lens. The cataract formed when DNP was injected on 8th day of incubation occurred when the 2 walls were apparently in contact (10). The oxidative enzyme systems are found only in epithelium, and the cortex is dependent on the epithelium for its metabolism(2.9). It is possible that this relationship may be involved in cataract formation.

Several hatched chicks were sacrificed for histological studies. Fig. 1 shows the lens of a newly hatched chick which received 500 μg of DNP on 8th day of incubation. There is a degeneration of lens fibers and a liquefaction of lens protein. This degeneration in the lens of the chick is similar to that previously observed in Vit. E-deficient turkey embryos(5,11).

Seventy-seven eggs were injected with 100 and 750 μg of DNP after 15 days incubation. The 100 μg level had no effect. The 750 μg level resulted in lens opacities in embryos from 20 hour post-injection sample and live-unhatched embryos. Hatched chicks appeared normal.

Summary. 1) Injections of 1-25 μg of DNP into chicken eggs, prior to incubation resulted in embryonic mortality after 3 days incubation, but did not produce lens changes. 2) Injections of 25-200 μg of DNP after 5 days incubation did not produce lenticular changes. 3) Cataracts were produced in embryos and hatched chicks from eggs injected with 200-500 μg of DNP after 8 days incubation. The size of cataract was roughly the same in hatched chicks as in embryos from the 500 μg group. 4) Injection of 750 μg of DNP after 15 days incubation produced an opacity evident after 20 hours. However, the opacity apparently regressed since the eyes of chicks hatched from this group appeared to be normal.

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Effect of Chlorpromazine on Swimming Time of Rats at Different Temperatures. (24138)

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Recently an analysis was made of the factors responsible for the marked hypothermia observed in rats treated with chlorpromazine (1). Chlorpromazine has also been shown to induce some muscle paralysis in rats(2). We have therefore studied the effect of chlorpromazine on swimming time of rats in water bath at different temperatures.

Methods. Male albino rats weighing 200 g were used. Swimming time of control and chlorpromazine-treated groups, composed of 6 rats, was measured when animals were swimming at 9, 19, 28 or 32°C. Chlorpromazine† 10 mg/kg was injected intraperitoneally 5 minutes prior to beginning of swimming and the rectal temperature was recorded with thermocouples. Room temperature was maintained at 21°C and water bath remained at

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† Chlorpromazine was graciously supplied by Smith, Kline and French (under trade name Thorazine).

TABLE I. Effect of Bath Temperature on Swimming Time of Control and Chlorpromazine (CPZ) Treated Animals.

Bath temp., °C	Swimming time, min. Control	CPZ†
9	9 ± 1*	9 ± 1
19	29 ± 7	18 ± 1
28	>90	22 ± 4
32	>90	>90

* Stand. error. † CPZ dose was 10 mg/kg.

constant temperatures for duration of experiment. In all experiments control and experimental animals swam at same time.

Results. When animals swam more than 1½ hr, the experiment was terminated, for it was observed that extremely wide variation occurred among normal animals in the time necessary to attain the limit of endurance in swimming. Furthermore, after 1½ hr the sedative and hypothermic effects of chlorpromazine disappeared gradually. Control animals swam longer than 1½ hr at 28 or 32°C, whereas at 19 or 9°C the swimming time dropped to 29 and 9 minutes, respectively (Table I). Chlorpromazine-treated animals swam longer than 1½ hr when the bath temperature was 32°C, whereas at 28, 19 and 9°C the swimming time (Table I) was greatly reduced. At bath temperature of 19°C, the rectal temperature drops at the same rate in the control as it does in chlorpromazine-treated animals (Fig. 1). The rectal temperature of control animals was 21.7°C when drowning occurred after 29 minutes of swimming, whereas the corresponding values

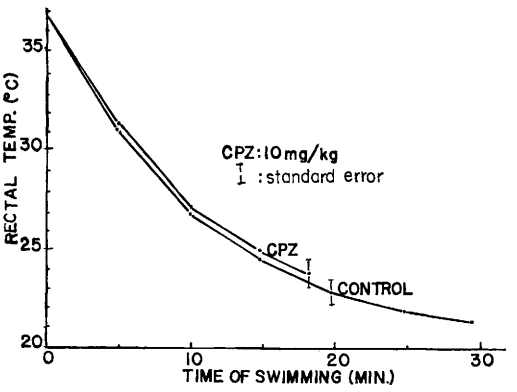

FIG. 1. Effect of swimming time on rectal temperature of control and chlorpromazine-treated animals swimming at 19°C.

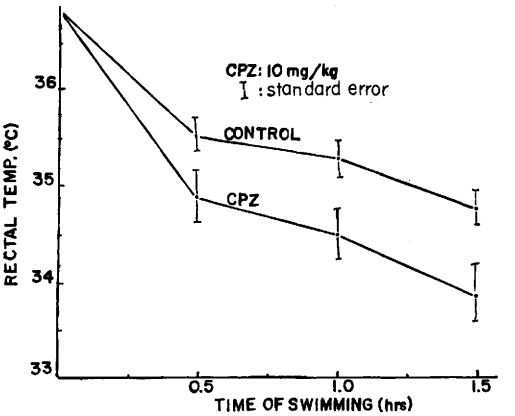

FIG. 2. Effect of swimming time on rectal temperature of control and chlorpromazine-treated animals swimming at 32°C.

for chlorpromazine-treated animals were 23.4°C and 18 minutes, respectively. When bath temperature is 32°C, the rectal temperature drops faster in chlorpromazine-treated group than in the control although both groups swim longer than 1½ hr (Fig. 2). When both groups swam the chlorpromazine-treated group was less disturbed and swam slower than the control group.

Discussion. Lowering of body temperature not only decreases speed of chemical reactions responsible for muscular contraction but also induces at certain levels a more or less pronounced state of narcosis. These responses to hyperthermia are probably the main factors responsible for decreased swimming time observed at certain bath temperatures in control animals. Because of muscle paralysis and sedation caused by chlorpromazine, it was suspected that this drug would potentiate the detrimental effect of low temperature on swimming animals. Sedation and muscular impairment in chlorpromazine-treated animals swimming at 32°C, probably explains the more rapid rate of body temperature drop. In spite of these effects the swimming time of both this group and the control exceeded 1.5 hr. However, at 28 and 19°C these reactions to chlorpromazine have a significant effect on swimming time. At 19°C the fall of body temperature was not faster in the experimental than in the control group, which indicates that factors other than changes in body temperature are responsible

for the difference in swimming time in both groups studied. It seems possible then that muscle paralysis and central sedation caused by both chlorpromazine and lower bath temperatures (28 or 19°C) become additive and explain the detrimental effect of chlorpromazine on animals swimming at temperatures lower than 32°C. At 9°C the effects of cold alone are so drastic and telescoped that chlorpromazine fails under these conditions to display its action.

Summary. When rats are swimming at 19 or 28°C, swimming time is markedly reduced by chlorpromazine (10 mg/kg) treatment. This difference is not due to differences in body temperature but is probably caused by sedation and muscular paralysis caused by this drug. At 9°C the detrimental effect of bath temperature on swimming time is so marked that chlorpromazine fails to display any action whereas at 32°C the stress is so small as to allow the animal to perform as well even when treated with chlorpromazine.

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Increase of Hexobarbital Sleeping Time by Certain Anticholinesterases.* (24139)

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Some organic phosphate insecticides, such as octamethyl pyrophosphoramide (OMPA) (1), p-nitrophenyl diethyl thionophosphate (parathion)(2) and ethyl-p-nitrophenyl thionobenzenephosphonate (EPN)(3) are converted by liver slices from relatively inactive to potent cholinesterase inhibitors. Conversion of OMPA(4), parathion(5), and hexobarbital(6) is an oxidative process, taking place in combined microsome and supernatant fractions of liver homogenates. Other organic phosphate anticholinesterases, such as S-(1,2-dicarbethoxyethyl)-O, O-dimethyl dithionophosphate (malathion), p-nitro-m-chlorophenyl dimethyl thionophosphate (chlorothion), and a mixture of bis-(dialkoxyphosphinothioyl) disulfides (phostex) are partially inactivated by liver slices(7). Since the alteration of these anticholinesterases by liver may involve the same enzyme systems as those detoxifying hexobarbital, their effects on duration of action of the latter were examined. Tetraethyl pyrophosphate (TEPP), and technical bis - dimethylamido - fluorophosphate (BFP) were used as examples of anticholinesterases not markedly activated nor rapidly inactivated by liver.

Methods and materials. Young adult male Swiss-Webster mice fasted 16 to 20 hours were used. Anticholinesterases† were given orally in corn oil 2 hrs before intraperitoneal injection of sodium hexobarbital in saline. TEPP was given to one group of mice 0.5 hr before the barbiturate. Sleeping time was the duration of loss of righting reflex from the side position.

Results. The highest doses of malathion and chlorothion and doses of other anticholinesterases used killed approximately 10% of the animals, all before injection of hexobarbital. Malathion, phostex and chlorothion produced the greatest prolongation of sleeping time (Table I). EPN and OMPA were also active, while BFP and TEPP were inactive.

Since malathion and chlorothion markedly prolonged sleeping time, it was expected that

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† Chlorothion, OMPA and BFP were supplied by Dr. K. P. DuBois of University of Chicago; EPN by E. I. duPont de Nemours Co.; malathion by Cyanamid Co.; phostex by Niagara Chemical Division, Food Machinery and Chemical Corp.; TEPP by Victor Chemical Works.