broken up and filtered on Whatman No. 2 paper through a large (size 6) Buchner funnel. The average yields $(\times 10^{13})$ obtained per tray were : 3.2 for T1, 3.8 for T2, 1.2 for T3, 2.0 for T4, 6.0 for T5, 4.3 for T6 and 1.1 for T7. These values are 25-50 times the yield obtainable in a normal size glass Petri dish without 'bottom' agar.

Summing up one can say that : (1) Routine assay of bacteriophage samples can be made on glass plates without 'bottom' agar, but a correction factor of 2 has to be taken into account for bacteriophages T2, T4, T5 and T6. (2) High yields of bacteriophages can be obtained when confluent lysis is carried out on glass plates without 'bottom' agar. (3) Confluent lysis can be adapted for large-scale bacteriophage production by carrying it out on large stainless steel trays.

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PHYSIOLOGY

A New Concept of Temperature Regulation by Amines in the Hypothalamus

NEARLY ten years ago it was found^{1,2} that adrenaline, noradrenaline and 5-hydroxytryptamine (5-HT) are present in relatively high concentrations in that part of the wall of the third ventricle known as the hypothalamus. Yet no definite function could be attributed to their presence in this diencephalic structure.

The hypothalamus is involved in the central control of a variety of important functions, one of which is concerned with regulation of body temperature. But what goes on in the hypothalamus to bring about this regulation? The experiments recorded here suggest that it is the release of adrenaline, noradrenaline and 5-HT.

The experiments are the outcome of two independent observations. First, that pyrogens injected into the cerebral ventricles^{3,4} or directly into the anterior hypothalamus⁵ of a cat cause fever and shivering, and second that, injected into the cerebral ventricles, adrenaline and noradrenaline abolish drug-induced shivering, whereas 5-HT has the opposite effect and evokes shivering. These effects, too, have been attributed to an action on the hypothalamus⁶⁻⁸. We have now shown that the injection of these amines through an implanted Collision cannula into the cerebral ventricles of an unanæsthetized cat also modify body temperature: adrenaline and noradrenaline lower, and 5-HT raises, the temperature.

To demonstrate the effect of adrenaline or noradrenaline, the body temperature has first to be elevated. This can be done by pyrogens. When a minute amount of pyrogenabout 1/1,000 of the dose effective on intravenous injection-is injected intraventricularly into an unanæsthetized cat the rectal temperature rises after a latency of about 1 h to a level of 2°-2.5° C above normal and remains elevated for several hours. The high temperature can then be brought down to normal, or to nearly normal, by an intraventricular injection of 50-100 µg of either adrenaline or noradrenaline. Within a few minutes the temperature begins to fall and the maximal fall is reached within about 45 min; then the temperature slowly climbs during the next 2-3 h until fever-level is again attained. When smaller doses of adrenaline or noradrenaline are injected intraventricularly at half-hourly intervals a reduction in temperature is maintained for longer periods. The injections of the catecholamines also cause cossation of the shivering produced by pyrogens.

To produce with 5-HT a rise in body temperature as well as shivering, 200 µg are injected intraventricularly into the unanæsthetized cat. Usually the rise occurs in two peaks. There is first a transient, relatively quick rise, which is followed within 1 h after the temperature has returned to normal by a second more gradual but prolonged elevation of up to 2° C. It is sometimes more than 20 h before the rectal temperature has returned to normal. When 5-HT is given during the pyrogen fever it appears to be even more effective. The intraventricular injection of 200 μ g then causes an additional steep elevation of up to 1° C and it requires more than 30 h before the pyrogen-5-HT fever subsides.

The fever and shivering produced by 5-HT are affected in the same way by the intraventricular injection of adrenaline or noradrenaline as the fever and shivering produced by pyrogens. The temperature is brought down and shivering ceases.

The findings reported here lead to a new concept about the mechanisms involved in the hypothalamic regulation They suggest that normal temof body temperature. peraturo is maintained by a delicate balance in the release of adrenaline, noradrenaline and 5-HT in the hypothalamus, thus attributing an important physiological function to the occurrence of these amines in this part of the brain; this, however, may not be their sole function. The effect of adrenaline and noradrenaline in lowering body temperature is seen only when the temperature has first been elevated. The reason may be because these amines are continuously released in sufficient amounts in the hypothalamus to keep the temperature down, in the same way as their release is thought to prevent us from shivering Additional adrenaline or noradrenaline continuously⁹. applied artificially to this region, therefore, would have no action either on the temperature which is already down, or on shivering which is not present. A rise in temperature as well as shivering could then be visualized as the result of two mechanisms: an inhibition of the release of adrenaline and noradrenaline, and an initiation or augmentation of the release of 5-HT. Fever produced by pyrogens, that is, the fever of infectious diseases, may be brought about in just this way. In addition, pyrogens may render the hypothalamus more sensitive to the action of 5-HT. and there is the further possibility that pyrogens do not act solely through the hypothalamic amines and their release, but also mimic the effect of 5-HT.

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Integration at an Inhibitory Interneurone: Inhibition of Renshaw Cells

THE spinal interneurones known as Renshaw cells have as their function the regulation of motoneurone activity: they appear to terminate on motoneurones directly inhibiting their firing¹, and to inhibit other inhibitory interneurones, thereby disinhibiting motoneurones and enhancing their discharge². Because of this widespread involvement of Renshaw cells in the control of motor