TABLE I. Effect of Androstenes on Hypertension.

Test	Derivatives of 4-androsten-3-one	Mean group blood pressure, mm Hg: Before inj.	2 hr*	4 hr*	5½ hr*
A	11β-hydroxy-4-androstene-3,17-dione	187	153†	140‡	138†
	Propylene glycol	187	186	177	187
B	4-androstene-3,11,17-trione	186	180	169†	178†
	4-androstene-3,17-dione	184	170‡	177‡	178‡
	Corn oil	182	188	186	190
C	11β-hydroxytestosterone	180	172	182	172
	Propylene glycol	181	180	182	178
D	11-ketotestosterone	183	168	160†	160†
	Testosterone	183	161‡	162†	164†
	Corn oil	178	180	182	182

* Hr after inj.
† $P<.01$ that treat mean = control mean.
‡ $P<.05$ " " " = " " .

metacorticoid hypertensive rats. Replacement of the 11-hydroxyl by hydrogen or a keto group appeared to decrease the activity of the 17-ketosteroids and increase the activity of the 17-hydroxysteroids. The depressor activity could not be related to anabolic or androgenic activity.

The technical assistance of Catherine Tsou and Ardys Magner is gratefully acknowledged.

1. Green, D. M., Saunders, F. J., Wahlgren, N., and Craig, R. L., *Am. J. Physiol.*, 1952, v170, 94.

2. Green, D. M., Saunders, F. J., Wahlgren, N., McDonough, F. J., and Clampit, J. M., *ibid.*, 1952, v170, 107.

3. Green, D. M., Craig, R. L., Saunders, F. J., and Sturtevant, F. M., *ibid.*, 1952, v170, 477.

4. Green, D. M., Saunders, F. J., Van Arman, C. G., Calvin, L. D., and Sturtevant, F. M., *ibid.*, 1952, v170, 486.

5. Selye, H., and Horava, A., *2nd Annual Report on Stress*, Montreal, Acta, Inc., 1952, pp 22 and 228.

6. Sturtevant, F. M., PROC. SOC. EXP. BIOL. AND MED., 1953, v84, 101.

7. Kersten, H., Brosene, W. G., Jr., Ablondi, F., and Subbarow, Y., *J. Lab. and Clin. Med.*, 1947, v32, 1090.

8. Snedecor, G. W., *Statistical Methods*, Ames, Iowa State College Press, 1946, p77.

9. Saunders, F. J., unpublished data.

10. Braun-Menendez, E., *Rev. Soc. Argentina de Biol.*, 1952, v28, 23.

11. Selye, H., and Rowley, E. M., *J. Urol.*, 1944, v51, 439.

12. Friedman, S. M. and C. L., *Endocrinology*, 1950, v46, 367.

13. Selye, H., *Stress*, Montreal, Acta, Inc., 1950, p631.

Received September 22, 1953. P.S.E.B.M., 1953, v84.

Resistance Strain Gauge Arches for Direct Measurement of Heart Contractile Force in Animals.* (20612)

K. J. BONIFACE, O. J. BRODIE, AND R. P. WALTON.

From the Department of Pharmacology, Medical College of South Carolina, Charleston, S. C.

While industrial uses of resistance wire strain gauges are highly diversified, the biologic application of this device has been limited almost entirely to the recording of hydraulic pressures. Actually there are numerous biologic changes of force which can be measured advantageously by this procedure which reacts isometrically and which, with the usual instruments, is capable of frequency recordings of 100 cycles/sec. In practice, it is

* This study was supported by grants from the National Heart Institute, U. S. Public Health Service.

only necessary to cement one of the standard coils to a metal strip which has elasticity characteristics suited to the force changes of the particular experiment. Garb(1), for instance, has used the principle to measure contractile force of an isolated papillary muscle. Robb(2) connected perfused, beating hearts of small mammals to the post of a Statham transducer and made similar records.

The present report describes the technic of preparing strain gauge arches which can be attached to the ventricles of large animals and made to record the force of each systolic contraction acting against the 2 points of attachment. Because of the unique compactness of this device, the chest wall can be closed after surgical attachment of the arch and lead wires brought through the wall for subsequent recordings in the post-operative animal. Recent experiments have established that the measurements of this method are representative of changes in different areas of both ventricles, are not directly influenced by variations in heart rate and are only moderately influenced by variations in arterial and venous pressure(3).

Methods. SR-4 strain gauges type A-7 were used as pick-up units(4) and their output was carried to a strain analyzer and amplifier (BL-310) and direct inking oscillograph (BL-202) of the Brush Electronics Co. Two types of arches have been used. In one, the strain gauge coil is covered with insulating resins and, in the other, the coil is protected by a thin metal tube (Fig. 1). Although a variety of insulating resins have been tested, none were found which did not lose resistance rapidly in the animal's chest. This resistance breakdown occurred so much more rapidly in body fluids than in saline that saline immersion was not considered a useful guide. Ordinarily, with the resin protected coils, resistance between the coil and some free point on the arch would be greater than 1000 megohms. On the first post-operative day resistance usually dropped to fractions of a megohm, this being determined by connecting the meter to one lead of the coil and the other to the animal's mouth. In all cases, with resistance reduced to fractions of a megohm, the animal was grounded. This permitted

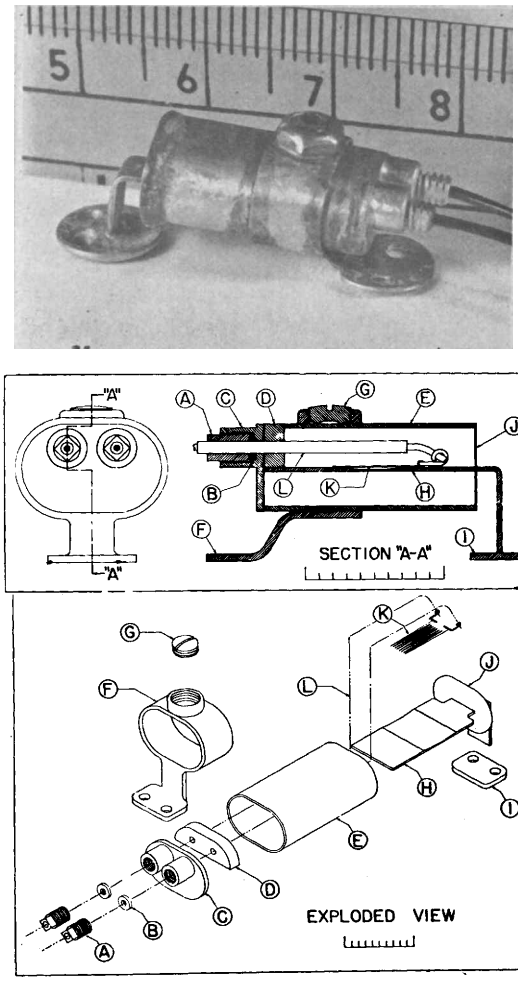

FIG. 1. Strain gauge arch with coil enclosed in brass tubing encasement. Above—photograph about twice actual size. Below—diagrammatic, sectional and exploded views with one cm scale. Parts designations as follows: (A) Stuffing box gland. (B) Stuffing box packing. (C) Body end integral with stuffing boxes. (D) Stop preventing upward movement of (H). (E) Tubular body or encasement. (F) Movable foot. (G) Set screw. (H) Elastic metal strip integral with rigid leg. (I) Foot. (J) Flexible metal diaphragm. (K) Strain gauge coil. (L) Lead wires.

satisfactory measurements for a few days and in some cases for a few weeks. With the metal protected coils, initial resistance would range in the area of 1000 megohms and would stabilize in the area of 25 to 100 megohms when tested during the period of use in the animal. Before using the strain gauge arches, they were customarily tested for sensitivity and their threshold of response determined in

grams. Desirably, the threshold of response should be less than 10 g.

It can be noted in Fig. 1 that the arch with metal protected coil is additionally equipped with provision for adjusting the distance between the 2 "feet" or points which are to be attached to the ventricle. This permits, even in hearts of widely varying size, a standardized degree of diastolic tension in the muscle segment between the 2 points of attachment. This is accomplished by calibrating the arch, leaving unaltered all adjustments of the analyser and oscillograph and making recordings immediately after the arch is surgically attached but before the chest is closed. The degree of diastolic tension can then be recognized and expressed in grams. It has been shown previously that the force of systolic excursion increases about 5% for each 1% increase in initial diastolic length (stretch) (5).

The systolic force commonly recorded at the time of surgical attachment of the arches was usually in the range of 50 g. This necessarily decreases in chronic experiments due to gradual loosening of the attachments with resulting decrease in initial diastolic tension. To adjust for this, the sensitivity of the oscillograph recordings must be increased. In all cases with these closed-chest observations, results are expressed in terms of percentage change rather than in grams force. It has been shown in experiments with stimulant drugs, that the percentage change is not greatly influenced by the initial diastolic tension in control periods, or, correspondingly, by the measured systolic force in control periods, so long as these features remained within the common ranges(3).

Preparation of the arch with metal-protected coil. The arch with electrical components enclosed in a hermetically sealed metal tube was constructed as shown in Fig. 1. The tubular encasement or body (E) was made of yellow brass, the flexible diaphragm end (J) was made of thin silicon-bronze and the elastic member (H) with integral rigid leg was made of heat-treated beryllium copper. The brass button or foot (I) was soldered to this leg. The lead wires, specially selected to withstand frequent bending, were made of 14 strands of 1-mil copper wire covered with a vinyl chloride sheath and commercially designated as Tensolite W 1748(6). A particular feature of this completely insulated device is its lack of interference with simultaneous ECG recordings.

Operative technic. The operations were performed under pentobarbital anesthesia with positive pressure mechanical respiration and with liberal administration of antibiotics. The chest was entered anteriorly through the

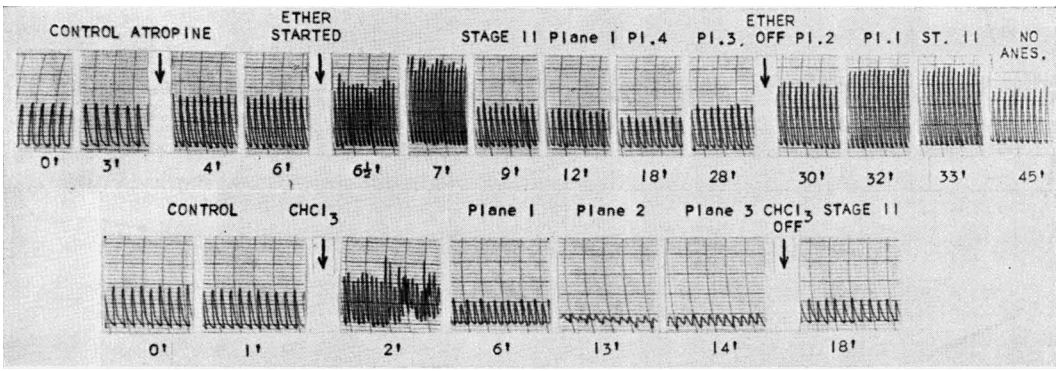

FIG. 2. Oscillograph recording of heart contractile force in chronically operated dog. Excursion amplitude is directly proportional to force. Anesthesia level (above) defined according to Guedel. Time (below) indicated in minutes. Ether anesthesia and chloroform anesthesia administered on successive days. Both experiments show increased and irregular force and rate during early struggling stage. Chloroform depression of contractile force is conspicuously greater than that with ether. During recovery from ether (in lighter planes of Stage III and in Stage II) there was a pronounced increase in contractile force considerably above control levels. This effect was frequently seen during recovery from anesthesia with all agents except chloroform and was tentatively ascribed to a sympatho-adrenal discharge.

fourth left intercostal space, the heart rotated to fully expose the anterior aspect of the right ventricle and the pericardium resected over this area. The arch was attached to the anterior surface of the right ventricle by cotton thread sutures, one set near the A-V sulcus and the other near the septum. Two or 3 sutures were laid at each point, threaded through the drilled holes in the feet of the arch and tied. Lead wires were brought out through the operative wound, the chest closed and aspirated. Chief complications in order of occurrence were adhesions, tearing out of sutures and breaking of lead wires. These complications were ordinarily diagnosed readily from the character of the tracing. The diagnosis was facilitated by the administration of epinephrine "test doses" of 0.5 to 1.0 γ/kg intravenously.

Results. The method has been used to measure heart force produced in the intact animal by cardiac glycosides(7), by hyperthermic agents(8), and by sympathomimetic amines(9). It is peculiarly suited to measure changes in heart force during the transitions of general(10) and spinal anesthesia(11), since it smoothly records the force of each contraction during the normal, conscious state as well as during anesthesia. Fig. 2 illustrates changes during induction and recovery from anesthesia with ether and, later in the same animal, with chloroform.

Summary. A strain gauge arch has been described which measures heart force changes in fully conscious, chronically operated dogs. Enclosure of the electrical component in a metal casing prevents insulation breakdown in body fluids.

1. Garb, S., *J. Pharmacol. and Exp. Therap.*, 1951, v101, 317.
2. Robb, J. S., *Am. J. Physiol.*, 1952, v171, 365.
3. Cotten, M. deV., *Am. J. Physiol.*, 1953, v174, 365.
4. Baldwin-Lima-Hamilton Corp., Philadelphia 42, Pa.
5. Walton, R. P., Cotten, M. deV., Brill, H. H., and Gazes, P. C., *Am. J. Physiol.*, 1950, v161, 489.
6. Tensolite Insulated Wire Co., Tarrytown, N. Y.
7. Walton, R. P., and Gazes, P. C., *South. Med. J.*, 1951, v44, 418.
8. Goldberg, L. I., Ezell, H. K., and Walton, R. P., *Am. Heart J.*, 1952, v44, 754.
9. Gazes, P. C., Goldberg, L. I., and Darby, T. D., *Circulation*, in press.
10. Boniface, K. J., Brown, J. M., and Kronen, P. S., to be published.
11. Richardson, J. A., and Walton, R. P., *J. Pharmacol. and Exp. Therap.*, 1953, v107, 141.

Received June 24, 1953. P.S.E.B.M., 1953, v84.

Effect of Antibiotic Dosage on Mortality from Whole Body X-Irradiation.* (20613)

GORDON E. GUSTAFSON AND SIMON KOLETSKY.
From the Institute of Pathology, Western Reserve University School of Medicine.

A large amount of data has accumulated on the effect of antibiotics on radiation injury. In general these drugs have been found to be slightly or moderately effective in reducing mortality. Varying amounts of antibiotics have been given at different intervals prior to and following radiation. This report is concerned with the effect of antibiotic dosage on the mortality from whole body x-irradiation.

Exp. 1. One hundred white male rats of the Wistar strain having a mean weight of 221 g, were separated randomly into 5 groups of 20 each. One untreated group served as a control while the 4 remaining groups received terramycin hydrochloride daily in amounts of 0.2 mg, 2.0 mg, 20 mg, or 200 mg, respectively. The antibiotic was given by stomach tube in a 2 cc aqueous solution beginning 72 hours and ending one to 4 hours prior to

* This work performed under contract between the U. S. Atomic Energy Commission and Western Reserve University. Terramycin furnished by courtesy of Chas. Pfizer and Co., Brooklyn, N. Y.