. Four different loads (5, 10, 15 and 20 kg) were carried on two measured gradients on Ben Lomond on each of 8 days. By arranging the experiment in the form of an 8×8 Latin square, the effect of the separate loads on each gradient could be found on the two subjects, and any effect due to the different order of carrying the loads and to the different days could be eliminated.

The mean oxygen consumption on a gradient of 1 in 5·7 varied from 2·22 l./min for the first subject while carrying a 5 kg load to 2·43 l./min for the 20 kg load; the corresponding values for the second subject were 2·09 and 2·44 l./min. The mean energy expenditures for the two subjects were 10·76 kcal/min for the 5 kg load and 12·17 kcal/min for the 20 kg load.

The coefficient of variation for the whole experiment was less than 4%. This value is highly satisfactory for a field experiment of this nature and is probably as low as could have been obtained had a laboratory treadmill been used.

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Cardiac glycosides and the potassium exchange of human erythrocytes. By C. R. B. JOYCE and M. WEATHERALL. *Department of Pharmacology, London Hospital Medical College, London, E.* 1

Schatzmann (1953) has shown that digitoxin and other cardiac glycosides delay the recovery of normal Na and K concentrations by erythrocytes which have been stored in the cold. We have therefore examined the effect of some cardiac glycosides on the potassium exchange of normal human erythrocytes. Freshly drawn blood, or washed red cells which had been allowed to stand for 4–5 hr in a dextrose-free medium at 37°, have been suspended in media containing Na, K, Ca, Mg, Cl, phosphate buffer and usually dextrose; ^{42}K has been used as tracer, and the rate of movement of K in and out of the cells has been followed for up to 6 hr at 37° and 3 days at 7°.

Except in the absence of dextrose, there were no great changes in the total K content of the cells. The rate of exchange of K decreased slightly during the experiments in the normal cells and decreased considerably in the presence of digoxin in concentrations from 10^{-8} to 10^{-5} (Table 1).

TABLE 1. K exchange of digoxin-treated erythrocytes

	Per cent of cell K exchanged per hour			
	37°		7°	
Treatment	First 2 hr	First 6 hr	First day	First 3 days
Controls	1·90–2·20	1·70–1·95	0·067	0·051
Digoxin: 0·01 mg/l.	1·85	1·30	—	—
0·1 mg/l.	0·82	0·47	0·068	0·052
1 mg/l.	0·32	0·23	0·047	0·035
10 mg/l.	0·25	0·20	0·032	0·023

In the absence of dextrose cell K was less well maintained and the rate of entry of K was diminished (as in the experiments of Glynn, 1954). In the presence of 10 mg/l. digoxin the entry was considerably slower, and was approximately the same whether dextrose was present or not. These relations between digoxin and dextrose were qualitatively similar in the presence of 2, 4 or 12 mM K.

Similar but less detailed results have been obtained with *k*-strophanthosid and digitaline.

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The collagen and elastin content of the arterial wall. By MARGARET L. R. HARKNESS, R. D. HARKNESS and D. A. MCDONALD. *Department of Physiology, University College and St Bartholomew's Hospital Medical College, London*

This investigation was prompted by an interest in the distribution of collagen and elastin in the body, especially in a tissue, such as the arterial wall, where their physical properties could be studied.

Arteries of dogs have been studied throughout. Samples of arteries from the same animals were used for the measurement of volume-elasticity curves. The aorta has been studied in most detail and the location of samples taken was recorded by measuring *in situ* from the aortic orifice, the diaphragm and the bifurcation of the aorta. Samples of large arteries (brachio-cephalic, carotid, subclavian, iliac and femoral arteries) and of one small artery, the saphenous, have been subjected to chemical analysis.

Dried samples were autoclaved at 30 lb./sq.in. for 6 hr. Collagen was estimated in the solution by hydrolysing it with 6 N-HCl and estimating hydroxyproline in the hydrolysate (Harkness & Harkness, 1954). Elastin was estimated in the solid residue by treating it with N/10-NaOH for 45 min at 95° C, washing it thoroughly, and drying to constant weight. This dried residue was then hydrolysed with 6 N-HCl and hydroxyproline and nitrogen estimated in the hydrolysate.

The total elastin and collagen only accounts for a proportion of the dry weight that ranges from about 60% down to only 30%. The relative composition of the wall is here expressed as the proportion of elastin to total elastin and collagen. In the thoracic aorta there is a high proportion of elastin—60·5% ± 4·0 (14 samples). In the abdominal aorta the proportion is much lower—27·3% ± 6·4 (7). The composition in other arteries studied has been much the same as in the distal aorta, e.g. iliac and femoral arteries—34·3% ± 10·0 (6).

The change in composition from thoracic to abdominal aorta takes place over a distance of not more than 5 cm; from 3 to 4 cm proximal to the diaphragm to 1 cm distal to it. If, as is usually assumed, the elastin in the large arteries is responsible for their elastic properties, this marked differentiation of arterial structure will have an important bearing on our concept of the reservoir, or 'windkessel', function of the arterial tree.

We wish to acknowledge a grant from the Nuffield Foundation for this work.

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The effect of 5-hydroxytryptamine, tryptamine and indolylacetic acid on the release of pigment from beetroot disks. By V. R. Pickles. *Physiology Department, King's College, Newcastle-upon-Tyne*

It is stated that indolylacetic acid and other substances which regulate growth in plants increase the rate of diffusion of pigment from slices of beetroot *in vitro* (Veldstra & Booij, 1949). This is attributed to an increased permeability of the cell membranes. From the structural requirements that have been

described for plant growth-regulator activity, it might be expected that 5-hydroxytryptamine would show this effect, and if so, this finding might be relevant to the mode of action of 5-hydroxytryptamine in animal tissues.

The substances to be tested were dissolved in distilled water or in 0·03 M-phosphate buffer, at pH 6, with the addition of 1% of ethanol which was necessary for rapid solution of indolylacetic acid. Batches of twenty disks 6 mm diameter and 1 mm thick, cut from fresh roots of *Beta vulgaris rubra*, were washed and then soaked in 5 ml. lots of the test solutions for two consecutive periods of 3 and 1–1½ hr. The pigment which exuded from the beet slices in each period was measured spectrophotometrically at 530 mμ and expressed in each case as a fraction of the pigment exuded from a control batch in the same period. The mean values in eight experiments on hydroxytryptamine (in the form of the creatinine sulphate), tryptamine and indolylacetic acid are shown in Table 1. All three substances were present in a concentration of 100 μg/ml.

TABLE 1

	Hydroxytryptamine	Tryptamine	Indolylacetic acid	Control
First 3 hr	1·50	1·00	1·30	1·00
Next 1–1½ hr	2·70	1·06	2·22	1·00

The values for hydroxytryptamine and indolylacetic acid are significantly different from 1·00.

It is concluded that 5-hydroxytryptamine is at least as potent as indolylacetic acid in causing pigment release, and more so than tryptamine, which in this series had no significant effect though in a concentration of 1 mg/ml. it approximately doubled the pigment exudation. The effect with 5-hydroxytryptamine was detectable at a concentration of 10 μg/ml., but not at 1 μg/ml.

In an attempt to differentiate between a possible effect on the cell wall and a general toxic effect which might equally lead to release of pigment, the oxygen consumption of beetroot slices was measured in the Warburg apparatus. Hydroxytryptamine in concentrations of 20, 40 and 80 μg/ml. caused no diminution in oxygen consumption over periods of 1–5 hr, although it increased pigment effusion by 7–60%.

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The potentiation of preganglionic impulses by histamine and pilocarpine. By U. TRENDELENBURG. *Department of Pharmacology, University of Oxford*

Evidence has been presented for the view (Trendelenburg, 1954) that both histamine and pilocarpine stimulate the superior cervical ganglion of the cat when the normal circulation of the ganglion is intact. The investigation of the

ganglionic actions of these two substances has been extended, and it has been found that they regularly potentiate the response to submaximal preganglionic stimulation. The doses required to potentiate preganglionic impulses are much lower than those necessary for stimulation of the ganglion. Whereas ganglionic stimulation was observed after injection of 2–20 μg histamine into the central end of the lingual artery (during occlusion of the external and internal carotid arteries), potentiation of the response to submaximal preganglionic stimulation has been observed after injection of 0·01–0·1 μg histamine by the same route. The potentiation of the stimulation by histamine was found to be blocked by mepyramine, and the potentiation by pilocarpine was found to be blocked by atropine; potentiation by both substances was found to be blocked by cocaine.

Both histamine and pilocarpine cause a fall of blood pressure followed by a rise in the spinal cat. This rise is not only due to liberation of pressor amines from the adrenal medulla since it persists after adrenalectomy. The evidence given above suggests that the rise after adrenalectomy is due to a transient potentiation of vasoconstrictor impulses from the spinal cord as they pass the sympathetic ganglia on their way to the vessels. Thus the rise is modified in the same way by substances like nicotine and cocaine as is the effect of histamine and pilocarpine on the ganglia.

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Squalene and other hydrocarbons in human sebum. By R. M. B. MacKenna, V. R. Wheatley and A. Wormall. *Departments of Dermatology and Biochemistry, The Medical College of St Bartholomew's Hospital, London*

In a study of surface skin fat or sebum from the human forearm we showed that about one-sixth of this fatty material consists of hydrocarbons. Squalene, an unsaturated hydrocarbon ($C_{30}H_{50}$), was isolated from this sebum in a pure state and shown to account for about 5% of sebum (MacKenna, Wheatley & Wormall, 1950). A method has been devised for determining the amount of squalene in as little as 5 mg of sebum, and it has been shown that sebum from the back contains more squalene than does forearm sebum (Wheatley, 1953).

Considerable interest has been aroused during recent years in the distribution of squalene in the animal kingdom, and in its significance as a possible intermediate in steroid metabolism. The secretion of squalene in sebum may represent the excretion of a metabolic waste product, but there is a possibility that this unsaturated hydrocarbon may have an important function as an antioxidant and fungicidal agent. A more complete study of the distribution

of squalene in sebum-like materials has now been made, and the results of these investigations, and others on the possible depilatory action of squalene, will be briefly summarized.

In other investigations it has been found that there is no significant difference between the squalene content of sebum from subjects suffering from certain skin diseases and normal individuals (Boughton, Hodgson-Jones, MacKenna, Wheatley & Wormall, 1954). The application of squalene (or the unsaponifiable fraction of shark liver oil) to the skin of subjects suffering from psoriasis or eczema had no beneficial effect on the skin condition.

Other hydrocarbons besides squalene are present in human sebum, and the total hydrocarbon content of sebum collected from single subjects or from groups of normal individuals shows a wide variation. The functions of these hydrocarbons have yet to be elucidated.

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Mathematical theory of oscillating flow in an elastic tube. By J. R. Womersley. *Physiology Department, Medical College of St Bartholomew's Hospital, London, E.C.* 1

The simple theory previously announced (Womersley, 1954, 1955*a*) has been extended, and the equations of motion solved for a viscous liquid in a thin-walled elastic tube. The solution is approximate, applying only to oscillations of long wavelength. The expression for the rate of flow is of the same form as that already published (Womersley, 1954) but with modified values of M'_{10} and ϵ. These are not much affected by different ratios of wall thickness to tube diameter (up to 1:5), but are fairly sensitive to the value chosen for the Poisson's ratio (σ) of the material of the arterial wall. If the tube is 'perfectly elastic' ($\sigma=\frac{1}{2}$) the flow is some 10–12% greater, and the phase lag between pressure gradient and flow some 2° more than for the simple solution for the rigid tube. At the other extreme, for a material which does not form a 'waist' on stretching, the flow is about 5% less than in a rigid tube and the phase lag is reduced by about $4\frac{1}{2}°$. (These values are for the first harmonic of the dog's pulse in the femoral artery.) These differences are caused by longitudinal oscillations of the wall of the tube, generated by the force exerted on the wall by the viscous drag of the moving liquid. A full account of this investigation is being published elsewhere (Womersley, 1955*b*). This account also considers the effect of the viscosity of the liquid on the pulse wave.

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Oscillatory flow in arteries: effect of radial variation in viscosity on rate of flow. By J. R. WOMERSLEY. *Department of Physiology, St Bartholomew's Hospital Medical College, London, E.C.* 1

In view of evidence that in an artery the red cells accumulate towards the axis (Bayliss, 1952) thus causing a variation in viscosity across it, a study has been made of the effect on the simple theory previously announced (Womersley, 1954, 1955) of some simple laws of variation of viscosity with radial distance. If the viscosity varies as an inverse power of the radius, the equation of motion can be integrated. The solution for steady flow is, for a tube of radius R and a viscosity law $\mu = \mu_1 (r/R)^{-m}$,

$$Q = \pi R^4 / 2(m+4)\, \mu_1,$$

and therefore an effective average viscosity $\bar{\mu}$ can be defined,

$$\bar{\mu} = \mu_1 (1 + \tfrac{1}{4} m).$$

For the inverse square law and the inverse fourth power law the solution can be expressed in terms of known tabulated functions. The expression for the rate of flow is of the same form as that already published (Womersley, 1954) but with slightly increased values of M'_{10} and ϵ (except at very large values of α, when ϵ is less than for the simple theory). At values of α such as occur in the femoral artery the difference is at its highest, of the order of 8–9 % in M'_{10} and two degrees in ϵ. The general shape of the curves is, however, so similar that they can be made almost identical by a suitable adjustment of the effective average viscosity.

It would seem that large radial variations in viscosity have little effect on the general form of variation in rate of flow and phase lag with frequency, and that quantitatively the experimental results already obtained (McDonald, 1955) could be fitted by either of these laws of variation. The highest value of m ($m=4$) taken for these calculations corresponds to a velocity profile

$$w = \frac{PR^2}{4\bar{\mu}} \{1 - (r/R)^6\},$$

and is very much flatter at the nose and steeper towards the wall, than the corresponding Poiseuille profile. It is thought that any variation in viscosity that may occur in practice will be less than this.

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Preliminary study of the mechanism of inactivation of vasopressin by kidney homogenates. By S. E. DICKER and A. L. GREENBAUM.
Departments of Pharmacology and Biochemistry, University College London

Kidney homogenates (1:10 in 0·25 M sucrose) were incubated with vasopressin (Pitressin, Parke Davis and Co.) in a Mg- and Ca-free Krebs-Ringer phosphate buffer solution pH 7·4 for periods up to 2 hr. After stopping the reaction by boiling, the preparation was centrifuged at 600 *g* for 10 min and the antidiuretic activity of the supernatant fluid was assayed by intravenous injections into rats in ethanol anaesthesia (Dicker, 1953). The antidiuretic activity decreased during the first 60 min, after which it remained constant at a value of approximately 5% of its initial activity. The inactivation occurred both in the absence and the presence of oxygen. When kidney homogenate was added to a solution of vasopressin which had been previously inactivated by kidney *slices* to 20% of its initial activity (Dicker & Greenbaum, 1954), further inactivation to a value of approximately 5% was observed. In investigating the inactivation process, it was found that vasopressin was bound to the proteins of the kidney homogenate. Fractionation of the homogenate into cellular debris and nuclei, mitochondria, microsomes and particle-free supernatant revealed that this binding occurred mainly on the proteins of the supernatant fraction. Once bound, vasopressin can be fully released from the proteins only by boiling in the presence of 0·3% acetic acid. Vasopressin which had been previously inactivated by kidney homogenate is not bound by fresh kidney homogenate.

To study the mechanism of vasopressin inactivation, kidney homogenates were resolved into their component fractions: (i) cellular debris and nuclei removed by centrifugation at 600 *g* for 10 min; (ii) combined mitochondrial and microsomal fraction, removed by centrifugation at 38,000 *g* for 30 min; and (iii) the particle-free supernatant. Preliminary results indicate that while the fraction containing mitochondria and microsomes reduces the activity of vasopressin to about 23% of the initial level in 60 min, that of particle-free supernatant reduces it to about 7% of the initial level in 60 min. These results seem to indicate that the binding of vasopressin is a preliminary to inactivation and that the inactivation itself may be brought about by two separate

enzyme systems. The binding of vasopressin to the kidney proteins is not specific (Heller & Urban, 1935) since similar binding was observed with liver, muscle and spleen protein.

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The response of the guinea-pig ileum to electrical stimulation by coaxial electrodes. By W. D. M. PATON. *Department of Pharmacology (Royal College of Surgeons), Examination Hall, Queen Square, London, W.C.* 1

A length of guinea-pig ileum, suspended in oxygenated Krebs solution, is threaded on a platinum electrode. The lower end of the gut is tied on to glass tubing into which the electrode protrudes so that it can move freely up and down with the intestinal movements; the tubing can be used for connexion to a volume recorder. The upper end of the gut is tied securely to fine polythene tubing which encloses the upper part of the platinum wire from its emergence out of the intestine and up through the bath fluid. The platinum is thus insulated from the bath fluid, but is in electrical connexion with the lumen of the intestine. The platinum wire is made sufficiently long to be attached to a frontal writing lever for recording the intestinal movements. A second platinum electrode dipping into the Krebs solution makes the whole bath a diffuse external electrode.

The arrangement permits a fairly uniform excitation to be applied over the whole length of the intestine, even if it is contracting or relaxing, and ensures that all the stimulation current applied traverses the intestinal wall.

Single electrical shocks applied through the electrodes elicit brief twitches of the muscle, lasting about 1 sec, this *twitch response* in the undistended preparation has the following properties:

(1) Its threshold to stimulation with shocks of 0·5 msec duration is about 1 V, but 5–25 V are needed for a fully maximal response. The threshold is usually slightly lower if the lumen electrode is made positive.

(2) The twitch can be obtained with square pulses of 50 μsec duration; the 'chronaxie' is about 200 μsec.

(3) The twitch is abolished by small doses of atropine (10^{-8}), and is greatly augmented and prolonged by eserine 2×10^{-8}, or the anticholinesterase compound 284C51, 10^{-8}. It is insensitive to mepyramine, to desensitization to histamine or serotonin, or to concentrations of hexamethonium far in excess of those required to paralyse the peristaltic reflex. Procaine 10^{-5} reduces the twitch response.

It is concluded from the character of the strength-duration curve and from the pharmacological responses that postganglionic nerve fibres are being excited, and that there is no evidence for any other than cholinergic activity at their endings.

If the intestine is distended at a pressure of $1\frac{1}{2}$–3 cm H_2O, the twitch response becomes irregular in its behaviour, but an *emptying reaction* can now be demonstrated in response to single shocks. This resembles the peristaltic reflex, and is sensitive to ganglion-blocking agents.

If the 'emptying' and 'twitch' reactions are abolished by atropine or similar drugs, shortening and emptying of the preparation can usually still be achieved by considerably lengthening the duration of the shock or by repetitive stimulation, and the 'chronaxie' is now about 80 msec.

It appears possible, therefore, by this type of excitation to elicit, and distinguish, in a single preparation, excitation of preganglionic, postganglionic and effector cell structures.

Haemoglobin E and Blood Groups in the Veddas. By JEAN A. E. GRAFF, ELIZABETH W. IKIN, H. LEHMANN, A. E. MOURANT, DOROTHY M. PARKIN and R. L. WICKREMASINGHE. *Department of Pathology St Bartholomew's Hospital, London, Blood Group Reference Laboratory, M.R.C. London, and Medical Research Institute, Colombo, Ceylon*

As a sequel to work on blood groups and sickle cells in South Indian aboriginal tribes (Lehmann & Cutbush, 1952), we have examined blood samples from nine pure or almost pure Veddas from Ceylon. Five are group B and four group O; eight are of the *Rh* phenotype *CCDee* (probably R_1R_1) and one *CcDee* (probably R_1R_0 or R_1r).

Paper electrophoresis of the haemoglobin showed seven to be homozygous for normal adult haemoglobin and two heterozygous for this haemoglobin and the E variant. Haemoglobin E has hitherto only been found in one American (Itano, Bergren & Sturgeon, 1954) of partially Asiatic origin (Sturgeon, personal communication) and in the Siamese (Chernoff, Minnich & Chongchareonsook, 1954).

The absence of the genes for blood group antigens A and Rhesus E and for sickling from this series, small though it is, suggests a relation to the Todas and Kotas of South India rather than to the so-called Veddoids. The presence of haemoglobin E here and in Siam raises wide anthropological issues.

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The source of the acid in the urine of man. By J. N. HUNT

Sex variations in the growth response of kittens to dietary penicillin G. By CECILIA D. DICKINSON and PATRICIA P. SCOTT

The excretion by the dog of administered sodium chloride. By W. J. O'CONNOR

Urine outputs during pregnancy in rabbits. By K. J. FRANKLIN and M. WISE

The absolute light-sensitivity of the planarian worm *Dendrocoelum lacteum*. By F. H. C. MARRIOTT and M. H. PIRENNE.