fective changes in the liver parenchyma. In the successful type of Rous fistula (ours were usually failures) Elman found very few ulcers. Berg's experience was similar. His smoothly functioning Rous fistulas developed many ulcers while the unsuccessful ones developed many.

It appears, therefore, that the development of duodenal ulcer in the absence of bile from the intestine is partially dependent on some factor other than acid. Possibly the effect on the gastric motility of liver damage, as suggested by Still and Carlson,^{τ} is the deciding factor.

7626 C

Electrocardiographic Studies of Chemical Pericardial Irritation.

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Pericardial effusions, clinical or experimental, may result in electrocardiographic changes much like those of coronary occlusion or of ligation of the coronary arteries.¹⁻⁷ In experimental effusions, one must consider the effect of pressure and of possible chemical influence. Indeed, Wiggers⁸ has demonstrated bizarre ventricular complexes, similar to those of effusions, resulting from applying a few cubic centimeters of potassium chloride solution to the visceral pericardium. Hence it seemed desirable to study the effects of various bland and irritating chemicals under conditions to exclude any pressure factor.

Dogs were used, with preliminary morphine sulphate 0.015 gm.

- ³ Smith, F., Arch. Int. Med., 1923, 32, 497.
- 4 Barnes, A. R., and Mann, F. C., Am. Heart J., 1932, 7, 477.
- ⁵ Scott, R., Feil, H., and Katz, L., Am. Heart J., 1929, 5, 68, 77.
- ⁶ Bay, E. B., Gordon, W., Adams, W., Am. Heart J. 1933, 8, 525.
- 7 Harvey, J., and Scott, J. W., Am. Heart J., 1932, 7, 532.

8 Wiggers, C., Am. Heart J., 1930, 5, 346.

⁵ Kim, M. S., and Ivy, A. C., J. A. M. A., 1931, 47, 1511.

⁶ Elman, R., and Hartmann, A. F., Arch. Surg., 1931, 23, 1030.

⁷ Still, K. S., and Carlson, A. J., Am. J. Phys., 1929, 89, 34.

^{*} I am deeply indebted to Dr. Louis Leiter and Dr. Emmet Bay for advice during this work.

¹ Smith, F., Arch. Int. Med., 1918, 22, 8.

² Smith, F., Arch. Int. Med., 1920, 25, 673.

about one-half hour before the first or control electrocardiogram. Light ether anesthesia followed, then rib resection just to the left of the sternum to expose the pericardium, followed by artificial respiration and opening the pericardial sac by a 3 to 5 cm. anterior incision. There was an electrocardiographic control at each step. The pericardium and chest were not closed again.

The chemicals used were liquids, solutions, and solids (crystals, powders), the fluids in amounts averaging one cubic centimeter applied at body temperature with a medicine dropper or camel's hair brush, so that pressure effects were absent. The solids were dropped on lightly. The initial application was made over the left ventricle just to the left of the septum and above the apex. Subsequent spreading of fluids was unavoidable.

The experiment was stopped if the dog went into shock, became asphyxiated, or developed ventricular fibrillation.

Electrocardiographic Results. Controls. These proved to be very important. The ST takeoff varied from +2 mm. to -1 mm., and in lead II half the T waves were negative or diphasic. Ether anesthesia caused surprising transient voltage decrease, as well as rate increase, and opening the pericardial cavity to atmospheric pressure and room temperature caused another voltage decrease (all leads) which did not tend to return to the control level.

Furthermore, the control ST segment was decidedly convex or concave in some cases; and about half the time, ST or T changed direction in at least one lead after ether anesthesia.

	during of Elevation as the omer Result.
Alcohol (95%)	ST rises starting in 12 seconds, with return to normal in 1 minute. An even greater rise occurred with reapplication over an artery.
Calcium Chloride (7%-10% sol.)	Marked ST rises within one-half minute, maximal in 3 minutes, then partial return to normal. (Concen- trations of less than 7% were ineffective.)
Ether (U.S.P.)	Marked sudden ST rise with sharp T inversion.
Ethyl Chloride (U.S.P.)	ST elevation and deep T waves.
Formic Acid (U.S.P.)	ST rise in 10 seconds, starting towards normal in 1 minute.
Hydrogen Peroxide (U.S.P.)	Transient ST and T change more marked when application was over an artery. Voltage decrease.
Lactic Acid (1%)	Instantaneous ST elevation.
'' '' (Conc.)	Rapid but not instantaneous ST elevation.
Mercurochrome (Crystals)	ST ^{elevations} starting in 6 minutes, maximum in 15 minutes.
Potassium Chloride (1%-10% sol.)	ST rises similar to those from calcium chloride, and agreeing with Wigger's results. ⁸
Sodium Chloride (Crystals)	Moderate ST elevation.
Tincture of Iodine (U.S.P.)	Similar to alcohol. (Tincture of iodine contains 83% alcohol.)

 TABLE I.

 Substances Producing ST Elevation as the Chief Result

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In a few instances, for control purposes, nothing was done for several hours after opening the pericardium; there were no additional electrocardiographic variations. In about half the experiments, the chemical was applied first to the intact parietal pericardium; there was never any significant change. Incidentally, lead II alone usually gave all the necessary information.

Application to the Visceral Pericardium. The most frequent change was a genuinely significant rise in the ST interval, amounting at times to RT fusion, and substances quite different chemically produced similar results. (Table I and Plate 1.) Complete bundlebranch block occurred 3 times, in each case with similar substances. (Table II.)

There was a group giving miscellaneous results. (Table III.) The time of appearance of the changes varied from instantaneous



PLATE I. (Lead II throughout).

		TABLE I	Ι.			
Substances	Producing	Complete	Bundle	\mathbf{B} ranch	Block.	

Oil of Cloves (U.S.P.)	Complete in 1 hour.
Sandalwood Oil (U.S.P.)	vi v 28 seconds.
Turpentine (U.S.P.)	" "9 minutes.

Ammonia Water

(In each of these instances, the PR interval was unaltered, the evolution of the block was gradual, with no transitional period resembling arborization block.)

	TAB	LE III.				
Substances	Producing	g Miscellaneo	us R	esults.		
C	Occasional	extrasystoles	and	slight	\mathbf{ST}	changes.

(1%-10% U.S.P.)	
Barium Chloride	Varying runs of extrasystoles.
(1.5% sol.)	
Chloroform (U.S.P.)	Sudden, sharp, diphasic T wave.
Potassium Permanganate	Slight QRS notching, diphasic T, and high P.
(0.1% sol.)	
Silver Nitrate (20% sol.)	Temporary QRS widening, but after bilateral vag-
	otomy extrasystoles occurred, and after atropine,
	nothing happened, except the slower rate.
Sodium Carbonate (U.S.P.)	Transient ventricular tachycardia of tremendous
	voltage. Later, ST and T high. Still later, return
	to normal.
Sodium Hydroxide	Bizarre notchings of uncertain significance. (Possi-
(10% sol.)	bly respiratory variations.)

(see lactic acid record on Plate 1) to an hour or more. The changes with alcohol, calcium chloride solution, lactic acid, formic acid, sandalwood oil, and sodium carbonate crystals were some of those occurring within one minute.

It is interesting to note the variety of substances that were without significant effect. (Table IV.)

	TABL	ΕI	v.	
Substances	Producing	No	Significant	Result.

Acetone (U.S.P.)Normal SalineChrysarobin (crystals)Potassium Chlorate (5% sol.)Ephedrin Sulphate (3% sol.)Talc (U.S.P.)Glucose (U.S.P.)Tannic Acid (5% sol.)		
Lactose (U.S.P.) Xylol (C.P.)	Acetone (U.S.P.) Chrysarobin (crystals) Ephedrin Sulphate (3% sol.) Glucose (U.S.P.) Lactose (U.S.P.)	Normal Saline Potassium Chlorate (5% sol.) Tale (U.S.P.) Tannic Acid (5% sol.) Xylol (C.P.)

End Effects. Some of the changes returned toward normal; others progressed into ventricular fibrillation, or were not observed. After several hours, it was sometimes difficult to tell whether the effects observed were due to the original application, shock, or asphyxia.

Preliminary Atropinization or Bilateral Vagotomy. These procedures gave important variations from the usual results in some cases. (The average dose of atropine was 0.36 mg. per kilo intravenously). Thus, alcohol caused a marked ST rise which failed to occur after atropine. Silver nitrate, which caused temporary widening of the QRS, resulted in extrasystoles after bilateral vagotomy, and in no change at all after preliminary atropine. However, the typical calcium chloride results were not prevented by atropine. Unfortunately, the experiments in which the volatile oils (with their bundle branch block type of curve) were used after preliminary atropine, gave unreliable results.

Postmortem Observations. Thirty-four hearts were autopsied. None showed gross myocardial lesions, nor gross pericarditis. Microscopic sections were made under and adjacent to the irritated areas in 9 dogs (in the experiments using formic acid, hydrogen peroxide, potassium permanganate sol., sandalwood oil, sodium hydroxide sol., turpentine, ammonia water, mercurochrome crystals, and tincture of iodine). In the last 3 of these, fragmentation and loss of striation were taken as evidence of a muscle injury to a depth of 0.1 to 0.3 mm. Otherwise there was no apparent muscle damage; pericardial injury was variable but slight.

Significance of the Changes. Can one explain the chief changes, ST elevation of various types, and 3 instances of bundle branch block? The experiments do not furnish proof, but they do show that demonstrable muscle injury need not be present to produce the changes described, and suggest that the extracardiac nerves may be a factor. Of course, the failure to find histologic evidence of muscle injury does not preclude the possibility that the observed effect of certain substances (e. g., salts) depends upon absorption, and passage of ions between muscle fibers. Moreover, bundle branch block need not depend upon absorption. There have been fairly numerous reports of transient bundle branch block, wherein there was held to be no heart damage, with increased vagal tone the factor responsible.⁹⁻¹³

The question of local or transient ischemia is not within this discussion. It is certainly questionable that any ischemia occurred in the experiments here reported. We note that alcohol or hydrogen peroxide applied over a coronary artery gave results more marked than over the muscle alone. One possibility is that the arterial application produced constriction and ischemia, but it is just as reasonable to assume increased reflex effects if the nerve supply is richer along the arterial course.

Summary. The electrocardiographic results of applying various

⁹ Wolff, L., Parkinson, J., and White, P. D., Am. Heart J., 1930, 5, 685.

¹⁰ Faulkner, J. M., Med. Clin. of N. Am., 1932, 15, 997.

¹¹ Newman, M., Br. Med. J., 1931, 2, 1134.

¹² Carr, F. B., New Eng. J. Med., 1933, 209, 1101.

¹³ Morris, R. S., and McGuire, J., Am. J. Med. Sci., 1932, 184, 202.

bland and irritating chemicals to the visceral pericardium, with pressure factors absent, are described. The chief of these are marked ST elevations of several types, occurring quickly; bundle branch block; and the rarity of extrasystoles. The controls proved very important, and are emphasized.

7627 C

Effect of Maximal Feeding on Metamorphosis in Amblystoma.

FRANCES DORRIS. (Introduced by R. G. Harrison.) From Osborn Zoological Laboratory, Yale University.

Twitty and Schwind¹ have shown that in heteroplastic grafting between the 2 species Amblystoma tigrinum and A. punctatum, comparable results with respect to growth are obtained only when the hosts are all maintained at the same nutritional level, an effect obtained by maximal feeding, thus insuring the rapidly growing voracius tigrinum larvae opportunity to realize their full capacity for growth. The effect of maximal feeding upon the more slowly growing species has not been emphasized, although various workers have noted that along with the spectacular acceleration of the growth rate, and a consequently earlier metamorphosis, there is a high mortality during the metamorphic period in maximally fed groups of A. punctatum, regardless of the type of diet.

The present experiments were undertaken in order to show the results of quantitative variation in a single diet upon the developmental rate and viability of *A. punctatum* from the earliest feeding stage through metamorphosis. Two hundred animals, taken from several bunches of eggs all at approximately the same stage of development, were reared from stage 39 onward in separate finger bowls. At the feeding stage the animals were divided into 4 groups of 50 each. The first 50 animals were starved, the second group given one feeding weekly, the third fed 3 times a week, and the fourth fed maximally. Enchytraeus, a small white worm, was used as the sole diet. All animals were measured at approximately 2-week intervals, the total length being recorded.

Fig. 1 shows the average growth rate for each group. The minimally fed larvae ate poorly, had low vitality, and remained of ap-

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¹ Twitty, V. C., and Schwind, J. L., *J. Exp. Zool.*, 1931, **59**, 61; Twitty, V. C., and Elliott, H. A., *J. Exp. Zool.*, 1934, **68**, 247.