small part of the total vitamin B_1 is present in these plants in the form of its pyrophosphoric ester. It should be noted, however, that there is no direct proportionality between CO_2 formation and the amount of co-carboxylase added, especially when too large amounts of the co-enzyme are to be estimated. For this reason in the case of dry yeast only 0.3 cc. of boiled yeast juice equivalent to 50 mg. of dry yeast was employed for the test. The results show that phosphorylation of vitamin B_1 by the mammalian organism is of vital importance as this co-enzyme plays an important rôle in the decarboxylation and dehydrogenation of pyruvic acid.[8] Furthermore animal tissues contain all of the vitamin B_1 as the pyrophosphoric ester.[8]

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Alleged Convulsant Properties of Brain Extracts.*

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Kroll[1] made the claim that convulsions could be produced in normal animals by the intravenous injection of extracts of brains removed from convulsing animals. Brain extracts from normal animals were said to be without convulsant properties. Both cats and rabbits were used but the former were regarded as more satisfactory. The minced brains were extracted 3 times with acetone and the remaining residue suspended in saline, extracted and filtered. This saline extract was employed in the experiments, the acetone extract being discarded.

Holmes[2] repeated these experiments on rabbits but used the acetone fraction of the extract. The acetone was evaporated and the remaining residue suspended in saline for administration. Such extracts were found to have marked constitutional effects when injected into animals. Death frequently occurred either with or without preceding convulsions. Extracts of normal brain as well as those from the brains of convulsing animals sometimes produced convulsions and both were equally lethal.

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[8] Lipmann, F., *Enzymologia*, 1937, **4**, 65.

* We thank Miss Doris Brophy for her assistance with these experiments.

[1] Kroll, F. W., *Z. f. d. ges. Neur. u. Psych.*, 1932-33, **143**, 780.

[2] Holmes, E., *J. Physiol.*, 1935, **85**, 400.

Despite the startling nature of Kroll's claim and the obvious pitfalls in the use of such crude extracts the subject merited investigation especially since Holmes used a different extract from that used by Kroll. Furthermore recent knowledge of explosive nervous activity mediated by chemical substances has made it necessary to think in such terms.

We have repeated the experiments using both types of extract. Cats have been used for the most part both as donor and recipient animals. Rabbits were used in a few instances as recipients. Our method of producing convulsions in the donor animals differed somewhat from that of the previous workers. They exposed the cerebral cortex under general anesthesia and stimulated electrically. In our experiments the unanesthetized animal was given a shock of 110 volts from the lighting main, one needle electrode being placed in the periosteum at the base of the skull and the other clipped to the lower lip. Such stimulation for 3 to 5 seconds is followed by a convulsion lasting several minutes, at first tonic and later clonic though the pattern varies. In 2 instances violent convulsions were produced by intravenous injection of thujone (1% by volume) to donor animals.

During progress of the induced convulsions the unconscious animal was bled through the carotids. Control animals were killed by intracardiac injection of air and similarly bled or simply bled under light ether anesthesia. The brain was removed at once, and ground thoroughly with sand in 80 cc. of acetone followed by 5 minutes' stirring with an electrical device. The acetone was then decanted and the remaining solid residue similarly treated with fresh acetone until thrice extracted.

Saline Extract of Residue (Kroll)—The stringy, solid residue remaining after acetone extract had been decanted off was dried by air blast, suspended in 60 cc. normal saline, stirred for 5 minutes and filtered twice through filter paper before use.

Acetone Extract (Holmes)—The three acetone extracts (240 cc.) were pooled and the acetone distilled off under negative pressure at 45°C. The remaining fatty residue was suspended in 60 cc. normal saline and traces of acetone removed by a bubbling air current.

Results. Extracts were made of the brains (wt. 20-25 gm.) of 10 cast, 2 of which were control animals and 8 of which had been convulsed in various ways. Twenty-five injections of brain extract were made intravenously into 19 animals (15 cats, 4 rabbits) in attempts to produce convulsions. The dose employed for rabbits was 1 to 2 cc. and that for cats 3 to 10 cc. Following 6 of these injections

TABLE I.

Donor					Recipient				
Cat. No.	Convulsive Agent	Type of Extract	Age of Extract, Minutes	Dose of Extract, cc.	Animal	Weight, Kg.	General Symptoms	Convulsive Symptoms	Death
1	110 volts 4 secs.	I	90	5	Cat		+++	±	—
		I	52	1	Rabbit		—	—	—
		I	124	2	" (same)		—	—	—
		I	60	2	Rabbit		+++	±	+
2	None. Control light ether	I	100	5	Cat		++	—	—
		I	130	5	"		++	—	—
		I	110	2	Rabbit		+++	—	++
		I	120	1	"		+++	—	++
3	110 volts 7 secs.	I	135	5	Cat		—	—	—
			150	10	" (same)		+++	—	+
4	110 volts 1 sec.	I	89	5	"	2.90	++	—	—
5	110 volts 3 secs.	I	89	5	"	2.05	++	±	—
6	Thujone 2 cc.	I	95	5	"		+	—	—
			107	3	" (same)		+	—	—
7	Thujone 1.8 cc.	I	95	5	"	2.65	±	—	—
8	None. Control air in heart	I	94	10	"	3.00	++	—	—
		II	163	7	"	3.00	—	—	—
		III	199	5	" (same)	3.00	+++	—	—
		III	174	3½	"	2.65	±	—	—
		II	182	10	" (same)	2.65	—	—	—
9	110 volts 4 secs.	I	97	9	"	2.65	+++	±	—
		III	135	3½	"	2.70	++	±	—
		II	213	7	"		++	±	—
10	Faradic 15 mins. 110 v. 3 secs.	I	75	8	"	3.10	+	—	—
		I	82	5	" (same)	3.10	++	—	—

Extract I = Saline of brain residue (Kroll).
II = Acetone residue filtered.
III = Acetone residue unfiltered (Holmes).

there were slight convulsive movements only. In the remaining 19 there were no convulsions whatever. When convulsive movements did occur they consisted of brief tonic spasms lasting 5 to 15 seconds followed by irregular clonic or running movements of equally short duration. Twenty of the 25 injections resulted in marked generalized symptoms consisting of collapse, flaccidity, dilatation of pupils, involuntary micturition and defecation and apparent unconsciousness. At the height of this reaction there was stoppage of respiration and absence of heart sounds followed by rapid, panting respiration and slow, irregular heart sounds. Recovery usually occurred in about 15 minutes. Two rabbits died following injection of normal brain extract and one rabbit and one cat after injection of convulsed brain extract. There were no convulsions in any of these animals prior to death. Death occurred 2 to 3 minutes after injection.

Holmes investigated the effects produced by injection of the acetone fraction into a rabbit and gave excellent tracings of the alterations in heart rate, blood pressure and respirations. Perfusion of isolated hearts with Ringer's solution containing small amounts of extract caused cardiac depression and arrest. He concluded that such extracts have no direct effect on the central nervous system and that they cause symptoms and death through their depressant effect on the heart and circulation. We have repeated this experiment on the anesthetized cat using the saline residue fraction (Kroll) for injection. This fraction also causes cardiac slowing, arrest and irregularity associated with fall of blood pressure and depression of respiration. This was true of brain extracts from control and from convulsed animals. The acetone fraction (Holmes) is more potent in this respect, however.

These experiments, therefore, offer no support for the claim that extracts prepared in this manner contain a convulsant substance won from the brain during a convulsion. It should be stated, however, that a convulsing substance might be present in amounts unrecognizable because of the general constitutional effects of the extracts. Furthermore if convulsions were associated with the appearance of some convulsive substance in the brain it seems probable that the substance would appear with explosive rapidity and disappear quickly. The substance might thus have vanished during the 10 or 15 minutes required to remove the brain for fixation in experiments such as these.

Summary. Saline extracts of the brain residue remaining after acetone extraction and also the acetone fraction were prepared from

normal cats and from cats undergoing convulsions due to thujone or electrical stimulation. Such extracts, when injected into normal cats or rabbits, caused marked constitutional symptoms due to cardiac depression but were without specific convulsant effect on the central nervous system. The claims of Kroll were therefore not substantiated.

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The Cure of Canine Blacktongue with Nicotinic Acid.*

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It has been reported by Elvehjem and coworkers[1] that canine blacktongue produced by subsistence on a diet of the Goldberger type is cured dramatically by administration of nicotinic acid. When this communication appeared we had 2 dogs exhibiting chronic blacktongue produced by maintenance on a slight modification of Goldberger's diet No. 123.[2] The modification consisted in the omission of the cowpeas and use of a slightly greater amount of casein. The disease, as exhibited by our animals, was characterized by poor appetite, progressive loss of weight, vermilion bands on the upper lips, general reddening of the oral mucosa, and, in one of the dogs, by persistent diarrhea. The vermilion bands on the lips and the reddening of the oral mucosa disappeared and reappeared repeatedly.

Presumably, the reason that the disease took a chronic rather than the acute form more commonly observed when using the Goldberger diets was the presence of a greater than usual amount of the antiblacktongue factor in the particular sample of corn used in our ration. This modified diet had been previously found to produce acute blacktongue.[3]

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2 Goldberger, J., Wheeler, G. A., Lillie, R. D., and Rogers, L. M., *U. S. Public Health Rep.*, 1928, **43**, 657.

3 Street, H. R., Doctor's thesis, 1936, University of Minnesota.