of muscle tissues and of 3.3°C. in the temperatures of both portions of the bone under test.

Conclusions. These experimental data show that, in living animals, the temperatures of certain different types of tissues are affected to different degrees by the systemic application of the short-wave electric field. Muscle tissue is affected slightly more than is subcutaneous tissue; intra-articular tissue is affected more than is muscle tissue. Furthermore, it has been shown that the reactions of anesthetized animals to general hyperthermia produced by this physical agent (short electric wave fields) are quantitatively different from those produced in unanesthetized animals. Measurements of temperatures of tissues of dead animals have shown that bone is heated much more markedly than is muscle tissue and they have indicated that the changes of temperature produced by this high frequency field are strictly dependent on the position and constitution of the various tissues.

7853 C

Thermal Changes Produced in Tissues by Local Applications of Radiothermy.

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The short electric wave generator developed in the Research Laboratories of the General Electric Company was used in these investigations. In utilizing the energy of this high frequency field for the investigations of thermal changes produced by local applications of the field, small insulated condenser plates were attached by means of tubular telescopic rods to the large condenser plates.

Measurements of temperatures were made (series of 30 dogs) on the intra-articular and subcutaneous tissues of both knee joints of each animal after local application of the short wave field to the region of the knee joints. Condenser plates 2.5 by 3 inches, separated by distances which varied from 2.5 to 4 inches, produced the high frequency field into which was placed the part of the animal to be tested. The current density applied to the knee joints varied from 0.1 to 0.05 ampere per square inch of surface of the small auxiliary condenser plates. The frequency of oscillation of the electric field

(which is not markedly affected by considerable variations in the distance and arrangements of the auxiliary plates) was 27.5 million cycles (wave length of 10.9 meters).

In order to evaluate the errors in the measurement of temperature produced by the introduction of a thermocouple needle into tissue and the errors caused by the presence of such a needle in tissue during application of the short wave field, the following procedure was carried out Thermocouple needles were introduced into the intra-articular and subcutaneous (at knee joint) tissues of one leg, and measurements of the temperatures were obtained over a 10-minute period. The leads were then detached from the needles, and the needles were left in position in the tissue while the short wave energy was passed through the knee joint. After cessation of the treatment, leads were again attached to the thermocouples and the measurements of the temperatures were taken over a 30-minute period. Immediately following this period, the short wave field was applied for the same length of time to the knee joint of the second leg of the animal. In this case the thermocouples were inserted immediately after the high frequency treatment had been completed, and the measurements of temperature were taken again over an interval of 30 minutes.

It was thus possible to ascertain the temperatures produced by application of the short wave field to tissue in which thermocouple needles were present during treatment. These temperatures theoretically should be somewhat higher than those of normal tissue in which no metallic needle is present. By delaying the insertion of the thermocouple needles into the second leg of the animal until after application of the high frequency field, it was possible to obtain readings of the temperatures produced by application of the short wave field to normal tissues, with, however, the recognition of the physical fact that these temperature readings were subject to losses due to the introduction of a low temperature needle of some thermal capacity and of considerable thermal conductivity. The temperatures thus obtained should be somewhat lower than the true temperatures of the tissues. By obtaining, on each animal, measurements of temperature by both of these methods (one somewhat higher than the true temperature and the other slightly lower than the true temperature) it is possible to estimate the effect of the high frequency field on the temperatures of tissues to a high degree of probable accuracy.

In 2 control dogs, examined in this manner and without subjection to the short wave field, significant changes in the intra-articu-

lar temperatures were not observed, but the subcutaneous temperatures rose slowly during the period that the thermocouple needle was inserted in the tissue. The average rectal temperature for the 30 dogs was 39.1°C. (102.3°F.). The average intra-articular temperature before application of the short wave field was 36.8°C. (98.2°F.). The average subcutaneous temperature in the region of the knee joints was 36.1°C. (96.9°F.). The rectal temperatures were not affected by local treatments of short duration.

Eleven dogs were subjected to the localized short wave field across the knee joint for 2 minutes, with a plate distance of 4 inches and a current density of 0.05 ampere per square inch. When thermocouples were present during treatment the intra-articular temperature rose 3.5°C. to a point slightly above the rectal temperature, whereas the subcutaneous temperature rose 2.5°C. but remained below the rectal temperature. These temperatures dropped sharply after cessation of the treatment. When thermocouples were inserted after application of the electric field, the intra-articular temperature rose about 1°C. and dropped very slowly with time, whereas the subcutaneous temperature apparently was not at all affected by the treatment. Two dogs were treated in this same field with an exposure of only one minute. The results for measurements with thermocouples present during oscillation of the field were practically the same as those stated in the foregoing, but there was no change in temperature indicated by thermocouples inserted after treatment in both the intra-articular and subcutaneous measurements.

Two dogs were treated for one minute in a field with a plate distance of 2.5 inches and a current density of 0.09 ampere per square inch. The effects on the thermal changes of tissue as indicated by thermocouples, inserted during and after the oscillation of the field respectively, were identical. The intra-articular temperature rose 4.5°C. to a value well above the rectal temperature, and decreased approximately exponentially with time after treatment. The subcutaneous temperature rose 5.5°C. to a value above both rectal and intra-articular temperatures.

The remaining 13 experimental dogs were treated under a constant distance of 3 inches between the plates of the auxiliary condenser and under a current density of 0.08 ampere per square inch.

Six dogs were treated for one minute through each knee joint. When thermocouples were present during application of the electric field, the intra-articular temperature rose 4°C. and the subcutaneous 3°C. Both temperatures were well above the rectal value and

both fell very rapidly after cessation of treatment. When thermocouples were inserted after application of the field, the rise of

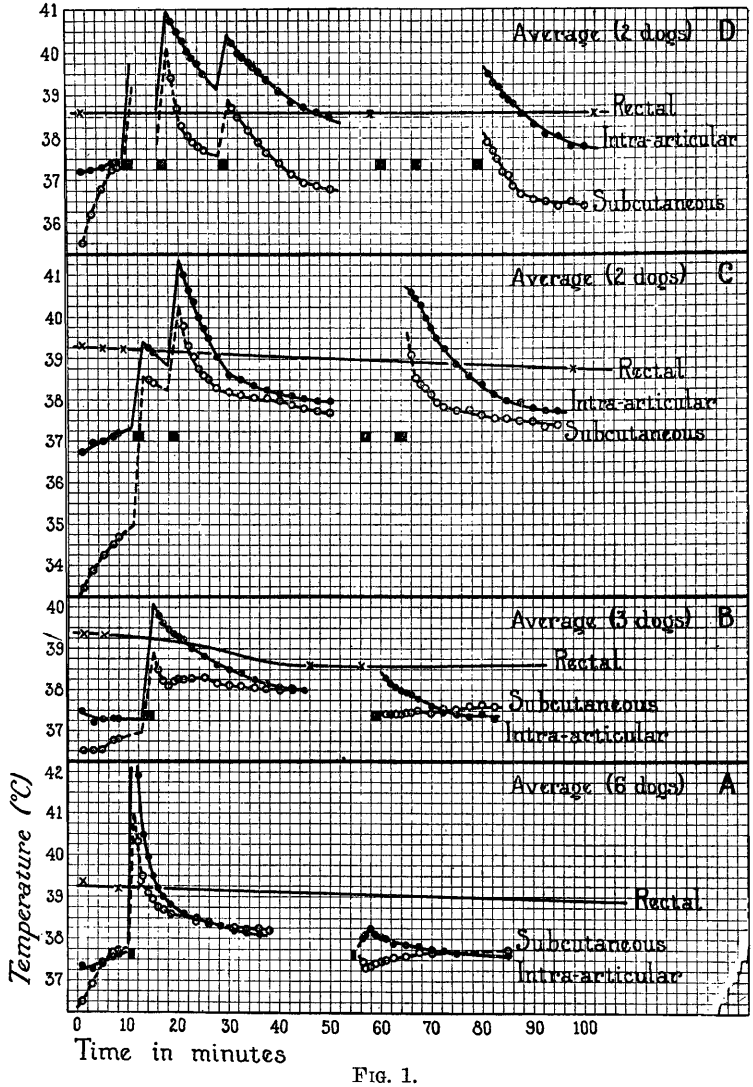

FIG. 1.

Curves showing the effects produced by the application of localized high frequency fields to the region of the knee-joints of dogs. (Current density of 0.056 to 0.11 ampere per square inch, frequency of 27.3×10^6 cycles per second, treatment plates insulated and separated 3 inches.) The curves give the intra-articular, subcutaneous and rectal temperatures after the application of varying doses. In obtaining the curves of the left portion of the diagrams, thermocouple needles were inserted in one leg of the animal throughout the treatment; in the right portion, the thermocouples were inserted in the other leg of the same animal after the cessation of the field. Time of treatment and chronological order are indicated by the blackened rectangles.

intra-articular temperature was only 0.4°C. and the subcutaneous temperature was apparently not affected.

Three dogs were treated for 2-minute intervals in this same fashion. By the first method of measurement, the increase in intra-articular temperature was 2.5°C. and the increase in a subcutaneous temperature 1.5°C.; both temperatures fell slowly with the passage of time after treatment. By the second method of measurement, the intra-articular temperature rise was 1°C., but the subcutaneous temperature again appeared to remain constant.

Two dogs were treated in this same manner by 2 applications of the field, each for 2 minutes, with an interval of 5 minutes between applications. In these experiments the results of measurements with thermocouples present during oscillation of the field and of measurements with thermocouples inserted after application of the field were identical. The intra-articular temperature rose 4°C. and returned in an approximately exponential fashion to a constant value at the end of the 30 minutes of observation. The subcutaneous temperature rose 3°C. and paralleled the drop of the intra-articular temperature. Both temperature values exceeded the rectal temperature at their peak. Two dogs were treated in the same way, but an additional 2-minute exposure to the electric field was made 10 minutes after the second exposure. Again the temperatures obtained by both methods of measurement were practically identical and qualitatively similar to those described.

Summary. It is apparent that errors in the measurement of temperature, due to the presence of a metallic needle (thermocouple, without leads) in tissue during exposure of that tissue to a high frequency electric field are greater when the time of exposure is short and when the intensity of the electric field is low. The relationship of the heat produced in deep-lying tissues to the heat produced in superficial tissues is dependent on the distance at which the condenser plates are placed with respect to the locations of the tissues. This fact is of importance in the therapeutic uses of high frequency fields (radiotherms). When a considerable air space separates these plates from the surface of the tissue, the change in temperature produced in the deep-lying intra-articular tissue is greater than that produced in the subcutaneous tissue. The converse relationship maintains when the plates are placed close to the surface of the tissue. This dielectric layer effect is superimposed on any specific heating due to difference in constitution of tissue and variation in wave length of radiation which may be present. Schlie-

phake[1, 2] first demonstrated this type of depth effect of the high frequency field, and has presented experimental evidence which indicates that high frequency treatment plates which are allowed to make contact with the surface of tissue produce a tissue heating which is closely comparable with that of diathermy, in which the production of heat is predominantly in the superficial layers of tissue.

The experimental evidence presented clearly demonstrates that it is possible to produce abnormally high temperature in a chosen region (*i. e.*, knee joint of a dog) by means of local applications of short wave electric energy of sufficient intensity. Furthermore, these relatively high temperatures may be produced in the deep (intra-articular) tissue of the region without the simultaneous production of high temperatures in the superficial (subcutaneous) tissues of the region (*i. e.*, portion of leg of dog) exposed to the high frequency electric field of the type used in these investigations.

7854 P

Precipitation of Apparent Creatinine from Serum Ultrafiltrates.

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In earlier isolation experiments[1, 2] on blood creatinine, the use of protein precipitants, of adsorbents, and evaporation in acid solution all made the interpretation of results difficult. In the case of sera showing various degrees of nitrogen retention a simpler path which avoids these difficulties is open. In the following experiments cellophane No. 300 was used as the membrane in an ultrafilter operated by a nitrogen pressure of 400 lb. per square inch. A few drops of toluene were added to the serum and the receiving vessel.

To 10 cc. of ultrafiltrate are added 250 mg. of pure picric acid. This is dissolved by shaking the tube under the hot water tap, and the solution is cooled to about 25° in cold water. One-tenth cc. of 10% potassium chloride solution is added, and the solution is mixed at once. An excess of picric acid may precipitate at this point, but unless

[1] Schliephake, Erwin, *Klin. Wchnschr.*, 1928, **7**, 1600.

[2] Schliephake, Erwin, *Strahlentherapie*, 1930, **38**, 655.

[1] Gaebler, O. H., and Keltch, A. K., *J. Biol. Chem.*, 1928, **76**, 337.

[2] Gaebler, O. H., *J. Biol. Chem.*, 1930, **89**, 451.