tion is the sole factor explaining the differences in the results which are obtained when the entire gastro-intestinal tract, or only a segment of this is used. The rapidity of emptying of the stomach and the motility of the small intestine may also be factors. When a jejunal segment is used no relationship exists between body weight and the rate of absorption of glucose while Cori[2] and Trimble, Carey and Maddock[4] have found that such a relationship exists when the gastro-intestinal tract is used as a physiological unit. This relationship must depend upon the rate of passage of the glucose solution into the small bowel or to differences in the rate of absorption from that portion of the intestine which acts as the absorbing membrane.

Conclusions. Data have been presented which demonstrate the rapidity with which solutions of glucose of varying concentrations when placed in the stomach of the dog are changed, so that when the solutions reach the small intestine the variations in the concentrations are of a small order. These findings may in part explain the differences in the rate of absorption when the gastro-intestinal tract is used as a physiological unit and when only a single segment of this unit is utilized.

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Bloodless Method for Recording Respiration and Quantitative Determination of Alterations of Sensation in Small Animals.

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Schmitz and Loevenhart[1] published a method for judging the onset and duration of anesthesia in the sciatic nerve of rabbits by the disappearance of changes in respiration when the distal portion of the nerve was stimulated. They recorded the respiration with a tambour attached to a cannula introduced into the trachea.

In order to study anesthesia (general, local and spinal) analgesia and hyperalgesia in small laboratory animals, without performing surgical operations, we have devised the apparatus shown in Fig. 1.

[4] Trimble, H. C., Carey, B. W., and Maddock, S. J., *J. Biol. Chem.*, 1933, **100**, 125.

[1] Schmitz, H. L., and Loevenhart, A. S., *J. Pharmacol. and Exp. Therap.*, 1924, **24**, 159, 167.

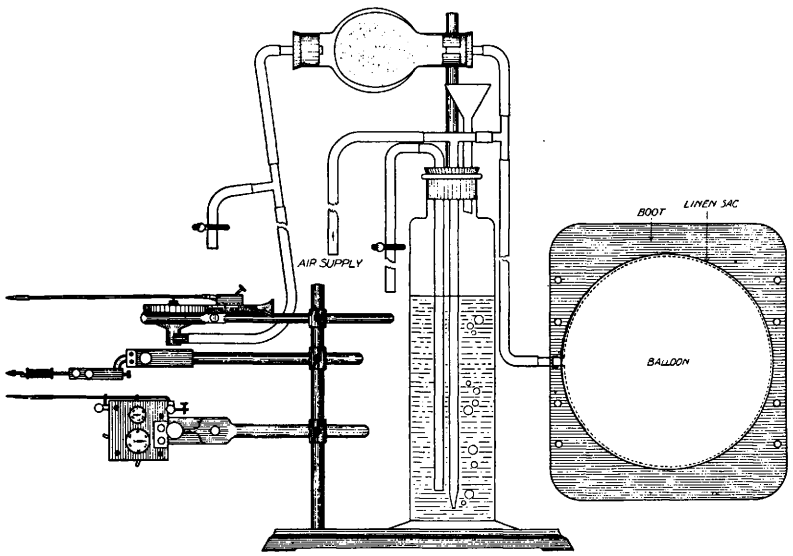

FIG. 1. Apparatus for bloodless registration of respiration.

The respiration is recorded using a modified blood pressure cuff which is laced around the chest and abdomen and connected with a tambour in the manner described below. Ordinary platinum electrodes are applied to the shaved skin (moistened with 0.9% NaCl) over the area to be tested. The stimulus is furnished by induction shocks from a Harvard induction coil, either faradic or break shocks being used. The coil distance is noted, so as to furnish a fairly quantitative measure of the stimulus.

For purposes of comparison, the threshhold of sensation can be taken as the minimal stimulus which causes a definite change in amplitude or rate of respiration.

The elastic sac of the respiration cuff for rabbits consists of a small toy balloon 18 cm. in diameter, covered with a linen sac (Fig. 1). The sac is placed inside of an ordinary tire boot through which a hole is made for the tube leading to the recording apparatus. The tire boot bears lacings and is applied to the animal's chest and abdomen. The rubber sac is connected by a rubber tubing and a T tube whose one branch inflates a rubber condom enclosed in a glass bulb. The other branch of the T tube is connected with a pressure bottle in which the pressure is kept constant by a slow stream of compressed air provided with a water valve maintaining about 15 cm. H_2O pressure as shown in the figure. Respiration movements are transmitted by pulsations of the condom to the air space in the glass bulb surrounding it and from this through a rubber tube to

a recording tambour. The purpose of the air valve in the pressure system is to insure a rapid return of the condom to its original volume after the animal moves or breathes violently.

Similar cuffs for recording the respiration of rats, guinea pigs, and probably mice, can be made by using 2 thicknesses of adhesive plaster plastered together, and provided with laces at opposite edges.

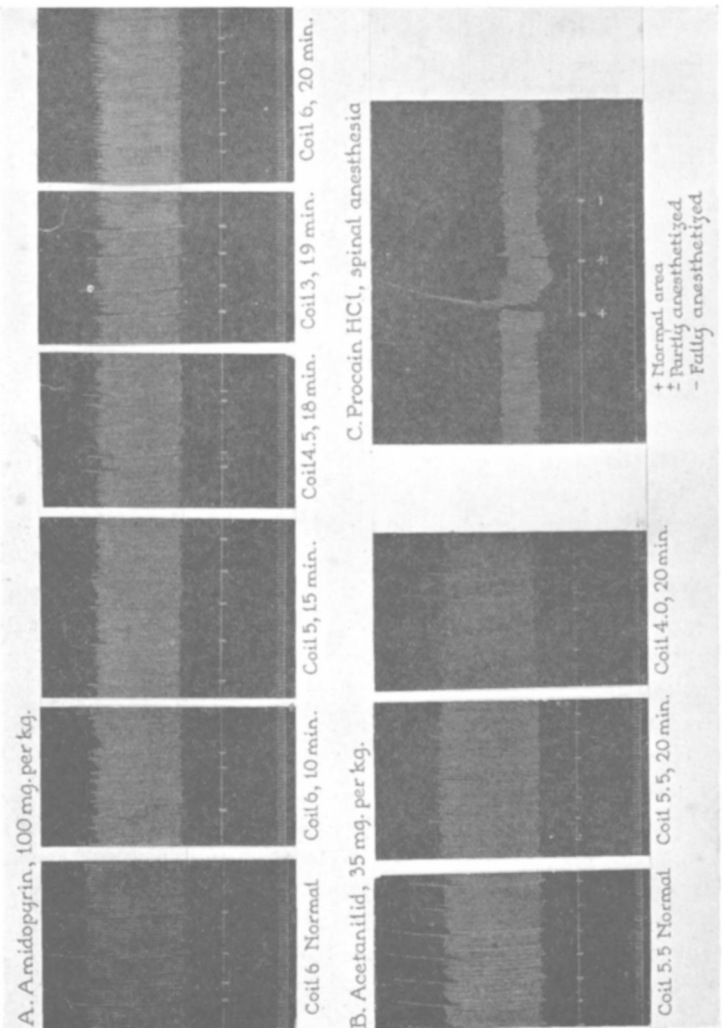

FIG. 2. Respiratory tracings.

A. Effects of amidopyrin at various intervals after injection and the coil distances of the stimuli used.
B. Effects of acetanilid.
C. Effects obtained in spinal anesthesia, when stimuli at same coil distances were applied over three different skin areas.

For such cuffs children's small toy balloons or finger cots provide the elastic sac. The pressure and recording apparatus is the same as for rabbits, the pressure in the cuff being adjusted to give the desired amplitude of recording.

By this method we have been able to study quantitatively the effects of analgesic drugs.

100 mg. amidopyrine (5% aqueous solution) per kilo subcutaneously raised the threshhold stimulus for brief faradic shocks with a Harvard induction coil from a normal of 6 cm. coil distance to 4.5 cm. (Fig. 2a). 35 mg. per kilo acetanilid raised it from 5.5 cm. coil distance to 4.75 cm. (Fig. 2b). Neither of these drugs caused any definite narcosis.

On the other hand, Hirschfelder and Cunningham[2] using the same method have found that 52 mg. morphine sulphate per kilo raises the threshhold of respiratory response from 6 cm. coil distance to 3 cm. and 50 mg. sodium amytal per kilo, raised it from normal of 6 cm. to only 5 to 5½ cm., although the animals were definitely soporous.

These findings harmonize well with the clinical observation that though the coal tar antipyretics and morphine relieve pain, the barbitals, sulphonal series, and most synthetic soporific drugs induce sleep but do not allay pain.

We believe that this method of testing affords the first satisfactory method for testing analgesic action quantitatively in laboratory animals. We have also used a similar method for determining sensitivity to pain in human beings, applying the electrodes to the mucous membranes on the inner aspect of the lip and determining both the stimulus which just produced a pain sensation and the stimulus at which the painful sensation became unbearable. Experiments on a small number of medical students indicated that an 0.6 gm. dose of acetphenetidin by mouth decreased both these stimuli by 0.5 to 1.0 cm. coil distance, *i. e.*, definitely increased the threshhold stimulus.

Our method is particularly well adapted for testing the onset and duration of local and spinal anesthesia. Rose[3] has used the minimal stimulus from a Harvard induction coil which just causes movement for testing local anesthesia with intracutaneous injections in the guinea pig. For this purpose our method furnishes a much more delicate index. We have also found it very satisfactory for testing the onset, degree, duration, subsidence and distri-

[2] Hirschfelder, A. D., and Cunningham, R. W., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 866.

[3] Rose, C. L., *J. Lab. and Clin. Med.*, 1929, **15**, 128.

bution of spinal anesthesia in rabbits (Fig. 2c). This subject is being investigated by Bieter and Ridges.[4]

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Variability Due to Technique of the Sedimentation Index.

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The striking variation in sedimentation rate as between individuals has led us to devote considerable attention to an analysis of this phenomenon. Studies of the influence of the technique employed and the interrelationships of the results by those techniques are proving fruitful in revealing important biological measures. Discussion of these results is being reserved until more extensive data can be accumulated, but it seems advisable at this stage to publish a note on the trustworthiness of a single determination of the sedimentation index.

Of fundamental importance at all times in the interpretation of the data of observation or experimentation is a knowledge of the variability to be expected in replicate measures of the same type. Not infrequently the worker in the fields of the so-called "exact sciences" is able to estimate *a priori* and from theoretical premises the error attaching to any method. Such estimates cannot, of course, be accepted as valid until verified in practical work, a fact which is all too often neglected. The biological worker can rarely follow such a procedure, if for no other reason than that the organism itself contributes an amount to the variability which can only be determined by the critical mathematical analysis of actual results.

Many techniques of making the sedimentation test have been in use during the past 10 years, but since the Cutler,[1] the Linzenmeier,[2] and Westergren[3] methods have had the greatest number of followers, the present discussion will be limited to these methods.

The extent to which any single measure, or average of replicate measures of blood sedimentation is reliable as a basis of generaliza-

[4] Bieter, R. N., and Ridges, A. H., unpublished experiments.

[1] Cutler, J., *Am. J. Med. Sci.*, 1926, **171**, 882; *Am. Rev. Tuberc.*, 1929, **19**, 544.

[2] Linzenmeier, G., *München med. Wchnschr.*, 1923, **120**, 1243.

[3] Westergren, A., *Am. Rev. Tuberc.*, 1926, **14**, 94.