

more in evidence the longer the period of stasis, and the higher the temperature of the peripheral surface. Short periods of stasis ($2\frac{1}{2}$ to 5 minutes) gave no tingling at the lower, but intense sensations at the higher temperatures.

Stasis of the finger alone even at the higher temperatures (*e. g.*, 39° for 5 minutes) gave only very slight tingling during stasis and on release, while if the compression was applied to the arm, the fingers appeared to share in the tingling sensations. In the fingers the nerve trunks must be peculiarly exposed to mechanical effects of pressure, and in this locality the changes in temperature also involved these nerve trunks.

It may, therefore, be concluded that the sensations of tingling are induced, directly or indirectly, by some chemical factor, the rate of formation of which varies with the temperature of the tissues. This factor presumably is formed more rapidly in the muscles, since stasis involving muscular regions is much more effective than stasis of the finger, which contains only smooth muscle.

A chemical factor seems the most legitimate hypothesis, but it might act indirectly through inducing osmotic changes.

It should be noted that the tingling was not investigated in detail, since the primary object of the experiments was to study temperature sensations and to arrange the experiments in such a way that tingling did not offer too great a complication.

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Carotid Sinus Reflexes to the Respiratory Center.

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According to Heymans¹ and Koch,^{2, 3} changes in pressure within the carotid sinuses set up reflexes which have a powerful influence upon the respiratory center. Their observations are fully confirmed by the results of perfusion of the carotid sinuses of 15 dogs, 5 rabbits, and 4 cats, with Locke's solution or with blood from a donor animal, by means of a pump. Heymans'¹ conclusion, that

¹ Heymans, C., and Bouckaert, J. J., *J. Physiol.*, 1930, **69**, 254.

² Koch, E., *Die reflektorische Selbststeuerung des Kreislaufes*. Dresden, 1931, 168.

³ Koch, E., and Mark, R. E., *Z. f. Kreislaufforsch.*, 1931, **23**, 319.

the respiratory stimulant effect of occlusion of both common carotids is entirely the result of carotid sinus reflexes, is not confirmed; denervation of the carotid sinuses, while usually diminishing and sometimes abolishing the stimulant effect upon breathing, occasionally does not decrease or may actually increase the respiratory effect of the occlusion, in decerebrate cats and narcotized dogs; hypertension as a result of the denervation introduces a new factor in that carotid occlusion does not reduce cerebral blood-flow to as low a level as before; a negative result from the occlusion does not then prove that a previous positive result was entirely due to reflexes from the carotid sinuses. Carotid occlusion lowers endosinusal pressure by 36% (average) in dogs; it reduces cerebral (torcular) venous outflow by about 45% (average) in dogs. Occlusion of the vertebral arteries reduces torcular outflow only by 25% (average) in dogs, and in one animal it had no measurable effect; absence of circulatory and respiratory stimulation from occlusion of the vertebrals does not therefore necessitate the conclusion that the stimulant effects of carotid occlusion are due entirely to reflexes from the carotid sinuses.

Heymans' conclusion¹ that the respiratory center is not directly affected by increase in its blood-supply is contradicted by the results of 4 sets of experiments in which medullary blood-flow was increased under such circumstances that reflexes from the carotid sinuses or aorta could not contribute to the results:

1. Reopening of occluded carotid and vertebral arteries produces apnea in dogs and cats. The result is exactly the same whether the occlusion is made proximal (common carotids) or distal (external and internal carotids) to the carotid sinuses; it is not significantly altered by sinus denervation. The apnea is not prevented by continuous inhalation of 10% CO₂, so that it is not due to the hyperpnea resulting from the occlusion.

2. Lowering of intracranial pressure to zero after a brief period of elevation to a level close to that of arterial blood-pressure (by way of a parietal cannula or cisternal needle) produces respiratory depression or apnea. Section of the sinus and aortic nerves does not modify the result. CO₂ inhalation shortens the apnea but does not prevent respiratory depression upon reduction of extramedullary pressure.

3. Adrenalin frequently produces apnea in dogs and cats, occasionally in rabbits, whose aortic and sinus nerves are completely

divided, or whose carotids (in sinus perfusion experiments) are isolated from the systemic circulation with aortic nerves cut.

4. Increase in vertebral perfusion flow was found⁴ to cause respiratory depression in dogs and cats; in those experiments the common carotids were closed, so that sinus reflexes were presumably excluded, and aortic reflexes operated in the reverse direction because increase in perfusion flow necessitated decrease in systemic blood-pressure. Recently the brains of 5 rabbits have been similarly perfused by way of the internal carotids, with sinus and aortic nerves cut; in these also respiration was regularly depressed by an increase in cerebral blood-flow, stimulated by a decrease (*e. g.*, increase in flow from 25.6 to 40 cc. per minute reduced breathing from 1280 to 640 cc. per minute; decrease in flow from 42.8 to 26.3 cc. increased breathing from 432 to 800 cc. per minute).

The experiments of Heymans, Bouckaert, and Dautrebande⁵ dealing with carotid sinus reflexes aroused by changes in gas-content of the carotid blood have been repeated. Of 10 dogs, only one showed repeatable and reversible effects of this sort and this one was least sensitive of all to the reflex respiratory effects of changes in carotid sinus pressure. Of 4 cats, however, all showed definite effects of the sort described by Heymans *et al.* In every case the possibility of patent carotid branches in the recipient animal was excluded. The influence of sinus denervation upon the respiratory effects of repeated exposure to CO₂ excess and oxygen-lack (nitrogen inhalation) was investigated in 4 dogs, one cat, and one rabbit. In general, the stimulant effect of either gas was less after sinus denervation than before, and that of oxygen-lack was reduced more than that of CO₂ excess. Sometimes anoxemia failed entirely to stimulate breathing after sinus denervation (one out of 7 inhalations in the cat, 4 out of 10 inhalations in the dogs), but in no case was this result obtained consistently in the same animal; other inhalations of the same gas-mixture by the same animal sometimes stimulated breathing more than they had before sinus denervation. In no case did CO₂ (10% in oxygen) fail to stimulate breathing after sinus denervation. These results are difficult to interpret; they indicate that while the sinus nerves apparently have some relation to the respiratory effects of asphyxia and anoxemia, the relation is not the simple one outlined by Heymans.⁵

It is concluded that while changes in carotid pressure undoubt-

⁴ Schmidt, C. F., *Am. J. Physiol.*, 1928, **84**, 202.

⁵ Heymans, C., Bouckaert, J. J., and Dautrebande, L., *Arch. internat. de Pharm. et de Therap.*, 1930, **39**, 400.

edly affect respiration reflexly through the sinus nerves, changes in blood-supply of the center can produce identical results. No qualitative differences have been disclosed; both influence depth of breathing more regularly and more readily than rate; both are effective only for a brief time after existing conditions of carotid pressure or cerebral flow have been changed, respiration returning toward normal when pressure or flow is maintained at a new level; both are rendered more effective by a preliminary period of sub-normal carotid pressure or cerebral flow. The importance of carotid sinus (and aortic) reflexes in the respiratory responses of the intact animal to changes in blood-pressure can be determined only by quantitative data concerning relative intensities, relative sensitivities, latent periods, effective ranges, etc., of the reflexes on one hand, of alterations in blood-supply of the center on the other. The significance of sinus reflexes to the chemical regulation of breathing is more complicated than was supposed by Heymans;⁵ in all probability factors are involved that have not yet been identified. Evidence now at hand suggests that sinus reflexes affect the respiratory center not directly, but through changes in caliber of the finer blood vessels supplying it. Experiments intended to yield quantitative data are being made.

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A Method of Assay of Extracts Containing the Suprarenal Cortical Hormone.

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This investigation was begun with the object of developing a method for the assay of extracts containing the cortical hormone which could be carried out with smaller amounts of extract than is required when bilateral adrenalectomized cats or dogs are used.

Hartman¹ has used the growth curve of treated suprarenalectomized rats of 100 to 150 gm. in weight as an alternative method of assay.

It was discovered that immature rats of the colony in this laboratory (Wistar strain) which has been inbred by us for a number of

¹ Hartman, F. A., and Thorn, G. W., *Proc. Soc. Exp. Biol. and Med.*, 1930, **28**, 94.