PROCEEDINGS OF THE PHYSIOLOGICAL SOCIETY

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DEMONSTRATIONS

Local action of drugs on the mouse foetus

By J. DAVIES, J. M. ROBSON and F. M. SULLIVAN. *Department of Pharmacology, Guy's Hospital, London, S.E.* 1

Hypophysectomy in the mouse by the trans-auricular route

By K. JAITLY and C. WILSON. *Department of Pharmacology, Guy's Hospital, London, S.E.* 1

Studies on an anti-inflammatory high molecular protein produced at a site of inflammation

By M. E. J. BILLINGHAM, B. V. ROBINSON, J. M. ROBSON and A. F. WINDER. *Department of Pharmacology, Guy's Hospital, London, S.E.* 1

Study of placental function in the rabbit

By J. M. ROBSON, F. M. SULLIVAN and J. F. TUCKER. *Department of Pharmacology, Guy's Hospital, London, S.E.* 1

Studies on uterine permeability in the rat

By P. B. MARLEY. *Department of Pharmacology, Guy's Hospital, London, S.E.* 1

Congenital malformations produced by physiological substances

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Peripheral neuropathy in the alloxan-diabetic rat

By G. M. PRESTON. *Department of Physiology, Guy's Hospital Medical School, London, S.E.* 1

The changes of segmental demyelination in the peripheral nerves of diabetic patients with neuropathy, were described by Thomas & Lascelles

(1965). They suggested that these changes could account for the slowing of conduction in the nerves of such patients. However, it is still not clear in man whether the development of neuropathy can be suppressed by good control of the patients' diabetes.

Male and female rats were made diabetic by the subcutaneous injection of alloxan and maintained for periods of up to 400 days. The animals were divided into two groups determined by the degree of the control of their diabetes. Rats of one group, designated well controlled, were given a daily injection of protamine zinc insulin, in a dosage of one unit per 100 g of rat, which had the effect of maintaining the animals' weights and sizes, at levels comparable with non-diabetic rats of the same age and sex. The second group of animals, designated badly controlled, were given insulin irregularly and in small dosage, sufficient only to maintain the rats' activity, prevent dehydration and hyperglycaemic coma. These animals were significantly lighter and smaller than non-diabetic rats of the same age and sex.

Compound action potentials were recorded *in vivo* from the exposed saphenous nerves of the diabetic rats and from normal animals of the same age. The conduction velocities of the fastest fibres were markedly slower in the nerves from the badly controlled diabetic rats than from the well controlled ones, which did not differ significantly from the normal animals. Measurements of internodal length and fibre diameter were made on teased preparations of the saphenous nerves from which compound action potentials had been recorded. In the normal animals there was a linear relationship between total fibre diameter and internodal length. In the nerves from the badly controlled diabetic animals this relationship was disturbed. Many of the fibres had short internodes, some fibres showed thin intercalated segments of myelin and others widening of the nodal gap. These changes suggest a process of chronic focal Schwann cell damage with regeneration. Nerves from the well controlled diabetic rats did not show these changes. Thus large doses of insulin prevent the electrophysiological and histological changes in the peripheral nerves of the alloxan diabetic rat.

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The use in teaching of an automated micro-method for blood glucose estimation

By J. N. CROSSLEY. *Department of Physiology, Guy's Hospital Medical School, London, S.E.* 1

Chronic catheterization of the portal vein in baboons

By J. N. Crossley and I. McColl. *Department of Physiology, Guy's Hospital Medical School, London, S.E.* 1

The baboon is widely regarded as a useful laboratory primate for studies of lipid metabolism in relation to atherosclerosis. Chronic catheterization of the portal vein has been used to study the absorption of carbohydrates and their influence on lipid metabolism in baboons eating high carbohydrate diets for prolonged periods.

The baboon (*Papio cynocephalus*) is tranquillized before handling by an intramuscular injection of phencyclidine (1 mg/kg body weight), intubated under thiopentone and anaesthesia maintained by halothane. The abdomen is opened through an upper transverse incision and the inferior mesenteric vein is tied where it crosses the left renal vein. A nylon catheter (Portex i.d. 2 mm) is introduced retroperitoneally through the left flank and advanced up the inferior mesenteric vein into the portal vein. The tip of the catheter is located at the porta hepatis by palpation and its position verified by portal venography.

The catheter is secured in its retroperitoneal course, leaves the abdomen through a small stab wound and is attached to the skin along the left costal margin. The catheter is filled with a heparin-saline solution (100 u./ml.) and the baboon is immediately fitted with a canvas jacket.

The catheter has been kept patent for up to 6 months by twice weekly flushing with the heparin-saline solution.

This work has been supported by a grant from the Medical Research Council.

Effect of humidity of inspired air on aural temperature

By H. F. Lunn. *Department of Physiology, Guy's Hospital Medical School, London, S.E.* 1

Breathing of warm moist air results in a rise in temperature in the wall of the external auditory meatus measured by the method of Cooper, Cranston & Snell (1964). In male subjects a rise of up to 0·5° C occurs within 15 min after changing from room air (at 22° C) to moist air at 40° C. Within that period rectal temperature shows no change. External auditory meatus temperature has been reported by Cooper *et al.* (1964) to be raised when warm saline is infused into the carotid artery or when the arm is immersed in a warm bath. It is not yet established whether the breathing of warm moist air causes its effect via the pulmonary circulation as in the experiments of Wessel James, Paul & Earle (1966) or via a countercurrent

heat exchange system between the arteries and veins of the neck as suggested by the observations on animals of Scholander & Scherill (1955) and by Hunter & Adams (1966).

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Method for assessment of the effects of gastrin on stomach emptying

By J. N. Hunt, M. T. Knox, N. Ramsbottom and Beatrice Wan. *Department of Physiology, Guy's Hospital, London, S.E.* 1

A fibroscope for intra-duodenal colorimetry

By J. N. Hunt and N. Ramsbottom. *Department of Physiology, Guy's Hospital, London, S.E.* 1

Total circulatory support in the dog using a low priming volume pump-oxygenator and peripheral cannulation

By E. Proctor. *Thoracic Research Department, Guy's Hospital, London, S.E.* 1

There are two main reasons why heart-lung machines have been little used in physiology: (1) the 'homologous blood syndrome' (Gadboys, Jones, Slonim, Wisoff & Litwak, 1963), often found in dogs when using apparently compatible donor blood to prime the oxygenators; and (2) the need for a thoracotomy in order to cannulate the cavae or right atrium to divert the venous return to the machine. Unacceptable artifacts can result from both of these factors.

The homologous blood problem has been avoided in the present machine by the development of an oxygenator having a priming volume sufficiently small that it can be primed with isotonic solutions and low molecular weight dextran, without undue dilution of the circulating blood (Proctor & de Bono, 1965). Fig. 1 shows a simplified version of this oxygenator suitable for both acute and survival studies. This gives full gas exchange and temperature control at blood flows up to 2·5 l./min in 25–30 kg dogs, with a priming volume of 750 ml. (550 ml. Ringer–lactate and 200 ml. low molecular weight dextran); 100 ml. of Ringer–lactate solution are added after each hour of perfusion to replace urinary, respiratory and metabolic losses of fluid. A vertical annulus formed by a stainless steel tube insert in a

Perspex tube gives efficient bubble oxygenation and heat exchange, followed by defoaming on stainless steel wool coated with baked-on Antifoam A in the cylindrical cartridge. Low-pressure filtration occurs in the reservoir, and the sump prevents vortex formation. The absence of reactions in the animals has been demonstrated in over 170 perfusions.

The need to open the chest is now avoided by using peripheral cannulation, in which a long, thin-walled, polythene or Teflon catheter (6·0 mm I.D. and 7·8 mm O.D.) is inserted via a femoral vein to the level of the right atrium (Fig. 1) to divert the venous return to the machine; the 'arterial-

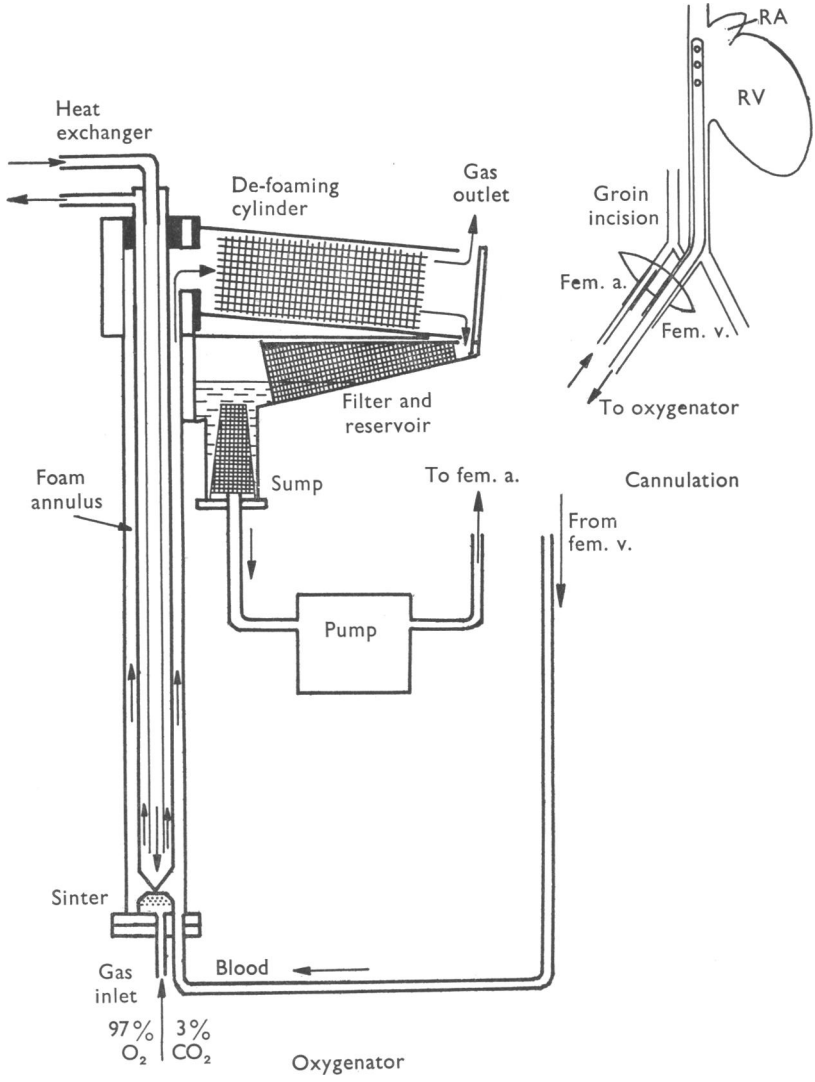

Fig. 1

ized' blood is returned to the circulation via a short cannula in a femoral artery. Used early in partial circulatory support (Galletti & Salisbury, 1958), and more recently in total circulatory support (Proctor, 1966), this technique permits a wide range of circulatory and respiratory studies in the closed chest dog.

With the heart beating, the cardiac output can be varied from near zero to normal output, while maintaining a normal systemic blood pressure, by controlling the venous return to the machine. Externally induced ventricular fibrillation (zero cardiac output) permits peripheral vascular studies unclouded by the cardiac variable; and the study of the effect of various agents on *in vivo* ventricular fibrillation in the presence of normal aortic and coronary blood flow and pressure is possible. The technique is being used here in experimental massive pulmonary embolism and myocardial ischaemia.

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Body extension in *Stentor*, a contractile ciliate protozoan

By L. H. BANNISTER and E. C. TATCHELL. *Biology Department, Guy's Hospital Medical School, London Bridge, S.E.* 1

Whereas the contraction of *Stentor* has been the subject of many investigations and its relationship to the fibre systems has been explored, the mechanism of extension of the animal has been largely neglected.

Preliminary investigations have shown that neither ciliary action nor the contraction of an organized set of fibres can account for body extension. Furthermore, it is unlikely that the completely extended form represents the resting state to which the body would return elastically.

For these reasons it is suggested that extension may be a result of general cytoplasmic movements similar to those postulated in dividing cells or in amoeboid streaming, and this possibility is being investigated.

The demonstration showed some aspects of the behaviour of *Stentor* during the various stages of re-extension from the contracted state.

The effect of fluoridated drinking water on the physical properties of the rat femur

By M. N. NAYLOR and R. F. WILSON. *Dental Clinical Research Laboratory, Guy's Hospital Dental School, London, S.E.* 1

Twenty-one-day old weanling albino rats were divided into paired control and experimental groups, both of which were given *ad libitum* supplies of rat cake diet and drinking water (fluoride ion content 0·2–0·3 p.p.m.). The drinking water of the experimental groups was supplemented by the addition of sodium fluoride to give fluoride ion concentrations of 10, 25, 100, 250 and 500 p.p.m.

After periods varying from 13 to 52 weeks paired control and experimental animals were killed and the femurs removed, dissected free of connective tissue and radiographed.

The breaking stress and deflexion of the femurs on bending were determined within 5 hr of removal by the method of Bell, Cuthbertson & Orr (1941). The bones were then ashed and their inorganic residue determined.

All animals thrived and there was no difference in the pattern of weight gain between the experimental animals and their controls, with the exception of those drinking 500 p.p.m. These animals soon developed toxic signs and all died within 1 week.

The results show that, in rats, consumption of drinking water with a fluoride ion content as high as 250 p.p.m. for up to 52 weeks has no effect upon the radiographic appearance, the breaking stress and deflexion pattern on bending and the ash content.

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A method for the rapid measurement of whole blood and plasma viscosity at physiological rates of flow

By WENDY GORDON. *Physics Department, Guy's Hospital, London, S.E.* 1

The viscometer consists of a horizontal capillary, of internal diameter 0·055 cm, 13 cm long, connecting two reservoirs; a mercury column provides a constant pressure head of about 100 mm mercury. The time of flow of a constant volume of fluid is registered on an electronic timer accurate to 0·01 sec. The calibration is therefore a viscosity against time of flow graph for fluids of known viscosities, and fits (to a good approximation) the equation

$$\nu = AT - B/T$$

which allows for turbulence in the exit reservoir. (ν = viscosity, T = time of flow, A and B are constants.)

This viscometer has the following advantages:

(1) Small samples only are required. A 9 ml. blood sample containing an anticoagulant is sufficient to estimate the whole blood and plasma viscosity, and the haematocrit.

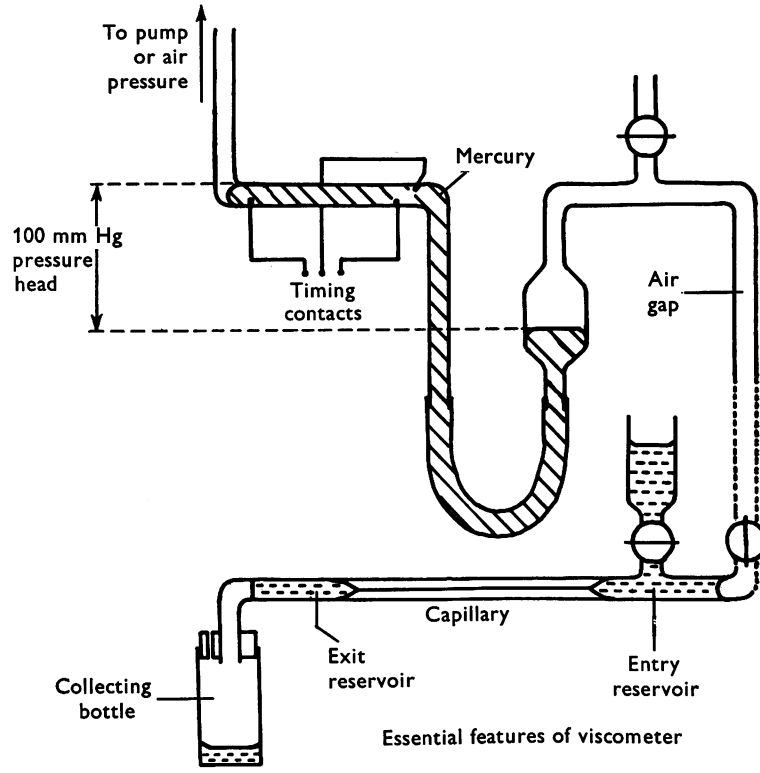

Fig. 1

(2) The measurements are made at high rates of shear, to simulate the physiological near-Newtonian flow.

(3) In order to calculate the viscosity, a measurement of the density of blood is not required, as the capillary and reservoirs are horizontal.

(4) The temperature of the capillary is kept constant at 30° C by means of a thermostatically controlled air bath.

(5) Each estimation takes $\frac{1}{2}$ hr, which includes washing out the capillary and reheating it.

(6) Readings for one sample may be repeated as often as required.

The accuracy of measurements is estimated to be 1 %.

Activity of cholinesterases in the brain and superior cervical ganglion of rats treated with nerve growth factor or its antiserum

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COMMUNICATIONS

The movement of noradrenaline in sympathetic nerves

By K. Kapeller* and D. Mayor. *University of Sheffield*

The accumulation of noradrenaline (NA) proximal to a single constriction in sympathetic nerves has been attributed to its proximo-distal movement along the axons (Kapeller & Mayor, 1966*a*, *b*). This movement has been investigated further after constricting guinea-pig and cat hypogastric nerves at two points, 0·5–2 cm apart, with either fine forceps or a fine silk ligature. Whole mount preparations of the guinea-pig nerves and 6–10 μ sections of the cat nerves were examined by the fluorescence microscopic method for NA at intervals up to 3 days after operation. Some cat nerves were also studied with the electron microscope.

Proximal to the proximal constriction there was a rapid accumulation of fluorescent material in fibres which became progressively more swollen. This was first seen 15 min after operation and was still evident after 3 days. A similar, but much smaller, accumulation was seen proximal to the distal constriction. It was less intense and affected a shorter segment of nerve than the accumulation proximal to the proximal constriction. It disappeared between 24 and 48 hr after operation.

Immediately distal to the constrictions the nerves gave a diffuse yellowish fluorescence, but in general showed no specific greenish NA fluorescence. Occasionally nerve fibres which exhibited the typical NA fluorescence have been found distal to the constrictions. These were seen more often beyond the distal lesion. Almost invariably, in the guinea-pig nerves, these fibres could be traced to a group of highly fluorescent ganglion cells situated more distally.

With the electron microscope an accumulation of granular vesicles, believed to carry NA, has been found proximal to both constrictions. This was more marked in relation to the proximal than to the distal constriction. No such accumulation has so far been found distal to either lesion. This corresponds to the behaviour of the fluorescent material in these nerves.

These findings support the view that NA travels proximo-distally along sympathetic nerves. Since an accumulation of NA also occurs proximal to

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