

has been decreased by toxic or fatal doses of morphine, chloral, alcohol or barbital. The stimulation compares favorably with that caused by caffeine. The improvement in respiration does not prevent death, if otherwise fatal doses of these hypnotics have been given; thus indicating that the respiratory depression *per se* is possibly not the primary cause of death from the hypnotics. During the period of maximum respiratory stimulation, there is little or no change in blood pressure and pulse rate, and the sugar, pH and CO<sub>2</sub>-combining power of plasma are unaltered. Hence the increase of temperature and respiration is not accompanied by an acidosis or the appearance of appreciable amounts of fixed acid in the blood. The rise of temperature is not prevented by destruction of the brain and spinal cord or by complete curarization, so that the mechanism of production would appear to be a peripheral one. When fever-producing doses are given repeatedly to dogs at intervals of 3 days over a period of 6 weeks, constant febrile responses are elicited, with little or no evidence of toxicity, either grossly or on microscopic study of the tissues. The other available isomers of nitro-, dinitro- and trinitrophenol are less effective in producing fever, or cause it only in fatal doses. Even with the  $\alpha$ -dinitrophenol the margin between the febrile and fatal dose is narrow.

Experiments are being made to elucidate the mechanism of the fever production, the details of the pharmacologic action, and the cause of death, and to determine possible antidotes, and therapeutic usefulness, of this drug in man.

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### Studies in Ageing Eggs. Changes in Permeability of Egg Membrane.

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The volume of unfertilized eggs of *Arbacia punctulata* aged in sea water at 19 to 22° C., pH 8.2, is not constant. The volume increases slowly and progressively during approximately the first 23 hours after shedding. The increase in volume of eggs from different females ranges from 1.8 to 3.2%. With further ageing the volume decreases progressively.

Samples of such ageing eggs were placed at successive ages in the

same concentration of dilute sea water, at 21.5°, pH 8.2, and the increase in volume of each egg measured during 5 to 7 successive minutes. Nine to 21 eggs were measured at each age. The average of these measurements at each age was plotted and the constant of the curve, *i. e.*, the permeability constant, *K*, was calculated by the method of Lucké and McCutcheon. *K* measured the amount of water passing through a unit of surface per unit difference of osmotic pressure per unit time.

TABLE I.

Showing increase in permeability (*K*) with increasing age of eggs. Calculations based on extrapolated and on average *V<sub>0</sub>* volumes.

Age in hrs.	Permeability <i>K</i>	Permeability <i>K</i>
	Extrapolated <i>V<sub>0</sub></i> .	Aver <i>V<sub>0</sub></i> .
1	.120	.121
3½	.134	.131
6	.132	.129
24	.139	.135
28	.171	.171
32	.167	.168
48	.166	.164
54	.162	.179
Increase in permeability—24.2%.		

The volume of the eggs before immersion in the hypotonic solution was determined in 3 ways: (1) average of 50 measured eggs, (2) by extrapolation, (3) average of all extrapolated *V<sub>0</sub>* values. The permeability constants were calculated by all 3 methods. The results, though varying, all agree in this, that a marked increase in permeability occurs with ageing of eggs.

The increase in permeability was 24.2, 41.0, 43.0, 47.0, and 68% in 5 different experiments, when 50 and 60% sea water was used. In one experiment with 80% solution of sea water the increase was 27%.

There appears in each experiment to be 3 stages in the increased permeability: (1) an initial low rate between 0 and 2 hours after shedding, (2) a higher rate between 3 and about 24 hours, (3) a highest rate between 24 and about 54 hours. These stages may represent 3 steps in a progressive increase of permeability with ageing of eggs.