decreases, but not in a relatively uniform manner. The ratio, $\frac{\text{action potential}}{\text{resting potential}}$, typically increases during the experiment.

Discussion. The parallel variations in magnitude of the resting and action potentials of the frog eye are in agreement with the observations of Brossa and Kohlrausch. These investigators measured resting and action potentials with the same electrodes and with the same recording device, a string galvanometer.

Under these conditions changes in contact resistance might conceivably affect both resting and action potential in the same manner. In the experiments reported here the same electrodes were used but with two types of recording instruments: a null-point type K potentiometer and a condenser-coupled high-gain amplifier. Changes in contact resistance would affect the amplified reading much more than the potentiometer reading. Therefore, the parallel variations in resting and action potential must be attributed to the photoreceptor.

The data obtained from excised intact eyeballs are rather uniform for flash intensities of 2.8 f.c. or lower. For higher flash intensities the magnitude of the action potential drops off more rapidly than does the resting potential, indicating inadequate recovery of sensitivity between test flashes. The data from the excised enucleated eyeballs indicate consistently action potentials whose magnitudes decrease much more slowly than do the resting potentials. This difference between intact and enucleated excised eyes may possibly be due to differences in retinal area illuminated.

In conclusion, the action potential obtained from intact and enucleated excised frog eyes in response to constant intensity, constant duration light flashes varies as the resting or demarcation potential. The electrical response of the excised eye to light is determined by the state of dark-adaptation and by the magnitude of the resting potential.

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Fat and Nitrogen Absorption after Folic Acid Administration in Dogs Deprived of External Pancreatic Secretion.

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Interest in folic acid was aroused in this laboratory because of the similarity of the steatorrhea in sprue and in obstruction of the pancreatic ducts. Spies[1-5] and co-workers have contributed most notably to the advancing knowledge of folic acid. We wished to determine whether or not absorption of fat and nitrogen was influenced in pancreatic steatorrhea by the use of folic acid. In earlier work Spies *et al.*[5] mentioned that changes in the size and consistency of the stools in tropical sprue occur after treatment with folic acid, in that the stools became less bulky and more solid.

Darby and others[6] in a report of sprue cases from the Vanderbilt University Hospital state that stool examinations in 2 cases 2 months after treatment was begun still showed an increased fat content though diarrhea had

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1 Spies, T. D., *Lancet*, 1946, **1**, 225.

2 Spies, T. D., *J.A.M.A.*, 1946, **130**, 474.

3 Spies, T. D., Lopez, G. G., Menendez, J. A., Minnich, V., and Koch, M. B., *South. M. J.*, 1946, **39**, 30.

4 Spies, T. D., Vilter, C. F., Koch, M. B., and Caldwall, M. H., *South. M. J.*, 1945, **38**, 707.

5 Spies, T. D., Milanea, F., Menendez, A., Koch, M. B., and Minnich, V., *J. Lab. and Clin. Med.*, 1946, **31**, 227.

6 Darby, W. J., Jones, H. C., *J.A.M.A.*, 1946, **130**, 780.

ceased. Their patients had received daily 15 mg of folic acid given intramuscularly. Fat determinations in their cases showed that prior to treatment in one case 37% of the dry weight of one stool specimen and 44% of a second dried stool were composed of fat. After treatment the fat fell to 29% of the weight of the dried stool. In another of their cases fat comprised 40% of the dry weight of a stool before treatment and a third case 23%. Stool analyses after treatment in these last 2 cases were not given. Fecal nitrogen was also determined in their 3 cases prior to treatment. The daily amount was 3.91 and 4.89 g in Case 1; 2.9 g in Case 2; and 4.11 g in Case 3. No figures were given for similar studies after treatment.

A report by Davidson *et al.*[7] indicates that folic acid did not improve fat-absorption, as estimated by fat balance tests, in 5 out of 6 cases of the sprue syndrome.

Some writers report a smaller percentage of fat in the stools after various forms of treatment in cases of sprue and pancreatic disease. The percentage of fat alone may give a false impression of the true state of affairs. It may fall simply because the patient is eating less fat. The only way to judge accurately increased absorption of fat resulting from treatment is to have the patient on a standard diet before, during, and after the prescribed treatment. It has been the practice of many investigators to express the fat content of the stools simply as percentage of dried matter. More important is the daily quantity of fat excreted in the stools. To determine the amount of fat absorbed it is necessary in addition to know the exact amount of fat in the diet; hence the importance of a standard diet in which the amount of fat and nitrogen has been determined.

Methods. Absorption experiments were carried out on 5 dogs deprived of external pancreatic secretion. Avoidance of complete pancreatectomy made it unnecessary for us to give our dogs insulin as they did not develop diabetes. The pancreatic juice was

[7] Davidson, L. S. P., Girdwood, R. H., and Innes, E. M., *Lancet*, 1947, **1**, 511.

TABLE I.

Folic Acid Added to Standard Diet of Five Dogs Deprived of Pancreatic Secretion.

Dog	I	I	I	I	I	I	II	III	IV	V
Date 1947	Mar. 24-27	Mar. 31-Apr. 2	Apr. 18-21	Apr. 25-28	May 2-5	May 9-12	June 19-22	June 19-22	June 19-22	June 19-22
Folic acid daily—mg	0	20	50	50	100	200	50	50	50	50
Wet wt feces—g	317	300	150	272	288	377	119	352	224	234
Dry " "	87	—	39	87	86	104	38	110	79	71
Percent solids	27.4	—	26.1	31.9	29.8	27.5	32.4	31.2	36.9	30.4
Nitrogen fed—g	14.6	12.9	9.2	14.6	14.6	14.6	10.7	12.9	12.9	12.3
" exer.—g	5.7	7.8	2.4	4.9	6.3	7.0	2.7	5.6	5.5	5.1
% N absorbed	60.6	72.7	75.2	66.5	56.5	52.2	74.8	56.7	57.1	61.8
Fat fed—g	26.8	25.1	21.6	26.8	26.8	26.8	18.9	23.5	20.7	20.2
" exer.—g	12.9	15.8	7.0	15.6	12.2	14.5	7.9	18.2	11.5	12.5
% fat absorbed	52.0	36.9	67.8	41.9	54.5	46.0	58.4	22.8	44.5	38.3

Notes: Weight of feces and food indicate the average daily weight. All experiments were carried out over three-day periods.

excluded from the intestine by ligating all the pancreatic ducts and interposing the omentum between the pancreas and duodenum. The pancreas of the dog frequently has more than 2 ducts so that care must be exercised in carrying out the procedure. A balanced diet containing known quantities of the various food components was fed and additions of 20, 50, 100, and 200 mg of folic acid were made to the diet.

In these experiments the dogs were fed diets composed of ground horse meat, evaporated milk and a commercial dog food, in some instances Gaines Meal, manufactured by General Foods Corporation and in other instances Kibble Dog Food, manufactured by the Wilson Company. Figures in Table I indicate that varying quantities of fat were fed in different experiments. Actually these figures represent the amount of food which the dogs ate. They were offered a diet on which normal animals in our laboratory gained weight and which was adequate in all components.

To mark the stools carmine was given at the beginning and charcoal at the end of 3-day feeding experiments. All the stools were collected and analyzed quantitatively for total solids, fat, and nitrogen. Fractional determinations were made for neutral fat, fatty acids, and soaps. The animals were later examined at autopsy in order to obtain evidence of definite occlusion of the pancreatic ducts and the presence or absence of aberrant pancreatic tissue.

Results. These are shown in Table I. Five experiments were performed on dog I giving 20 to 200 mg of folic acid daily. Two hundred mg of folic acid are far in excess of the usual amounts required in the treatment of sprue. In the control experiment when no folic acid was given, 52% of the fat fed was absorbed. After folic acid was added to the diet, the average percentage of fat absorbed was 50. There was not only no correlation between the fat absorption and the quantity of folic acid administered, but no increase in absorption even when a very large amount of folic acid was given.

Studies were made on 4 additional dogs deprived of pancreatic digestion. They were given 50 mg of folic acid daily, an amount well above the usual therapeutic dose of folic acid used in gastrointestinal diseases. The percentage of fat fed that was absorbed ranged from 22.8 to 58.4; the average being 41%. The evidence is conclusive that folic acid did not prevent great loss of fat in the stools.

At autopsy of the dogs no evidence was found of any connection between the atrophic pancreatic remains and the duodenum, and there was no aberrant pancreas.

The stools were larger than those of normal animals, yet the percentage of solids varied from 26.1% to 36.9%, which is within the normal range. Nitrogen absorption during the period of folic acid administration varied from 52.2% to 75.2%.

Determinations of the components of the total fecal fat, while folic acid was given, resulted in figures for neutral fat, fatty acids, and soaps which are no different from the results obtained in stool examinations previously made in other studies in our laboratory on animals deprived of the external secretion of the pancreas.

From the results obtained there is no evidence that folic acid given to animals with steatorrhea due to absence of pancreatic digestion will further the absorption of fat or nitrogen.

As normal stools contain a certain quantity of fat, even in starvation, sufficient quantities of fat must be given to produce an amount definitely in excess of the normal figure of intestinal "fat secretion." Normally, fecal fat is considered to be largely endogenous. Previous work with animals in our laboratory indicates that this secretory figure lies somewhere between 0.5 and 2.0 g daily. The figures of fat lost in the feces as given in the table are greatly in excess of this amount. In earlier experiments on one of the animals we observed marked variations in absorption of food components. It first appeared that improved absorption was due to the folic acid, but later found to be only the usual variation in absorption which occurs in animals deprived of pancreatic digestion.

TABLE II.
Chart Showing the Difference Between Percentage of Fat in Stools and Percentage of Fat Excreted.

Dog Date	VI 12/20/46	VI 1/8/47	I 12/20/46	I 1/8/47	VII 12/23/46	VII 1/8/47
Wt dry stool (g)	107	65.9	113	110	55	28
Total (g) fat excreted	18.3	19.9	14.9	21.6	4.6	3.5
% dry weight	17.1	30.2	13.2	19.7	8.4	12.6
Fat fed (g)	38.1	38.1	38.1	38.1	38.1	38.1
% fat excreted	48.1	52.3	39.2	56.8	12.2	9.2
	Dogs deprived of external pancreatic secretion				Normal dog	

Weights indicate average daily weight. All experiments were carried out over 3-day periods.

The percentage of fat in the dried stool in normal dogs on a standard diet varies widely. In healthy human beings on the Schmidt diet, the average in our clinic has been 25%. In steatorrhea of pancreatic origin the percentage of fat in the dried stool is frequently less than the maximum occurring in health; hence no definite conclusion regarding the absorption of fat can be drawn from the percentage of fat in the stool unless it is greatly elevated. In Table II are given the results of absorption studies on 2 dogs deprived of pancreatic secretion, and for comparison those on a normal dog. All were fed the same amount of fat daily, namely 38 g, and all had a percentage of fat in the dried stools that was within normal limits, yet the dogs without pancreatic digestion lost in their feces from 39.2% to 56.8% of the fat fed. It is evident from this that the amount of fat in the stools is all important. In obstruction of the pancreatic ducts the weight of the dried stools is definitely increased as is shown in Table II.

Summary. Data on the absorption of fat and nitrogen following folic acid therapy in dogs deprived of external pancreatic secretion have been presented. Folic acid was shown to be of no value as far as absorption of these substances was concerned.

The importance of employing a standard diet of known composition and of determining the amount of fat lost in the stools and not relying on the percentage of fat present in the dried stool is emphasized.

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Blocking and Protecting Actions of Amines and Ammonium Compounds on a Crustacean Synapse.

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The central nervous system of the crayfish provides a highly satisfactory preparation for the study of synaptic transmission. It contains 4 giant fibers, up to 250μ in diameter, which extend the entire length of the ventral nerve cord. These fibers synapse with motor fibers in each of the abdominal ganglia. A single impulse in a giant fiber normally causes a single response in the motor fibers (Wiersma[1]).

Nicotine is a particularly active drug on this synapse, causing an initial facilitation followed by block. However, approximately 40 minutes after block by nicotine, transmis-

[1] Wiersma, C. A. G., *J. Neurophysiol.*, 1947, **10**, 23.