TABLE I.
Mitotic Activity in the Hypophysis of Rats.

Group		No.	Age, avg and range, days	Mitoses per mm² Mean ± S.E.
1	Pregnant 6-8 days with estrogen	9	92 (89-93)	17.33 ± 3.27
2	Pregnant 12-15 days with estrogen	13	94 (83-106)	4.35 ± 1.41
3	Pregnant without estrogen	3	95 (94-98)	.72 ± .64
4	Ovariectomized with estrogen	10	83 (76-90)	22.09 ± 5.46

the injected ovariectomized Group 4. In comparing Groups 2 and 4, the difference is definitely significant statistically ($P. < .01$).

The 3 animals not receiving injections and killed on the 13th day have an average mitotic activity of .72. This is essentially the same as the low mitotic activity found previously in somewhat older animals after the 3rd day of pregnancy[3] and is also not significantly different from the average found in ovariectomized animals of the same age.[2]

The results show that during pregnancy something is produced that, in most cases, suppresses the mitosis-stimulating effect of estrogen. The fact that the suppression does not occur until after implantation suggests that the placenta produces the inhibiting substance. Since, in some cases, the mitotic activity in the hypophysis is not suppressed, it is necessary to assume either that the inhibiting effect may be overcome or that the cells of the hypophysis are less refractory to mitosis-stimulating substances in some animals.

15742

The Use of a Resistance Wire, Strain Gauge Manometer to Measure Intraarterial Pressure.

EDWARD H. LAMBERT AND EARL H. WOOD.
From the Acceleration Laboratory and Section on Physiology, Mayo Foundation, Rochester, Minn.

For use in measurement of intraarterial pressure in man under ordinary circumstances in the laboratory or clinic, the high frequency hypodermic manometer developed by Hamilton and his associates[1] has not been excelled in respect to its combination of accuracy and simplicity of operation. In certain unusual situations, however, this manometer is inconvenient to use, because it must be rigidly fixed with respect to the recording camera and records must be made within a few feet of the subject. Attempts to overcome these disadvantages have led to development of means of converting pressure to electrical energy,[2-4] so that arterial blood pressure might be recorded with more freedom at some distance from the subject by means of a galvanometer. The purpose of this paper is to describe the use of a resistance wire, strain gauge pressure transmitter to accomplish electrical translation in measurement of arterial blood pressure.

The strain gauge pressure transmitter[*,5] consists of a balanced Wheatstone bridge

1 Hamilton, W. F., Brewer, G., and Brotman, I., *Am. J. Physiol.*, 1934, **107**, 427.

2 Rein, H., *Arch. f. d. ges. Physiol.*, 1940, **243**, 329.

3 Hampel, A., *Arch. f. d. ges. Physiol.*, 1940, **224**, 171.

4 Lilly, J. C., *Rev. Scient. Instruments*, 1942, **13**, 34.

* Manufactured by Statham Laboratories, 8222 Beverly Blvd., Los Angeles, Calif.

5 Meyer, R. D., *Instruments*, 1946, **19**, No. 3.

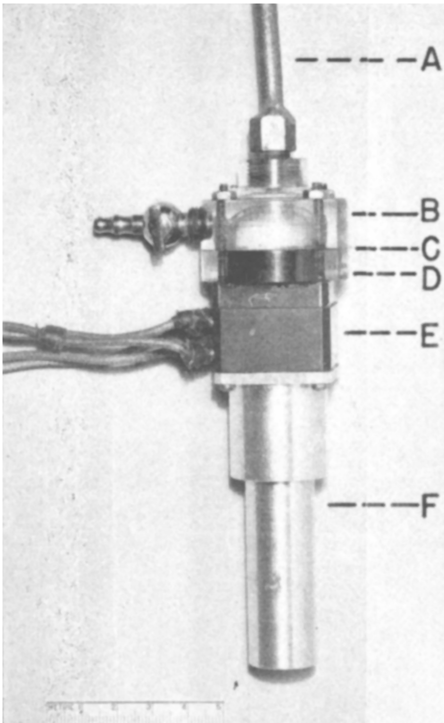

FIG. 1.
Strain gauge pressure transmitter adapted for measurement of arterial blood pressure. A. Lead tube to which needle is attached. B. Lucite chamber filled with anticoagulative solution. Stopcock for fluid reservoir. C. Plastic membrane (Koroseal). D. Lucite chamber filled with oil. E. Case containing strain gauge. Wires lead to battery and galvanometer. F. Holder.

whose 4 elements are made up of strain sensitive wire. The 4 wires are mounted on a cantilever suspension, movement of which increases the strain on one pair of wires and decreases it on the other. Since the resistance of the wires changes with variation in strain, movement of the suspension destroys the balance of the bridge and causes current to flow in the output circuit. The magnitude of the current is directly proportional to the amount of movement of the suspension. The bridge may be powered by dry cells (6 to 20 volts) and the output current measured by means of a microammeter or suitable recording galvanometer. No amplification is necessary. In utilizing this device as a pressure transmitter the cantilever suspension is connected to a bellows or diaphragm. Movement of the bellows or diaphragm caused by application of fluid or gas pressure alters the strain on the bridge circuit so that the amount of pressure applied can be determined by measuring the output current.

In order to adapt the pressure transmitter for use in measurement of blood pressure, the housing which surrounds the bellows through which pressure is transmitted to the strain sensitive wires has been replaced by a cylindric lucite chamber (Fig. 1). The latter is filled under vacuum with nonvolatile oil (evacuated hydraulic fluid) and is separated from a second lucite chamber by means of a loose plastic membrane (Koroseal). To the second chamber is attached a lead tube and needle used for arterial puncture and a stopcock which leads to a fluid reservoir. This system is filled with anticoagulative solution consisting of air-free solution of 0.9% sodium chloride containing 20 mg of sodium heparin per liter. Use of oil in the first chamber prevents corrosion of the metal bellows by the action of the anticoagulative solution. Isolation of the first chamber from the second by means of a plastic membrane eliminates the possibility that air bubbles may become lodged in the folds of the bellows whenever the manometer is filled and washed with anticoagulative fluid.

Strain gauge pressure transmitters which have several ranges of sensitivity are manufactured. The gauge which has been used for measurement of arterial blood pressure has a closed circuit output of about 14 microamperes for a pressure equivalent to 100 mm of mercury (bridge resistance 273 ohms) over a total range of $\pm$ 780 mm of mercury. With use of this gauge, a lead tube $\frac{1}{8}$ inch (0.3 cm) (inside diameter) by 18 inches

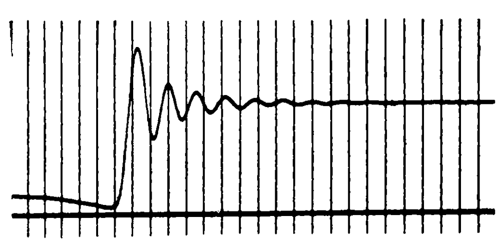

FIG. 2.
Natural frequency of strain gauge manometer with 18-inch lead tube and 19-gauge needle. Time interval is 0.01 second.

TABLE I.
Natural Frequency of Manometers Using Various Strain Gauge Pressure Transmitters.

Strain gauge No.	Full scale range, mm Mercury	Needle* gauge	Natural frequency, cycles per second	
			18-inch lead tube†	No lead tube
PV-107	± 780	19	63	78
		17	80	106
P6-8D-350	± 415	19	29	33
		17	33	50
P6-4D-250	± 208	19	20	25
		17	24	36

* 1¼ inches in length.
† ⅛ inch internal diameter.

(45.7 cm) and a 19-gauge needle 1¼ inches (3.2 cm) long, the natural frequency of the manometer is about 60 cycles per second (Fig. 2) as determined by the method described by Hamilton and his co-workers.[1] The displacement of fluid into the needle is about 0.5 cu mm when a pressure of 100 mm of mercury is applied.

More sensitive strain gauge pressure transmitters are available, such as those which have a total range of ± 415 mm of mercury or ± 208 mm of mercury, but their fluid displacement is greater and the natural frequency of the manometer using these gauges is considerably lower than that described in preceding sentences (Table I).

The galvanometer which has been used with the pressure transmitter is the Type A manufactured by the Heiland Research Corporation.† The natural undamped frequency of this galvanometer is 40 cycles per second. When critically damped, its deflection is within ± 3% of the true response up to a signal frequency of about 35 cycles per second but falls to 50% at about 60 cycles per second. With the galvanometer located 2 meters from the recording camera, the sensitivity of the entire manometer system is such that a deflection of 50 mm is equivalent to a pressure of 100 mm of mercury. The calibration of the system is strictly linear throughout its range and is stable so long as the voltage of the batteries is maintained. Hysteresis is approximately 0.5%. Moderate changes in temperature have only a negligible effect on the system.

† Heiland Research Corporation, 130 East Fifth Avenue, Denver, Colo.

With the exception that recording is done by galvanometer, the technics and precautions used in measuring pressure with the strain gauge manometer are the same as those employed with the Hamilton manometer.[1] However, because of the relatively large volume of fluid which enters the strain gauge manometer when pressure is applied, special care has been taken to avoid clotting of blood which enters the needle while measurement of blood pressure is being made. The bore of the stainless steel needle is polished by drawing through it a thread impregnated with thick grease containing fine emery dust. Before the needle is used, its inside surface, particularly near the point, is coated very thinly with paraffin. While the needle is in the artery, it is flushed periodically with a very small quantity of sterile anticoagulative solution. With these precautions, pressures have been measured continuously for more than an hour.

The disadvantage of the strain gauge manometer which has been described herein is the low natural frequencies of the manometer and the galvanometer. To determine the limitation which this may impose on use of the strain gauge manometer, the accuracy of this manometer for recording arterial blood pressure has been tested by comparison with a Hamilton manometer which had a natural frequency of 115 cycles per second. Simultaneous recordings obtained by use of the 2 manometers in studies on dogs have demonstrated that the strain gauge manometer accurately records normal peripheral pulses (Fig. 3), but that it may introduce instrumental errors in recording more abrupt cen-

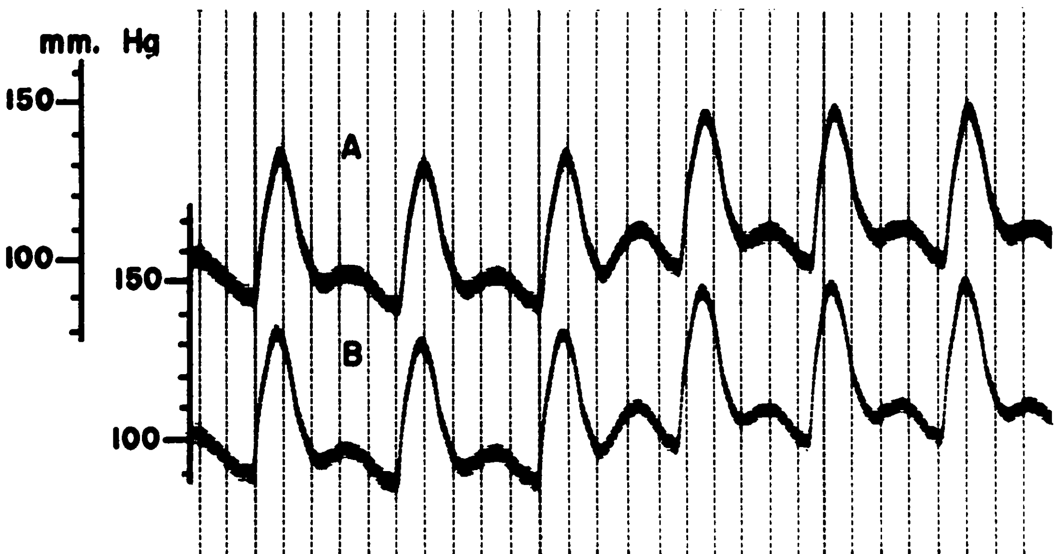

FIG. 3.
Femoral arterial blood pressure of a dog recorded simultaneously by Hamilton manometer (A) and strain gauge manometer (B). Time interval is 0.1 second.

tral pulses as, for example, those of the common carotid artery. For this reason the strain gauge manometer cannot be recommended for the study of arterial blood pressure and pulse wave forms in clinical investigations in which the Hamilton manometer can be employed.

To increase the natural frequency of the strain gauge manometer would require sacrifice of its sensitivity. Because of the limited sensitivity and the low frequency response of recording devices presently available, the use of electronic amplifiers would then be necessary to obtain satisfactory records. Other arrangements of strain sensitive, resistance wire designed for use with amplifiers have been employed in physiological research,[6] but their suitability for recording arterial blood pressure has not yet been reported.

In its present stage of development, however, the strain gauge manometer which has been described herein is useful for measuring the pressure in peripheral arteries in situations in which electrical translation is necessary. For example, this manometer has been

[6] Grundfest, Harry, Hay, J. J., and Feitelberg, Sergei, *Science*, 1945, **101**, 255.

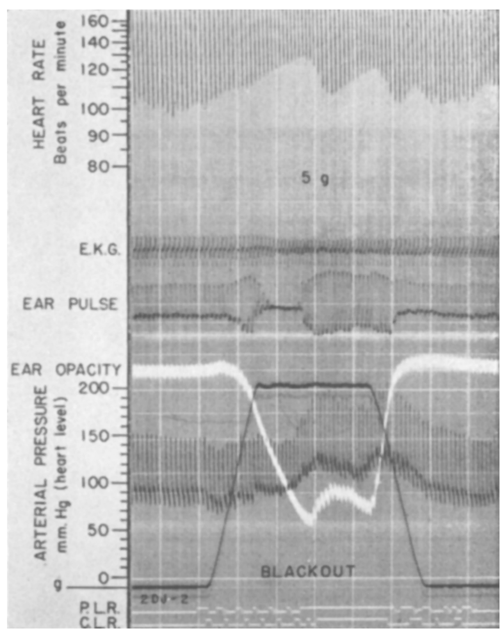

FIG. 4.
Arterial blood pressure and other physiologic variables in man during exposure to centrifugal force (g). Pressure measured in radial artery with wrist at heart level by means of strain gauge manometer. Vertical white lines are spaced at intervals of 5 seconds. P.L.R. and C.L.R. show subject's response to light signals in peripheral and central fields of vision.

useful in determining the changes in arterial blood pressure which occur in man during exposure to centrifugal force on a human centrifuge[7,8] (Fig. 4). In this case the output current of the strain gauge was carried from the rotating centrifuge through mercury ring contacts and recorded in another room about 60 feet from the subject.

Summary. The use of a resistance wire strain gauge to convert pressure to electrical energy in making direct measurements of arterial blood pressure is described. The electrical circuits involved are simple. Recording is by means of a galvanometer without the use of electronic amplifiers. The calibration of the manometer is linear, stable and relatively insensitive to temperature changes. The natural frequencies of the manometer and galvanometer are 60 and 40 cycles per second, respectively.

Addendum. Manometers constructed with strain gauges of a more recent model (P6-15D-250, serial No. 275) have natural frequencies up to 100 cycles per second when fitted with an 18-inch (45.7 cm) lead tube and a 19-gauge needle. Their sensitivity has remained the same as that of previous strain gauge manometers.

7 Lambert, E. H., and Wood, E. H., *Fed. Proc.*, 1946, **5**, 59.

8 Wood, E. H., Lambert, E. H., Baldes, E. J., and Code, C. F., *Fed. Proc.*, 1946, **5**, 327.

15743

Sodium Cyanide: Time of Appearance of Signs as a Function of the Rate of Injection.*

ARTHUR A. WARD, JR. (Introduced by W. S. McCulloch.)

From the Department of Psychiatry, University of Illinois College of Medicine, Illinois Neuropsychiatric Institute, Chicago, Ill.

The effects of sudden intravenous injections of NaCN in animals have been described elsewhere.[1] On the basis of both human and animal studies,[2] certain conclusions have been drawn as to the probable detoxification rate for this compound based on the assumption that this rate is constant. Because of possible therapeutic applications, it is important to determine in what manner the body responds to slow, constant infusions of dilute solutions of the sodium salt of cyanide, and whether the detoxification rate varies as a function of the rate of injection.

Method. Experiments were carried out on cats of about 2 kg paralyzed with dihydro-beta-erythroidine hydrobromide† (10 mg *i.v.* followed by about 0.1 mg per min. continuously) and maintained on artificial respiration at 25 strokes/min. of 35 cc/stroke. The skull was laid bare and the electrical activity of the cortex obtained with skull electrodes was recorded with a 6-channel, ink writing Grass oscillograph, the EKG being recorded with the same apparatus, using the conventional leads. Changes in the oxygen tension of the cortex were concurrently recorded.[3] NaCN was injected continuously‡ by an accurately calibrated 50 cc syringe driven by a synchronous motor, delivering from 0.033 ml/min. to 0.54 ml/min. By

* The work described in this paper was carried out under a contract between the Medical Division, Chemical Corps, U. S. Army, and the University of Illinois College of Medicine.

1 McCulloch, W. S., and Wheatley, M. D., in press.

2 Loevenhart, A. S., Lorenz, W. F., Martin, H. G., and Malone, J. Y., *Arch. Int. Med.*, 1918, **21**, 109; Loevenhart, A. S., Malone, J. Y., and Martin, H. G., *J. Pharm. and Exp. Therap.*, 1922, **19**, 13.

† The author wishes to thank Merck & Co. who kindly supplied this drug.

3 Davis, E. W., McCulloch, W. S., and Roseman, E., *Am. J. Psychiat.*, 1944, **100**, 825.

‡ The author wishes to thank Dr. R. K. Richards of the Abbott Laboratories who loaned to us this apparatus.