

**The Dilator Effect of Histamine on the Cerebral Vessels in Man.**

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Direct evidence as to whether or not the cerebral vessels in man possess vasomotor play is still lacking.

The following observations on patients indicate that the arterioles, capillaries, and venules of the human brain respond with prompt dilatation to histamine.

Following the intravenous administration of an average dose of 0.07 mg. (0.7 cc. of a solution of 1:10,000) of histamine phosphate the spinal fluid pressure showed a marked rise. The onset of this rise occurred about simultaneously with the circulation time of the injected histamine. During and slightly after the rise of the spinal fluid pressure the excursions of the oscillatory pulsation of the spinal fluid were greatly increased, although there was no demonstrable rise in the simultaneously registered arterial or venous blood pressure. Coincident with these objective changes there was a sensation of throbbing and pressure in the head.

A small amount of histamine phosphate administered intravenously, when the hemisphere was exposed for the purpose of removal of tumor, caused a prompt bulging of the brain, a distinctly increased cerebral pulsation, and a visible bright flush of the brain surface. These changes, just as other bodily responses following the single intravenous dose, lasted but 0.5 to 3 minutes. Forbes, Wolf and Cobb have observed a similar behaviour of the small pial vessels of the cat.

Adult subjects tolerated well the continuous intravenous administration of 0.05 to 0.1 mg. of histamine phosphate per minute of a solution of 1:10,000. The oxygen and carbon dioxide content of the arterial blood flowing to, and the venous blood returning from the brain was measured. It was observed that while the arterial blood during the administration of histamine showed an average increase of 8% in the oxygen content, because of increased concentration of the blood; the oxygen content of the blood obtained from the internal jugular vein showed an average rise of 20% over the value found before the injection of histamine. During identical experimental conditions the average increase in the oxygen content of the blood obtained from the external jugular vein was 12%, and that from the

basilic vein 24%. The average decrease of the carbon dioxide content of the blood obtained from the internal jugular vein was 9%.

Among the 9 subjects whose blood from the internal jugular vein was studied, 2 failed to show a rise in the oxygen content during the administration of histamine. As rise in the spinal fluid pressure occurs with regularity following histamine injection, one has to conclude that histamine in these individuals produced only a dilatation of the venules. Further evidence that histamine may induce dilatation of the veins directly is revealed through observations of the small veins of the conjunctiva which respond with a dilatation following continuous administration of histamine. Diffuse dilatation of the sub-papillary venous plexuses of the skin also developed in certain persons during the administration of histamine, without simultaneous arteriolar dilatation.

One part of epinephrin chloride antagonized the effect of 10 parts of histamine phosphate on the minute vessels of the skin. Epinephrin chloride in the same ratio also abolished the changes induced by histamine in the cerebral vessels.

The evidence thus presented indicates that histamine produces marked vasomotor response in the minute vessels of the brain. Comparative quantitative observations demonstrate that the sensitivity of the cerebral vessels to the minimal effect of histamine is marked, and the sensitivity is at least as great as that of the facial vessels, which are the most sensitive of the cutaneous vessels. The sensitivity of the cerebral vessels to histamine and epinephrin suggests that these chemical substances through their local action may play a rôle in the physiologic and pathologic regulation of the cerebral circulation in man. Whether or not, in addition to the local *chemical vasomotor regulation*, direct central nervous vasomotor regulation of the cerebral vessels is active in man, is still an open problem.

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### Thirteen Thousand Generations of Paramecium.

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As a matter of record it seems well to summarize the data and give the present status of the long-continued culture of *Paramecium aurelia* at Yale University.