

that the kidney of most fresh water fish contains renin. Just why the kidney of marine fish, whether glomerular or aglomerular, should be devoid of detectable renin and the kidney of fresh water fish richly supplied with this same substance is a question which cannot be answered at this time. As has been noted, already, there is evidence that the tubular function in the kidneys of these two varieties of fish is probably not identical.

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### Temperature Characteristics for Respiration in the Newt Under Chloretone and Nembutal\* Anesthesia.

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It is well known that various narcotics and anesthetics have a depressing effect upon respiration but this has not been systematically investigated as a function of temperature. Thus, while something is known of the influence of this class of drugs on the absolute respiratory rate, little information is available for changes in the relative respiratory rate.

The newt, *Triturus viridescens*, was used in the present experiments both because it is a poikilothermous animal and therefore useful for temperature analyses and because its respiration has already been investigated by means of a Warburg apparatus suitably modified for this purpose.

The minimum dose required to maintain newts immobile for 24 hours under the conditions of temperature variations was determined experimentally for two suitable drugs. After preliminary anesthesia for 15 minutes in a 1-10 dilution of a saturated aqueous solution of chloretone, animals were transferred to modified Warburg vessels containing 1 cc of a 1-20 dilution of a saturated solution of chloretone. Comparable fluid was introduced into one unit serving as a thermobarometer. Nembutal (sodium pentobarbital) produced the desired effect with an intraperitoneal injection of 0.2 cc of a 0.6% solution.

Thermal adaptation and the procedure for measuring oxygen consumption followed that described by Pomerat and Zarrow.<sup>1</sup>

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\* Supplied through the courtesy of the Abbott Laboratories.

<sup>1</sup> Pomerat, C. M., and Zarrow, M. X., *J. Cell. and Comp. Physiol.*, 1937, **9**, 397.

All data reported were based on animals which remained immobile during the entire period of measurement and which recovered from the anesthetic at its conclusion.

Arrhenius plots of the data for oxygen consumption during chloretone anesthesia yielded a temperature characteristic ( $\mu$ ) of  $17,200 \pm$  (Fig. 1). This is the same value as that found for unanesthetized animals by Pomerat and Zarrow<sup>1</sup> and for newts studied in relation to their endocrine system by Pomerat.<sup>2</sup> A similar treatment of the values obtained for 10 different animals under nembutal anesthesia is represented in Fig. 2. A distinct shift in the  $\mu$  is seen to have occurred. A value of  $22,080 \pm$  was found for temperatures from  $6.5^\circ\text{C}$  to  $16.5^\circ\text{C}$  and of  $10,100 \pm$  for the temperature range of  $17.0^\circ\text{C}$  to  $21.0^\circ\text{C}$ . A critical temperature (break) was found at approximately  $16.5^\circ\text{C}$ . It is noteworthy that the three values for  $\mu$  which have been found for the newt are commonly associated with processes in which oxygen is utilized.

Shifts in temperature characteristics such as that resulting from nembutal anesthesia are relatively rare in the literature.<sup>3</sup> They may be looked upon simply as a modification of a fundamental constant, but from a more speculative standpoint<sup>3, 4, 5</sup> they are believed to represent a change of "pace-setter" in a catenary

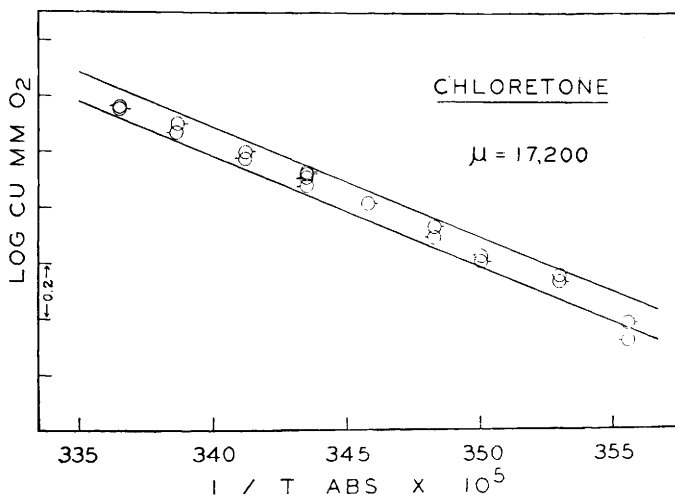


FIG. 1.

Arrhenius equation plot for the rate of oxygen consumption in the newt, *Triturus viridescens*, under chloretone anesthesia.

<sup>2</sup> Pomerat, C. M., *Endocr.*, 1939, **25**, 385.

<sup>3</sup> Crozier, W. J., *J. Gen. Physiol.*, 1935, **18**, 801.

<sup>4</sup> Crozier, W. J., and Hoagland, H., *Handbk. of Gen. Exp. Psych.*, 1934, Chap. 1.

<sup>5</sup> Hoagland, H., *Cold Spring Harbor Symp. on Quant. Biol.*, 1936, **4**, 267.

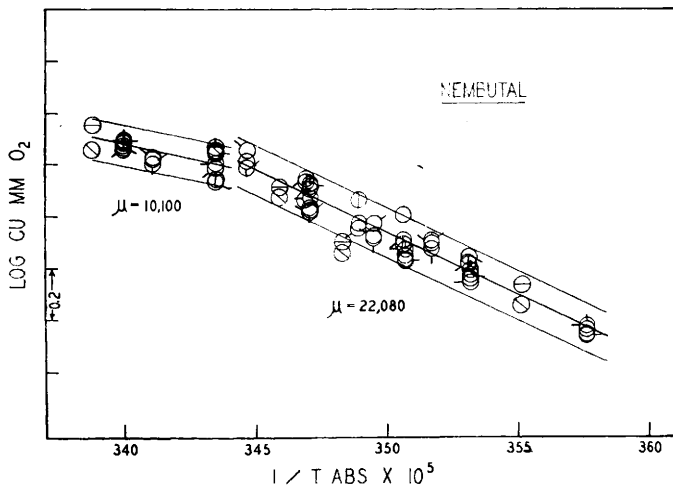


FIG. 2.

Temperature characteristics for the rate of oxygen consumption in the newt, *Triturus viridescens*, under the influence of nembutal anesthesia.

series. Among the recent studies supporting this interpretation are Hadidian and Hoagland's<sup>6, 7</sup> findings concerning a respiratory enzyme system extracted from beef heart. Following poisoning with a critical amount of NaCN the value of  $\mu$  shifted abruptly from  $11,200 \pm 200$  to exactly 16,000 calories. This is believed to represent a change from a "pace-setter" mechanism involving a dehydrogenase to one characterized by an oxidase.

Promising among the various theories of narcosis is the view that the phenomenon is due to interference with oxidative mechanisms. According to Holmes<sup>8</sup> oxidation is inhibited in tissues which are anesthetized by urethane and the higher alcohols and cytochrome remains in the oxidized form following the action of these agents as well as after treatment with chloroform and ether. Anesthetics and cyanide are believed to inhibit at different points. That these effects involve brain tissue has been supported by the work of Jowett and Quastel<sup>9</sup> who found narcotic inhibition of glucose oxidation in the presence of brain slices *in vitro*. Jowett<sup>10</sup> concludes upon further study of anesthetics acting upon brain slices that the mechanisms of these depressants lies in their capacity to inhibit cell oxidation.

<sup>6</sup> Hadidian, Z., and Hoagland, H., *J. Gen. Physiol.*, 1940, **23**, 81.

<sup>7</sup> Hadidian, Z., and Hoagland, H., *J. Gen. Physiol.*, 1941, **24**, 339.

<sup>8</sup> Holmes, E., *The Metabolism of Living Tissues*, 1937, Cambridge University Press.

<sup>9</sup> Jowett, M., and Quastel, J. H., *Bio. Chem. J.*, 1937, **31**, 565.

<sup>10</sup> Jowett, M., *J. Physiol.*, 1938, **92**, 322.

Depressants of the barbiturate series are known to suppress respiration and transform mammals into poikilothermous animals.<sup>11, 12</sup> In contrast to chloretone it would seem that nembutal, a barbiturate, may bring about narcosis by shifting some enzymatic reaction whose presence can be detected by the measurement of the oxygen consumption as a function of temperature.

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#### Study of the Papilloma Virus Protein with the Electron Microscope.\*

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Information relative to the physical character of the papilloma virus protein<sup>1</sup> has been obtained by means of ultracentrifugation,<sup>2</sup> electrophoresis,<sup>3, 4</sup> diffusion and viscosity.<sup>2</sup> Recently, more direct studies of this animal virus have been undertaken with the electron microscope. In the present paper are described the preliminary observations dealing chiefly with data gathered with this instrument relative to the appearance and size of the virus.

Papilloma virus protein isolated in 0.05 M phosphate buffer pH 6.5 by previously described ultracentrifugal procedures<sup>1</sup> was diluted with water to concentrations of the order of 0.05 to 0.5 mg per cc. The salt concentration in the final solutions was approximately 0.005 M. Preparations for study were made by pipetting the solutions onto collodion membranes supported on 200-mesh wire gauze. Free fluid was removed with the pipette, and the resulting

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<sup>11</sup> Herrmann, J., *J. Pharm. and Exp. Therapeutics*, 1940, **72**, 130.

<sup>12</sup> Hemingway, A., *Am. J. Physiol.*, 1940, **134**, 350.

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<sup>1</sup> Beard, J. W., Bryan, W. R., and Wyckoff, R. W. G., *J. Infect. Dis.*, 1939, **65**, 43.

<sup>2</sup> Neurath, H., Cooper, G. R., Sharp, D. G., Taylor, A. R., Beard, D., and Beard, J. W., *J. Biol. Chem.*, 1941, **140**, 293.

<sup>3</sup> Sharp, D. G., Taylor, A. R., Beard, D., and Beard, J. W., *J. Biol. Chem.*, 1942, **142**, 193.

<sup>4</sup> Sharp, D. G., Hebb, M. H., Taylor, A. R., and Beard, J. W., *J. Biol. Chem.*, 1942, **142**, 217.