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Ganglion cells in the mammalian tongue. By F. W. GAIRNS and H. S. D. GARVEN. *Institute of Physiology, University of Glasgow*

This work is an extension of observations already made on the gum and palate (Gairns, 1951).

Schumacher (1926) and Kolmer (1927) recognize the existence of ganglion cells in the vallate papillae. More recently Kane (1950, personal communication) has investigated the possible relationship of these ganglion cells to the sense of taste. Kolmer (1927) also states that larger compact ganglia exist in most mammals, including apes and man. These ganglia lie deeper in the substance of the tongue. Okamura (1936) shows figures of ganglia within the musculature of the tongue of the cat. On the other hand, Carleton (1938), using the rabbit, Weddell, Harpman, Lambley & Young (1940), using the rat, and Boyd (1941), also using the rabbit, do not report the presence of any ganglion cells within the tongue.

Our findings are as follows. In the rat, hedgehog and man there are ganglion cells within and below the vallate papillae. In the rat, rabbit and man they have also been found at the edge of the tongue posteriorly in the region of the foliate papillae. In the cat and man a few have been seen deep to fungiform papillae on the upper surface near the tip of the tongue. In the rat, rabbit, cat, hedgehog and man small and large ganglia have been observed in intimate relationship to the intrinsic serous and mucous glands of the tongue (Fig. 1). In the rat, cat, hedgehog and man small groups of ganglion cells have been found closely associated with the walls of the arteries. In the rat, rabbit, cat and hedgehog small and large groups of ganglion cells have been observed on the course of intramuscular nerve bundles at considerable distances either from glands or from the surface epithelium. In the rat and cat some of the cells lie on the course of very small nerve bundles in close proximity to the motor end-plates supplied by these bundles (Fig. 2). These last are reminiscent of cells figured by Kulschitsky (1924) in snake muscle. In man small ganglia lie between the epithelium of the upper surface and the subjacent muscle or gland.

In considering the functional significance of these findings it is necessary to examine the following possibilities. The ganglion cells in some instances may be related to (*a*) the taste buds and/or other sensory endings in the vallate and

foliate regions and may therefore be homologues of posterior root ganglion cells which, like those of the spiral ganglion, have come to lie more peripherally; (*b*) possible proprioceptive mechanisms in the tongue; (*c*) the intrinsic salivary glands of the tongue in the same way as the parasympathetic ganglia are related to the large paired salivary glands; (*d*) blood vessels, being concerned

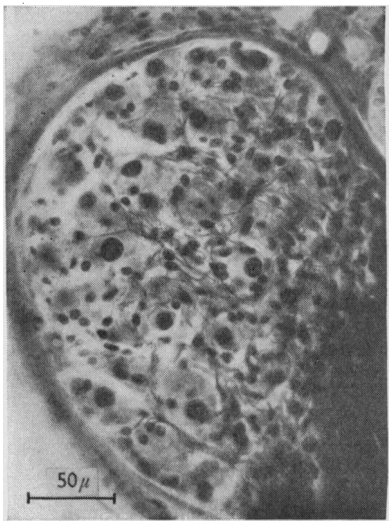

Fig. 1.

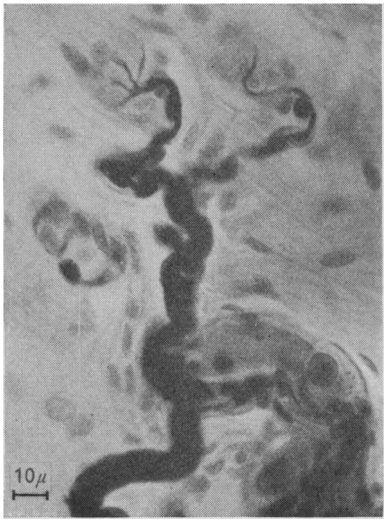

Fig. 2.

Fig. 1. Human tongue. Large ganglion adjacent to serous gland and deep to vallate papilla.

Fig. 2. Cat's tongue. Ganglion cells in small intramuscular nerve twig. These lie in close proximity to the two motor end-plates. Bielschowsky-Gros silver diammine ion stain.

Untouched photomicrographs.

with vascular changes, probably vasodilatation, not only in the glands but throughout the tongue; (*e*) the function of the motor end-plates either directly, or indirectly through vascular changes in their immediate neighbourhood; (*f*) smooth muscle in the tongue.

Further investigation is in progress.

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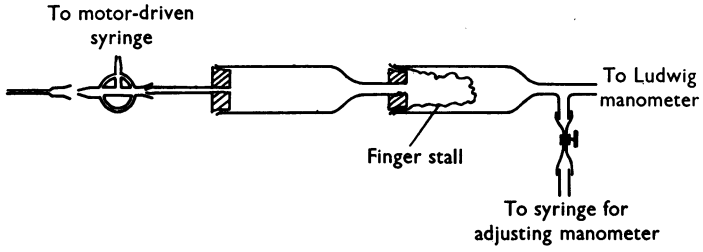
Direct recording of arterial blood pressure in man. By R. S. J. CLARKE, F. DUFF and I. D. THOMPSON. *Department of Physiology, The Queen's University of Belfast*

It is sometimes necessary, particularly when investigating the mechanism of alterations of blood flow, to measure changes in the mean arterial pressure. In such cases it is unnecessary to employ a system capable of following rapid fluctuations and, indeed, if the mean pressure is to be directly recorded rather than deduced from a curve following the pressure changes through the pulse cycle, the system must be a slow one. A mercury manometer is convenient and adequate for the purpose.



A 0·5 mm bore needle is inserted into the lumen of the artery, and connected by about 15 cm of 3·5 mm bore polythene tube to a chamber filled with saline designed to detect any reflux of blood. This leads to a second chamber containing a flaccid thin rubber finger-stall which transmits the pressure via a water filled tube to a conventional mercury manometer, while providing a barrier against infection or the reflux of mercury. A flow of about 1 ml. of saline per min delivered from a motor-driven syringe is maintained to prevent clotting. All except the mercury manometer is sterilized before use.

Static calibration. The zero point is found by holding the needle in the horizontal plane through the artery, with saline flowing through as during an actual experiment.

Dynamic calibration. The mercury is forced to the 100 mm mark and held there by closing the T tap. Saline is passed through the needle. The tap is then suddenly opened and the rate of fall of the mercury recorded. With the system used, it takes about 2 sec to fall 50 mm and 4 sec to fall 75 mm.

As the venous occlusion plethysmograph is not usually employed for making observations on flow at intervals shorter than 10–15 sec, the speed of response of the manometer is adequate for most purposes.

A combination of ergometry and plethysmography for investigating the circulation through the leg muscles. By E. J. FINNAN and J. T. SHEPHERD

Measurement of the blood flow in the umbilical cord of the foetal guinea-pig. By A. D. M. GREENFIELD and J. T. SHEPHERD

A class experiment on hand calorimetry. By A. D. M. GREENFIELD, J. T. SHEPHERD and I. D. THOMPSON

Equipment for human limb plethysmography. By A. D. M. GREENFIELD

High titre cold agglutination. By G. M. NELSON

Histological changes in the liver in experimental siderosis. By J. A. NISSIM. *Department of Pharmacology, Guy's Hospital Medical School*

Repeated intravenous injections of saccharated iron oxide in total doses up to 2·16 g Fe/kg, and subcutaneous or intraperitoneal injections of 'ferric hydroxide ferrous ascorbate' in total doses up to 1·0 g Fe/kg were used in the production of siderosis in animals. The animals studied included mice, rats, rabbits and guinea-pigs, but the ascorbate preparation was studied only in the last species. Some guinea-pigs were given 'ferric chloride caramelate' (Nissim, 1949). Histological sections were examined after different total quantities of iron, but doses of the order of about four times those given by Cappell (1930) were reached in several animals.

Saccharated iron oxide, first picked up by the reticulo-endothelial cells, was later altered into a diffusible form, which could enter parenchyma cells in different organs. The ascorbate and caramelate are diffusible preparations, and both penetrated parenchyma cells directly, whilst their uptake by the reticulo-endothelial cells was much slower.

With the passage of time a number of organs become saturated with iron. Previous workers failed to produce lesions in the body with repeated iron injections. This is attributed partly to the smaller amounts of iron used, and partly to the nature of the compounds injected. In the present experiments the animals receiving the larger doses died some 5–6 months from the first injection and showed unmistakable lesions in the liver and sometimes in other organs, e.g. kidneys, suprarenals. The clump of reticulo-endothelial foci became surrounded and infiltrated with cells of the histiocyte-leucocyte series. Gradually, the infiltration extended among the hepatic cells, and in extreme

cases these lesions came to resemble lymphomatous masses. The liver parenchyma showed signs of damage with atrophy of the cytoplasm and nuclear pyknosis and karyolysis. The sinusoids became widened and engorged with white and red cells. In one rat the damage progressed further, whole liver lobules disappeared in certain areas, the giant cell foci and portal tracts approximated, and the liver capsule became collapsed and wrinkled. Some islands of parenchyma cells were present and a minimum amount of fibrous tissue was noted between the reticulo-endothelial clumps, but no true cirrhosis with collagenous tracts was evoked.

Some of the hepatic cells showed intranuclear oval iron-reacting bodies. Others showed diffuse staining of their nuclei, often progressing to granular massive iron impregnation as heavy as that seen in phagocytes.

Guinea-pigs receiving the iron ascorbate preparation also showed overt damage of their liver parenchyma with patches of acute necrosis without fibrosis. As there were no giant-cell foci, the surrounding white cell proliferation was also absent.

In all the siderotic livers examined in the present work no true fibrosis has been observed. At most there was the small cell proliferation, and it is possible that some of them may have been young fibrocytes, but there was no cirrhosis comparable to that occurring in haemochromatosis in man, or to that obtained experimentally with other agents (Himsworth, 1947).

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Variations in the appearance of the cells of the guinea-pig brain after routine histological methods. By B. G. B. Lucas and Dorothy H. Strangeways. *Surgical Unit, University College Hospital, London, W.C.* 1, *and Department of Physiology, The Queen's University of Belfast*

During an investigation on the effect of anoxia on the guinea-pig brain, variations were found in the histological picture of the brain of the control animals which have been attributed to the anoxia by many previous workers. In the brains which were well fixed the cells were evenly and lightly stained and there were few or no pericellular or perivascular spaces. In other brains two variations were found, first, shrinkage of nerve cells and blood vessels with the production of pericellular and perivascular spaces, and, secondly, the presence of a variable number of shrunken hyperchromatic cells which appeared to have undergone chronic cell change. No explanation was found for the first variation, but injury to the brain during its removal was a factor in the production

of the second. Mechanical damage to the cortex leads not only to localized deeply staining cells, but also to cell damage extending for some distance from the site of injury. The cells immediately surrounding the injury and extending for some distance into the deeper layers of the cortex are small and deeply staining and cannot be distinguished from cells which have undergone chronic cell change.

Surface injury may cause changes in cell structure at a considerable distance from the site of injury, and the large pyramidal cells of the Vth layer of the cerebral cortex are particularly vulnerable. This is the layer which is often reported as being most affected by anoxia, and it may be that these cells are the most fragile and so more likely to be damaged by any factor, be it trauma, anoxia or drugs.

The pilomotor axon reflex. By N. AMBACHE and P. A. ROBERTSON

Sterols, temperature and metabolism. By JAMES M. O'CONNOR

Placental production of glucose and fructose in the sheep. By D. PAULINE ALEXANDER, R. D. ANDREWS, A. ST G. HUGGETT, D. A. NIXON and W. F. WIDDAS. *Physiology Department, St Mary's Hospital Medical School, London*

Experimental hyperglycaemia in the pregnant ewe or her foetus causes a slow prolonged hyperfructosaemia (Huggett, Warren & Warren, 1951). Using glucose labelled ^{14}C it was possible to show that labelled glucose formed labelled fructose, even though the rate and quantity of glucose given was such that there was no rise in blood glucose (Alexander, Huggett & Widdas, 1951).

This communication describes results following perfusion of the placental vessels through the umbilical arteries. The foetus was replaced by a Henry-Jouvelet pump. There were two types of perfusion, circulating and non-circulating or through perfusion. In the former the umbilical vein perfusion fluid leaving the placenta entered a reservoir from which it was sucked by the pump and returned to the umbilical artery. In the latter the perfusion fluid entering the umbilical artery is drawn from a bank of fluid and flows out from the placenta into a separate receiving beaker. The perfusion fluid was sometimes plasma and sometimes heparinized blood.

The level of fructose under circulating conditions is a dynamic balance between fructose formation and utilization by the placenta. If the fructose of the perfusing fluid is adjusted to too low a value the placenta brings about a

rise in concentration and vice versa. Non-circulating perfusion shows that the rate of formation is constant at 8–13 mg/min in different sheep and relatively independent of the maternal glucose level in any one experiment. Hyperglycaemia does not increase the rate of fructose formation under these conditions. This is in contrast to the rate of glucose collection which does rise with elevation of maternal glucose. In the light of these observations it seems probable that the slow rise in fructose concentration which occurs in hyperglycaemic experiments with intact foetuses or circulating perfusions may be brought about by inhibiting or reducing the fructose consumption. This would fit in with Mann's (1951) findings that glucose is preferentially utilized by spermatozoa in glucose-fructose mixtures so that an increase in glucose concentration reduces the fructose utilization.

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Responses to temperature in the isolated rabbit ear. By I. D. Ferguson and N. Levinson. *Institute of Physiology, University of Glasgow*

Perfusion of the ear through the central artery was commenced within 3 min of removal of the ear from the rabbit. Oxygenated Locke's solution at pH 7·3–7·4 containing 0·154 M-NaCl, 0·0054 M-KCl, 0·00225 M-$CaCl_2$, 0·000052 M-$MgCl_2$, 0·00596 M-$NaHCO_3$ and 0·000417 M-NaH_2PO_4 was perfused under constant pressure (Ferguson & Garry, 1952). The temperature of the perfusion fluid (F_t) and of the ear environment (E_t) could be varied at will. The rate of inflow and of weight increase due to oedema were recorded. Forty-six experiments were carried out.

At $F_t = 38°$ C the inflow rate was initially rapid but then fell quickly to reach a minimum at the end of 2 hr. During this period the oedema increased steadily and rapidly. Thereafter the inflow rate rose steadily while the rate of oedema formation decreased. At $F_t = 16°$ C the initial inflow rate was slow, due to an observed spasm of the central artery. Subsequently the inflow rate became rapid and remained significantly greater than the inflow at $F_t = 38°$ C. The oedema, meanwhile, increased steadily but only slowly. These characteristic responses were also obtained in one and the same ear by changing the temperature of the perfusing fluid.

More rapid inflow and greater oedema formation occurred at $F_t = 45°$ than at $F_t = 38°$ C, but vascular damage was indicated by bullae formation.

Perfusion at $F_t = 38°$ C with an E_t artificially lowered from 21 to 16·5° C led to a slightly greater inflow and to a significant reduction in rate of oedema

formation. Perfusion at $F_t = 16°$ with an E_t artificially raised from 16 to 23·5° C led to a significant increase in the rate of oedema formation, but the inflow rate was not consistently affected.

These results may be explained by postulating that in the isolated ear the responses to temperature are similar to those in the intact ear (Grant, 1930; Grant, Bland & Camp, 1932; Van Dobben-Broekema & Dirken, 1950).

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Acetylcholine metabolism of axotomized sympathetic ganglia.

By G. L. Brown, H. McLennan* and J. E. Pascoe. *Department of Physiology, University College, London*

It has already been shown (Brown, McLennan & Pascoe, 1952) that 3 weeks after section of the postganglionic nerves (axotomy) of a sympathetic ganglion, the ganglion cells are inexcitable by preganglionic impulses. In an attempt to explain this loss of function we have investigated the acetylcholine metabolism of such axotomized ganglia.

The amount of acetylcholine liberated into the perfusate from the axotomized cat's superior cervical ganglion on stimulation of the sympathetic trunk was found to fall within normal limits.

Manometric estimations were made of the cholinesterase in the superior cervical ganglia of rats in which the internal and external carotid nerves had been sectioned on one side 3 weeks previously. We have found that about 50% of the activity was lost in the axotomized ganglion when compared with the normal from the other side. This represents a drop in the 'true' cholinesterase, since 'pseudo' cholinesterase, as judged from the hydrolysis of triacetin or benzoylcholine, is not present in these ganglia.

The synthesis of acetylcholine *in vitro* by the axotomized ganglia, incubated in the usual Krebs-bicarbonate medium, is the same as that by the control. When the potassium concentration of the medium is raised, which in the normal ganglion produces a tenfold increase in the synthesis, no enhancement is found in the axotomized ganglion.

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* Fellow of the National Research Council of Canada.

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Inhibition of activity in single fibres of the rabbit's optic nerve. By L. C. THOMSON

Renal function before and after birth. By R. A. MCCANCE and E. M. WIDDOWSON. *Medical Research Council Department of Experimental Medicine, Cambridge*

It is well known that the urine passed immediately after a normal birth is very dilute, and that within the next few hours it becomes more concentrated. To find out if the low osmotic pressure of the urine passed at birth was due to events connected with birth, urines and bloods taken from mothers and babies at Caesarian sections have been compared with those taken at normal deliveries. No essential differences have been found. The first urines formed after birth have also been collected and studied. All the results have been most consistent. Examples are shown in Table 1.

TABLE 1

		m.mole/l.			m.equiv/l.		
		Osmotic pressure	Creatinine	Urea	Na	Cl	K
		Normal delivery. Full term					
Mother:	Serum	324	0·09	2·7	135	103	5·4
	Urine	640	6·70	117·0	88	113	122·0
Baby:	Serum	298	0·11	3·6	136	101	9·5
	Urine at birth	156	0·49	17·2	49	40	4·1
	First urine after birth	324	3·90	125·0	29	23	39·5
		Caesarean section. Premature					
Mother:	Serum	338	0·09	3·2	137	107	4·7
	Urine	585	7·00	228·0	83	98	77·0
Baby:	Serum	323	0·07	2·7	125	105	8·2
	Urine at birth	118	0·21	8·0	60	52	4·0
	First urine after birth	151	0·72	29·5	26	25	17·4
	Amniotic fluid	312	0·09	3·7	124	109	4·3

Note. (1) The high concentration of K in cord serum. In other respects, including O.P., there have been no consistent differences. (2) The low concentrations of creatinine, urea and K in infant urine before birth and their *rise* after birth. (3) The moderate concentrations of Na and Cl before birth and their *fall* after birth. These results indicate that per millimole of creatinine or urea excreted, and therefore presumably per ml. of glomerular filtrate formed, 3–5 times more water and about 10 times more Na and Cl are excreted before birth than after it. If imbibition of amniotic fluid, which certainly seems to take place *in utero*, is invoked to explain the high excretion of water there, relatively more of the Na and Cl than of the water in the imbibed fluid must leave the foetus through the placenta.

The relationship of shivering to respiration. By J. H. CORT and R. A. MCCANCE

The nerve cells of the pig's circumvallate papilla. By F. KANE.
Department of Physiology, University College, Cork

The pig has only two circumvallate papillae: they are large oval structures (5 × 4 mm), one on either side and between the foliate papilla and the middle line. The centre of the papilla is occupied by a large ganglion whose cells taper backwards to a nerve of readily dissectable size. This is joined almost immediately by that from the foliate papilla and by about five twigs from the pharyngeal and tonsillar region. Within an inch or so—before crossing the hyoid—it has become the main trunk of the glossopharyngeal nerve. A small artery supplies the ganglion entering its inferior surface quite separately from the main nerve. A number of small groups of nerve fibres leave the ganglion and ramify among the surrounding glands of von Ebner.

The taste buds on the papilla are confined to the vallum wall and vary in number from 600 to 1200. In only one case have we found them absent and then the ganglion was absent too. The cells of the ganglion are of two kinds, one larger, clear and smooth in outline, the other smaller, obviously multipolar and tending to be in the tail and periphery of the ganglion. It is possible to count the two categories, and in our counts we have followed Gasser & Grundfest (1939) in adopting the methods of Hursh (1939). The nerve leaving the ganglion has about 700 fibres, and osmic acid and silver preparations show the curious feature, which struck Koch (1916) and Zotterman (1935), that it consists of a small group of relatively large (8–10 μ) and a large group of very small myelinated (2–4 μ) fibres. The total of fibres in the IXth nerve as it crosses the hyoid is about 2500 and as it enters the jugular canal about 3000.

We have cut the nerve to the papilla by two routes—from the skin under the jaw, to pick it up as it crosses the hyoid, and by a superficial transverse cut through the tongue mucosa behind the vallum. We generally used the simpler method. Apart from the classical taste-bud degenerations (Parker, 1922) we find degenerative changes in some, but not all, of the larger cells, the small being not much affected. A small number (70–150) of the cells of the petrous ganglion degenerate. This is about the number which would be affected if the coarse fibres of the nerve have their cell bodies there. Degenerative changes also show in the upper medulla; fibres on the damaged side going to the 'gustatory nucleus' are clearly degenerated, whilst a part of the nucleus itself shows striking changes. Marchi preparations of the upper medulla show an interesting crossing of the mid-line by degenerate large fibres which are found also at the mesencephalic root of the Vth nerve.

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Plasma iron levels after the intravenous administration of different iron preparations. By J. A. NISSIM. *Department of Pharmacology, Guy's Hospital Medical School*

Plasma iron levels were studied at 0, ½, 3 and 6 hr after the intravenous injection into rabbits of different iron preparations. Three important factors influencing the rate of fall of plasma iron must be considered: (1) precipitation, including its rate and threshold at which it begins; (2) excretion, mainly renal; (3) diffusion into tissues. These factors did not depend on valency but on the nature of the whole molecule.

After the injection of 22·5 and 45 mg Fe/kg of saccharated iron oxide, the first levels were 62 and 120 mg % respectively, and corresponded to the calculated values, on the assumption of even distribution in plasma. Following 180 and 360 mg Fe/kg the figures obtained were 340 and 500 mg %, corresponding to three-quarters and one-half of the theoretical values respectively. Histological study showed abundant iron precipitation, so that one-quarter and one-half of the iron precipitates immediately on injection at these respective doses. The rate of fall of plasma iron was also more rapid than with doses of 22·5 and 45 mg Fe/kg. The plasma iron value of 500 mg % is the highest ever recorded.

Examples of plasma iron levels (in mg Fe %) after intravenous injection of different iron preparations (22·5 mg Fe/kg)

Hr after injection	Saccharated iron oxide	Ferric glucosate	Ferric chloride lactate	Colloidal ferric hydroxide	Ferrous chloride pyruvate	Ferric ammonium citrate	Ferric chloride caramelate	Ferric hydroxide ferrous ascorbate
0	62	65	65	11	42	45	46	22
½	42	50	61	9	23	17	25	8
3	28	21·5	41	1·25	5	7	15	4
6	10	7·5	12	0·9	2·5	2	8	2

After intravenous ferric glucosate, abrupt precipitation begins to occur at lower plasma levels than with saccharated iron oxide, so that after a dose of 90 mg Fe/kg the first value was only one-half the theoretical.

Colloidal ferric hydroxide precipitates heavily and immediately, and even after 22·5 mg Fe/kg the first plasma Fe value was only 11 mg.

After ferric ammonium citrate, 'ferric chloride caramelate' and 'ferric hydroxide ferrous ascorbate' (Nissim, 1949), the fall of plasma iron was rapid. These preparations did not precipitate, and their disappearance from the plasma depended on their urinary excretion and diffusion into the tissues.

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Urinary iron excretion and diffusibility of different iron preparations. By J. A. NISSIM. *Department of Pharmacology, Guy's Hospital Medical School*

The amount of iron excreted in the urine of rabbits during the first 24 hr after the intravenous injection of different iron preparations was studied. Correlation of plasma-iron levels with urinary-iron excretion showed that iron preparations fell into three groups. The first included compounds like saccharated iron oxide, ferric glucosate and 'ferric chloride lactate', which showed no precipitation at a dose level of 22·5 mg Fe/kg, and a very slow rate of disappearance from the blood associated with poor urinary excretion. Compounds of the second group, e.g. colloidal ferric hydroxide and 'ferric chloride pyruvate', showed rapid fall of plasma levels associated with rapid precipitation of the iron and poor urinary excretion. In the third group were such compounds as ferric ammonium citrate, 'ferric chloride caramelate' and 'ferric hydroxide ferrous ascorbate' which showed rapid fall in plasma iron associated with high urinary iron excretion and no precipitation.

TABLE 1. (*a*) Percentage urinary iron excretion in first 24 hr after intravenous injection of 22·5 mg Fe/kg in rabbits. (*b*) Diffusibility measured as concentration of iron in peritoneal fluid after intravenous injection of 90 mg Fe/kg in mice (average of 2–4 animals, mg Fe %)

	Group I			Group II		Group III		
	Saccharated iron oxide	Ferric glucosate	Ferric chloride lactate	Colloidal ferric hydroxide	Ferrous chloride pyruvate	Ferric ammonium citrate	Ferric chloride caramelate	Ferric hydroxide ferrous ascorbate
(*a*)	2·5	2·7	1·5	0·27	0·25	16·1	18·7	27·4
(*b*)	0·16	0·2	0·35	—	—	5·4	4·7	6·9

The difference in urinary iron excretion between saccharated iron oxide and ferric ammonium citrate could not fully account for the difference in rate of fall of plasma iron, since this was still observed after renal ligation. As no evidence for iron excretion into the alimentary tract was obtained following either preparation, it was concluded that there was greater extravascular diffusion of ferric ammonium citrate.

The diffusibility of the various iron compounds was therefore investigated using the live peritoneum as the dialysing membrane. Mice were first injected with 2·0 ml. physiological saline intraperitoneally. This was followed by a

slow intravenous injection of the iron preparation studied (90 mg Fe/kg given in 10 min). The concentration of iron in the peritoneal fluid was then measured. The averages of figures obtained in 2–4 mice are given in the table. The three most diffusible preparations were those which showed the highest renal elimination, and by contrast the diffusibility of saccharated iron oxide, ferric glucosates and 'ferric chloride lactate' was negligible.

Accommodation of the human eye in a bright and empty visual field. By T. C. D. WHITESIDE. *R.A.F. Institute of Aviation Medicine, Farnborough, Hants*

An investigation is being carried out to determine whether, in the presence of a bright field of vision in which there is no detail to fixate, accommodation can be relaxed voluntarily to infinity. The method consists in employing a test object which is so small as to be visible only when it is near the point at which the eye is focused. This test object consists of a glass plate on which is a regular pattern of black spots each of which subtends $\frac{1}{2}$–1′ of arc. The test is observed through a +4D lens, by means of which, when the spots are out of focus and therefore invisible, the subject is presented with an empty field, the brightness of which is 180 foot lamberts.

The subject views this empty field binocularly although recognition of the test object is monocular. The experimental procedure consists in telling the subject to 'look in the distance' whilst the test object is slowly brought towards him. The test object is always suddenly and clearly recognized, although the direction from which it comes is unchanged and familiar to the subject. The results are calibrated by placing a fixation spot at predetermined distances and noting at which point the test objects become visible.

Ten subjects were examined, and it was found that, although an attempt was being made to relax accommodation to infinity, a mean of 1·7D was being exerted within 10 sec of looking at a point 12–18 in. away. Progressive relaxation took place until after about 45 sec a mean of 1·16D was reached. Beyond this there was little improvement in relaxation. The majority of the subjects were slightly hypermetropic, the mean value of the far points being −0·06D (standard deviation 0·619).

The problem appears to have some bearing to the findings of Campbell & Primrose (1952) that under scotopic conditions there was a failure to relax accommodation to infinity.

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Adrenaline and the forearm blood flow. By R. F. WHELAN. *Sherrington School of Physiology, St Thomas's Hospital, London*

The sustained increase in blood flow in the normal forearm during continuous intravenous infusions of adrenaline (10 μg/min) is still obtained after blocking the nerves to the forearm with local anaesthetic and also in the early days following surgical sympathectomy. It is not found when the adrenaline is infused intra-arterially (1 μg to $\frac{1}{1000}$ μg/min). The sustained dilatation is therefore not due to a direct action of the adrenaline on the vessels, nor is it due to a sympathetic nervous reflex response, and it is suggested that a secondary hormone release by the circulating adrenaline is responsible.

Adrenaline as a histamine liberator in man. By J. L. MONGAR and R. F. WHELAN. *Department of Pharmacology, University College and the Sherrington School of Physiology, St Thomas's Hospital, London*

The vasodilator effect of intravenous adrenaline on the human forearm is not due to the direct action of this hormone on the blood vessels nor is it a sympathetic nervous effect (Whelan, 1952). Several workers have shown that adrenaline releases histamine from tissues (Koch & Szerb, 1950; Eichler & Barfuss, 1940), and Staub (1946) reported an increased plasma-histamine level during intravenous adrenaline in man and suggested that histamine release might be responsible for some of the cardiovascular effects of adrenaline.

In ten normal subjects intravenous infusions of 10 and 20 μg/min of adrenaline were given and the plasma-histamine level estimated by a method based on that of Code (1937). No increase in plasma histamine was observed.

It is therefore concluded that the effects of adrenaline on the circulation cannot be explained by a release of histamine into the blood stream.

An attempt was made to demonstrate that a known histamine liberator would have a measurable effect on plasma-histamine level by infusing D-tubocurarine intra-arterially in doses from 0·5 to 5·0 mg/min for 5 min in two normal and five anaesthetized subjects. Little effect was produced unless the circulation through the limb was arrested for 2 min immediately after injection of the D-tubocurarine, when increases up to 80 times the resting level were obtained.

Infusions of 0·2–2·0 μg/min adrenaline into the brachial artery in four subjects produced no change in the histamine level of the venous return from the limb.

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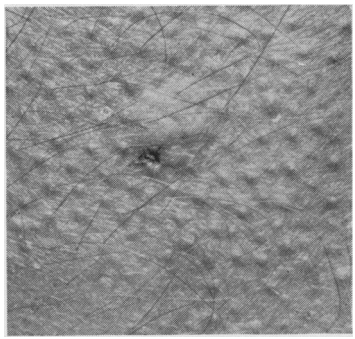
Nicotinic actions of *m*-bromo- and 3:5-dibromo-phenyl ethers of choline (M.B.F. and D.B.F.). By N. AMBACHE and P. A. ROBERTSON. *Ophthalmological Research Unit (Medical Research Council), Institute of Ophthalmology, Judd Street, London, W.C.*1

M.B.F. and D.B.F. were first synthesized by Hey (1952); tested on the cat's blood pressure, they were found to have the greatest nicotinic, activity of any compounds examined hitherto being 4–5 times more powerful than nicotine. The action of M.B.F. and D.B.F. has now been investigated on the following preparations:

(1) *Superior cervical ganglion (cats).* Nictitating membrane records show that ganglionic stimulation can be obtained by injecting as little as 0·1 μg M.B.F. or 0·05 μg D.B.F. into perfused ganglia. Larger doses produce a reversible block to preganglionic stimuli.



(2) *Skeletal muscle.* Both ethers contract the sphincter iridis in the pigeon and the frog's rectus abdominis; the action on the latter is abolished by D-tubocurarine.

(3) *Rabbit ileum.* M.B.F. regularly elicits longitudinal muscle contractions which are abolished by hexamethonium. The response to D.B.F. is also motor, but with higher doses there is a mixture of motor and inhibitory components in the response. More extensive use has therefore been made of M.B.F., which is 0·5–2 times as active as nicotine. Increasing doses may produce a diminishing effect, and may be followed by a depression of the contraction to a fixed dose of nicotine; both observations suggest a second, 'paralytic', or blocking, type of action like that of nicotine.

In preliminary experiments the motor response to M.B.F. has been greatly reduced, abolished, or even reversed (in five out of seven experiments) by botulinum toxin; the 'reversed' or inhibitory action of M.B.F. is abolished by hexamethonium.

These results suggest that the motor effects of M.B.F. arises 'indirectly', but whether this indirect action is purely ganglionic or whether the motor nerve endings in the gut are also involved (by an axon reflex mechanism) remains in doubt in view of the following observations which illustrate the 'axonic' action of these compounds.

(4) *Skin; pilomotor axon reflex.* Several nicotine-like substances evoke pilomotor axon reflexes in the human skin (Coon & Rothman, 1940). M.B.F. (0·3 μg intradermally as in the figure) and D.B.F. do the same; hexamethonium abolishes this 'axonic' effect and that of nicotine. Higher concentrations of the ethers block the effect of nicotine.

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The influence of cortisone on the plasma proteins. By E. F. McCarthy

The effect of local temperature on blood flow in the human foot. By M. J. Allwood and H. S. Burry

Cardiovascular reflexes in the foetal guinea-pig. By A. D. M. Greenfield and J. T. Shepherd. *Department of Physiology, The Queen's University of Belfast*

Observations have been made on forty-nine guinea-pig foetuses examined as described by Shepherd & Whelan (1951). Arrest of the blood flow in the umbilical veins of mature foetal guinea-pigs causes gradual slowing of the heart, often with a latency of only 2–3 sec. Arrest of the maternal uterine circulation causes similar slowing, but with a latency of 7–8 sec. Both effects are abolished by injecting atropine into the foetal circulation, and both are distinct from the heart block of sudden onset seen after prolonged occlusion of the umbilical or uterine vessels whether or not atropine has been used. Gradual slowing is also caused, but with a delay of about 23 sec, by administration of 6% oxygen, but not of 7–8% CO_2, to the mother. These findings suggest that the slowing is provoked by the effect of anoxia on some foetal chemoceptor. The view that chemo- rather than baroceptors are involved is supported by the finding that occlusion of the umbilical veins alone produces an effect indistinguishable from occlusion of both arteries and veins, although the pressure changes must be very different in the two cases.

Bauer (1938) was able to detect a similar reflex in the rabbit 4 days after, but not before, birth. In the foetal sheep (Bauer, 1937) the reflex develops late in prenatal life. In the guinea-pig the reflex develops in the last third of foetal life. The guinea-pig, like the sheep, is born in a very mature state, and the results presented here are consistent with the view that the development of the reflex is related to general foetal maturity rather than to the time of birth.

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Vascular responses in persons with high serum titres of cold agglutinins. By R. J. MARSHALL, J. T. SHEPHERD and I. D. THOMPSON. *Department of Physiology, The Queen's University of Belfast*

Persons whose serum has a high titre of cold agglutinins are unusually liable to develop numbness and cyanosis of the digits and other parts on exposure to local cold. Reversible intravascular haemagglutination has been observed in the conjunctival vessels when these are cooled (Iwai & Mei-Sai, 1925; Stats & Bullowa, 1943), and it is likely that similar changes occur in the digital vessels. It has been suggested, however, that vasospasm plays a part in reducing the blood flow (Carey, Wilson & Tamerin, 1948; Kramer & Perilstein, 1951).

We have examined the responses of the hand circulation to local cold in two persons whose serum at 0–10° C has a cold agglutinin titre of 1:20,480. Vasomotor tone was reduced by immersing the feet and legs in a stirred water-bath at 42–44° C and wrapping the subject in blankets (Gibbon & Landis, 1932). The circulation to both hands was then arrested and one hand exposed to water at 10° C. On release of the circulation 10–15 min later there was practically no flow through the cooled hand.

These responses have been compared with those obtained in patients suffering from Raynaud's disease, in whom spasm of the digital arteries occurs on exposure to local cold (Lewis, 1929). In these patients a high blood flow was maintained through the cooled hand.

In addition, patients with Raynaud's disease show the normal large increase in blood flow in the fingers when these are immersed in water at about 1° C (Thompson, 1952, to be published). In one of the persons with cold agglutinins there was no increase at all.

These results can be adequately explained by supposing that the vessels of the patients with cold agglutinins become blocked with agglutinated red cells. It is unnecessary to postulate that the vessels themselves behave abnormally.

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The response to acetylcholine and histamine of the blood vessels of the human hand and forearm. By F. DUFF, A. D. M. GREENFIELD and I. D. THOMPSON