Glaser

Proc. Soc. Expt'l Biology & Med 72 432-434 (1949)



*Summary and conclusions.* A choleretic response to cinchophen was observed in guinea pigs.

The cinchophen output in the bile was found to be greatest in guinea pigs and to decrease in the following order: rats, cats and rabbits.

The following is the order found for susceptibility to cinchophen ulceration: cat, dog, guinea pig and rat. Rabbits were found completely resistant.

There appears to be no obvious relationship between the species susceptibility to cinchophen ulceration and the choleretic response of that species to cinchophen or to the concentration of cinchophen in the bile after intravenous administration.

It would appear that the ulcer susceptible animals investigated have a low basal bile flow whilst the unsusceptible have a high flow.

Received October 4, 1949. P.S.E.B.M., 1949, **72**.

## Focal Neurological Lesions Produced by Microwave Irradiation. (17458)

W. H. OLDENDORF (Introduced by George A. Jervis)

*From the Binghamton State Hospital, Binghamton, N. Y.*

Prewar and wartime research allowed the development of electronic equipment capable of efficiently producing large quantities of radiation above 1000 megacycles (microwaves). Notable among these advances was the development of the magnetron tube which is used in radar equipment[1] and has been incorporated recently in a microwave diathermy machine.* The frequency at which this machine operates (2450 megacycles, 12.2 cm) allows good penetration of animal tissue and even of bone, as demonstrated by Osborne and Fredericks[2] and Krusen, Herrick and Wakim.[3] These findings and the fact that radiation at this frequency travels in substantially straight lines suggests that the application of toxic doses of this radiation to a small area of the cerebral cortex is possible without injury to the scalp and skull.

However, a review of the literature reveals no report of the utilization of microwave radiation for the artificial production of focal neurological lesions. With the technic to be described focal lesions were produced in rabbit brains without surgical procedure. The site of the cortical lesion, moreover, was accurately determined before the irradiation.

*Method.* Adult rabbits weighing about 3 kg were utilized. Under intravenous pentothal anesthesia sufficient to immobilize the animal (80-100 mg) the animal's head was placed on a wooden block approximately 7 cm in thickness. The area of the scalp over the proposed site of irradiation was shaved. A thin copper shield with an oval hole 2 x 3 cm was then placed with the long axis of the hole parallel to the rabbit and over the proposed site, in the present cases the right cerebral hemisphere. It was found convenient to braze a guide on the upper surface of the shield to maintain the intersection of the lead-in conductor and dipole directly over the hole in the shield. In the "C" type of director, which was used throughout, the point of maximum radiation was directly underneath the small screw which held the dipole in place.

The plastic protector of the radiating elements was then placed in contact with the shield and the shield in contact with the scalp over the proposed site. It was found convenient to mark the site lightly with a dot of colored crayon before putting the shield

1 Argento, H. F., Centimeter-wave Magnetrons. QST, Dec. 1945.

* Available as the "Microtherm" from the Raytheon Mfg. Co., Waltham, Mass., who courteously supplied the machine with which this work was done.

2 Osborne, Stafford L., and Frederick, Jesse N., *J.A.M.A.*, 1948.

3 Krusen, F. H., Herrick, J. F., and Wakim, K. G., *Proc. Staff Meet. Mayo Clin.*, 1947, **22**, 209.

FIG. 1.
Circumscribed area of coagulation necrosis in the cerebral cortex of the rabbit. Nissl's stain. Very low power.

in place. The shield interferes considerably with the efficiency of the radiator but some shielding is necessary lest the ears be seriously burned, since they protrude directly beside the dipole. Prior to irradiation, 30 cc of 5% glucose in water and 100 mg caffeine sodium benzoate were injected intraperitoneally. With the output at 100% the machine was turned on for 3 minutes.

No quantitative temperature readings were taken. They were considered to be grossly inaccurate and misleading since the area of increased temperature within the intracranial cavity was so small.

*Results.* Seventeen rabbits were used but only 2 representative experiments will be described.

*Rabbit 18*: The animal received irradiation exactly as described above under "Method." He responded in 30 minutes after irradiation but refused to eat for three days. During this time he received 100 cc 5% glucose in water intraperitoneally daily. Following this he gradually rallied and took food spontaneously. At no time was an asymmetrical motor defect noted. Fifteen days after irradiation the animal was living and well and showed only a crusting lesion of the scalp over the irradiated area. The animal was sacrificed on the 15th day by intracardiac ethyl alcohol. The brain grossly showed a yellow-green coagulation lesion 0.7x1 cm on the superior surface of the posterior portion of the right cerebral hemisphere. The dura was grossly intact and was not adherent to any area of the cortex. Histologically, as seen in Fig. 1, there was a small lesion which appeared sharply circumscribed. It involved the cortical gray matter in its entire width and extended somewhat into the subcortical white matter. The whole lesion contained no intact nerve cells or glia and was delimited by a wall of intensely proliferating glia cells.

*Rabbit 16*: This animal received irradiation according to the above technic but with elimination of the shield, intraperitoneal fluid and caffeine. The animal did not respond and expired three hours later despite post-irradiation parenteral fluids. Sections of the brain showed a large sloughed area with a slight polymorphonuclear infiltration in the surrounding surviving tissue.

*Comment.* It appears from the experiments reported that by means of microwave irradiations a focal lesion can be produced in the cerebral cortex of the rabbit without incising the scalp or opening the skull. The only injury to the scalp was a crusting lesion without bleb formation.

A possible explanation of the extremely small size of the lesion is that the plastic protector in contact with a small area of the scalp has dielectric properties which allow much more efficient entrance of the radiation into tissue in the area in contact, than is possible from air to tissue.

The histological lesions produced by this type of irradiation into the cerebral cortex are similar to those described in detail by Silver and Walker[4] in experiments of thermocoagulation of the cerebral cortex by the direct application of a heated piece of metal, except that microwave destruction apparently penetrates more deeply within the tissue.

Since microwave diathermy heating is dielectric heating, it is presumed to be nonionizing and any toxic effects would be those of excessive heating. In fact, no significant hematopoietic effects were observed in the work of Lidman and Cohen,[5] Fallis[6] and Daily[7] upon exposure to intensities of radiation likely to be experienced in practical radar work. It should be noted, however, that Imig, Thomson, and Hines[8] indicate that testicular degeneration may occur from microwave heating at a lower temperature than from infra-red heating, and Richardson, Duane, and Hines[9] showed that upon intentional overdosage, lenticular opacities appeared at about 50°C.

Further work is now in progress using a special butyl rubber impregnated with a titanium compound which allows an intermediate dielectric constant without excessive absorption of the radiation by the rubber. With this technic it is hoped to allow penetration in an area of any shape and, because of the greater efficiency of transfer into the tissue, in a larger area. A modification of this technic may eventually allow the easy destruction of cortical tissue without any surgical procedure both in experimental neurology and in therapeutics.

*Summary.* A technic is described of producing focal lesions in the cerebral cortex of rabbits by microwave irradiation without incising the scalp or skull. The results on two animals are reported and future possibilities of this work are discussed.

4 Silver, M. L., Walker, A. E., *J. Neuropath. Exp. Neur.*, 1947, **10**, 311.

5 Lidman, B. I., and Cohen, C., *Air Surg. Bull.*, 1945, **2**, 448.

6 Fallis, R. H., Jr., *Am. J. Physiol.*, 1946, **147**, 281.

7 Daily, L. E., *U. S. Naval Med. Bull.*, 1943, **41**, 1052.

8 Imig, C. J., Thomson, J. D., and Hines, H. M., PROC. SOC. EXP. BIOL. AND MED., 1948, **69**, 383.

9 Richardson, A. W., Duane, T. D., and Hines, H. M., *J. Neuropath. Exp. Neur.*, 1947, **10**, 311.

Received October 18, 1949. P.S.E.B.M., 1949, **72**.

## Ultrafiltration and Ultracentrifugation Studies of Coxsackie Virus. (17459)

JAMES J. QUIGLEY (Introduced by Gilbert Dalldorf)

*From the Division of Laboratories and Research, New York State Department of Health, Albany.*

The physical properties of the Coxsackie group of viruses[1-4] have been under investigation since their isolation, and preliminary studies indicated that the original strain is very small. The present report is a summary

1 Dalldorf, Gilbert, and Sickles, G. M., *Science*, 1948, **108**, 61.

2 Dalldorf, Gilbert, Sickles, G. M., Plager, Hildegard, and Gifford, Rebecca, *J. Exp. Med.*, 1949, **89**, 567.

3 Gifford, Rebecca, and Dalldorf, Gilbert, PROC. SOC. EXP. BIOL. AND MED., 1949, **71**, 589.

4 Sickles, G. M., and Dalldorf, Gilbert, PROC. SOC. EXP. BIOL. AND MED., 1949, **72**, 30.