bile in the duodenum is indicated by the time of response, 3.5 hr after introduction of bile into the duodenum, and by observations on 3 control dogs not given chloroacetylcholine. In these dogs, as in several others given glycine or other inactive agents, a latent response was not observed.

The volume of bile secreted during each 12-min period is also noted on the graph. At the time of maximum response, the flow of bile following injection of chloroacetylcholine was 350% of the control level, and after decholin it was 417% of the corresponding control level. Since the control level of secretion before decholin was given was higher than the initial control level, decholin must be considered to be relatively more potent than these values indicate.

Major differences were observed in the color and specific gravity of bile secreted under the influence of the 2 agents. After injection of chloroacetylcholine, the specific gravity increased considerably and attained a peak at the time of maximum flow, while the color was unchanged, indicating a true choleretic effect. After decholin, the usual hydrocholeresis was noted; the bile became pale and the specific gravity fell below the control level of 1.012.

The similarity of the delayed choleretic response to chloroacetate and chloroacetylcholine indicates that the latter rapidly liberates chloroacetate in the body, which then reacts slowly to evoke choleresis. This view is in accord with the hypothesis that a free carboxyl group is essential for the choleretic action of halogenated hydrocarbon derivatives,[1] and the evanescence of other pharmacologic effects of chloroacetylcholine also indicates rapid hydrolysis in the body.[3] Chloroacetylcholine appears to cause a stronger choleretic response than equivalent amounts of chloroacetate, but this may be due to a greater hepatotropism of the ester as compared to the free acid, which is probably distributed as uniformly throughout the tissues as is tribromoacetate.[4] The cholinergic properties of the ester are unrelated to its choleretic action, because of the difference in time of the 2 types of response and also because of the general lack of choleretic effect of other cholinergic agents.[5]

Summary. Chloroacetylcholine chloride provokes a large but delayed increase in the formation of bile in the dog, similar to the choleresis following administration of chloroacetate. The comparative choleretic effects of the 2 agents are discussed in regard to the mechanism of chloroacetate choleresis.

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14041 P

Phosphocreatine as Energy Source of the Action Potential.

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The parallelism between the concentration of choline esterase and the E.M.F. of the action potential in electric organs and the localization of the enzyme at the neuronal surface suggest that formation of acetylcholine is intrinsically connected with the nerve action potential and may be responsible for the electrical changes during nerve activity.[1-3]

* Aided by grants of the Dazian and Josiah Macy, Jr., Foundations.

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TABLE I.

	Exp. I	Exp. II
Length of specimen	185 cm	179 cm
Girth of the section used	36.6 cm	36 cm
Volume of electric tissue used	400 ccm	380 ccm
Number of discharges	1600	1600
External electrical energy	9.2 g cals	5.9 g cals
Initial phosphocreatine P_2O_5	1.07 mg/g	0.98 mg/g
Final phosphocreatine P_2O_5	0.50 mg/g	0.52 mg/g
Phosphocreatine split in 100 gr	178 mg	142 mg
Phosphocreatine split in section measured	712 mg	540 mg
Energy released by breakdown of phosphocreatine	32.0 g cals	24.5 g cals

The resynthesis of acetylcholine requires energy. Energy-rich phosphate bonds are considered to be the most readily available source of energy for endergonic life processes. In muscle the release of phosphate from adenosine triphosphate (ATP) seems to be the primary source of the contraction energy[4] and possibly directly connected with the mechanical change during the contraction.[5] The adenosinephosphate is rapidly rephosphorylated by the breakdown of phosphocreatine, a substance in which the phosphate bond is also rich in energy, the breakdown of one mole of phosphocreatine yielding about 10,000 g calories. The phosphocreatine thus acts as a storehouse for the energy of phosphate bonds.[6] The presence of phosphocreatine in nerve suggests that there too its phosphate bond is the storehouse for the energy of the action potential, ATP acting as catalyst.

In ordinary nerve, however, it is difficult to compare the energy output of the action potential with the energy released by the breakdown of phosphocreatine and only some general estimates are possible.[7] In the electric organ, on the other hand, the discharge of which is generally recognized as identical with the action potential of nerve, both electrical and chemical changes are within the range of possible measurement. The breakdown of phosphocreatine and the energy of the action potential have been compared in the electric organ of the electric eel, *Electrophorus electricus* (Linnæus).

The discharge of a section 10 cm long containing about 350-400 g of electric tissue has been photographically recorded by means of a cathode-ray oscillograph. The current was passed through an external resistance chosen to give approximately the maximum external energy. The number of dicharges was counted by means of an electric scaling circuit. Immediately before and after the counted series of discharges, a piece of the electric organ was quickly cut out and thrown into liquid nitrogen, and the phosphocreatine was determined.

The results of two experiments are given in Table I as examples.

The rate of respiration in the electric organ is slow, the Q_{O_2} being about –0.3 to –0.4 The lactic acid formation is small. Since the duration of the experiments is generally only 3-5 min it seems probable that during this period there is no marked resynthesis and that the amount of phosphocreatine actually split corresponds to the difference measured.

The energy released externally is only part of the total electric energy produced. To estimate this total energy it would be necessary to know what electrical characteristics of the tissue vary in bringing about the discharge. If the organ is supposed to have a constant E.M.F. and a variable resistance, the total energies in the two observations would be 18 and 14 g cals respectively. Assuming constant resistance and variable E.M.F., the values would be 16 and 10 g cals. Whatever assumption is made the experiments give evidence that the breakdown of phosphocreatine is adequate to account for the energy produced by the action potential.

[4] Meyerhof, O., *Biological Symposia*, 1941, **3**, 239.

[5] Engelhardt, W. A., *Yale J. Biol. and Med.*, 1942, **15**, 21.

[6] Lipmann, F., *Adv. Enzymology*, 1941, **1**, 99.

[7] Gerard, R. W., and Tupikova, N., *J. Cell. Comp. Physiol.*, 1938, **12**, 325.

It is not known how much acetylcholine is actually released during the discharge. But the amount which can be split during the time of a discharge may give an indication of the possible amount which can be involved in the process if we assume that acetylcholine is released during that period at a rate similar to that at which it can be split. The duration of one discharge is about 3 millisec. The duration of 1600 discharges would be about 5 sec. 400 g of electric organ can split about 500 g acetylcholine chloride in 60 min or about 700 mg in 5 sec which is about 4 millimoles. This would be the maximum amount which can be split, but it is not probable that the whole amount is actually released. The amount of phosphocreatine split during these discharges corresponds to 3 millimoles. It appears thus possible that the amounts of acetylcholine and phosphocreatine metabolized are of the same order of magnitude and that even a stochiometric relation exists. The explanation would be that for each molecule of choline acetylated there occurs an endothermic phosphorylation of one molecule, possibly of acetate forming acetylphosphate, the intermediate described by F. Lipmann.[8] Phosphocreatine would yield this phosphate using ATP as catalyst. The energy required for the resynthesis of the phosphocreatine would be derived from the oxidative breakdown of pyruvic acid, ATP acting again as catalyst.

[8] Lipmann, F., *Symposium on Respir. Enzymes*, 1942, p. 195.

14042 P

Comparative Effects of Gastroenterostomy and Pedicle Jejunal Graft on the pH of the Gastric Mucosa.*

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Recently, the authors,[1] in a study of the effects of jejunal transplants on gastric acidity, reported a reversal of the normal response to histamine as reflected in direct measurements of the pH of the mucosal surface of seven different regions of the stomach. The present report deals with the comparative effects of gastro-enterostomy and a jejunal transplant

TABLE I.

pH of Gastric Mucosa Before and After Gastroenterostomy and Following Conversion of the Jejunum About the Anastomosis to a Pedicle Graft.
Each figure represents the Average of 7 different regions of the stomach.

	Before gastroenterostomy			After gastroenterostomy			After conversion to pedicle graft		
Dog	Fasting	10 min after Histamine	20 min after Histamine	Fasting	10 min after Histamine	20 min after Histamine	Fasting	10 min after Histamine	20 min after Histamine
1849	6.4	4.7	2.0	6.9	6.1	5.9	7.1	7.4	7.6
1854	4.7	4.0	2.3	5.9	4.0	2.9	5.6	7.0	7.1
1909	6.3	2.0	0.9	5.2	5.3	3.5	3.6	5.3	5.4
1917	5.5	4.7	2.1	4.1	5.4	4.9	6.2	6.7	7.0
1934	4.6	4.1	2.4	5.9	2.6	1.9	3.5	4.4	5.3
1967	3.0	2.6	1.7	6.2	4.5	1.8	2.5	3.5	3.9
Average	5.1	4.0	1.9	5.7	4.6	3.5	4.8	5.9	6.1

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[1] Stefko, Paul, Andrus, Wm. DeW., and Lord, J. W., Jr., *Science*, 1942, **96**, 208.