Sensory adaptation and the mechanism of vision. By
K. J. W. CRAIK. (From the Psychological Laboratory, Cambridge)

The absolute sensitivity of the human eye increases in dim illumination and decreases in strong; thus the adaptative mechanism affords a system of compensation for slow changes in illumination. The details and limits of this compensatory process have been further investigated, extending the observations of Wright [1935], Lythgoe [1932] and of Mellone & Rawdon-Smith [unpublished]. Craik has shown that brightness-discrimination [1938] and acuity [1939] deteriorate at illuminations far above or below that to which the eye is adapted; thus as adaptation to any intensity proceeds, acuity and brightness-discrimination progress towards the optimal for that illumination. The effect of adaptation on subjective brightness has now been investigated, using binocular comparison of test fields presented to the two eyes in succession, immediately after they have been adapted to equal or unequal intensities. Fields exposed to the two eyes separately were adjusted in intensity till they had equal subjective brightness; the estimation was accurate to within $\pm 10\%$ of the physical illumination of either field; yet the state of adaptation of the two eyes might be so different that the fields which were judged subjectively equal differed 500-fold in illumination. It appears that there is little or no increase in the subjective brightness of illuminations from 100 to 15,000 E.F.C. (the upper limit of the apparatus) provided that the eye is adequately adapted to each illumination in turn; the adapted response appears to "saturate" at approximately 100 E.F.C. Thus, the adaptative mechanism provides compensation, in respect of subjective brightness, for changes in illumination, over almost as large a range (above 100 E.F.C.) as that over which it provides compensation for disturbance of acuity and brightness-discrimination by changes of illumination (i.e. above 1 E.F.C.). Certain of these results are shown in Fig. 1. (The lower ends of the curves are dotted, since certain phenomena there require further investigation.)
This compensation for changes in illumination applies, of course, to comparatively slow variations, occupying several minutes; it does not cause rapid changes of illumination to pass unnoticed. Indeed, this compensatory mechanism actually increases the sensitivity to rapid changes, as evidenced by the optimal values of acuity and brightness-discrimination found at nearly equal test and adapt illuminations. Thus a sudden increase in the illumination of an eye adapted, e.g. to 100 e.f.c., produces an initial large increase in subjective brightness, followed by a gradual return to the same subjective brightness as before, though the physical illumination is maintained at its higher value; a sudden change

\[
\log I_{\text{left}} = 3.4
\]

\[
\log I_{\text{right}} = 2.8 \quad 1.5 \quad 0.5
\]

Fig. 1. The relation between the subjective brightness of fields presented to eyes in equal or different states of adaptation. Abscissa: illumination in equivalent foot-candles to which the right eye is adapted. Ordinates: test illuminations whose subjective brightness, as seen by the left eye, equals that of the adaptation field seen by the right eye, when the left eye has been adapted to the illuminations marked on the curves as \(I_{a \text{ left}}\).

to the original illumination would cause a large drop in subjective brightness, again followed by a return to its previous steady value. There is insufficient evidence as to the neural or photochemical nature of this adaptation.

REFERENCES
The site of resistance to diffusion through the cell membrane, and the role of partition coefficients. By J. F. Danielli. (From the Biochemical Laboratory, Cambridge)

Assuming that the cell-plasma membrane is a lipoid film about 50 Å thick, stabilized by adsorbed protein films at the two interfaces, the membrane may be represented by the potential-energy diagram of Fig. 1. The rate of flow of molecules of a penetrating solute from water into the membrane is $aC$, from the membrane into water is $bC'$, and across the minor potential-energy diagrams in the interior of the membrane is $eC''$. $C$ is concentration and $a$, $b$, $e$ vary with molecular species and can be calculated approximately. The partition coefficient is $a/b$. The permeability of the membrane is

$$P = \frac{ae}{nb + 2e}.$$  

$n$ is the number of minor barriers, and cannot exceed 50. For molecules of, for example, glycerol, penetrating the ox erythrocyte, the greatest possible values of $a$ and $b$ are $10^{-11}$ and $10^{-7}$, and the least possible value of $e$ is 2 per sq. cm. of membrane. Hence for such molecules and probably for all molecules having smaller partition coefficients, $nb$ is negligible compared with $2e$, and we have $P = \frac{1}{2}a$, i.e. the resistance to diffusion lies almost entirely at the membrane interface. In fact the membrane could be a hundred times thicker without significantly altering its permeability to glycerol.

For molecules such as propyl alcohol $2e$ may be negligible compared with $nb$, and $P = a/b \cdot e/n$: the interior of the membrane contributes

$$a$$
appreciably to the resistance to free diffusion, and permeability varies inversely with $n$, i.e. is inversely proportional to the membrane thickness.

In the second case permeability is directly proportional to the partition coefficient $a/b$. In the first case permeability is proportional to “$a$”, and the partition coefficient is $a/b$. Since, however, variation in $a/b$ is mainly due to variation in “$a$”, “$b$” remaining relatively constant, there is a general parallelism between the values of “$a$” and the partition coefficient. Hence in both cases permeability varies with partition coefficient, but since several other variables are also involved, there are minor differences between the series of molecules arranged in order of partition coefficient and the same molecules arranged in order of permeability.

**Gonadotrophin from horse pituitaries.** By P. Eggleton and J. M. Robson. *(From the Departments of Physiology and Pharmacology, The University, Edinburgh)*

Attempts to isolate from acetone-dried horse pituitary material two qualitatively different gonadotrophic preparations after the manner of Fevold [1937] have failed. A gonadotrophic material of “mixed” activity, i.e. producing follicular growth, ovulation and luteinization, has been obtained. It contains a third of the activity of the original dried gland, concentrated into about 1/150th of its bulk. It is soluble in all degrees of acidity and alkalinity, and is not toxic to human subjects when injected intravenously.

The dried gland is extracted with dilute pyridine solution, and the extract precipitated with ammonium sulphate and dried. The extracted material is re-extracted and reprecipitated twice in the same manner. The product is taken up in water and dialysed for 48 hr. Normal HCl is added to the salt-free residual solution until no further material precipitates from it. After removal of the precipitate, the remaining solution is poured into five volumes of acetone, and a trace of strong NH$_3$ solution added to promote flocculation. The product is a white powder of albumin-like properties (empirical formula C$_{92}$H$_{196}$O$_{77}$N$_{15}$S). In the largest single preparation of this material 1.5 g. were obtained from 250 g. of dried pituitary.

Attempts to derive from this preparation pharmacologically different fractions by partial precipitation with methyl alcohol, trichloroacetic acid or picric acid have failed.
Of this material 0.1 mg. will double the ovarian weight of immature female rats (40–50 g. body weight). According to tests kindly made by Dr Parkes on one batch of material in hypophysectomized rats, a daily dose of 0.2 mg. given for 5 days results in ovaries of about 38 mg. weight, and the total effect is one of follicular stimulation, luteinization, and interstitial cell stimulation. A single intravenous injection of about 0.015 mg. produces ovulation in the oestrous rabbit. Intravenous injection of 5 mg. produced no ill-effects in women, according to the preliminary report of a clinical investigation by Prof. Dugald Baird.

Intravenous injection of 0.05–0.2 mg. into female rabbits 5–7 hr. after hypophysectomy produced ovulation, and the ovulated follicles developed into active corpora lutea following the administration of either oestrone or oestradiol.

In rabbits hypophysectomized 12 or more days previously, quantities of 0.25–0.5 mg. injected intramuscularly twice daily over 7–8 days induced follicular growth without either ovulation or luteinization. Similar findings were obtained with doses of 0.5–1.0 mg. of an extract (Antex) from the serum of pregnant mares, of which the makers state that 0.2 mg. doubles the ovarian weight in immature rats.

In both cases the subsequent intravenous injection of 0.2 mg. of our material produced ovulation, and the ovulated follicles developed into active corpora lutea as a result of the administration of oestrone or oestradiol.

Hisaw, Fevold, and their co-workers, claim to have separated two distinct gonadotrophic principles by fractional precipitation in acid solution. We have failed (as did Saunders & Cole [1938]) to repeat this result, and further have obtained a product soluble in all degrees of acidity, which nevertheless produces both follicular growth and luteinization.

In view of the fact that a gonadotrophic preparation may exert qualitatively different actions according to the circumstances of administration, it is clearly desirable that any preparation reputed to possess exclusively one type of activity should be tested in several laboratories under different experimental conditions. Only if all observers agree could the existence of more than one gonadotrophic principle be regarded as established.

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The effect of insulin hypoglycaemia and $B_1$-avitaminosis on the acetylcholine content of brain. By F. C. MacIntosh. (From the National Institute for Medical Research, London)

The synthesis of acetylcholine (ACh.) is promoted by glucose and by pyruvate, both in excised brain tissue [Quastel, Tennenbaum & Wheatley, 1936; Mann, Tennenbaum & Quastel, 1938] and in the intact sympathetic ganglion [Kahlson & MacIntosh, 1939]. It might thus be expected that under conditions in which glucose or pyruvate is not being normally metabolized, the ACh. content of nervous tissue would be lowered as a result of inefficient ACh. synthesis. Among such conditions are insulin hypoglycaemia (deprivation of glucose) and $B_1$ avitaminosis (faulty utilization of pyruvate). I have therefore estimated the ACh. content of the brains of mice in insulin convulsions, and of pigeons in which advanced polyneuritis had been induced by a diet of polished rice. In neither case, however, did the values obtained fall outside the normal limits of variation for the species: these were, for the whole brain of the mouse (seven animals) 1.5–2.6$\mu$g./g., and for the cerebral hemispheres of the pigeon (four animals) 1.8–3.0 $\mu$g./g.; the corresponding values for six insulin-treated mice, and for four $B_1$-deficient pigeons, were respectively 1.5–1.8 and 2.0–3.0 $\mu$g./g. A few determinations have indicated no effect of $B_1$ avitaminosis on the ACh. content of the superior cervical ganglion of the mouse, the cerebellum of the pigeon, or the brain of the rat.

Extracts of brain for ACh. estimation were made with trichloroacetic acid, only the fraction soluble in absolute alcohol being retained, and tested on the eserinized leech preparation or on the blood pressure of the chloralosed cat [cf. Brown & Feldberg, 1936]. A variety of control experiments has shown that ACh. is quantitatively extracted from brain tissue by trichloroacetic acid, that no ACh. is lost in subsequent stages of the procedure, and that the response of the leech strip to ACh. is not modified by other substances present in the extracts. Higher values for ACh. in brain, which may irregularly be found when extracts are prepared by heating the minced tissue in eserinized saline, are due to sensitization of the leech muscle to ACh. by other substances present in such extracts, and not to any more complete extraction of ACh. by this means.

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Pyruvate oxidation in brain, not involving a succinate cycle.

By C. Long, S. Ochoa and R. A. Peters. (From the Department of Biochemistry, University of Oxford)

Washed minced pigeon brain tissue readily oxidizes pyruvic acid (c. 67% of the pyruvate disappearing is oxidized to CO₂ and water, 25% appears as acetic acid, 5% as lactic acid [Long, 1938]) in conditions under which a cyclical system involving C₄ dicarboxylic acids does not appear to be possible because (1) succinic acid which gives rise to a large O₂ uptake does not evolve CO₂ [Weil-Malherbe, 1937], and (2) fumaric or l-malic acids give neither O₂ uptake nor CO₂ production. This means that succinic acid is oxidized only to fumaric-malic acids under these conditions [Quastel & Wheatley, 1931]. It does not seem that the “citric acid cycle” of Krebs & Johnson [1937] can play a part either, as it involves succinic, fumaric, malic and oxalacetic acids as intermediates, and also because added citric acid does not increase the O₂ uptake. It is doubtful whether oxalacetic acid can arise in any other way.

It may be added that early observations in this laboratory showed no catatorulin effect with succinate, and in further experiments since then comparatively large additions of fumarate or l-malate have not influenced the catatorulin reaction with pyruvate. The above evidence reinforces previous views from this laboratory [McGowan & Peters, 1937] upon the nature of the oxidation of pyruvate in pigeon brain.

Minced pigeon brain washed three times with ice-cold Ringer, pH 7.3

<table>
<thead>
<tr>
<th>Duration min.</th>
<th>Substrate</th>
<th>µl./g. tissue O₂ uptake</th>
<th>µl./g. tissue CO₂ production</th>
</tr>
</thead>
<tbody>
<tr>
<td>150</td>
<td>Pyruvate 0-02 M</td>
<td>442</td>
<td>1626</td>
</tr>
<tr>
<td>120</td>
<td>Succinate 0-04 M</td>
<td>361</td>
<td>1112</td>
</tr>
<tr>
<td>120</td>
<td>Fumarate 0-046 M</td>
<td>527</td>
<td>543</td>
</tr>
<tr>
<td>180</td>
<td>l-Malate 0-04 M</td>
<td>336</td>
<td>286</td>
</tr>
<tr>
<td>120</td>
<td>Citrate 0-018 M</td>
<td>308</td>
<td>145</td>
</tr>
</tbody>
</table>

Respiration medium: NaCl 0-126 M; KCl 0-018 M; MgSO₄ 0-0011 M; NaHCO₃ 0-0013 M; KH₂PO₄ 0-0097 M.

REFERENCES


1 More recently, Weil-Malherbe (Biochem. J. [1937], 31, 2202) has favoured the view that succinic acid is an actual intermediate in pyruvic acid oxidation.
(From the Department of Medicine, Cambridge)

Experimental work [Committee for the Investigation of Dental Disease, 1936] has shown that the incidence of dental hypoplasia and of caries is reduced or even abolished by adequate amounts of vitamin D in the diet. Indeed, the association of rickets and "bad teeth" has been recognized in this country since Glisson's [1651] original description of the disease. One would therefore expect that in a community where rickets was widespread the teeth would be much worse than in a similar community in which there was no clinical rickets. This is not necessarily the case, as the following observations show.

During the past three years comparative diet surveys have been carried out amongst various Indian communities, and over 9000 children (5–15 years) have been examined clinically by the same observer. The examination included a search for past and present signs of rickets and an inspection of the teeth. The number of teeth present in the mouth was recorded and the number which were carious to naked eye examination.

It was exceptional to find children who had had dental care, but in such cases teeth treated by a dentist were counted as carious. The incidence of hypoplasia and hypocalcaemia sufficient to give a sensation of roughness with a probe was also noted.

Rickets and osteomalacia are exceedingly common in certain parts of north India, notably in the Kangra valley which lies in the Himalayan foothills. In an examination which was carried out there it was found that twenty-four out of a total of forty-five children showed signs of rickets, late rickets or osteomalacia. The same children had almost perfect teeth, with a very low incidence of caries and little hypoplasia. The teeth of these children were, in fact, no worse than those of 938 children in the Central Provinces living on a similar diet and among whom no case of rickets was discovered. These dental findings were communicated to Dr Marshall Day, who, at my suggestion, examined fifty children in the Kangra valley, all of whom had severe rickets, but nearly all of whom he found to have excellent teeth. His results have just been published [Taylor & Day, 1939].

REFERENCES

Excitability changes in a nerve fibre during the passage of an impulse in an adjacent fibre. By Bernhard Katz and Otto H. Schmitt. (From the Department of Physiology, University College, London)

A pair of single fibres isolated from the limb nerve of Carcinus maenas is separated along a part of its length and is mounted on electrodes as illustrated in Fig. 1a. Fibre I is excited at B by a quick induction shock, and then as the impulse is passing through the region CDE, the excitability of fibre II is tested at D by a short condenser discharge applied between D and C. The action potentials are led off to a cathode-ray oscilloscope from D and E.

The excitability of fibre II varies, during the passage of an impulse in the adjacent fibre, in a triphasic manner, as illustrated in Fig. 1b. As the action potential in fibre I approaches D, fibre II becomes at first less excitable, then passes through a more excitable phase, and finally again through a period of slightly reduced excitability.
These changes are readily explained as being due to the effect of the action currents of fibre I, remembering that the direction of these currents with respect to the nerve membrane reverses twice, and that current lines which leave the conducting fibre enter the adjacent resting fibre and vice versa.

**Discharges in nerve fibres produced by potassium ions.** By G. L. Brown and F. C. MacIntosh. (*From the National Institute for Medical Research, London*)

The injection of KCl into a perfused ganglion is known to set up impulses in the postganglionic fibres and to liberate acetylcholine from the preganglionic nerve endings [Brown & Feldberg, 1936]. The effect of KCl is, however, not confined to these actions. We have injected KCl into the carotid artery of the cat, all branches being tied other than those supplying the superior cervical ganglion, together with the nodose ganglion of the vagus, and the IX, XI and XII nerves where they are in close relation to the ganglia. Records have been taken with amplifier and oscillograph from the pre- and postganglionic sympathetic trunks, from the vagus on either side of the nodose ganglion, from its superior and recurrent laryngeal and depressor branches and from the hypoglossal nerve. In all instances, the central connexions of the nerves had been cut. The arterial injection of 0.16–0.4 c.c. of an isotonic solution of KCl (2–5 mg.) causes a discharge of impulses in all these nerves. The discharge lasts many seconds in all cases except that of the postganglionic sympathetic trunk, in which it is cut short by the paralysing effect of persisting KCl. In the hypoglossal, and in a small twig of the superior laryngeal nerve carrying motor fibres, we have recorded synchronized discharges with a perfectly regular rhythm of about 150 per sec.

The discharge evoked by KCl in the preganglionic sympathetic trunk is unaffected by paralysing the ganglion cells with nicotine. An isotonic solution containing KCl and CaCl₂ in the proportion of 1:2 does not evoke the discharge. The similar injection of acetylcholine sets up a discharge only in the postganglionic sympathetic trunk.

In one experiment we succeeded in making an injection into the circulation of the sciatic nerve at the point where the gluteal artery crosses it. The injection of KCl caused sustained contraction of the small muscles of the foot.
These experiments suggest that K ions, when suitably applied, can cause the repeated discharge of impulses from nerve fibres in their continuity, and not only from nerve cells; indeed, the question whether certain effects of injecting KCl into the sympathetic ganglion were rightly attributed to stimulation of the ganglion cells may need reconsideration.

REFERENCE


**Congenital myotonia in the goat.** By G. L. Brown and A. M. Harvey. *(From the National Institute for Medical Research, London)*

We have been able to obtain from the United States a strain of goats suffering from a congenital myotonia, which is indistinguishable from Thomsen's disease as it occurs in man, and, like it, relieved by quinine [Kolb, 1938]. The muscles are extremely sensitive to mechanical stimulation; tapping, stretching and the insertion of needle electrodes cause contraction of the muscle. This contraction is due to a long-lasting irregular tetanus in groups of muscle fibres, and is accompanied by oscillatory action potentials, best revealed by means of concentric needle electrodes. It is independent of the connexion of the muscle with the central nervous system.

The response of the muscle to a single motor nerve volley is repetitive in nature, and the twitch tension is at least twice that developed by the same muscle of a normal English goat of similar weight. At the end of tetanic stimulation of the motor nerve at a frequency of 50 per sec. the muscle remains tetanically contracted, as it does naturally after sudden exertion. On the other hand, stimulation at frequencies of 5 per sec. produces a progressive diminution of the abnormal activity. The sensitivity to mechanical stimulation is not diminished by full curarization of the muscle, and 8 days after section of the nerve supply of the muscle the myotonic reactions are still unchanged.

The amount of acetylcholine required to produce, by close arterial injection, a given tension maximum is the same in normal and myotonic muscles, and only the duration of the response is greatly increased in the myotonic. The myotonic muscles, on the other hand, are abnormally sensitive to K⁺. A normal goat tibialis muscle requires the injection of 100 mg. KCl in 2 c.c. to evoke a brief contraction as great as a maximal
motor nerve twitch, whereas a myotonic muscle may give with 20 mg. a
response much greater than the twitch tension and lasting some minutes.

We believe that this myotonia is due to an abnormality of the muscle
fibre itself, and that the neuro-muscular transmitting apparatus is not
directly involved.

REFERENCE


**Potassium content of human muscle.** By J. N. Cumings. (*From the
Biochemical Laboratory, National Hospital, Queen Square, London*)

An investigation into the potassium content of normal and abnormal
muscle and the effect of prostigmin on the muscle K is reported.

Twenty-seven normal voluntary muscles were examined and an
average K content of 0.289% by wet weight and 0.989% by dry weight
of muscle was found.

Abnormal muscles could be grouped according to whether there was
a normal, a low, or a raised K level. All muscles except those from cases
of myasthenia gravis, dystrophia myotonica and those with gross
replacement of muscle fibres by fat or by fibrous tissue contained a
normal K content. Muscles from myotonic patients and those muscles
with replacement fibrosis contained a low K content. Myasthenic muscles
contained a very raised K level, often twice the normal amount being
found.

Prostigmin did not alter the K level in normal muscles, but in
myotonia there was a raising of the K to within or nearly within the
normal level, whereas in myasthenia there was a drop in K content to
within the normal range.

**The effect of asphyxia on inhibition of respiratory movement in
the sheep's foetus.** By J. Barcroft, D. H. Barron, A. T. Cowie,
P. H. Forsham and A. MacDonald. (*From the Department of
Physiology, University of Cambridge*)

Experiments designed to explore the degree of asphyxia necessary to
release respiratory movements in the foetus from their normal inhibitory
control have been carried out as follows. Blood has been taken from the
fontanelle under as nearly normal conditions as may be. The umbilical
cord is then occluded until respiratory movements appear, when a second sample of blood is taken from the fontanelle. The oxygen level at which release takes place is remarkably constant, dropping from about 25% saturation at 100 days to about 15% at term. The CO₂ level is variable. The hydrogen-ion level has not been determined. In the absence of the last determination it is not possible to say that the release is due to oxygen deficiency, but merely that the oxygen level forms a surprisingly exact indicator of the degree of asphyxia required.

Observations on intestinal secretion. By R. D. Wright, M. A. Jennings, H. W. Florey and R. Liem. (From the Department of Pathology, University of Oxford)

In an oral communication to the Society on 12 November 1938 evidence was produced that in decerebrate or decapitate cats:

1. Stimulation of the vagi in the thorax produced considerable secretion from the upper part of the duodenum. Histological examination showed depletion of secretion from Brunner's glands. No secretion was obtained from the rest of the small intestine.

2. The administration of eserine caused a secretion not only from the duodenum but also from other parts of the small intestine.

3. Cutting the greater splanchnic nerves in the thorax produced secretion from the duodenum but not elsewhere.

These experiments have been continued and it has been found that the cutting of all preganglionic fibres to the coeliac and superior mesenteric ganglia causes a "paralytic" secretion from all the small intestine. If at aseptic operation these fibres are cut and the animal allowed to recover an initial diarrhoea disappears in a few days. If after 10 days, when the animal is in good condition, it is decapitated and the ganglia removed a free secretion occurs from the whole length of the gut.

Previous work, showing that a duodenal fistula totally transplanted beneath the skin secretes in response to a hormone liberated after feeding, has been repeated on the cat with the same results. This type of experiment has also been extended to the pig. The portion of the duodenum between the bile and pancreatic ducts has been transplanted beneath the skin by a two stage operation. These transplants secrete well. After 24 hrs. starvation secretion ceases, but it starts again very soon after the administration of food, so that in this species also a hormone appears to be active.
The only enzymes constantly found in centrifuged juice obtained by the various methods are enterokinase and amylase. This confirms the view that other enzymes which have been reported, notably erepsin, are not secreted into the juice but come from broken-down cells. After adding mucosal scrapings to centrifuged juice erepsin is found.

**Reflex vaso-motor responses from the paws of the cat.** By C. B. B. Downman, A. F. Goggio, B. A. McSwiney and M. H. C. Young. (From the Sherrington School of Physiology, St Thomas’s Hospital)

Reflex vaso-motor responses were recorded by means of small plethysmographs applied to the front and hind paws of the cat; these were connected by rubber tubing to Wiggers’s capsules covered by light rubber membranes, on which were mounted extremely light mirrors for optical recording of volume changes. The method reduces dead space and inertia to a minimum, and volume changes of 0.01 c.c. can be recorded.

The responses were abolished by a tight ligature round the pads; responses, however, were still obtained if the pad of one toe was left out of the ligature, indicating that the vessels of the pads were responsible for the whole of the measurable response from the paw.

Reflex vaso-constriction was elicited in both front and hind paws by pinching the ear, by sound stimuli, by single break shocks or faradic current applied to either somatic or visceral afferent nerves, by pinching the gut or the mesentery, and by distending a balloon in the gut. These reflexes were obtainable in cats anaesthetized with urethane, dial, nembutal, or pernocton, and in the decerebrate cat. Maximal reflex vaso-constriction was obtained with stimuli which produced a rise, a fall, or no change in the blood pressure. The reflex response was obtained after removal of both suprarenal glands, and also in the decerebrate cat after curarization.

The efferent pathway of these reflexes is through sympathetic fibres, since section of the appropriate sympathetic pathways abolished the response from the front or hind paws.

The latent period of the reflex vaso-constriction is extremely variable, ranging from 0.5 to 2.0 sec.; it appears to depend mainly upon peripheral conditions. The central reflex time was fairly constant, for similar peripheral conditions, in all experiments, being of the order of 0.4–0.6 sec.
Summation of subliminal stimuli, applied either to the same afferent nerve or to two different afferent nerves, has been obtained. Summation has also been shown on stimulation of the appropriate preganglionic or postganglionic nerve fibres.

The role of light in the action of several drugs upon the hypophyseal melanophore hormone secretion of frogs (Rana temporaria). By T. C. R. Shen. (From the Department of Pharmacology, University of Ghent)

Köller & Rödewald [1933] demonstrated that total darkness influences the hypophysis of frogs in such a manner that an extract made from such a hypophysis contains little or no melanophore hormone. This fact was confirmed by Jores [1934] and Schroff [1935]. Stutinsky [1936] showed that exposure of frogs to strong electric light continuously for one week alters the cellular structure of the hypophysis. The chromophobe cells increase at the expense of chromophile cells. This indicates that the gland is actively secreting. In previous papers [Shen, 1937, 1938 a, b, 1939] we have shown that several drugs induce a melanophore hormone secretion. Indeed the melanophores of hypophysectomized frogs do not react to these substances. In the present study an effort has been made to examine the effect of these drugs upon melanophore hormone secretion of the hypophysis of frogs which have been exposed to either a period of total darkness or a period of continuous light.

Seven series of experiments were made to study the effect of complete darkness upon the melanophore hormone secretion induced by drugs. Each series consisted of 7–10 frogs weighing 15–30 g. (Rana temporaria). After exclusion from light for periods varying from 30 min. to 24 hr. appropriate doses of either piperido-methyl-3-benzo-dioxane (F 933), yohimbine, nicotine, sodium phenobarbital, allylisopropyl barbituric acid (numal, "Roche"), sodium barbital, or chloralosane were injected subcutaneously. This was done under a dim red light in a dark room. The animals were again returned to the dark. At intervals of ½, 1 and 2 hr. from the time of injection their melanophore responses were controlled under a dim red light in the dark room. The experimental results show the following points: (1) Frogs which have been kept in total darkness still react to the examined drugs by a melanophore expansion. (2) Frogs blinded by previous extirpation of their eyes and kept in total darkness react to F 933 by a darkening of the skin. (3) Animals kept in a light environment and darkened by drugs cannot be rendered pale by
putting them in total darkness, and conversely it is not possible to further deepen the colour of animals kept in complete absence of light, once darkened after drug injection by exposing them to light. (4) Application of local anaesthetics (2% novocaine or 0.1% percaine) to the exposed hypophysis region of pale frogs kept in complete darkness still induces the dark skin response.

The effect of continuous light on the drug action upon the melanophore hormone secretion was examined in two series of experiments. A method similar to that of Stutinsky [1936] was employed. Male frogs weighing 20–25 g. were used. After exposure continuously for one week to a white background under a light from a 75 W. electric lamp, appropriate doses of yohimbine or sodium barbital were injected subcutaneously. The results show that constant and continuous light does not appreciably affect the dark skin response obtained by injecting barbital or yohimbine.

The above experiments thus show that neither total darkness nor prolonged, continuous light have any appreciable influence on the stimulating action of the examined drugs upon the hypophyseal melanophore hormone secretion of frogs.

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The effects of certain aldehydes upon the growth of cells in vitro.

By E. N. WILLMER and K. WALLERSTEINER. (From the Department of Physiology, Cambridge)

During certain investigations on the carbohydrate metabolism of chick periosteal fibroblasts growing in vitro it was found that growth and cellular activity were inhibited by certain aldehydes, notably glyceraldehyde, methyl glyoxal, propyl aldehyde, butyl aldehyde and benzaldehyde, but not by the corresponding acids. The critical concentration for
inhibition was in the region of 0-002 \( M \), and at least with certain aldehydes (glyceraldehyde, propyl aldehyde and butyl aldehyde) the effect was reversible, for when the aldehyde was removed, growth and cell division were resumed. During the inhibition many of the cells withdrew their processes and became completely spherical. On removal of the inhibitory substance they put out pseudopodia and started to migrate within the first hour, and cell divisions occurred without any significant latent period.

Several other substances containing the aldehyde group have also been tested in relation to the growth and activity of tissues in vitro. Acrylaldehyde (\( \text{CH}_2: \text{CH} . \text{CHO} \)) and crotonaldehyde (\( \text{CH}_3 . \text{CH}: \text{CH} . \text{CHO} \)) produce similar inhibitory effects but at very considerably lower concentrations, e.g. 0-00002 \( M \). Furfural

\[
\begin{align*}
\text{H} & \quad \text{C} \\
\text{H} & \quad \text{C} \\
\text{C} & \quad \text{CH} \\
\text{O} & \quad \text{C} \\
\text{CHO} & \quad \text{CHO}
\end{align*}
\]

inhibits at 0-01 \( M \). Preliminary experiments suggest that heptaldehyde inhibits at 0-002 \( M \) and that citral (\( \text{[CH}_3\text{]}_2\text{C}:\text{CH} . \text{CH}_2 . \text{CH}_2 . \text{C}[\text{CH}_3] : \text{CH}.\text{CHO} \)) becomes effective at 0-001 \( M \).

The effects of many of these aldehydes have been tested on the growth of the cells of a dibenzanthracene chicken sarcoma in vitro, but there has so far been no indication that the sensitivity of these cells differs in any way from that of normal cells.

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**A simple differential volumetric method for obtaining the time-course of oxygen usage by stimulated frog’s muscle.**

By D. K. Hill. (*From the Physiological Laboratory, Cambridge*)

The volumeter consists of two bulbs joined by a capillary tube of fine bore. A spot of fluid in this tube acts as indicator, and is viewed by a travelling microscope. The movement of the spot can be followed over a minimum distance of \( \frac{1}{100} \) mm. 1 mm³ volume change causes a movement of the spot of 5 mm.

A pair of frog’s sartorii is used, one in either bulb supported on a frame which is part of the stopper. Both bulbs are filled with oxygen. The muscles are stimulated by platinum electrodes. The whole apparatus is immersed in finely crushed ice and water: the ice is cleared away round the part of the capillary tube containing the spot of fluid and the microscope objective is placed beneath the surface of the water. The
spot is illuminated by a small flash-lamp bulb pushed down in the ice. A temperature of 0° C. is preferred, first because melting ice provides an excellent thermostat, and secondly because the time course of metabolic events in the muscle is greatly drawn out by a low temperature, and diffusion processes then become of less importance.

When working differentially there is no movement of the spot when both muscles are resting. When one muscle is stimulated tetanically for 5 sec. there is first a volume increase due to heat liberation: this can be allowed for by a control heating. There is then a slow uptake of oxygen shown by a volume decrease: an average sartorius will use a total of about 1 mm.³ of oxygen for complete recovery.

The carbon dioxide produced in the early stages of recovery is completely absorbed by the muscle itself, which becomes alkaline owing to breakdown of phosphocreatine. In the later stages the carbon dioxide diffuses across to the walls of the vessel and is absorbed by soda placed on filter-paper. It has been shown that the amount of carbon dioxide present at any moment in the gas is insufficient to cause any complication.

The record obtained can be analysed to allow for the rate of oxygen diffusion into the muscle. The result shows that the time course of oxygen usage is exactly the same as the time course of the delayed heat production at the same temperature.

The transient response of a primitive ear. By K. J. W. Craik, A. F. Rawdon-Smith and R. S. Sturdy. (From the Psychological Laboratory, Cambridge)

The response of the vertebrate ear to transient stimuli has been investigated in some detail, notably by Derbyshire & Davis [1935] and Rawdon-Smith & Hawkins [1939]. The response of such ears, however, exhibits considerable complexity in that the nervous response proper is invariably in some degree contaminated by admixture with potentials of cochlear origin. It has been shown by Adrian [1938], however, that the response from the ear of the tortoise consists almost entirely of action potentials, phenomena analogous to the vertebrate "cochlear effect" being of very small magnitude. We have, therefore, studied the response from the ear of the land tortoise, Testudo graeca, to electrically generated transients, controllable both in amplitude and in wave-form.

As would be predicted, the electrical response from this primitive ear to such stimuli comprises one or more action potential volleys, the
number present in each discharge depending both on the intensity and on the complexity of the transient stimulus. Provided that this is of brief duration, however, one response volley only will be elicited, since stimulus waves following that which first yields a response arrive during the refractory period of the acoustic nerve fibres. As the duration of the stimulating transient is lengthened, however, one or more succeeding phases will be produced in the response. It is, however, possible to obtain a stimulus which consists of a single initial phase whose amplitude is great relative to that of the succeeding phases. Such a stimulus, provided it is applied at an intensity sufficient for this initial phase to excite, though insufficient for those following to do so, will, of course, yield a single volley response irrespective, within limits, of its duration. Such a stimulus may be conveniently employed to determine which phase of a complex stimulating wave elicits the succeeding response. This may be done in one of three ways: by determining whether a just detectable response is obtained at lower stimulus intensity for a positive or for a negative pressure wave; by assessing the magnitude of the responses obtained to transients of identical amplitude and form, but in the two different phases; and by measuring the latency of the response for the two stimulating phases, using a supraliminal stimulus. In the latter method, the change in latency on moving from one phase to the other is correlated with the arrival at the ear of a negative or positive pressure wave.

In this manner, we have shown that the essential phase of the stimulus for the tortoise ear corresponds to the development of positive pressure at the ear drum. This observation is in contrast with that of Derbyshire & Davis on the cat, who have shown that in this animal the stimulating phase is the negative pressure wave. There is good reason to suppose that this latter condition will hold for all the more highly developed vertebrate ears.

It would appear difficult to reconcile our observation with the belief that the crude auditory apparatus of the tortoise represents the evolutionary forbear of the mammalian cochlea, since it does not appear readily possible that in the course of development the adequate stimulus could change from a positive to a negative pressure change.

REFERENCES

Adrian, E. D. [1938]. *J. Physiol.* 92, 9 P.
