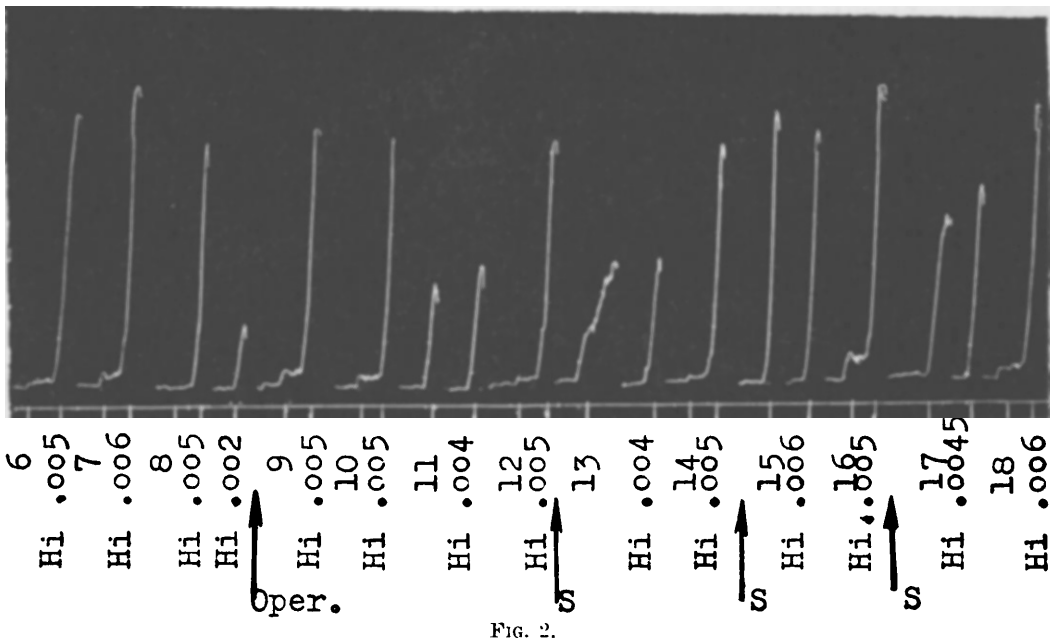

FIG. 2.

Effect on the ileum of standard histamine solutions (Hi., in γ) and of skin dialysates (samples 6-18). Samples 7 and 8, 9 and 10, etc., are duplicates. Odd numbered samples were heated in acid; even numbered samples, untreated. Oper, application of electrodes; S, stimulation.

occurred. However, a slight increase in the histamine equivalent of the skin samples occurs following application of the electrodes to the splanchnic nerve, without there having been an electrical stimulation. This may be due to irritation or mechanical stimulation of the nerve by the application of the electrodes.

Summary. A method for the study of skin histamine has been described. The histamine equivalent of skin extracts obtained by this method has been shown to increase following injection of histamine into the skin and following burning or chemically irritating the skin. That the substance studied is closely related to histamine has been shown by several tests. Using the method described, experiments have given suggestive evidence that histamine may be liberated in the abdominal skin upon the application of electrodes to and stimulation of the splanchnic nerve.

14132

The Neurenteric Canal in the Frog, *Rana Pipiens.*

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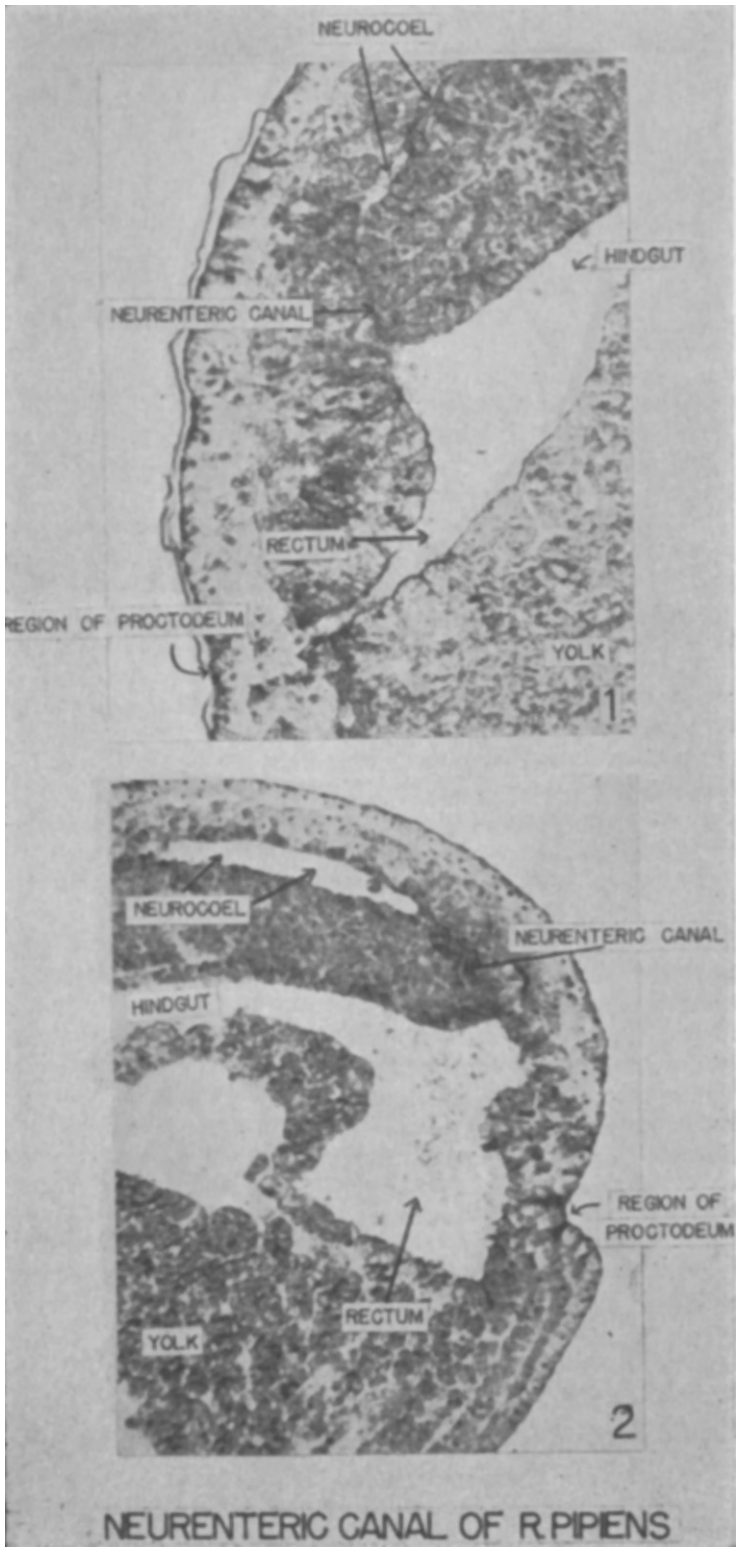
Even the temporary appearance of a tubular connection in the embryo between the neurocoel and the hindgut, known as the neurenteric canal, has considerable phylogenetic significance if its presence can be demonstrated and the parts homologized in such a variety of forms as Amphioxus, Fish, Amphibia, Reptiles, Mammals and possibly even in birds (duck, goose, Sterna., Lillie[1]). It is the purpose of this paper to add another link in the chain of evidence of the embryological existence of such a canal, using the Anuran, *Rana pipiens.*

[1] Lillie, F. R., *The Development of the Chick,* Henry Holt Co., 1919.


NEUROCOEL
HINDGUT
NEURENTERIC CANAL
RECTUM
REGION OF PROCTODEUM
YOLK
1
NEUROCOEL
NEURENTERIC CANAL
HINDGUT
REGION OF PROCTODEUM
RECTUM
YOLK
2
NEURENTERIC CANAL OF R.PIPIENS

The neurenteric canal has been variously described as a tubular connection between the neurocoel and hindgut; the post-anal gut (Shumway[2] and Huettner[3]); the dorsal cavity of the closing blastopore; the short bent posterior portion of the neurocoel plus the remains of the blastopore; the notochordal canal; the anterior end of the primitive streak; and also the connection between the amniotic and yolk sacs of the mammal. Huxley and DeBeer,[4] for instance, are very cautious in stating that the blastopore becomes an enclosed tube with the approximation of the parallel neural ridges at that region so that "in this manner, a neurenteric canal, actual or virtual, according as to whether the blastopore is or is not still open, is formed, connecting the cavities of the neural tube and the gut."

Over 100 frog embryos (*Rana pipiens*) of stages 15 to 17 (Shumway[5] and Rugh[6]) were serially sectioned sagittally at 10 μ and examined for the possible existence of this canal. In practically every embryo the canal was either present as such (Fig. 1) or its lining of pigmented cells could be easily discerned (Fig. 2). Those embryos which had recently closed blastopores showed the most perfect neurenteric canals. In slightly older embryos (*i.e.*, stage 18) the neurenteric canal was occluded, but its earlier position could be determined by the column of pigmented cells, even though the neurocoel and hindgut were permanently separated.

An examination of the arrangement of cells in Fig. 1 will indicate the continuity of the neurocoel and the posterior archenteron and will also emphasize the differences, particularly in size, of the overlying posterior integumentary cells originally derived from the blastoporal lips.

There is no dispute as to the existence of this canal in Amphioxus where it persists through late larval life (Arey,[7] Conklin,[8] McEwen[9]). In Teleost Fish, Kupffer's vesicle is supposed to represent in part a rudiment of the neurenteric canal (McEwen[9]) even though a canal as such never develops. In Amphibia the available data refer only to the Anura and even here it is not consistent. Huettner[3] says, "This" (neurenteric) "canal does not exist in the embryo of the wood frog, at least not as a spacious passage between the neurocoel and the primitive gut. However, there are certain structures developed by the closure of the blastopore which may be considered as homologous to the neurenteric canal of Amphioxus." In the chick, McEwen[9] says, "Thus there is formed a typical neurenteric canal in just the region where such a canal would be expected to appear, were the primitive groove a blastopore," while Jordan and Kindred[10] state, "The neurenteric canal is derived by a perforation of the floor of the primitive pit." Lillie[1] says, "In the chick the neurenteric canal is never typically developed. Usually it is represented only by the primitive pit. In exceptional cases I have found traces of it in the head process." In the Mammal, McEwen[9] says, "It is perhaps doubtful whether the perforation, when present, even persists until the fusion of the neural folds in this region is actually complete. During its existence, however, the opening in question is so closely homologous with the neurenteric canal of the frog that it is frequently so named," and Jordan and Kindred state that "The primitive node" (of the mammalian embryo) "is pierced by a patent neurenteric canal, the homologue of the primitive pit."

It must be emphasized that this neurenteric canal as a tube is small; that it exists for a maximum of about 17 hours at 18°C; and that it can be seen only in stages No. 15 to

[2] Shumway, W., *Introduction to Vertebrate Embryology*, John Wiley & Co., 1941.

[3] Huettner, A. F., *Comparative Embryology of the Vertebrates*, 1941.

[4] Huxley, J., and DeBeer, G. R., *The Elements of Experimental Embryology*, Macmillan & Co., 1934.

[5] Shumway, W., *Anat. Rec.*, 1940, **78**, 139.

[6] Rugh, R., *Experimental Embryology, a Manual of Techniques and Procedures*, N. Y. University Bookstore, 1941.

[7] Arey, L. B., *Developmental Anatomy*, W. B. Saunders Co., 1940.

[8] Conklin, E. G., *J. Morph.*, 1932, **54**, 69.

[9] McEwen, R. S., *A Textbook of Vertebrate Embryology*, Henry Holt Co., 1931.

[10] Jordan, H. E., and Kindred, J. E., *A Textbook of Embryology*, D. Appleton-Century Co., 1937.

No. 17 of early embryonic development. Its transient nature may be the reason for the denial, or questioning, of its existence in the various references mentioned. Nevertheless, it is the contention of this paper, based upon the study of many sectioned embryos during this particular period of development that

a. A neurenteric canal actually does exist in fact as a tubular connection between the neurocoel and the hindgut of the embryo of *Rana pipiens.*

b. The cells of the floor of the neurocoel, of the floor of the neurenteric canal, and of the roof of the archenteron are of the same type and are, in all probability, continuous in early development.

c. The post-anal gut and the neurenteric canal are not synonymous but may be continuous.

d. The neurenteric canal is very small, tubular, and transient. It is formed by the depression of the posterior medullary plate along with the dorsal lip of the blastopore, concurrently with coalescence of the posterior neural folds and the lateral lips of the same blastopore which together form the sides of the temporary neurenteric canal.

14133

Effect of Quinones on Acid Formation in Saliva.

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Fosdick, Fancher and Calandra[1] noted that a saliva-glucose mixture containing 1 mg per 100 cc of synthetic vitamin K (2-methyl-1,4-naphthoquinone) "forms no acid in a 4-hour incubation period, while the same mixture will produce up to 2 m.eq. of acid under the same conditions in the absence of the vitamin K." These authors emphasized that the effect on bacterial metabolism observed by them to be a property of synthetic vitamin K and discussed the possible uses of this compound in the prevention of dental caries.

The possibility suggested itself to us that the bacterial inhibitory action of synthetic vitamin K in saliva might be due to the fact that this compound is a quinone and that its antibacterial property has no actual relation to its vitamin K activity. It was already known[2] that benzoquinone possesses a substantial bacteriostatic ability. Recently reports[3,4] have appeared of a remarkable bacteriostatic effect exerted *in vitro* by certain dimethoxy quinones related structurally to fumigatin. Fumigatin (3-hydroxy,4-methoxy,2:5-toluquinone), produced by *Aspergillus fumigatus,* in itself possesses a definite ability to inhibit the multiplication of several gram-positive organisms.[5]

All points in Fig. 1 referring to a particular quinone were determined with solutions incubated concurrently using the same lot of pooled saliva to which 10% of its weight of glucose had been added (recommendation of Fosdick *et al.*[1]) Other experiments demonstrated that essentially the same results were obtained when only 2% of glucose was added to the saliva. Those quinones which were not sufficiently soluble in water were made up in alcohol, or chloroform in the case of 2,6-dimethoxy-benzoquinone, so that equal volumes contained equal molecular amounts of the several substances. The required volumes (0.05 to 1.0 cc) of these solutions were added to dry 25 cc volumetric flasks and the solvent evaporated under reduced pressure so that a

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1 Fosdick, L. S., Fancher, O. E., and Calandra, J. C., *Science,* 1942, **96**, 45.

2 Graham-Smith, G. S., *J. Hyg.,* 1919, **18**, 1.

3 Oxford, A. E., *Chemistry and Industry,* 1942, **61**, 189.

4 Oxford, A. E., *J. Chem. Soc.,* 1942, p. 577.

5 Oxford, A. E., and Raistrick, H., *Chemistry and Industry,* 1942, **61**, 128.