over a period of one week, showed no pathological reaction to the injection.

As it had been reported that anaphylaxis plays a part in thiamine toxicity, those animals surviving were given a sensitizing dose of 100 mg. of thiamine, and one week later injected intravenously with 100 mg./cc. of thiamine solution until death occurred. The reaction of the animals was the same as previously described, but the toxic dose was almost doubled (from 375 to 500 mg./rabbit). There was no evidence of anaphylaxis, but auricular extrasystoles were seen in five of six animals injected. The usual rate was 3:1.

TABLE 1

RESULTS OF INTRAVENOUS INJECTION OF 100 MG./CC. THIAMINE HYDROCHLORIDE

Animal	Weight (kg.)	Total dose (mg.)	Results
21	1.591	220	Extreme vasodilatation at 220 mg., convulsions, cyanosis, inability to stand; animal recovered.
22	1.704	180	Vasodilatation at 120 mg., convulsions at 140 mg., death by respiratory paralysis at 180 mg. Autopsy showed lungs collapsed but normal; other organs normal; auricular extrasystoles, rate of 3:1.
23	1.818	220	Vasodilatation at 200 mg., convulsions at 220 mg., at which point respiration stopped but started again, with ensuing death by respiratory paralysis. Blood was definitely venous and the animal cyanotic. Autopsy revealed the same conditions as in #22.
24	1.591	200	Vasodilatation at 120 mg., death by respiratory paralysis at 200 mg. No convulsions; otherwise the same as #22.
25	1.704	240	Vasodilatation followed by collapse at 240 mg. No convulsions. Respiration very slow and animal cyanotic; recovered in five minutes.

Electrical stimulation of the muscles of the diaphragm showed that the muscles were still able to contract. Further, electrical stimulation of the phrenic nerve caused the diaphragm to contract, thus showing that the observed respiratory paralysis was central in origin. This could only mean that the respiratory center of the medulla was paralyzed.

CONCLUSIONS

(1) The above results are the same in every way as those observed when a solution containing 100 mg./cc. of thiamine hydrochloride and 0.35 per cent chlorobutanol was injected intravenously.

(2) The toxicity encountered upon injection of 100 mg./cc. of thiamine hydrochloride solutions is due to the thiamine content and not to the preservative.

(3) Symptoms of thiamine hydrochloride toxicity may be summarized as follows: (a) peripheral vasodilatation; (b) decreased respiration due to direct action on the respiratory center in the medulla; (c) asphyxial convulsions due to anoxia resulting from decreased oxygenation of the blood; (d) death by paralysis of the respiratory center; and (e) cardiac arrhythmias, probably due to anoxia and not a direct action of thiamine hydrochloride on the cardiac muscle or the conducting system.

(4) Anaphylaxis plays no part in thiamine hydrochloride toxicity as seen in rabbits. However, injection of a sensitizing dose apparently increases the resistance of the animal to toxic injections of thiamine hydrochloride.

(5) The lethal dose of thiamine hydrochloride by intravenous injection into rabbits is approximately 126 mg./kg.

(6) After a sensitizing dose of 100 mg. of thiamine hydrochloride the lethal dose is approximately 238 mg./kg.

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Effects of Whole-Wheat and White Bread Diets on Susceptibility of Mice to Pneumococcal Infection

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It was reported recently (*1*) that when mice are maintained on a "synthetic" diet they are much more resistant to the intraperitoneal injection of Type I, SV-1 strain pneumococcus than mice maintained on the usual laboratory diet. The explanation was advanced that the cruder diet supplies some factor (or factors) which is necessary for the rapid multiplication of the pneumococcus *in vivo*, and maintains a higher level of this factor in the tissues and fluids of the mouse than prevails during its absence from the diet. Belief in the validity of this explanation has been strengthened by the outcome of later experiments. When certain crude foodstuffs are added to the "synthetic" diets, the susceptibility of the mice to pneumococcal infection is increased. Moreover, extracts of these foods are capable of stimulating the *rate of growth* of the pneumococcus *in vitro*.[1]

[1] Unpublished experiments with Marion B. Sherwood.

Whole-wheat flour was found to be much richer than white flour in the factor stimulating pneumococcal growth *in vitro*. This suggested that mice eating whole-wheat bread might be more susceptible to pneumococcal infection than those eating white bread. The results of two experiments designed to test this possibility are shown in Table 1. The mice were maintained on either white or whole-wheat bread for 6 days before the injection of the pneumococci (10^{-4} or 10^{-6} ml. of a 17-hour culture). In both experiments the mice eating white bread were more resistant to the infection than those receiving whole-wheat bread. Thus, only 1 of 49 mice (2 per cent) on the whole-wheat diet survived the infection, whereas 20 of the 50 (40 per cent) eating white bread survived 6 days (and presumably indefinitely). In line with previous experience, the difference in response between the two dosages was small (*1*).

Obviously, these experiments provide insufficient evidence on which to decide the white vs. whole-wheat

TABLE 1

EFFECT OF DIET ON THE SURVIVAL OF MICE INFECTED WITH PNEUMOCOCCUS TYPE I

Exp. No.	Diet	Dose	No. of mice	Number surviving on day indicated						Average survival (days)
				1	2	3	4	5	6	
I	Whole-wheat bread	10^{-4}	24	24	9	4	3	1	0	1.71
	White bread	10^{-4}	25	25	19	16	14	13	11	3.92
II	Whole-wheat bread	10^{-6}	25	25	9	6	2	1	1	1.76
	White bread	10^{-6}	25	25	19	12	12	10	9	3.48

bread controversy or to base a dietary treatment of pneumonia. However, they do cast considerable doubt on one tenet of the nutritionist's credo. It is generally assumed that, when known essentials are present in equal amounts, a cruder foodstuff is to be preferred to a refined. This point of view implies that the unknown factors of the crude foodstuff are always beneficial. The assumption has an a priori validity which is supported by the history of the isolation of the vitamins and has not, up to now, been contradicted experimentally. The experiments described in this paper provide such a contradiction and cast doubt on the validity of the basic assumption. They show that, in one instance at least, the unknown factor of the crude foodstuff is more beneficial to the parasitic organism than to the animal consuming the food.

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The Production of Electricity by Nerve

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Five years ago we reported (*7*) that acetylcholine produces a pronounced phase-boundary potential of negative sign at the junction of oil and saline. It was suggested that this acetylcholine potential is the basis of the electrical negativity which arises in nerve during activity. A long series of additional experiments (*1–9*) have supported this theory that the chemical mediator of the nerve impulse, acetylcholine, sets up a negative phase-boundary potential in the lipoid layer of the nerve fiber—a theory which reconciles the "chemical" and "electrical" theories of nervous transmission. In a recent review, Feldberg (*12*) states that our experiments explain the "depolarizing" action of acetylcholine at synapses and at the end-plate. The term "depolarize" does not imply that acetylcholine renders an imaginary sieve membrane permeable to ions like potassium. We have previously shown (*6, 9*) that the old Bernstein concept of an ionic sieve membrane is untenable on both theoretical and experimental grounds. Actually, the lipoid-soluble acetylcholine dissolves in the oil layer to a much greater extent than the saline, thus establishing a true phase-boundary potential which we can demonstrate on an oil layer several centimeters thick, thereby eliminating any "permeability" change in an imaginary sieve membrane.

Recently the "oil-cell" model of the nerve impulse previously described (*7*) has been modified to conform to "physiological" conditions. For example, cholesterol (from spinal cord) or brain extract is added to the oil layer, thereby increasing the phase-boundary potential. Seventeen grams of cat brain extracted with 20 cc. of guaiacol at 80° C. was cooled and filtered. The resulting brain solution in guaiacol gave 45 mv negative with 0.05 per cent acetylcholine, in contrast to 30 mv established by 0.05 per cent acetylcholine on guaiacol without brain extract. Thus, acetylcholine can produce a phase-boundary potential with brain substance.

The addition of human serum which contains "serum cholinesterase" and small amounts of "cell cholinesterase" (*14*) to the saline phase brings the "oil-cell" model still closer to living nerve. Four cc. of human serum added to 200 cc. of 0.9 per cent NaCl with bicarbonate to make the pH 8.2 (at 37° C. for 8 hours) destroys the electrogenic activity of 0.05 per cent acetylcholine as tested in the "oil-cell." This experiment shows that it is the acetylcholine and not