Progress Report

Effect of Changes in Blood Volume on Body Impedance

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Loss or gain of blood in amounts as small as 3 per cent of the estimated total blood volume was detected by an electronic instrument, in animals ranging in weight from 2.0 to 30.0 kg. The principle of the instrument is based on the detection of a change in body impedance when blood enters or leaves the body confines. Infusion of normal saline produced a 50 per cent greater change in body impedance than infusion or removal of whole blood. Electrocardiographic potentials and changes in body impedance due to respiration may also be detected and recorded apart from the changes in blood volume. Stability, linearity and freedom from artifact are satisfactory and the instrument would seem to offer a potential method for instantaneous detection of surgical blood loss.

We have previously reported on an electronic method of detecting changes in total blood volume.[1] This method, based on electrical impedance plethysmography, enabled us to detect changes in blood volume of approximately 5 to 10 per cent of the total blood volume, in animals ranging in size from 2.5 to 27.0 kg. At the suggestion of one of us (G. I. J.), the electronic circuitry has been modified in a way such that the sensitivity is at least five-fold greater and the stability greatly improved. This report will deal with the initial results obtained on laboratory animals using the improved circuitry.

Material and Methods

Electronic Apparatus. Figure 1 is a block diagram of the electronic circuitry. The apparatus works as follows: A 1 kc. square wave generator presents a 200 microampere peak to peak square wave signal to the summing point of amplifier 1. The animal is placed in the negative feedback path of this amplifier via two subcutaneous needle (current) electrodes placed as widely apart as possible, *e.g.*, from occiput to hind leg. The capacitor in the circuit blocks direct current and helps prevent polarization of the electrodes while the amplifier assures that regardless of impedance, the 200 microampere peak to peak current flowing through the animal is constant. Since the peak to peak current is truly constant, then the voltage detected by the potential electrodes will be directly proportional to that impedance. According to Ohm's law, $E = IR$ and $I = K$ (constant) so $E = KR$ and R is the independent variable. R (the impedance of the animal) will be inversely proportional to changes in total blood volume. To detect this impedance two potential electrodes are connected to the animal at a point about 1 inch proximal to each of the input (current) electrodes. These electrodes are connected to a high gain, high input impedance, low level amplifier capable of passing a 1 kc. signal with a bandwidth of at least 200 cps. For this purpose, the Tektronix Type 2A61 oscilloscope preamplifier was quite suitable and this is shown in the block diagram as the amplifier connected to the potential electrodes. Detection is via these two additional electrodes to eliminate the effect of electrode polarization impedance which might occur at the current carrying electrode-tissue interface. Such potentials can appear as artifacts indistinguishable from the physiological signals. The differential input characteristic of this amplifier also minimizes detection of the 60 cps. and radio frequency common mode signals usu-

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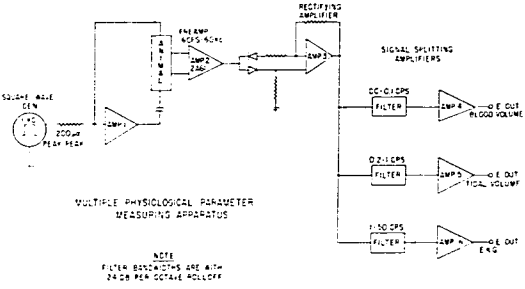

FIG. 1. Block diagram of electronic circuitry.

ally present in the environment where physiological measurements are made.

The amplified 1 kc. square wave output of the 2A61 amplifier is then full-wave rectified in an operational amplifier circuit (amplifier 3 in the block diagram). The output of this amplifier is a d.c. signal with 2 kc. "spikes" present from rectification. These are easily filtered electrically. The absolute d.c. level will vary with three entities: (1) the changing impedance caused by blood volume changes, (2) the changing impedance caused by respiration, and (3) the electrocardiographic potentials. Fortunately, the frequencies of these signals are sufficiently different to be separable by electrical filtering. The output of amplifier 3 is fed to amplifiers 4, 5, and 6. Each of these amplifiers incorporates filters to tailor the bandpass to that required to pass only one of the three physiological signals. Amplifier 4 has a bandpass from 0 to 0.1 cps., suitable for monitoring the d.c. impedance of the animal which is proportional to blood volume. It rejects those frequencies above 0.1 cps. which includes the ECG and respiration signals. Amplifier 5 passes frequencies from 0.2 to 1 cps. which is appropriate for the respiration signal but not for the blood volume and ECG signals. Similarly, amplifier 6 passes frequencies from 1 to 50 cps. thus providing ECG but not blood volume or respiration. The gain of each of these amplifiers can be adjusted to make the signal amplitude appropriate for the recorder used. Each signal at the output can, if desired, be made approximately the same peak amplitude.

Animal Experiments. Five cats weighing from 2.0 to 3.0 kg. and 7 dogs weighing from 12 to 30 kg. were studied. General anesthesia was induced with thiopental in the dogs and chloroform in the cats. Anesthesia was maintained in both groups by endotracheal halothane nitrous oxide-oxygen with respiration controlled by a Bird respirator. A femoral vein was cannulated for bleeding and reinfusion, and the input (current) and output (potential) electrodes consisted of 18 gauge 1½ inch needles. The usual locations for the current electrodes were on the occiput and one of the hind legs. The potential electrodes were placed about 1 inch proximal to the current electrodes. Blood was removed in amounts of up to 300 ml. in increments of 20 to 50 ml. in the dogs, and 30 ml. in increments of 5 to 10 ml. in the cats, using heparinized syringes. The output of the blood volume and tidal volume amplifiers described above were each connected to a Heathkit * penwriter. In one cat and one dog withdrawn blood was replaced by the same amount of normal saline. In all animals checks of stability were made for periods of up to one hour duration during which time no bleeding or fluid infusion was carried out.

Results

Bleeding or reinfusion in all animals caused a prompt and reproducible impedance change. Changes as small as 3 per cent of the total blood volume (estimated as 7 per cent of body

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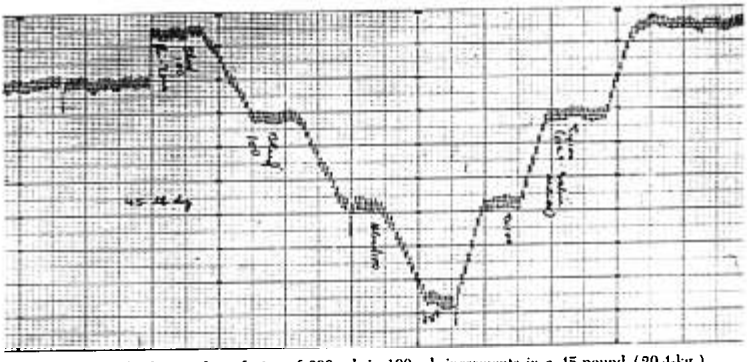

FIG. 2. Bleeding and reinfusion of 300 ml. in 100-ml. increments in a 45-pound (20.4-kg.) dog. Record obtained with a Heathkit penwriter. Time scale: 1 minute = 2 large divisions. Baseline was re-zeroed just before bleeding to permit display of entire record. Superimposed sawtooth pattern is caused by respiration which was controlled by a Bird respirator. Occasional downward spikes are due to spontaneous breathing. 100 ml. is approximately 7 per cent of the estimated total blood volume.

weight) were easily detected. Figures 2 and 3 show representative records obtained as a result of bleeding and reinfusion in a 20.4-kg. dog and a 2.5-kg. cat. The superimposed sawtooth pattern was caused by changes in intrathoracic volume owing to respiration. In all instances there was good linearity and return to baseline with reinfusion. Removal of more than 20 per cent of the estimated total blood volume was usually avoided to prevent hemorrhagic shock.

Figure 4 is a record obtained as a result of slow removal of 20 ml. of blood from a 2.0-kg. cat, bleeding required approximately 6 minutes. Rapid reinfusion of the blood resulted in prompt return of the recording to baseline.

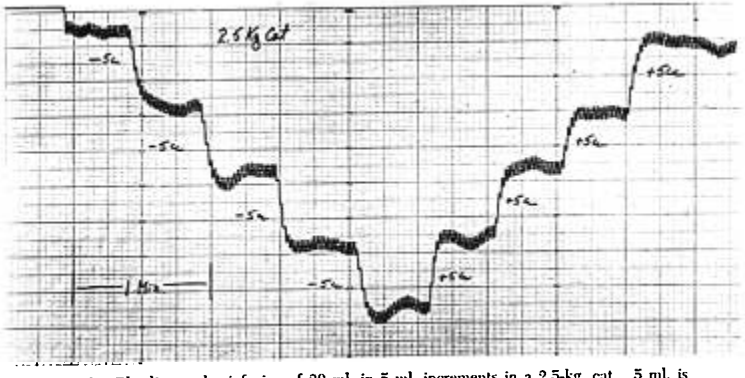

FIG. 3. Bleeding and reinfusion of 20 ml. in 5 ml. increments in a 2.5-kg. cat. 5 ml. is approximately 3 per cent of the estimated total blood volume.

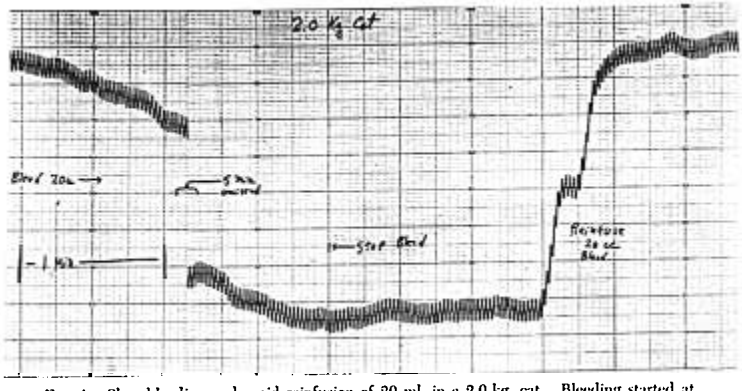

FIG. 4. Slow bleeding and rapid reinfusion of 20 ml. in a 2.0-kg. cat. Bleeding started at left hand edge of record and took approximately 6 minutes.

Figure 5 shows the difference in body impedance changes caused by blood withdrawal versus changes caused by infusion of the same amount of normal saline. The record is from a 12.0-kg. dog and shows that infusion of 50 ml. of normal saline produces a change in impedance approximately 50 per cent greater than removal of 50 ml. of blood. The same experiment was performed on one cat, and the same relationship between saline and blood held, that is, a 10-ml. saline infusion produced a 50 per cent greater change in body impedance than removal of the same amount of blood.

Figure 6 is a recording of the output of amplifier 5 and represents a spirographic tracing. The figures written on the record are readings from an Air Shields Ventimeter, with changes in volume resulting from changes in pressure settings of the Bird respirator. Changes in amplitude of the tracing with changes in tidal volume seem to be linear except at extremes

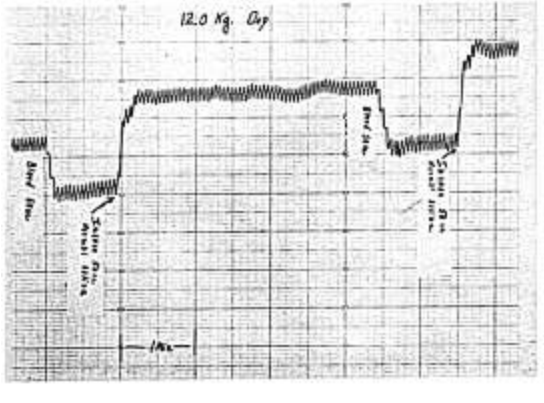

FIG. 5. Blood withdrawal versus saline reinfusion in a 12.0-kg. dog. Infusion of 50 ml. of normal saline produces a change approximately 50 per cent greater than removal of 50 ml. of blood.

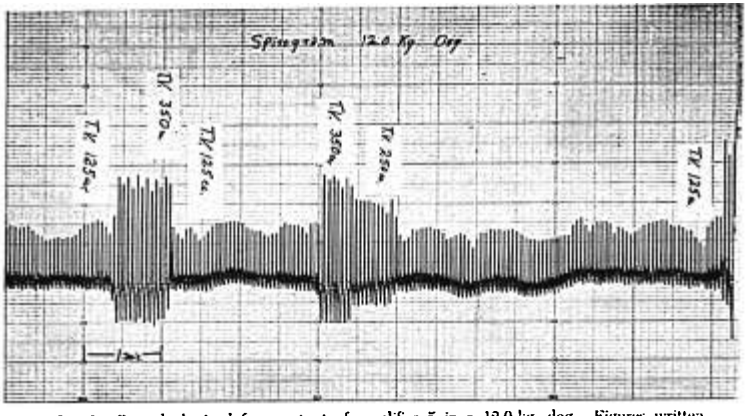

FIG. 6. Record obtained from output of amplifier 5 in a 12.0-kg. dog. Figures written above tracing indicate readings from an Air Shields Ventimeter, with changes in volume due to changes in pressure settings of Bird respirator.

of tidal volume, but we do not yet have enough data to support a definite conclusion.

Checks of stability with the equipment attached to a dummy load resistor equivalent to the approximate impedance of the animals (370 Ω as determined in previous experiments)[1] showed no drift in periods up to three hours. With the experimental animals connected to the equipment, checks of stability showed a maximum drift equivalent to a 3 per cent change in blood volume, in a one hour period in all animals except one cat. In this animal there was a pronounced, continuous drift in the same direction that would have been caused by bleeding. With replacement of the output electrodes with new needles and securing these needles firmly to the animal with adhesive tape, the drift was eliminated.

Discussion

The principle of the instrument described in this study is approximately the same as that described in our initial report[1]: body impedance is inversely proportional to the volume of conductive material available for the flow of electric current. If blood is removed from the confines of the body, the total body impedance increases. The inverse is true with blood infusion. The major difference between the apparatus described in this report and in our initial study is the use of a four terminal system, with constant current input and examination of the output signal by full wave rectification and measurement of the resulting d.c. level. A square wave input was selected because of the simplicity of generation and amplitude control of such a signal.

The primary purpose of the instrument is to detect changes in blood volume, thus the ability to measure respiratory volume and to detect electrocardiographic changes are added advantages. Measurement of tidal volume is a well known application of electrical impedance plethysmography and is discussed in an excellent review on physiologic electrical impedance by Geddes and Hoff.[2]

In any practical application of this method, it would be important to know the effect on body impedance of intravenous infusion of solutions other than whole blood. Our initial experiments indicate that infusion of normal saline produces a 50 per cent greater decrease in body impedance than does whole blood. This relationship agrees fairly well with the *in vitro* specific resistances of saline and whole blood[3, 4, 5] (approximately 112 ohm cm. for

normal saline at 37° C. versus 160 ohm cm. for normal human blood at 37° C. However, since a moving stream of blood is known to be more conductive than a stationary one,[6] the *in vitro* values for blood resistance may not hold. We intend to perform further experiments to determine the effects of various commonly used intravenous solutions on body impedance.

The sensitivity and linearity of this instrument offer great promise as a means of quantitation and instantaneous measurement of surgical blood loss. The problems of drift and artifact are not great, and can probably be minimized by good electrical shielding and secure electrode placement. We are now building a solid state model which we hope will enable us to carry our experimental work into the operating room.

Summary

An electronic instrument has been described which can detect blood volume changes as small as 3 per cent of the total blood volume in animals ranging in size from 2.0 to 30.0 kg. The principle of the instrument is based on the detection of a change in body impedance when conductive material enters or leaves the body confines. Infusion of normal saline produces a 50 per cent greater change in body impedance than infusion or removal of whole blood. Electrocardiographic potentials and changes in body impedance resulting from respiration may also be detected and recorded apart from the blood volume changes. Stability, linearity, and freedom from artifacts are satisfactory and the instrument would seem to offer a potential method for instantaneous detection of surgical blood loss.

References

1. Underwood, R. J., and Cowing, D.: An electronic method of detecting blood volume changes, ANESTHESIOLOGY 26: 199, 1965.
2. Geddes, L. A., and Hoff, H. E.: The measurement of physiologic events by electrical impedance, a review, Amer. J. Med. Electronics 3: 16, 1964.
3. Rosenthal, R. L., and Tobias, C. W.: Measurement of the electrical resistance of human blood; use in coagulation studies and cell volume determinations, J. Lab. Clin. Med. 33: 1110, 1948.
4. Wolf, A. V.: Aqueous Solutions and Body Fluids. New York, Hoeber Medical Division, Harper and Row, 1966, pp. 17–20.
5. Nyboer, J.: Electrical Impedance Plethysmography. Springfield, Ill., Charles C Thomas, 1959, Ch. IV, pp. 210–216.
6. *Ibid.*: Chapter IV, p. 215.

Anesthesia

UTERINE VASOCONSTRICTION Phenylephrine (0.05 mg.) was injected into dog fetuses *in utero* under conditions of maternal hypovolemia or normovolemia. In both cases fetal hypertension was observed with no change in fetal heart rate, fetal P_{O_2}, maternal blood pressure, heart rate or P_{O_2}. A previous study has shown that phenylephrine was injected into the hypovolemic mother will cause a fall in fetal heart rate and fetal P_{O_2}, and if injected into the normovolemic mother fails to change fetal P_{O_2} or heart rate. From these two studies it is concluded that fetal hypoxia following maternal phenylephrine injections during hypovolemia is secondary to the constrictive effects of the drug on the material side of the circulation. (*Linkie, D. M., and others: Fetal Effects of Phenylephrine Injection, Amer. J. Med. Sci. 252: 277 (Sept.) 1966.*)