

of the P wave to the peak of the auricular systole was shorter than the normal limits calculated above. In one case of a 59-year-old male diagnosed as scleroderma with involvement of the lungs, marked pulmonary hypertension and evidence of partial heart block, the latent period was 0.17 sec. The time from the beginning of the P wave to the peak of the auricular systole was 0.20 sec. in this case. This may represent some delay in the spread of the sinus impulse through the right auricle.

Summary. 1. In 8 adult subjects with essentially normal hearts the latent period between the beginning of the electrical P wave and pressure pulse wave corresponding to the right auricular systole averaged 0.11 sec. 2. In one case of a child with a rapid pulse and Tetralogy of Fallot the latent period was much shorter, 0.055 sec. 3. In one case of scleroderma with pulmonary hypertension and partial heart block the latent period was prolonged to 0.17 sec.

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Influence of Thiourea on Development of the Chick Embryo.

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While investigating the effect of several substances which may influence the growth of rickettsiae in the yolk sac of the chick embryo, some effects on the embryo itself have been observed, and these have been followed up for thiourea.

Thiourea and related substances have been shown to affect the thyroid function in adult animals, viz., rat,^{1,2} mouse and dog,¹ rabbit,³ and chick.⁴ Thiourea has also been found to inhibit metamorphosis in tadpoles⁵⁻⁷ and

cleavage of sea urchin eggs.⁸

Thiourea is introduced into the yolk sac of Leghorn embryos according to the technic described by Cox.⁹ Aseptic precautions are strictly adhered to throughout the whole procedure. Fertile eggs incubated at 39°C for 7-17 days are used. The shell covering the air sac is washed with 5% phenol and the injections are made into the yolk through a needle-sized opening in the air sac by means of a hypodermic syringe and a 22-gauge needle. The hole is then sealed with paraffin and the eggs are returned to the incubator. Amounts of thiourea used were 0.3 to 3 mg per egg. In order to avoid mechanical damage to the embryo, the fluid introduced should not exceed 0.5 ml; a similar volume of distilled water serves as control. Eggs were daily inspected by candling and dead ones were discarded.

Results. While the controls hatched after 21 days (on very few occasions after 20 or 22 days), hatching of embryos treated with thiourea was retarded up to 10 additional days. The retardation seemed to depend on 2 factors, (a) age of the embryo at the time of injection; (b) concentration of thiourea. For example, 1 mg thiourea delayed hatching by only 1 day in 17-day egg embryos, while the same amount applied to younger

* The author is indebted to Dr. M. Aschner for his valuable suggestions.

¹ Mackenzie, C. G., and Mackenzie, I. B., *Endocrin.*, 1943, **32**, 185.

² Astwood, E. B., Sullivan, J., Bissel, A., and Tyslovitz, R., *Endocrin.*, 1943, **32**, 210.

³ Bauman, I., Metzger, N., and Marine, D., *Endocrin.*, 1944, **34**, 44.

⁴ Mixner, J. P., Reineke, E. P., and Turner, C. W., *Endocrin.*, 1944, **34**, 169.

⁵ Gordon, A. S., Goldsmith, E. D., and Charipper, H. A., *Nature*, 1943, **152**, 504.

⁶ Gordon, A. S., Goldsmith, E. D., and Charipper, H. A., *Growth*, 1945, **9**, 19.

⁷ Hughes, A. M., and Astwood, E. B., *Endocrin.*, 1944, **34**, 138.

⁸ Bevelander, G., *PROC. SOC. EXP. BIOL. AND MED.*, 1946, **61**, 268.

⁹ Cox, H. R., *Science*, 1941, **94**, 399.

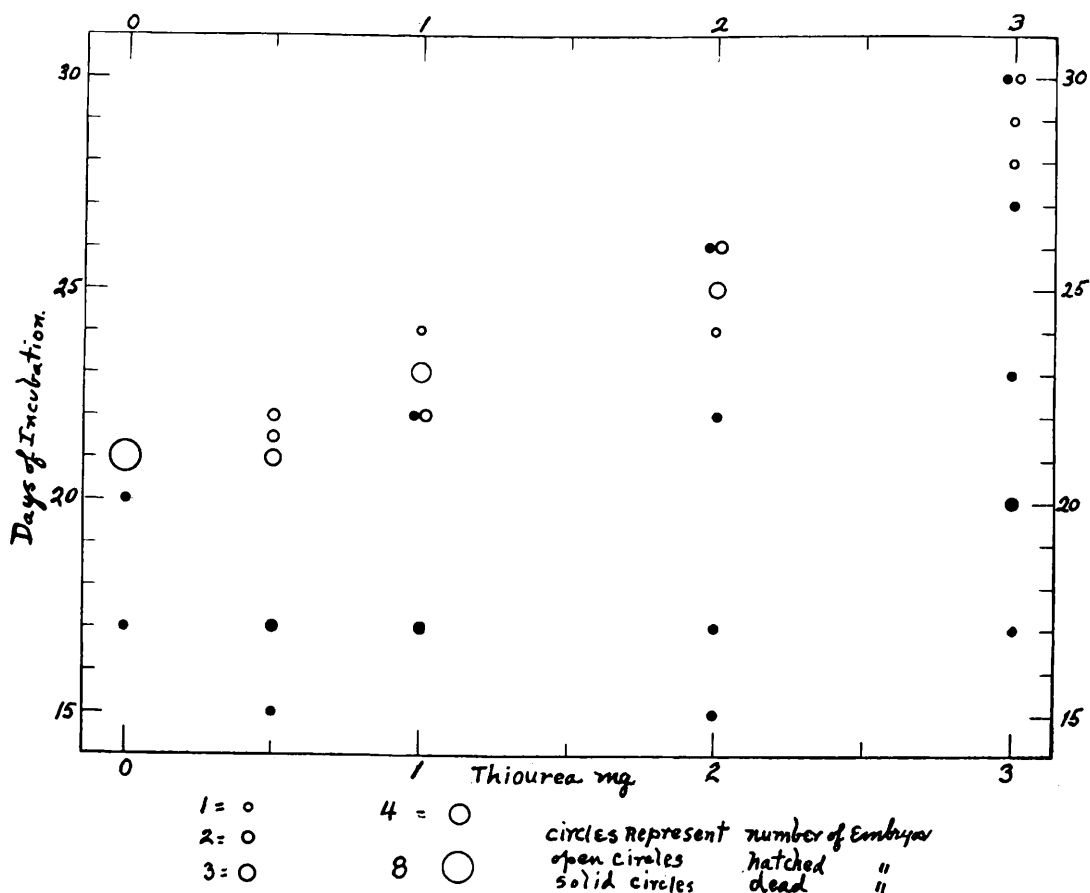


FIG. 1.

Delay in hatching time of Leghorn egg embryos after injection of thiourea at the 14th day of incubation.

embryos (10 days old) caused a delay of 3 days. Two mg of thiourea retarded hatching by 3-7 days, the effect again depending on age. Though hatching time can be extended up to the 30th day by still higher amounts of thiourea (3 mg), hatchability is much impaired being equivalent to only about 5-10% of the controls. In addition, the delay in hatching is associated with other signs of inhibition. Whereas in normal embryos the yolk sac begins to retract on the 19th day, and by the 20th day has entirely entered the abdomen, the yolk sac is not much reduced in size at this stage in eggs treated with thiourea; it can still be found on the 30th day of incubation in those embryos previously treated with a dose of 3 mg thiourea. While in the controls the "egg tooth" enters the air-chamber on the 20th day, treatment with 2 mg thiourea at age of 10-14 days delays

this phenomenon by 2-5 days. The results of a typical experiment are given in Fig. 1.

Experiments were also carried out in order to elucidate the mode of action of thiourea. Gordon *et al.*⁶ were able to show that the inhibiting effect of thiourea on tadpoles can be reversed by thyroxine. In our experiments it was difficult to prove the reversing effect of thyroxine as it was found to be very toxic especially for embryos up to 14 days. Thyroxine in nontoxic concentrations had no antagonizing activity at all. However, in some experiments with 17-day-old eggs, 10 μ g of thyroxine fully neutralized the action of 2 mg thiourea when the 2 drugs were simultaneously applied (molecular ratio 1:2,000). The experiments suggest that in the chick embryo, as in other animals, the inhibiting effect of thiourea may be due to interference with normal thyroxine metabolism.