acetyl choline on the intestine in the dark in concentrations in which a mixture of nitrogen and oxygen of similar percentage composition had no such effect. This indicates that carbon monoxide acts specifically in this case, the action being independent of asphyxial complications due merely to an insufficiency of oxygen. If such a carbon monoxide-poisoned preparation which has responded feebly to a drug be illuminated there is a fairly immediate increase in contracture which lasts throughout the period of illumination and which returns to the initial level upon discontinuance of illumination.

Some 25 experiments were performed on the blocking action of cyanide, 10 on the blocking action of carbon monoxide, and 4 on the light reversal of the carbon monoxide block. In none of these experiments have we observed any exceptions to the blocking actions of these substances or its reversal by light, as described above.

It would appear that some mechanism is involved in the response of smooth muscle to drugs and possibly also to autonomic nerve impulses which has the characteristics of a heavy metal catalytic system.

6572

Relative Depressant Effects of Certain Barbiturates on Heart of Elasmobranchs.

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Apparently no comparative study has been made of the relative cardiac depressant effects of the widely used barbiturates, perhaps because the effects on the central nervous system are so pronounced, as compared with the effects on the heart, that attention centers largely on their central actions.

Opportunity was afforded for studying the relative degree of cardiac depression produced by certain barbiturates, nembutal (sodium ethyl-methyl barbiturate), amytal (sodium iso-amyl barbiturate; luminal (sodium phenyl-ethyl barbiturate), and veronal (sodium di-ethyl barbiturate).

The study was carried out on the isolated heart of elasmobranch fishes, chiefly the *Squalus acanthias* or spiny dogfish, which is admirably adapted for such a study. The number of animals used

totaled 14, all dogfish except one *Raia stabuliforis* (barndoor skate). The procedure for the dogfish heart was as follows:

The heart was removed from the animal with the sinus and great veins intact. A sino-auricular-ventricular preparation was prepared by cutting off the aortic arch and its vessels, then by means of a vertical incision the auricle on one side and about half the ventricle was cut off, thus exposing the endocardium. When the heart preparation was thus made, it was suspended in a balanced saline solution which was constantly supplied with oxygen and whose temperature was maintained at 16°C.

The balanced Locke-Ringer's solution was made by dissolving the following amounts of salts and urea in each liter of freshly distilled water (Barnstead still): Sodium chloride, 15 gm.; urea, 20 gm.; potassium chloride and calcium chloride, each 400 mg.; magnesium chloride, 1 gm.; sodium bicarbonate, 500 mg.; sodium acid phosphate, 100 mg.

When freshly distilled water was used, the pH of this solution was 7.55.

Graphic records obtained by means of a light heart lever were taken from the isolated rhythmically beating sino-auricular ventricular dogfish preparation and after a maximum rhythm was attained, 50 mg. of each of the above named barbiturates as the sodium salt was added to each 100 cc. of the saline solution bathing the heart preparation. This amount of barbiturate caused heart stoppage in a short time when nembutal, amytal and luminal were used, whereas when veronal was employed the heart rhythm persisted during the period of observation, which lasted for over an hour. While there was no great difference in the length of time required for this dosage of the 3 more toxic barbiturates to stop the heart, the degree of toxicity, judging by the average time required to produce heart stoppage, followed in a certain order.

Table I shows the individual variation for each series and the average time required. It also shows that these barbiturates fall into 2 groups, the more toxic being nembutal, amytal, and luminal; the least toxic being veronal, which does not stop the heart in this dosage after an hour or more.

As a further check on the relative toxicity between the least and one of the more toxic, namely veronal and nembutal, an experiment was carried out on the heart of the elasmobranch, *Raia stabuliforis* (barndoor skate). In this animal the heart is large enough to be divided into halves, and when mounted in separate chambers under identical conditions, the 2 halves will beat synchronously. Thus

TABLE I.

Barbiturate (as sodium salt)	Time to stop heart after 50 mg. Min.	Aver. Min.
Nembutal	4	7.5
	7	
	11	
	8	
Amytal	6	
	9	9—
	11	
Luminal	9	
	9	11—
	14	
Veronal	>68	
	>70	>68
	>157	

arranged, the usual dose (50 mg.) of each of the above was added to the saline. (Temp. 19°C.) and it was shown that nembutal stopped the heart preparation in 2 minutes, whereas veronal had little or no effect after several hours.

Conclusion. The depressant activity of nembutal, amytal, and luminal is high compared with veronal on the sino-auricular-ventricular preparation of *Squalus acanthias,* each given as the sodium salt.

6573

Maintenance Dose of Parenteral Liver Extract in Treatment of Pernicious Anemia.

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Gänsslen[1] and Castle and his co-workers[2, 3] have shown that the active principle of liver (fraction G of Cohn) is much more effective when given parenterally than when given orally to patients with pernicious anemia. Since this discovery, it has been of interest to know the average frequency of injections and the amount of active

[1] Gänsslen, M., *Klin. Wchnschr.*, 1930, **9**, 2099.

[2] Castle, W. B., and Taylor, F. H. L., *J. Am. Med. Assn.*, 1931, **96**, 1198.

[3] Strauss, M. B., Taylor, F. H. L., and Castle, W. B., *J. Am. Med. Assn.*, 1931, **97**, 313.