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see ref #1 for part I ✓

Microwave Radiation to the Anterior Mediastinum of the Dog (II)

II. Thermal, Cardiovascular, Respiratory and Blood Enzyme Observations*

JACK MARKS, M.D., EARL T. CARTER, Ph.D., M.D., DANTE G. SCARPELLI, Ph.D., M.D., and JESSE EISEN, M.D.

Introduction

IN a previous communication[1] we cited those considerations that prompted us to undertake this study. Briefly we wished to investigate the possibility of using microwave radiation to increase myocardial blood flow. Previous investigators have presented evidence to show that microwaves in addition to producing heat in tissues also produced a marked and significant increase in blood flow.[2] It was our purpose to study some of those physiologic effects that attend the application of microwave diathermy to the anterior mediastinum of the dog. We wished to determine whether this modality might be rationally applied to increase myocardial circulation in man in the presence of coronary artery disease. This report, or our prior one, describes certain preliminary investigation done in dogs.

Methods and Materials

Twelve (12) mongrel dogs were used in these experiments. After intravenous administration of Sodium Nembutal® (pentobarbital), 30 mg. per-kilogram body weight, the animals were placed on a dog board in supine position. The animals had balloon cuffed endotracheal tubes placed in their tracheae to permit spirometry with a 6 liter Benedict-Roth spirometer. Venous blood was taken from a modified cardiac catheter which was introduced into the right atrium via the internal jugular vein. Blood samples were collected from the femoral arteries by an indwelling Cournand needle and blood pressure was recorded by means of a Stetham strain gauge, through a Brush pre-amplifier and recorder, utilizing the same needle. Cardiac output determinations were done by the Fick method. Either a single-channel Sanborn Viso-Cardiette or a single-channel Cambridge Simpli-Scribe electrocardiograph was used to monitor the electrocardiogram. Recordings were made of the standard limb leads and of the augmented limb leads.[1]

Temperatures were measured at the cardiac apex, in the retrocardiac esophagus and in some experiments in the liver by means of a 25 gauge needle-type thermistor resistance thermometer for which Dr. Richard Stowe** kindly provided the circuit diagram. Rectal temperatures were recorded by means of a mercury thermometer which had been used earlier to calibrate the thermistor resistance thermometer. Thermistors were placed adjacent to the cardiac apex by percutaneous puncture at the palpable apical beat. The V lead of electrocardiograph was placed in electrical contact with the thermistor needle and, when a current of injury was detected, the needle was withdrawn in minute increments until the S-T displacement disappeared.

A commercial Raytheon microwave diathermy generator was used in these experiments. Physical characteristics of this device have been discussed comprehensively elsewhere.[3] The character of the wave length is one of 2400 to 2500 megacycles per second with a wave length of approximately 12.2 cm.

The four inch, so-called, "A" reflector was used in each experiment. In the first experiment the reflector was placed one inch above the chest. In the second experiment a distance of one and one-half inches was used and in the last 10 experiments the reflector was placed two inches above the chest.

The midpart of the microwave reflector was placed in the same vertical plane as the needle thermistor which had been previously placed at the cardiac apex. Full power of 125 watts was used in all heating periods.

It is characteristic of electrical conductors that they are themselves heated when placed in a high intensity microwave field. Accordingly, we had the choice of either inserting the 25 gauge thermistor needles each time a reading was to be made or of removing the source of radiation momentarily while making recordings. Preliminary studies showed that while the tiny thermistor at the end of the needle did assume a temperature higher than the surrounding tissues during radiation, the thermistor assumed adjacent tissue temperature in 12 to 30 seconds after removal of the microwave reflector, hence, all temperature data were obtained while the microwave reflector was momentarily shifted away from the animal.

Blood enzyme studies were done during various phases of these experiments in four dogs. These included Serum Glutamic Oxalacetic Transaminase, Serum Pyruvic Transaminase, and Malic and Lactic Dehydrogenases.[4,5,6] These were done so as to ascertain whether myocardial tissue was sufficiently damaged by microwave radiation to increase the blood content of these enzymes.

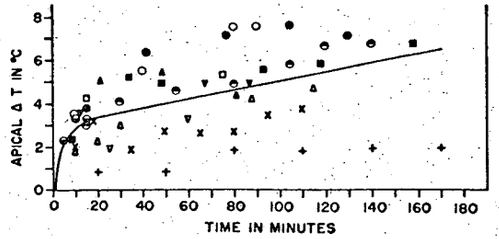
The animals were heated for periods of from 15 to 140 minutes and subsequently autopsied within one hour of death in each case by Dr. Dante Scarpelli.

Heating Patterns

Figure 1 depicts the observed increments in cardiac apical temperatures in all 12 dogs following the initiation of microwave heating. While scatter between animals is evident, it will be noted that the individual animal, each designated by a separate symbol, behaved in a fairly uniform fashion. There was a characteristic rapid cardiac heating during the first 10 to 15 minutes after which the temperature continued to rise more slowly and essentially linearly with time. The straight portion of the solid line in figure 1 does not represent a "least squares" fit but rather represents an average slope with respect to the individual slopes of the animals. The intercept of the line also represents the average of the 12 individual intercepts obtained by extrapolation of the linear portion of the temperature curve to the ordinate. The initial curved portion of the line is an assumed form. The value for this average slope (after the initial 10 to 15 minute time period) is approximately ±.02°C. per minute.

FIGURE 1

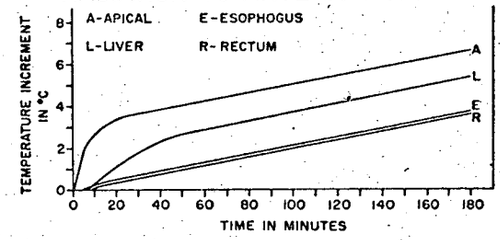
APICAL TEMPERATURE CHANGE



Curves for the esophageal, rectal, and liver temperatures were obtained in a similar manner and are plotted with the apical temperature function, just discussed, in figure 2. The average control values for

FIGURE 2

HEATING PATTERN DURING MICROWAVE RADIATION TO ANTERIOR CHEST



the temperatures of the cardiac apex, esophagus, rectum, and liver in degrees Centigrade were 36.5, 37.0, 34.5 and 36.5, respectively, with standard deviations of ±1.13, ±1.32, ±1.97, and ±0.79. It is noted that the anterior cardiac surface rapidly assumes a temperature higher than those of the other three sites, an observation not surprising in view of the position of the microwave reflector. The rather prompt heating of the liver at first appears surprising but, when one considers the anatomical position of the dog liver, it is evident that at least the medial portion of the liver comes into the direct beam of the 4 inch diameter reflector placed over the anterior chest.

The esophageal and rectal temperatures followed very similar patterns even though the former, located in the posterior mediastinum, was directly beneath the microwave dish. Apparently the depth of the esophagus, the interposition of the heart between it and the microwave source, and other factors

The Authors

● Dr. Marks, Columbus, a member of the courtesy staffs, St. Anthony, and University Hospitals, and associate staff, Grant Hospital, is instructor in Clinical Medicine, Ohio State University College of Medicine.

● Dr. Carter, Rochester, Minnesota, consultant in Medicine, Rochester Methodist Hospital, and assistant professor (Medicine), Mayo Foundation and University of Minnesota, formerly was a member of the Department of Preventive Medicine, The Ohio State University Health Center, Columbus.

● Dr. Scarpelli, Columbus, is pathologist, University Hospital and assistant professor of Pathology, The Ohio State University College of Medicine.

● Dr. Eisen, Columbus, is a member of the staffs of Grant, Children's, and St. Anthony Hospitals, and instructor, Department of Surgery, The Ohio State University College of Medicine.

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**Department of Physical Medicine, The Ohio State University Hospital.

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such as a possible cooling function of the pulmonary airways accounted for the fact that the esophagus behaved like an area remote from the microwave source.

Cardiovascular Dynamics

A consistent moderate increase in heart rate was found in all animals. The increase was in the order of 20 to 40 beats per minute from an average initial value of 137 beats per minute with a standard deviation of ±22.

The average pre-exposure cardiac output was quite variable from animal to animal, averaging 170 cc. per kilogram of body weight for 10 animals with a standard deviation of ±107 cc. The initial mean blood pressure was 123 mm. Hg and the standard deviation was ±28, while the peripheral resistance determinations averaged 938 dynes per cm.^{5} with a standard deviation of ±32. Analysis failed to reveal any systematic effect with respect to these three variables following various periods of microwave radiation.

Moderate declines in cardiac output in a range from 26 to 32 per cent occurred at intervals of from 118 to 174 minutes in four animals. A somewhat larger decline of 49 per cent in cardiac output was observed at 11 minutes in one animal. Rise in cardiac output of 8 per cent at 170 minutes, 19.6 per cent at 25 minutes and 89 per cent at 105 minutes were observed in three other animals while two animals exhibited increases of cardiac output of 254 per cent at 75 minutes, and 300 per cent at 157 minutes, respectively. While these latter two dogs did have fairly high rises in apical temperatures, 6.5 and 6.0°C., respectively, other animals with even greater rises failed to show much change in cardiac output. No definitive relationships between any of the cardiovascular data and the temperature data already described could be demonstrated.

It must be noted that the venous blood samples were withdrawn from the right atria, a source without complete homogeneity of venous blood having therefore slightly varying degrees of hemoglobin saturation, pO_2 and pCO_2, from place to place in the right atria.

Respiratory Effects

The mean pulmonary ventilation observed in 10 of the experimental animals immediately prior to heating was 211 cc. per minute with a standard deviation of ±94 cc. In every instance, after approximately two hours (105-170 minutes range) of microwave exposure, the pulmonary ventilation increased, producing an average of 410 cc. per minute (BTPS) with a standard deviation of ±252 cc. The probability of this increase being other than random variation was between .05 and .10 but the relatively large variance with respect to the ventilatory data probably accounts for this somewhat high probability level.

The oxygen intake averaged 7.15 cc. per minute (STPD) per kilogram body weight with a standard deviation of ±2.5, while after approximately two hours of heating the average was 8.1 cc. ±3.9. The mean increase of 0.95 cc. was not statistically significant. The carbon dioxide elimination averaged 6.10 cc. per minute per kilogram body weight (STPD) with a standard deviation of ±2.2 cc. prior to heating and rose to an average value of 7.15 ±3.9 after heating, a change not statistically significant.

TABLE 1. *Serum Enzyme Activity of the Sera of Dogs Receiving Microwave Radiation*

Dog No.	Period of Heating (Min)	Enzyme Activity GOT*	GPT**	LDH†	MDH‡
9	0	10	0	50	225
	15	10	0	100	375
	96	17	0		
10	0	19	0		
	15	15	0		
	120	13	13		
11	0	19	6	50	150
	14	9	15	50	150
	120	19	7		
12	0	13	0	75	125
	17	13	10	75	150
	137	37	9		

*GOT — Serum Glutamic Oxalacetic Transaminase
**GPT — Serum Pyruvic Transaminase
†LDH — Lactic Dehydrogenase
‡MDH — Malic Dehydrogenase

Blood Enzyme Studies

No significant changes were observed in the Serum Glutamic Oxalacetic Transaminase, Serum Pyruvic Transaminase, and Lactic Dehydrogenase for the time periods involved. In two instances, increased Serum Malic Dehydrogenase activity was observed, the significance of which was difficult to assess due to the hemolysis of blood by microwave radiation. These data are summarized in Table 1.

Discussion

With respect to the heating pattern as shown in figure 2, it is of interest that the rates of heating of the different sites chosen were all approximately 0.02°C. per minute once initial adjustments were completed. These data, in addition to the predominance of myocardial engorgement in the anterior portion of the mediastinum,[1] suggest that the initial rapid cardiac heating, especially during the first 10 minutes, reverts over to the slower process as total body heating is brought about. The rectal temperature does not begin to rise significantly until after 5 to 10 minutes of microwave exposure; the deeper posterior mediastinum behaves in a similar manner. Thus, in the first few minutes the major portion of the microwave energy is absorbed by the anterior chest wall and anterior myocardium. Blood flowing through the heart will carry more and more heat away, the steeper the temperature gradient between the myocardium and the blood. This means an ever greater portion of the microwave energy will be distributed to the body as a whole. This has the effect of commuting local precordial heating to whole body heating.

One would be tempted to predict two effects to permit widespread distribution and hence elimination of heat received locally, especially in view of the effects well documented in man.[7] First, one would expect a consistent fall in peripheral resistance and, second, an increase in cardiac output. Either or both mechanisms would serve to dissipate body heat. Neither effect was clearly demonstrated in the 10 dogs so studied. However, it should be recalled that the dog, unlike man, does not have a major reliance on peripheral vasomotor control in heat regulation. In our animals the peripheral resistance was just as likely to decrease somewhat as to increase.

The dog does rely heavily on the respiratory avenue for heat loss and a consistent increase in pulmonary ventilation was noted in our series. Of course, there need be no change in cardiac output or peripheral resistance at all for blood to distribute heat from the heart to the periphery. Furthermore, the continued temperature rises shown in figure 2 certainly indicate that a balance between heat gain and heat loss, the latter by any route, had not been achieved during the periods of observation.

These studies and those reported in our earlier communication[1] are preliminary and inconclusive, but seem sufficiently interesting to warrant further investigation. We believe that since tissue heating is so prominent an aspect of microwave radiation of this frequency, energy and wave length that those cardiopulmonary effects observed here are probably in large part attributable to precordial heating, and after 15 minutes, to total body heating. Our data suggest that microwave application should be of about 15 minute duration exposure time and of an energy level low enough to avert cutaneous discomfort which might be subjectively gauged in man. Under these conditions we believe that human studies should be safe.

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MERCAPTOMERIN AND AMINOPHYLLINE were used for treatment of cardiac failure and ascites that was resistant to continued treatment with previously used diuretics. The 35 patients studied ranged in age from 18 to 75 years. Their heart diseases were of rheumatic, congenital, arteriosclerotic, hypertensive, or pulmonary etiology. Throughout the period of study, all patients were treated with bed rest, digitalis, and salt restriction. Potassium supplements were given to some patients, including all those who were receiving benzthiazide derivatives. When mercaptomerin was substituted for a previously used diuretic, intramuscular injections of 2 ml. were usually given three times weekly; when the regimen of mercaptomerin plus aminophylline was begun, aminophylline was injected intravenously (0.5 Gm. in 20 ml. of CO_2-free water) two hours after administration of the mercurial and over a span of at least 10 minutes to avoid excessive respiratory stimulation. The 2-hour time lapse was arbitrarily chosen as being most likely to ensure maximal potentiation and is in accord with that recommended by other clinicians. The present authors note that they now find it prudent to estimate the blood-urea level before each pair of mercaptomerin-aminophylline injections and to withhold this treatment whenever this level exceeds 70 mg./100 ml.

Of the 35 patients studied, 28 responded to mercaptomerin-aminophylline with sustained diuresis and clinical improvement; 31 showed maximum rate of loss of weight while receiving the combined therapy.

With the exception of patients with blood-urea levels in excess of the 70 mg./100 ml., it is suggested that the combined injections described here are always worthy of trial where mercurials alone or benzthiazide derivatives fail to clear cardiac edema. — (ABSTRACT): J. G. Domenet; D. W. Evans, and O. Brenner, Birmingham, England: *British Medical Journal*, 1:1130-1133 (April 22) 1961.