Session A. General Effects of Microwave Radiation

Chairman: *H. P. Schwan*
Vice-Chairman: *Z. V. Gordon*
Rapporteurs: *T. V. Kalada and M. L. Shore*

THERMAL EFFECTS OF SINGLE AND REPEATED EXPOSURES TO MICROWAVES — A REVIEW*

S. M. Michaelson

University of Rochester, School of Medicine and Dentistry, Department of Radiation Biology and Biophysics, Rochester, New York, U.S.A.

INTRODUCTION

Review of the literature on biologic effects of microwaves reveals several areas of established effects and mechanisms on the one hand and speculative effects and mechanisms on the other. This has created a dilemma in trying to assess the real or imaginary from the actual or potential hazard to man from exposure to this energy. Part of this dilemma is based on semantic differences and/or lack of appreciation of past scientific achievements as well as a lack of conceptual approaches in the planning and/or analysis of studies.

Although most of the experimental data support the concept that the effects of microwave exposure are primarily a response to altered thermal gradients or hyperthermia, there are large areas of confusion, uncertainty and actual misinformation. To put the question of microwave bioeffects in its proper perspective, a critical analysis of the published literature is essential to differentiate the known and substantiated from the speculative and unsubstantiated effects.

BIOPHYSICS

For this presentation, microwaves will be defined as that portion of the electromagnetic energy spectrum encompassing the frequency range of 300 MHz — 300 GHz with

* The work upon which this paper is based was performed pursuant to Contract No. FDA 73-30 with the Public Health Service, Food and Drug Administration, Department of Health, Education and Welfare, with support by the Bureau of Medicine and Surgery, U.S. Navy, and with the U.S. Atomic Energy Commission at the University of Rochester Atomic Energy Project and has been assigned Report No. UR-3490-317.

WHO – Biologic effects & health hazards of microwave radiation 1974

wavelengths in free space of 1 meter to 1 millimeter. In order to understand the consequences of microwave exposure, consideration of biophysical principles and mechanisms of action is essential. These will be presented by Drs. Schwan and Illinger.

THE PHYSIOLOGY OF THERMAL REGULATION

The mammal is a complicated self-regulating organism, composed of different organs with diverse cell types. The effects of heating can be subdivided into those acting at (a) the cellular level, (b) the organ level, and (c) the total self-regulatory mechanism. When we are dealing with the whole organism, the effects at all these three levels occur simultaneously and are more or less interrelated (10).

One of the main factors in temperature regulation of mammals is their capacity to alter the temperature gradient between the "shell" (peripheral) and the core (deep tissue) of the body. That a gradient exists at all is due to the fact that the body loses heat from its surface by conduction, convection, radiation and evaporation (9).

It is appropriate at this time to define what I mean by thermal effects, namely effects that result from heating of tissue through the application of electromagnetic fields. The effect may be a result of, or a response to, heating the body, a specific organ, or a controller (i.e. nerve, blood vessel, endocrine organ) of an organ or body system. This definition also invokes the concept that selective heating or alteration in thermal gradients may occur which may not necessarily manifest themselves by a measurable increase in core or colonic temperature. The basis for this definition is that thermal gradients in the body can vary under normal circumstances. The body, however, has the physiologic capability to accommodate to such changes without a change in core temperature. The core temperature of a mammal can remain constant when the heat generated by the metabolism of the body is equal to the heat lost from its surface (16). As both the rates of heat production and of heat loss vary in different tissues and organs of the body, local temperatures also vary. Generally, temperatures of peripheral tissues are lower than those of deep tissues, but both peripheral temperature and core temperature reflect unmeasurable means of many different temperatures (3).

Gordon and Tolgskaja (14, 38) define thermal as the presence of an overall heat effect as measured by the core temperature response of the animal. Such temperature implies an integral thermal effect reflecting thermoregulation in the entire body. It is important to realize, however, that the absence of a temperature rise in the colon does not exclude the possibility of such an effect in tissues and internal organs absorbing microwave energy. Although the rectal temperature is a reasonably representative measure of deep body temperature in steady state conditions, it is slow to indicate changes in body temperature, and its use cannot be recommended for thermoregulatory studies of the relations between thermal stimuli and thermoregulatory responses (3).

The temperature control system is an example of a dynamic system approaching the accuracy of an engineered one (12). All the complicated mechanisms of heat regulation are integrated by hormonal and nervous control as well as by a direct temperature effect of the blood supplying the hypothalamus which can also be influenced experimentally by direct heating. The threshold for direct heat activation is an increase in temperature of 5 to 6°C (10).

Temperature changes can act as stimuli to different organs, influencing their behavior. The rate at which the heat is dissipated will vary in different species depending on heat-regulating mechanisms or metabolic characteristics. The breakdown of protective mechanisms for heat control causes an uncontrolled rise in body temperature.

WHO – Biologic effects & health hazards of microwave radiation 1974

The maintenance of a certain temperature is of vital importance to the organism because all biologic processes are conditioned by temperature. The temperature of the tissues is an important factor which determines the extent of the physiologic response to heat. Below a certain temperature threshold, no reactions are observed. A change in tissue temperature could produce a change in the degree of the physiologic response.

Specific organ or tissue systems may "function" at a significantly different rate if local thermal gradients are altered. Based on an extensive review of the literature on thermal regulation, Thauer (37) concluded that relatively large changes in circulation are provoked by quite small deviations from neutral temperature. Also, the cardiovascular system is subject to the combined influence of both skin temperature and deep temperature. Under certain conditions, the thermal stimuli to the skin can be of greater significance in causing cardiovascular reactions than the level of core temperature.

Within a few degrees, nerve fiber transmission rates are temperature dependent (6, 42). In mammals the central nervous system ceases to function at 44 to 45°C and the heart stops beating at 48°C. A rise in temperature of 5°C causes a twofold to threefold increase in pulse rate, oxygen consumption, etc. The mechanisms of heat regulation are activated in several ways: by thermal receptors in the skin, by direct stimulation of the hypothalamus, and by receptors in the spinal cord and viscera.

Heat receptors are distributed in a definite pattern in the skin. Sensory summation may occur so that the threshold for stimulation decreases as the size of the area stimulated increases. Sensations occur for changes in temperature of a few thousandths of a degree in a second (12).

THERMAL EFFECTS OF MICROWAVE ABSORPTION

In assessing the biologic effects of microwaves, it is essential that the investigation be well-conceived and appropriately conducted, and that an intelligent relationship of exposure to an appropriate biologic endpoint be established. It is difficult, however, to extrapolate to larger animals or man from small laboratory animals with differences in methods and capacities of thermal regulation, different absorption cross section, body size, surface area, and with differences in energy distribution within the body and in metabolic rates.

Under normal circumstances, animals have an average rate of physiologic cooling, whether they are active or at rest, which is determined by (a) geometry — ratio of body volume to surface area, (b) insulating factors — fur or hair, and (c) environmental factors — i.e. temperature differences between the body and its surroundings. The absorption of microwave energy in the animal manifests itself in the form of heat. The irradiated animal must compensate for this heat input or else suffer a rise in body temperature.

The extensive investigations into microwave bioeffects during the last 25 years conclusively show that exposure to power density of 100 mW/cm² for several minutes or hours, depending on the animal species, can result in pathophysiologic manifestations of a thermal nature characterized by a temperature rise which is a function of the thermal regulatory processes and active compensation of the animal. The end result is either reversible or irreversible change depending on the conditions of the irradiation and the physiologic state of the animal. At power densities below 100 mW/cm², however, evidence of pathologic change is nonexistent or equivocal for large animals (24, 25).

Temperature increase in the body during exposure to microwaves depends upon the following factors: (a) animal species, (b) the specific area of the body exposed and the efficiency of heat elimination at that site, (c) thickness of skin and subcutaneous tissue,

WHO – Biologic effects & health hazards of microwave radiation 1974

(d) body type or mass and covering of exposed areas, (e) orientation or position in the electromagnetic field, (f) intensity or field strength, (g) duration of exposure, (h) frequency or wavelength of the energy, (i) environmental temperature, air currents, humidity, (j) condition of the exposed subject, such as state of health, method of restraint, anesthetization or other medication (32, 33).

In partial-body exposure, under normal conditions, the unexposed portion acts as a cooling reservoir to stabilize the temperature of the exposed part. This stabilization is due to an equilibrium established between the energy absorbed by the exposed part of the body and the amount of heat carried away from that area. The heat is transported via increased blood flow to cooler parts of the body that are maintained at normal temperature by heat regulating mechanisms. If the amount of absorbed energy is in excess of the optimal amount of heat energy which can be handled by the mechanisms of temperature regulation, a continuous temperature rise, and under some circumstances local tissue destruction, can result (32, 33).

The thermal response of male Long-Evans rats (350—425 g) exposed to 2450 MHz (CW) in an anechoic chamber maintained at 22°C is shown in Figure 1. All rats were pre-handled and gentled for two weeks prior to exposure. The body temperature was

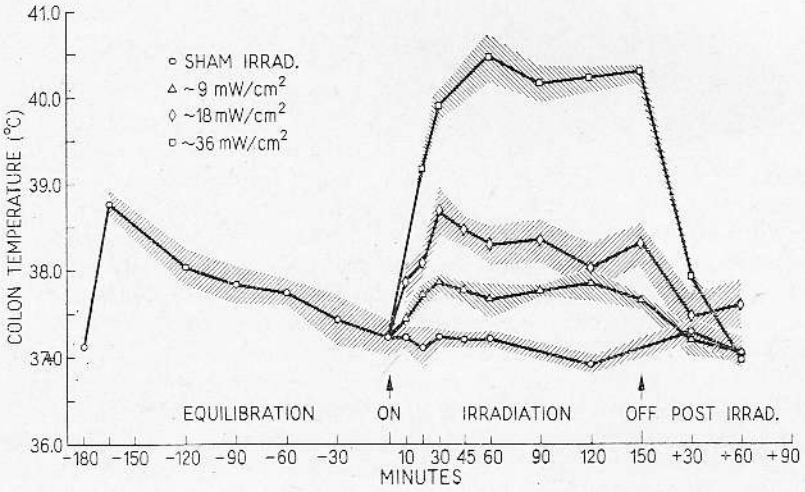


Fig. 1. Colonic temperature response in rats exposed to 2450 MHz CW microwaves.

allowed to equilibrate in the chamber for three hours before irradiation. After 15 minutes in the chamber, the colonic temperature showed an increase which required three hours to return to baseline (17). The results of exposing rats to 9 mW/cm², 18 mW/cm², and 36 mW/cm² for 150 minutes are shown. The 9 mW/cm² level caused a distinct colonic temperature rise, when compared to the sham-irradiated group. A similar temperature response in rats exposed to 2450 mHz (CW), 10 mW/cm² has been reported by Djordjevič and Kolak (8). Incident energy of 18 mW/cm² caused approximately twice the temperature rise as 9 mW/cm². All of the temperatures demonstrated in the irradiated rats were within a range observed in the first fifteen minutes of the equilibration period. Exposure to 36 mW/cm² caused a fourfold increase in colonic temperature. These data suggest the lability of the temperature response of rats as a result of experimental manipulation and the importance of ascertaining the relation of the expo-

WHO – Biologic EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION 1974

sure to the equilibration period in studies involving temperature measurements in rats exposed to microwaves.

The thermal response in the dog exposed to 165 mW/cm², 280 MHz pulsed (360 pulses/sec, 2—3 μsec pulse width) at 30% humidity consists of three phases (25) (Fig. 2). In phase 1, initial thermal response, body temperature increases by 1—2°C, $^1/_2$ hour

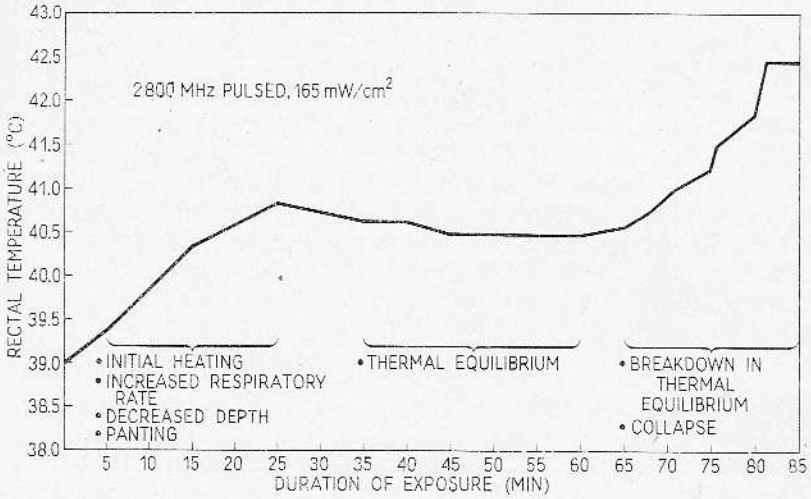


Fig. 2. Thermal response of the dog exposed to 2800 MHz pulsed microwaves, 165 mW/cm².

after onset of exposure. In phase II, period of thermal equilibrium, rectal temperature stabilizes; this may last 1 hour, during which the temperature will cycle between 40.6 and 41.1°C. In phase III, period of thermal breakdown, the temperature rises above 41.1°C, continues increasing rapidly until a critical temperature of 41.7°C, or greater, is reached. If exposure is not stopped, death will occur. Exposure of dogs at 100 mW/cm² for periods up to 6 hours does not cause a critical rectal temperature. Initial heating is slight, the animal remaining in thermal equilibrium during the remainder of exposure (Fig. 3).

On the basis of observations on rats exposed to microwaves, Gordon (13) has concluded: (a) there is an inverse relationship between the microwave intensity and the elapsed time until death of the exposed animals; (b) the reaction of animals to micro-

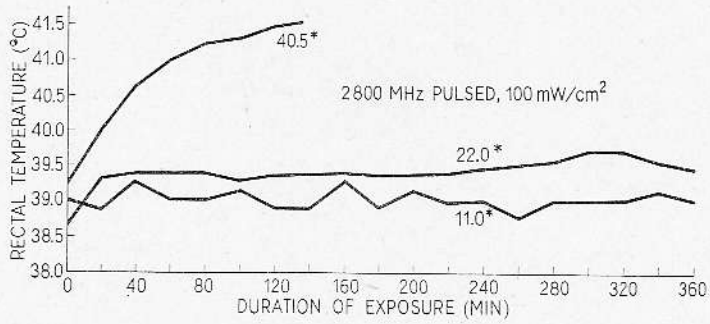


Fig. 3. Response of dogs exposed to 2800 MHz pulsed microwaves, 100 mW/cm² at various environmental temperatures*.

WHO – Biologic effects & health hazards of microwave radiation 1974

wave exposure always involves the following three periods: an orientation period, an excitation period, and a passive period (with occasional spasms) leading to death from hyperthermia; (c) hyperthermia is due to absorption of the incident energy and its conversion to thermal energy by dielectric losses in the tissues; there is evidently also a direct effect of microwaves on the thermoregulatory centers; (d) the most rapid lethal outcome is produced by irradiation with 10-cm waves of high power density; the effect of decimeter, 3-cm and 5-mm waves is less pronounced; (e) for the same power density of 10-cm waves, lethality is higher and more rapid with pulsed than CW waves; (f) the survival of animals exposed to microwaves, of even low power density, may be affected by changes in their diet or water intake. Irradiation impairs the animal's tolerance to subsequent physical stress. Temperature response obtained by Gordon (13) is shown in Table 1. She showed that for a constant exposure time of 15—30 min, decimeter (dm), centimeter (cm) and millimeter (mm) waves produced rises in rectal temperature at different threshold intensities. The limiting suboptimal power densities were respectively, 5—7 mW/cm² for mm waves, 10 mW/cm² for 10-cm waves and >40 mW/cm² for dm waves. A comparable wavelength dependence of thermogenesis has been seen in the dog where 2800 MHz pulsed caused a greater thermal effect than 200 MHz CW (Fig. 4).

Table 1

Increment of Body Temperature upon Exposure of Rats to Continuous or Pulsed 10-cm Waves for 30 Min*

Irradiation intensity (mW/cm²)	CW λ = 10 cm	Pulsed λ = 10 cm
	Δt (°C)	Δ (°C)
2.5	−0.3	−0.2
5.0	−0.2	−0.3
7.5	−0.3	−0.1
10.0	+0.3	+0.1
control animals	−0.1	−0.1

* From Gordon (13).

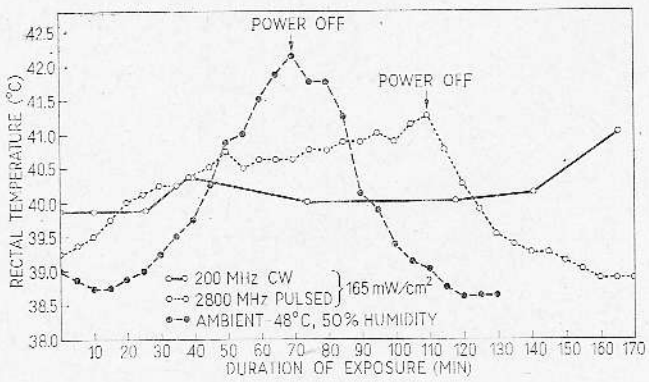


Fig. 4. Comparison of the thermal response of the dog exposed to 2800 MHz pulsed and 200 MHz CW microwaves, 165 mW/cm².

WHO – Biologic effects & health hazards of microwave radiation 1974

The influence of body size

Evidence is available on the relationship of species or body size and sensitivity to microwaves. The survival time of rats exposed to microwaves (13) is noted in Table 2. In contrast, exposure of dogs to 2800 MHz pulsed, 100 mW/cm² could be continued

Table 2

Survival Time of Rats Exposed to Microwaves*

Wave range	Time of death (min)		
	100 mW/cm²	40 mW/cm²	10 mW/cm²
Decimeter	60 (50%)	Survived for 2 h	Survived for 5 h
10-cm	60 (100%)	40 (50%)	Same
3-cm	110 (50%)	Survived for 3 h	,,
Millimeter	180 (50%)	Same	,,

* From Gordon (13).

for 6 hours or more (Fig. 3). The apparent greater sensitivity of smaller animal species (rats and rabbits) can be seen in Figure 5. Although a greater sensitivity of rabbits and rats is shown, it is not quite clear whether it is only the body size which is a factor or whether specific differences in physiologic regulation among species may play an equally important part in the response (25). In whole-body exposure of different species of

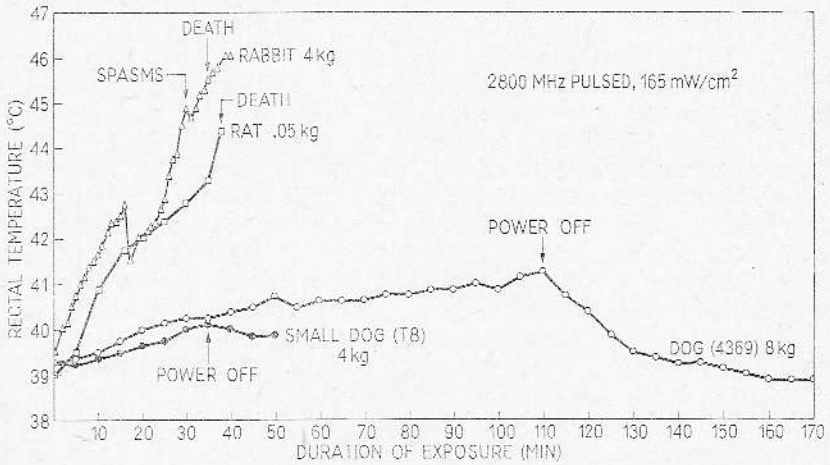


Fig. 5. Thermal response of various species of animals exposed to 2800 MHz pulsed microwaves, 165 mW/cm².

animals, Tjagin (39) demonstrated that the response was dependent not only upon the power density but also upon the animal's size and the quality of its thermoregulatory apparatus. Exposure to 300 mW/cm² raised the rectal temperature by 1—1.5°C in dogs, 6.6—7°C in cats and rabbits, and 7.9—10°C in rats. Subbota (36) noted that of the variations in respiration, pulse rate and blood pressure of dogs exposed in short-term ex-

WHO – Biologic effects & health hazards of microwave radiation 1974

periments to high power densities (200—300 mW/cm²), the blood pressure was the most stable parameter. Other experimental animals (cats and rabbits) were killed by such intensities. At 10 mW/cm² no changes in the cardiovascular system appeared. These results emphasize the need for appropriate scaling, gauging or proportionality factors that have to be invoked in any interspecies comparison of microwave bioeffects among laboratory animals and especially between animals and man.

Thermal gradients and distribution of heat

The distribution of heat induced by microwaves in the body and particularly the brain has been of interest to various investigators using models and confirming the results by animal experimentation (15, 18, 19, 34). These investigations and their implications will be discussed by Drs. Schwan and Guy.

Using the percentage of EM energy absorbed in various body tissues which can be estimated approximately from the electric parameters of the tissues, Presman (30) made calculations for the case of exposure of the occipital region of the head of man, rabbits, and rats to EMF's of superhigh frequency. He found that the amount of energy that penetrates into the subcortical structures varied according to animal size (Tab. 3).

Table 3

Percent of Microwave Energy that Penetrates into Subcortical Structures of Various Animals*

	1000 MHz	2000 MHz	4000 MHz
Rat	30	20	5
Rabbit	20	10	<5
Man	5	<5	0

* Estimated from Presman (30).

In considering the implications of these studies it is important to realize that brain temperature is not uniform. There is a gradient of approximately $^1/_2$°C between surface and deep brain structures (7). Further, the brain regions which are directly sensitive to temperature (i.e. central thermodetectors) and control peripheral thermoregulatory mechanisms during heat stress are located in the anterior hypothalamus/preoptic area (AH/PO) (21). Since microwave power absorption in the brain is non-uniform owing to the nature of EM/tissue interactions and the possibility of hot spots, the choice of brain location for temperature measurement will materially affect the results. It should also be pointed out that so-called core or high colonic temperature is a poor substitute for brain temperature. Numerous reports, where cranial and rectal temperatures were simultaneously measured, have demonstrated that the temperatures diverge with unpredictable phase and amplitude differences (1).

Brain temperature elevations more than about 2°C above set-point are sufficient for paradoxical thermoregulatory responses (20). Successful thermoregulation takes place within this span of AH/PO temperature increases. Once beyond this range, the hyperpyrexia could become irreversible due to positive feedback. It has been demonstrated that 0.1°C is the smallest temperature elevation with physiological significance. Von Euler (40) has shown that a 0.1°C elevation in anterior hypothalamus/preoptic area temperature results in the generation of a 100 mV steady potential in that structure.

WHO – Biologic effects & health hazards of microwave radiation 1974

Peripheral evidence of heat loss mode processing by central thermoregulators occurs with about $^1/_2$ to 1°C AH/PO temperature elevation (35).

In essence, investigations of the distribution of heat reveal that analysis of microwave bioeffects and attempts to extrapolate them to man must take into consideration the importance of animal size, thermal gradients and species differences in regard to brain circulation and regulation of brain temperature. It is apparent that physiologic responses to subtle temperature changes may occur in small animals which have no relevance for larger animals and man.

Repeated exposures — compensation, adaptation or acclimatization

Gordon (13) has reported that rats exposed to sublethal levels (10 mW/cm²) of mm, cm or dm waves showed greater tolerance to repetitive exposures and were in a satisfactory state after 5—10 sessions. She suggests that presumably the increased tolerance is due to compensatory mechanisms that are called into play.

A similar pattern has been observed in dogs exposed to 2800 MHz or 1280 MHz pulsed. Repeated exposures to 165 mW/cm², 2800 MHz pulsed resulted in improved tolerance as evidenced by the ability to successively prolong exposure time with minimal increase in temperature and progressive depression of "basal" temperature (Fig. 6). Exposure of dogs to 1280 MHz pulsed, 100 mW/cm², six hours/day, five days/week for four weeks revealed an increase in rectal temperature during each exposure for

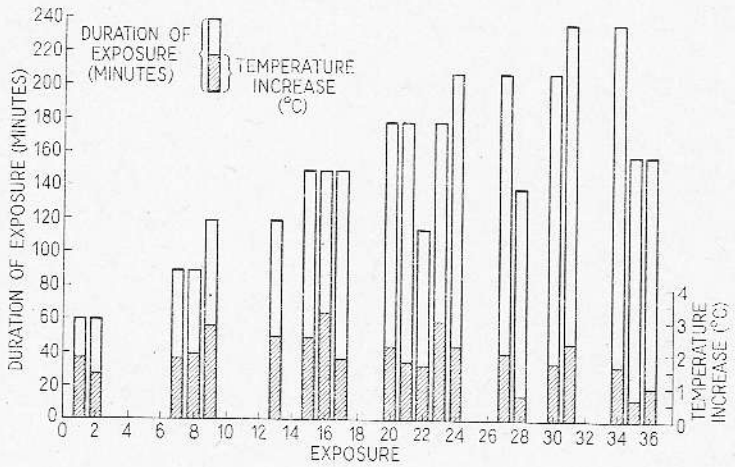


Fig. 6. Microwave tolerance in dogs repetitively exposed to 2800 MHz pulsed microwaves, 165 mW/cm².

the first week. During the subsequent three weeks, temperature increases were moderate. A progressive lowering of pre-exposure temperature was evident as the number of exposures was increased. Exposure to 50 mW/cm² initially resulted in slight temperature increase. Progressive lowering of the pre-exposure temperatures was noted as the exposures were repeated (Fig. 7).

Phillips et al. (28) noted acclimatization in rats exposed repetitively to 2450 MHz pulsed (20 mW/cm² or 30 mW/cm² estimated) using temperature response, ECG and heart rate as criteria.

In rats exposed to 2450 MHz (CW), 10 mW/cm², 2 hours a day for 30 days, a slight thermal effect and increase in some blood elements occurred during the first phases

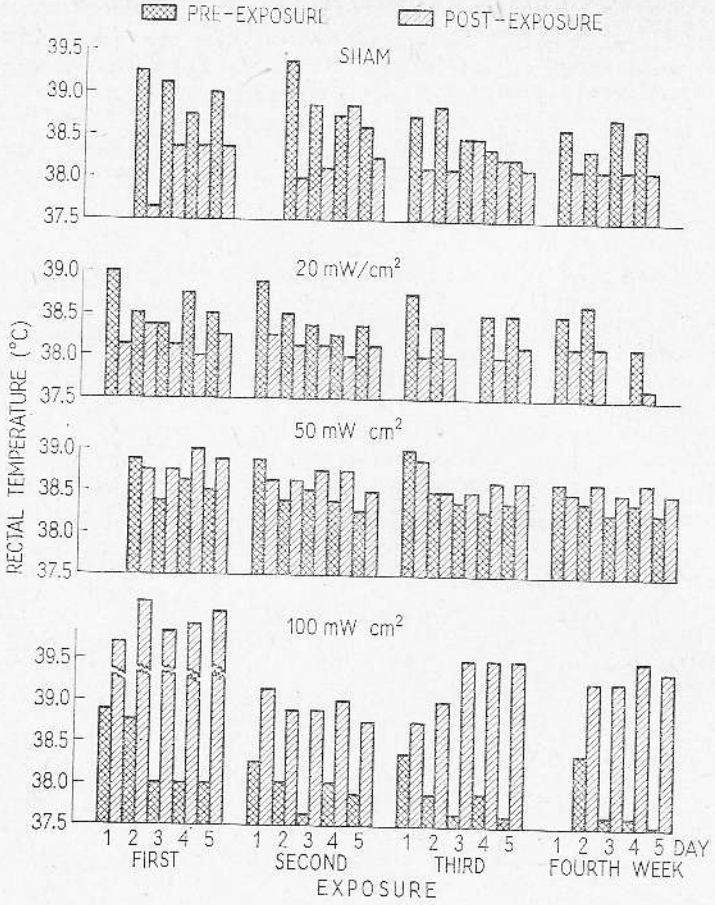


Fig. 7. Microwave tolerance in dogs repetitively exposed to 1285 MHz pulsed microwaves.

of irradiation with a later tendency towards normalization or adaptation (8). Exposure of rats to 3000 MHz at 16—94 mW/cm² for 1 min per day led at first to enhanced excitability (after 14—20 exposures) and then to reduced excitability (26, 27).

No cumulative effect of microwaves has been demonstrated if maintenance of adequate thermal regulation is used as the criterion. Intermittent exposure of the normal animal can be tolerated for extended periods of time and is related to the interval between exposures which permits the animal time to recover. These findings of physiologic adjustment to repeated exposures make one ponder the validity or meaning of the reports which suggest cumulative effects of microwave exposure below injury threshold levels.

Cataractogenesis

Thermally induced opacification of the lens of the eye can occur as a result of microwave energy absorption. Dr. Carpenter will review these findings.

I might just point out that careful analysis of the work of Carpenter et al. (4, 5), as well as Williams et al. (41) and Birenbaum et al. (2), reveals that whenever cataracts

WHO – Biologic effects & health hazards of microwave radiation 1974

are produced among animals subjected to different power-density-time relationships, a threshold becomes obvious. No one has yet been able to produce cataracts even by repetitive exposures when the power-density-time relationship is really below threshold.

It is important to note that lens opacity has consistently been produced in only one species, namely the rabbit. Although the rabbit has been traditionally used for studies of microwave cataractogenesis, one might ask whether this species is the most appropriate model? We cannot exclude the possibility that there may be a true difference in threshold values for lens changes in various species *in vivo,* even though this may not be readily or easily confirmed (11). No doubt one also has to be concerned with thermal gradients in the eye. For example, in the normal rabbit, with a corneal temperature of 32.3°C, the aqueous humor will have a temperature of 33°C; the anterior surface of the lens, 33.6°C; the interior of the lens, 35.4°C; the vitreous humor, 36.5°C and the retina, 37°C (31). Such temperature differences have to be taken into consideration when trying to relate cataractogenesis with temperature measurements in the eye. In addition, the metabolism of the eye is influenced by temperature. Thus, interspecies relationship of biochemical constituents has to be taken into consideration.

Neural effects

Reported neural effects and behavioral changes resulting from exposure to microwaves are not necessarily inconsistent with thermogenesis. It should be noted that behavior is not a simple process but is the expression of different effects in various body systems. Temperature input signals arise in many body structures that have been shown to evoke behavioral and/or physiological responses to changes in local temperature.

Pinneo et al. (29) have postulated that many so-called "non-thermal" effects of microwave exposure may actually be specific thermal effects on certain neural structures. They examined the thermal stimulation of peripheral nerves exposed to 3000 MHz and 10,000 MHz microwaves and infrared energies. They showed that all three sources of energy produced the same effects on the central nervous system, and suggested that experiments purporting to show non-thermal effects should be examined with the possibility in mind that a thermally-induced neuro-physiological response may have occurred.

McAfee (23) points out how data can be misinterpreted as the result of some unknown effect of microwave radiation, when hyperthermal effects are not involved. In cats, when peripheral nerves are stimulated by 45°C temperature, adrenal medullary secretion occurs and a rise in blood pressure is developed as a result of adrenal secretion (22). It appears that functional cardiac changes can occur as a result of microwave exposure, no doubt as a response of the autonomic nervous system to the thermal effects. Thermal stimulation of peripheral nerves can produce the neurophysiological and behavioral changes that have been reported. The interaction between the peripheral nervous system and the central nervous system would account for the reported effects on heart rhythm, blood chemistry, etc.

EXTRAPOLATION FROM ANIMAL TO MAN

It is apparent that extrapolation from animal to man is most complex. Observations in the living animal indicate some of the variables that are a result of the interplay of physical factors and physiological controls in a living dynamic system with multiple

WHO – Biologic effects & health hazards of microwave radiation 1974

integrative functions, feedback mechanisms, and redundancy for which the individual relies upon homeokinesis.

One of the problems in studying biologic effects of microwaves, as in all biomedical investigations, is the selection of the most appropriate animal species for study. Animals are quite often selected only on the basis of convenience, economy or familiarity and without regard to their suitability for the problem under study. Because of the lack of awareness and concern in the selection of the experimental animal, many investigations have no inherent value in so far as extrapolation to man is concerned and, in some cases, have led to incorrect interpretations necessitating expensive, time-consuming attempts at confirmation or logical application of the data.

Many animal studies on the response to RF or microwave exposure have been done with small rodents, the responses of which are not readily applicable to human beings, owing to differences in coefficients of heat absorption, different thermal distribution, small body surfaces, and relatively poor thermal regulation in contrast to man who has one of the best thermal regulatory mechanisms.

A comparative approach with appropriate "scaling" or use of proportionality factors is basic to the elucidation of the nature of vital processes among animals and to place man in his proper biological perspective; it relates the different ways in which various species maintain homeostasis, characterizes animals particularly suitable for demonstrating specific responses, integrates and coordinates anatomic, physiologic, biochemical, and pathologic similarities of various groups of animals. From a comparative approach we can learn what biologic attributes are unique or common among different animals, study interrelations with environmental stresses and find animals that are most suitable for study of important functions to provide a basis for biological generalization. It behoves the investigator to become aware of the attributes of various animals to obtain the most meaningful results for studying the effects of RF or microwave exposure so that reliable and relevant extrapolation to man can be made.

CONCLUSION

I would like to conclude on a personal note. We, as scientists, concerned with the biologic effects and health implications of microwave exposure should relate to the concerns and needs of society. It is paramount, nevertheless, that we do not succumb to social and political pressures or aspirations. Science is knowledge based on various activities and disciplines which involve systematic and unbiased observation.

In this year, the quincentennial of the great Polish scientist Nicholas Kopernik (Copernicus), let us not lose sight of the contributions by which he, through penetrating analysis, observations, and mathematical calculations, fought and overcame the prevailing view held since the time of Ptolemy, of the geocentric construction of the Universe and replaced it with his scientifically proved heliocentric theory. Kopernik was followed by other great philosophers of science, such as Francis Bacon in the 16th century, who insisted on the close and methodical observation of facts, setting the basis for a considerable portion of the scientific method. In the 17th century, René Descartes strove to create a new methodology in science based more on deduction than experience, resulting in a monumental discourse on methods. Finally, in the present century, with the thoughts and works of Albert Einstein and his concepts, a system that is mathematically verifiable, based upon time-space relations, is now possible.

From these great philosophers of science the scientific or hypotheticodeductive method has evolved to which we all should subscribe. This philosophy can be separated into

WHO – Biologic effects & health hazards of microwave radiation 1974

four parts which may be classified as: 1) collecting a series of observations, 2) forming an hypothesis that links the observations, 3) testing the truth or falsehood of the hypothesis and 4) using the hypothesis in examination of further observations or re-examinations of those already considered. When the hypothesis answers suitably to repeated or sufficiently delicate tests, we have a finding.

It is disturbing to read certain "scientific" articles or reports which are contrived to convince the reader of the truth of certain views or to put him in possession of certain knowledge. Such works quite often obscure the process by which the expounded views were reached, which usually consists of a series of improvised judgements of working hypotheses interspersed with a provisional series of observations. Many such judgements are normally found untenable and many observations irrelevant, ill-chosen, badly-made or in need of further tests.

In this presentation, an attempt has been made to review, synthesize, and critically analyze the thermal response to microwave exposure. Although there is considerable agreement among scientists, there are lacunae of disagreement. It is highly recommended that apparent discrepancies be studied and analyzed in detail, taking into consideration all the biophysical, biochemical and physiological factors inside the body and external factors that might influence the response of the organism. One must consider the homeokinetic systems that might be involved in regulation as a result of exposure to microwave energy. Free international exchange of information and closer personal contact between scientists would be invaluable in helping to resolve the discrepancies and divergence of opinion that exists in the understanding of some of the biologic and clinical effects of exposure to microwave energy.

REFERENCES

1. BENZINGER, T. H.: *JAMA.*, 1969, **209**, 1200.
2. BIRENBAUM, L., GROSOF, M., ROSENTHAL, S. W., ZARET, M. M.: *IEEE Trans. Biol. Med. Eng.*, 1969, **BME-16**, 7.
3. BLIGH, J.: *Temperature Regulation in Mammals and Other Vertebrates.* American Elsevier Publishing Co. New York, 1973.
4. CARPENTER, R. L., BIDDLE, D. K. VAN UMMERSEN, C. A.: *Proc. Third Int. Conf. Med. Electr.* (London), 1960, **3**, 401.
5. CARPENTER, R. L., VAN UMMERSEN, C. A.: *J. Microwave Power* 1968, **3**, 3.
6. CURRIER, D. P., NELSON, R. M.: *Phys. Ther.* 1969, **49**, 146.
7. DELGADO, J. M. R., HANAI, T.: *Amer. J. Physiol.*, 1966, **211**, 755.
8. DJORDJEVIC, Z., KOLAK, A.: *Aerospace Med.*, 1973, **44**, 1051.
9. DUBOIS, E. F.: *Bull. N. Y. Acad. Med.*, 1934, **15**, 143.
10. FISCHER, E., SOLOMON, S.: Physiological Responses to Heat and Cold. In: *Therapeutic Heat.* 5th ed. Ed.: S. H. Licht, Elizabeth Licht. New Haven, Conn., 1958, p. 116.
11. GEERAETS, W. J.: *Industr. Med.*, 1970, **39**, 441.
12. GILSTRAP, L. O., JR., McNEIL, J. S.: GREENBERG, L. P., SPODAK, R. B.: *A Compilation of Biological Laws, Effects, and Phenomena, with Associated Physical Analogs.* Wright-Patterson Air Force Base, Ohio, 1964.
13. GORDON, Z. V.: *Biological Effect of Microwaves in Occupational Hygiene.* Izdatelstvo Medicina, Leningrad, Otdelenie, 1966 (TT 70-50087, NASA TT F-633, 1970).
14. GORDON, Z. V.: Occupational Health Aspects of Radio-Frequency Electromagnetic Radiation. In: *Ergonomics and Physical Environmental Factors.* Occupational Safety and Health Series 21. International Labour Office. Geneva, 1970, p. 159.
15. GUY, A. W.: *IEEE Trans. Microwave Theory and Techniques* 1971, **MTT-19**, 205.
16. HORVATH, S. M., RUBIN, A., FOLTZ, E. L.: *Amer. J. Physiol.*, 1950, **161**, 316.
17. HOUK, W. M., MICHAELSON, S. M., LONGACRE, A., JR.: *The Physiologist.*, 1973, **16**, 347.
18. JOHNSON, C. C., GUY, A. W.: *Proc. IEEE.* 1972, **60**, 692.
19. KRITIKOS, H. N., SCHWAN, H. P.: *IEEE Trans. Biol. Med. Eng.*, 1972, **BME-19**, 53.

WHO – Biologic effects & health hazards of microwave radiation 1974

20. LARSEN, L. E., MOORE, R. A., ACEVEDO, J.: An RF Decoupled Electrode for Measurement of Brain Temperaturi During Microwave Exposure. In: *Proc. 1973, IEEE G-MTT Intl. Microwave Symp.* (in press).
21. MAGOUN, H. W., HARRISON, F., BROBECK, J. R., RANSON, S. W.: *J. Neurophysiol.*, 1938, **1**, 101.
22. McAFEE, R. D.: *Amer. J. Physiol.*, 1962, **203**, 374.
23. McAFEE, R. D.: *IEEE Trans. Microwave Theory and Techniques*, 1971, **MTT-19**, 251.
24. MICHAELSON, S. M.: *IEEE Trans. Microwave Theory and Techniques*, 1971, **MTT-19**, 131.
25. MICHAELSON, S. M., THOMSON, R. A. E., HOWLAND, J.: *Biologic Effects of Microwave Exposure.* Griffiss Air Force Base, New York, Rome Air Development Center. ASTIA Doc. No. AD 824-242, 1967.
26. MINECKI, L., OLUBEK, K., ROMANIUK, A.: *Medycyna Pracy*, 1962, **13**, 255.
27. MINECKI, L., ROMANIUK, A.: *Medycyna Pracy*, 1963, **14**, 355.
28. PHILLIPS, R. D., KING, N. W., HUNT, E. L.: *Thermoregulatory, cardiovascular and metabolic response of rats to single or repeated exposure to 2450 MHz microwaves.* Presented at 8th Annual Microvawe Power Symp. Loughborough, U. K., 1973.
29. PINNEO, L. R., BAUS, R., MCAFEE, R. D., FLEMING, J. D.: *The Neural Effects of Microwave Radiation.* Arlington, Virginia. AD 722684, RADC-TDR-62-231, 1962.
30. PRESMAN, A. S.: *Usp. Fiz. Nauk*, 1965, **86**, 263.
31. PRINCE, J. H. (Ed.): *The Rabbit in Eye Research.* Charles C. Thomas. Springfield, Ill., 1964.
32. SCHWAN, H. P., PIERSOL, G. M.: *Amer. J. Phys. Med.*, 1954, **33**, 371.
33. SCHWAN, H. P., PIERSOL, G. M.: *Amer. J. Phys. Med.*, 1955, **34**, 425.
34. SHAPIRO, A. R., LUTOMIRSKI, R. F., YURA, H. T.: *IEEE Trans. Microwave Theory and Techiniques*, 1971, **MTT-19**, 187.
35. STROM, G.: Central Nervous Regulation of Body Temperature. In: *Handbook of Physiology.* Sect. 1. Neurophysiology, vol. 2. American Physiological Society. Washington, D. C., 1961, p. 1173.
36. SUBBOTA, A. G.: Tr. Voj. Med. Akad. im. Kirova (USSR), 1957, **73**, 111.
37. THAUER, R.: Circulatory Adjustments to Climatic Requirements. In: *Handbook of Physiology.* Sect. 2. Circulation. vol. 3. Ed.: Hamilton, W. F., Dow, P.: American Physiological Society. Washington, D. C., 1965, p. 1921.
38. TOLGSKAJA, M. S., GORDON, Z. V.: *Pathological Effects of Radio Waves*, Medicina, Moscow, 1971 (Consultants Bureau. New York, 1973).
39. TJAGIN, N. V.: *Tr. Voj. Med. Akad. im. Kirova* (Leningrad), USSR, 1957, **73**, 9.
40. VON EULER, C.: *J. Cell. Comp. Physiol.*, 1950, **36**, 333.
41. WILLIAMS, D. B., MONAHAN, J. P., NICHOLSON, W. J., ALDRICH, J. J.: *AMA. Arch. Ophthalmol.*, 1955, **54**, 863.
42. ZYSNO, E. A., REICHENMILLER, H. E.: *Arch. Phys. Ther.* (Leipzig), 1968, **20**, 465.

WHO – BIOLOGIC EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION 1974

RAPID WARMING FROM HYPOTHERMIA BY MICROWAVES

H. D. Baillie

Crumpsall Hospital, Manchester, England

INTRODUCTION

There has been a plea for further research on the possible nonthermal effects of microwave radiation (1). The importance of this subject in assessing health hazards and establishing safety standards was stressed when strong evidence was presented indicating that nonthermal effects could be cumulative (2).

A recent report suggested that hypothermia could be used for unmasking nonthermal effects during powerful exposures of short duration (3). This suggestion could be applied with advantage.

The following study describes a microwave method for producing rapid warming from hypothermia in the rat. It was developed for investigating the physiological responses to rapid warming but it may prove of value for research on the nonthermal effects of microwaves.

In a preliminary report (4) unmodified exposure of a hypothermic rat in a microwave cavity was shown to produce burns of the animal's extremities. This overheating was prevented by converting the animal's body to a uniform geometric shape by immersing it in a water jacket during exposure.

The final design of the water jacket and details of the rapid warming method are described in this communication.

APPARATUS, METHODS AND MATERIALS

Wistar rats weighing between 200 and 250 g were used in this study.

Anesthesia

All experiments were performed with the animals under general anesthesia. The anesthetic gas mixture was nitrous oxide 70%, oxygen 30% with halothane vapor 0—2.5%. The percentage of halothane was reduced during cooling and it was discontinued at 30°C. At lower temperatures anesthesia was maintained by cold narcosis. As cooling proceeded the oxygen concentration was rapidly increased to 100% so that the body fluids were saturated with this gas at the lower limit of hypothermia. The technique was reversed during warming.

Colling and Warming by Conduction

Surface cooling and warming were accomplished by spraying the upturned thorax and abdomen with water at the appropriate temperature. The apparatus consisted of a water reservoir and a spray driven by an electric pump. The animal's body was held in a small plastic box. This had a head recess for administering the anesthetic gases

and an outlet pipe for returning the water to the reservoir. Water at 4°C was used for cooling and its temperature was maintained by adding ice. The ice-water was replaced by water at 40°C for surface warming. This temperature was maintained by a thermostatically controlled electric heating element located in the base of the reservoir.

Monitoring

The body temperature was recorded by rectal and mid-esophageal thermocouples during surface cooling and warming. The respiratory rate was counted by observing the chest movements and the heart rate was recorded by electrocardiography.

The Control Group of Rats

Twelve rats were cooled to 18°C and warmed to normal body temperature using the water spray. The cooling and warming times were recorded with the other parameters.

All other rats were cooled by the water spray and warmed by microwaves.

Microwave Warming

The apparatus was a 3 m × 1 m × 1 m cavity which was energized at a nominal frequency of 2.5 GHz by three water-cooled magnetrons. It contained a mode stirrer and a series of reflector plates which prevented the formation of static points of focal concentration in the random field of microwaves which was formed by reflection from its metallic interior. The magnetrons were each rated at 1.5 kW giving the cavity a dielectric heating power of 4.5 kW under optimal conditions. This heating power could be adjusted between zero and the maximum from a control console. The field in the center of the cavity was uniform in terms of its heating ability as shown by tests with a water load placed at different positions. This was the working area of the cavity and it contained a thin plastic staging for supporting the water jacket. The frequency of the microwaves corresponded to a free-space wavelength of 12.4 cm when measured with a coaxial wavemeter (Fig. 1).

The water jacket was made of plastic (Perspex). It was a vertical cylinder closed at the lower end by a 15 cm × 15 cm plate. This plate was supported at the corners by legs which were 3 cm high. The cylinder was 32 cm in height and it had an internal diameter of 6.5 cm. Compressed air was piped through the base to ensure gentle agitation of the water during exposure. The immersed rat was prevented from drowning by enclosing the head in a cylindrical plastic helmet. The anesthetic gases were piped through the upper surface of the helmet and they escaped from its lower border to the surface of the water. The rat's head was secured within the helmet by a collar. This was a circular disc with a slot cut away for the neck. The collar was fixed to the base of the helmet by a screw ring (Fig. 2).

Hypothermic rats were warmed from 18°C to determine the exposure time which would raise the body temperature to 38°C with the apparatus working at full power. During these observations the initial water jacket temperature was varied to determine the value which would ensure a water temperature of 40°C at the end of the exposure. This was repeated with the apparatus working at two thirds and one third of the power.

When these values had heen obtained three groups of twelve rats were warmed from 18°C to 38°C, one group for each power setting. The condition of the rats following

WHO – Biologic effects & health hazards of microwave radiation 1974

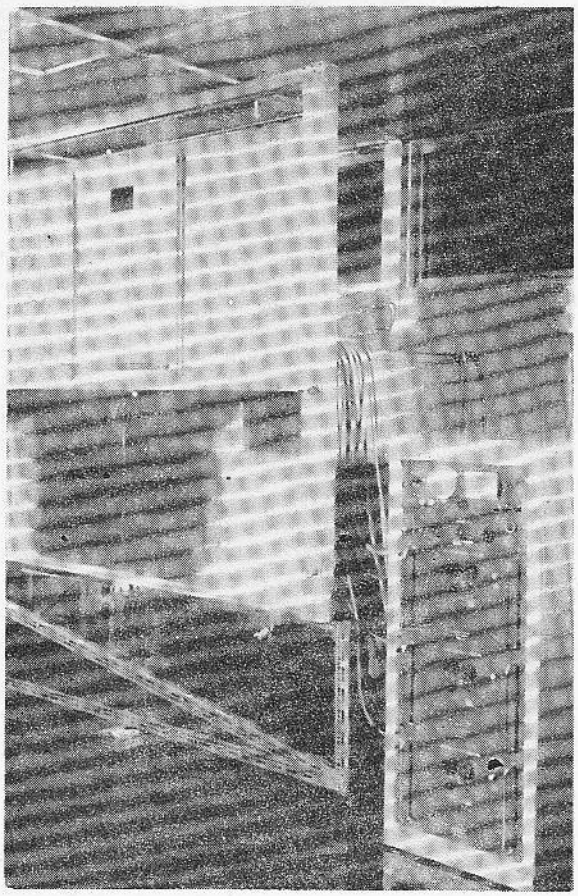


Fig. 1. The M. H. 1500 Microwave Cavity and Control Console. Original design of this experimental model by Elliot Electronics: England. One magnetron housing is seen on the top of the cavity behind the sliding door. The mode stirrer is located in the roof of the cavity behind the lower edge of the sliding door.

warming was observed. Damaged survivors were destroyed. The remaining survivors were allowed to recover from the anesthetic and they were returned to their cages for observation. Where minor burns became apparent after a delay, these animals were also destroyed. The others were maintained for three months before being subjected to post mortem examination.

Variations in the temperatures of the body tissues were studied in two rats following microwave warming from 18°C. One of the animals was killed before warming to eliminate circulatory effects. The tissues were probed with a thermocouple needle immediately after warming and again after a delay of two minutes.

Finally one rat was killed and skinned. The outline of the skin was traced on graph paper so that an estimate of the animal's surface area could be made for power calculations.

WHO – Biologic effects & health hazards of microwave radiation 1974

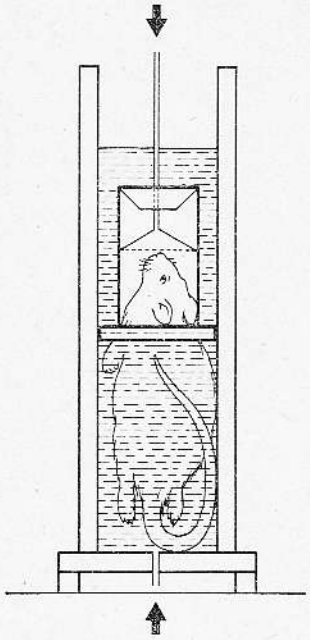


Fig. 2. The Perspex water jacket with the rat and helmet. The lower arrow indicates the inlet for the piped air supply. The upper arrow indicates the inlet for the anesthetic gases.

RESULTS

The twelve rats of the control group (those cooled and warmed by the water spray) all survived. The mean cooling time was 20 minutes and the mean warming time was 30 minutes (Fig. 3).

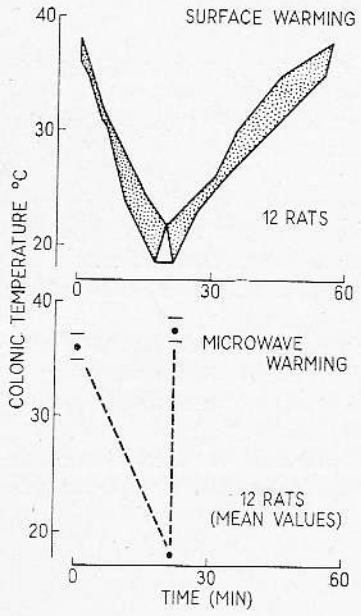


Fig. 3. The cooling and warming graphs of body temperature with time. The horizontal dashes bordering the pre-cooling and post-warming temperatures enclose two standard deviations.

WHO – Biologic effects & health hazards of microwave radiation 1974

The preliminary experiments with microwave warming indicated that a 20-second exposure was required to raise the body temperature of a 220 g rat from 18°C to 38°C when the apparatus was working at full power. The exposure time for warming through this range was shown to be inversely proportional to the power setting. Accordingly the exposure time required for warming at $^1/_3$ power was 60 seconds.

The volume of water required to cover the upper surface of the helmet with an adequate safety margin was in the region of 420—430 ml when the rat weight was approximately 220 g. This volume varied slightly according to the position adopted by the body. The initial water temperature needed to be no higher than 14°C to ensure that it did not exceed 40°C at the end of exposure.

The recordings of the heart rate and the respiratory rate were used for estimating the clinical state of the animal during cooling and warming. The measurements were obviously restricted to the pre- and post-warming periods where microwave warming was used. The values varied considerably with the level of hypothermia and the depth of anesthesia. In general the heart rate fell from the region of 420/minute to 100/minute during cooling. Similarly the respiratory rate fell from 100/minute to 10—20/minute. The heart rate and respiratory rate were if anything slightly faster than normal after warming by both methods.

The rectal and mid-esophageal temperatures did not differ significantly.

There were three deaths during microwave warming in the group of twelve rats warmed in the apparatus at full power. Two of the survivors developed superficial burns of the rump and they were destroyed.

Two deaths occurred in the group of twelve rats warmed at $^2/_3$ of the power. There were no obvious detrimental effects of microwave warming in the survivors.

All deaths during warming were due to cardio-respiratory failure as there was no evidence of thermal damage at post mortem.

All twelve rats warmed at $^1/_3$ of the power survived unharmed. This was cosidered to be the successful group. Accordingly this warming rate of 20°C in 60 seconds was considered to be the safe limit of microwave warming under the experimental conditions. For this reason the comparison of microwave warming with conventional conduction warming was restricted to this group (Fig. 3, Tab. 1).

During the three month period of observation all the undamaged survivors behaved in a normal manner. Several litters were produced and the offspring were bred through two generations. No specific studies were made on these animals but their apparent

Table 1

The mean values of results for rats warmed from 18°C to 38°C using $^1/_3$ of the rated power of the cavity. Standard Deviations in parenthesis.

Body Weight	216 g	(15 g)
Initial Temperature	36°C	(1°C)
Hypothermic Temperature	17.8°C	(0.5°C)
Cooling Time	21 min	(2.4 min)
Post Warming Temperature	37.7°C	(1.2°C)
Rise in Body Temperature	19.9°C	(1.3°C)
Volume of Water in Jacket	428 ml	(4.6 ml)
Initial Water Temperature	14.4°C	(0.3°C)
Final Water Temperature	39.8°C	(1.4°C)
Rise in Water Temperature	25.7°C	(1.2°C)
Exposure Time	60 s	

WHO – Biologic effects & health hazards of microwave radiation 1974

Table 2

Variations in tissue temperature following microwave warming. Rat one killed before warming. First temperature reading made immediately after warming. Second temperature reading made two minutes after warming.

Tissue	Rat One Readings °C		Rat Two Readings °C	
	Ist	2nd	Ist	2nd
Skin	37	36	34	34
Liver	39	38	38	37
Large Intestine	36	37	34	28
Small Intestine	37	36	33	32
Kidney	39	38	38	36
Stomach	38	37	37	36
Lungs	35	35	37	36
Heart	38	37	36	36

normality was remarkable in view of the physiological stress suffered by their antecedents.

The variations in tissue temperature following microwave warming were virtually unaffected by the state of the circulation or a delay in making the measurements (Tab. 2).

The surface area of the 216 g rat was estimated to be 225 cm².

DISCUSSION

Safe microwave warming from 18°C to 38°C was achieved under the experimental conditions. This was twenty times faster than conventional surface warming. The experiments indicated that the physiological stress of rapid warming was well tolerated by the rat.

The division of power during microwave warming was calculated from the results. The mean rat weight, 216 g, was raised through 20°C in 60 seconds. The specific heat of the body was assumed to be 0.83 (5) and 1 kW was represented as 239 cal/s. The calculation indicated that power dissipation in the rat was at a rate of 0.25 kW. The mean water volume was 428 ml and this was raised through 27° C. Accordingly, power was dissipated in the water surrounding the rat at a rate of 0.75 kW. These were the figures with the cavity working at one third of its rated power. Inefficient coupling of the microwave field to the dielectric load, heat loss and power dissipation in the plastic accessories were thought to account for the remaining 0.5 kW.

It was impossible to measure the field strength of the microwaves in terms of mW/cm² for comparison with other studies where biological materials were exposed to beamed microwaves in free space. However it was desirable to make some estimate in these terms in view of the popular interest in the biological hazards of microwaves and safety standards for this type of electromagnetic energy.

One may suggest that the non-reflected part of the field incident on the animal had a power density which was functionally equivalent to 1100 mW/cm² as the estimated surface area of the 216 g rat was 225 cm².

WHO – Biologic effects & health hazards of microwave radiation 1974

REFERENCES

1. CLEARY, S. F.: *Am. Ind. Hyg. Ass. J.*, 1970, **31**, 52.
2. CARPENTER, R. L., BIDDLE, D. K., VAN UMMERSEN, C. A.: *IRE Trans. Med. Electron*, 1960, **ME-7**, 152.
3. BAILLIE, H. D.: Thermal and nonthermal cataractogenesis by microwaves, In: *Biological Effects and Health Implications of Microwave Radiation*. Symposium Proceedings. Cleary, S. F. ed. U. S. Department of Health, Education and Welfare technical report BRH/DBE 1970, **70**, 59.
4. BLOOR, K., BAILLIE, H. D.: *Brit. J. Surg.*, 1966, **53**, 992.
5. BURTON, A. C.: *J. Nutrition*, 1935, **9**, 261.

WHO – Biologic effects & health hazards of microwave radiation
1974

MAIN DIRECTIONS AND RESULTS OF RESEARCH CONDUCTED IN THE USSR ON THE BIOLOGIC EFFECTS OF MICROWAVES

Z.V. Gordon, A.V. Roščin and M.S. Byčkov

Labor Order of the Red Banner Institute for Scientific Research on Industrial Hygiene and Occupational Diseases, Academy of Medical Sciences of the USSR, Moscow, USSR

The research programe in the USSR uses three approaches, i.e., hygienic, clinical and experimental studies, directed to the investigating the biologic effects of a whole range of radiofrequencies, and particularly of microwaves which constitute the most biologically active part of the radiofrequency spectrum.

In the field of hygiene we have studied the working conditions accompanying various processes of production, from the development and building of a prototype to its serial production, then the conditions of daily performance and, finally, servicing and research work.

With the accumulation of hygienic, experimental and clinical data it became apparent that more strict assessment of occupational conditions is necessary for those working with microwave sources, including recording of the actual irradiation of the people, and particularly combination of microwave irradiation with other factors in the environment (soft X-rays, heat) which will be dealt with in the paper by Dr. K. V. Nikonova later during this meeting, as well as the mode of irradiation.

As our investigations have shown, the regime of microwave irradiation to which the workers are exposed has a pronounced intermittent character. While one group of activities is characterized by relatively or absolutely constant levels of irradiation (Fig. 1), in the other irradiation is changeable both in its intensity and time-course (duration of irradiation periods and of intervals between them, Fig. 2). From the statistical point of view, the actual exposure levels of those regulating microwave radio sets are subject to haphazard fluctuations, and therefore for the analysis of the irradiation data use was made of the appropriate theory of random processes.

The characteristics of random processes, such as statistical probability, dispersion and correlation functions, have shown that the random process under investigation is not a static one.

The results obtained determined our approach to hygienic studies in factories and

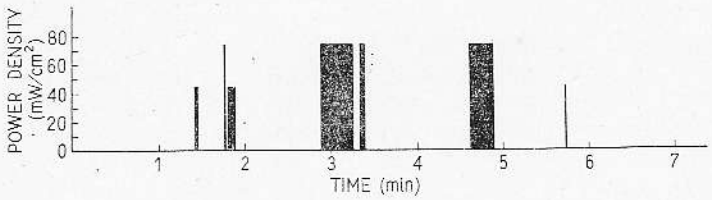


Fig. 1. Exposure to irradiation with two intermittent parameters, the duration of the irradiation periods and the intervals which separate them, the intensity of irradiation being relatively constant.

WHO – Biologic effects & health hazards of microwave radiation 1974

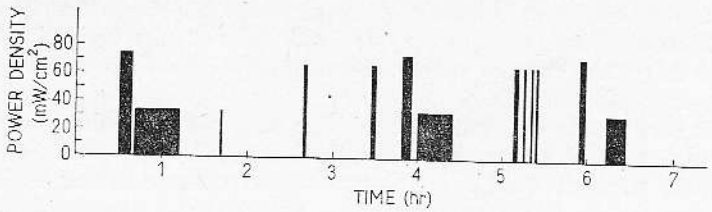


Fig. 2. The regime of irradiation in which both the intensity and the time parameters (the duration of irradiation periods and the intervals between them) have intermittent character.

led to the requirement for graphic recording of intensity and duration of irradiation during working shifts.

It has been possible to define some of the factors which influence to various degrees the characteristics of the irradiation process: number of radiation sources, particular design features of radiosets in production, sequence of technological steps, and many others.

Previous investigations conducted in our laboratory, coupled with evaluation of basic aspects of the biologic action of microwaves, made it possible to elucidate the importance of intermittent exposure factors for the biological effects of microwaves.

We used an experimental model of intermittent irradiation based on actual regimes of irradiation accompanying production. We found that, according to a number of indicators (fluctuations in weight and blood pressure, electroencephalography and electromyography, neurosecretory activity of hypothalamic nuclei), intermittent exposure to irradiation results in more pronounced biologic effects than those of steady irradiation under conditions of equal strength and time parameters. One could hypothesize that intermittent exposure is much more strenuous for the adaptation and compensation mechanisms owing to the frequent changes in the irradiation parameters.

Without dwelling upon the clinical direction of research, to which a separate paper by Dr. M. N. Sadčikova is devoted, we will only note that clinico-hygienic correlations made it possible to link the clinical indicators with intensity of microwave irradiation under industrial conditions. This unique material accumulated as a result of 20 years' observations made it possible to establish a very important fact, namely, that the biologic effects become more severe with increasing duration of work accompanied by irradiation of low intensities (less than 1 mW/cm²).

Before going into experimental research, it is necessary to define certain terms which are frequently treated ambiguously. These are thermal and non-thermal effects.

Thermal effects are those biologic suquelae which are due to integral rise of temperature of the body and its separate parts during whole body or local irradiation.

Thermal effects are those biologic sequelae which are due to integral rise are the result of uneven heating of microstructures of a heterogeneous biologic tissue and may occur in the absence of the integral thermal effect. Finally, non-thermal or "extrathermal" effects are due to conversion of electromagnetic energy within an object into another form of non-thermal energy (molecular resonance absorption, photochemical reaction, etc.).

The present lack of adequate methods for separating nonthermal from thermoselective effects is the sole reason for their being put together under the provisional name of "non-thermal" effects.

The occurrence of pronounced biologic effects of microwaves of intensities which do not evoke the integral heat effect (less than 10 mW/cm²) has been con-

WHO – Biologic effects & health hazards of microwave radiation 1974

vincingly shown independently by a number of Soviet and foreign authors. Although there are differences of opinion on the "non-thermal" or "microthermal" nature of the biologic effects of low levels of energy, there should be no doubt at present as to the actual existence of these effects.

From this perspective, the studies on biologic effects of microwaves carried out 20 years ago in the USSR concerned high intensities (8, 25) and were limited only to establishing the minimal lethal doses, thermal action and some other effects (Tab. 1).

Table 1

Changes induced by microwave irradiation of high intensity (data of Belova, Gordon and Lobanova)

Investigated indicators	Radiation intensity (mW/cm^2)	Duration of life or exposure	Character of the changes
1. 50% lethality, 10 cm band (rats)	100	15 min	Marked symptoms of overheating. Morphologically in the internal organs and nervous system significant vascular disturbances; slight evidence of dystrophic changes
2. Cataract formation (rabbits)	10	60 min	Opacity of the lens after 7 h irradiation
3. Thermal reaction (rats)	10	15—30—60 min	Maximal intensity which does not lead to elevated body temperature
4. Blood pressure (rats)	100	6—12 weeks 10 min each time	Lowered arterial pressure

The investigations were performed primarily at the levels of intensity which do not result in the integral thermal effect (less than 10 mW/cm^2). The results obtained can be arranged provisionally into two groups: one presents the phenomenology of effects at various levels of life activities, while in the other various mechanisms of action are dealt with.

The phenomenology of the biologic effects of microwaves has been studied in most detail. Particular attention has been paid to the nervous system, as it is most sensitive (8, 22) and plays a key role in the pathogenesis of radiation sickness (8, 24, 29).

Some of the biologic effects resulting from microwave irradiation of non-thermogenic intensities are shown in Table 2 (only statistically significant results are quoted).

It can be seen that microwave radiation (intensity, 10 mW/cm^2), when acting for long periods of time, constitutes a pathogenic factor (morphologic lesions in the nervous system, changes in reproductive function and some borderline conditions). The interpretation of these borderline conditions is equivocal and they cannot be confidently regarded as purely regulatory or adaptive and compensatory reactions which would be practically harmless. The include such effects as lowered endurance, retarded weight gain, inhibition of conditioned reflexes and neurosecretion, neurophysiologic disturbances.

However, irradiation that is lower in intensity by one order of magnitude (1 mW/cm^2) is also significant from the medical point of view according to a number of indicators.

WHO – Biologic effects & health hazards of microwave radiation 1974

Table 2

Changes in certain functions of the organism of animals irradiated with microwaves of nonthermogenic intensity

Investigated functions	Radiation intensity (mW/cm²)	Type of experiment	Duration of each irradiation (min)	Animal species	Character of the changes
I. *General indicators*					
1. Endurance to effort — swimming	10	chronic	90	rats	decrease
2. Weight	10	chronic 4—8 weeks	60	rats	retarded weight gain
II. *Nervous system*					
1. Examination of electric activity of various brain structures by means of macro- and microelectrodes and stereotaxic technique (Byčkov, Dronov)	0.03—10	acute	30—40	rabbits cats rabbits	predominantly generalized inactivation of the brain, domination of hypothalamic function;
		chronic	30—60		dissociation of integration of specific and nonspecific afferent systems at the thalamo-cortical level
2. Examination of behavioral reactions (Lobanova, Kicovskaja, 1968; Asabaev, 1970)	10	chronic (1—2 weeks)	60	rats mice	inhibition of conditioned reflexes, lowered excitability, weakening of the processes of stimulation and inhibition, increased spontaneous motor activity
	1	chronic (12—16 weeks)	60	birds	
3. Neuropharmacologic investigations (Kicovskaja, 1968; Zenina, 1964)	10	chronic (10 weeks)	60	rats rabbits	application of camphor, strychnine, nicotine and other neurotropic substances revealed lowered excitability of the motor zone of the cortex, subcortical structures and sensitive centers in the spinal cord with dissociation of the sensorimotor mechanisms at the spinal level

Tab. 2

Investigated functions	Radiation intensity (mW/cm^2)	Type of experiment	Duration of each irradiation (min)	Animal species	Character of the changes
4. Morphological changes in the nervous system (Tolgskaja, Gordon 1971)	10	chronic (8—25 weeks)	60	rats	changes in interneuronal axodendritic and axosomatic structures of the brain, and sensory nerves and receptors of various internal organs and the skin
5. Changes in neurosecretory function of the hypothalamus (Tolgskaja, Gordon 1968, 1971)	10	chronic (4—14 weeks)	60	rats	morphological and histochemical changes in secretory nuclei of the hypothalamus anterior suggesting inhibition of anterior activity
		chronic (20—26 weeks)	60		
III. *Cardiovascular system*					
1. Blood pressure	10	chronic (18—20 weeks)	60	rats	lowered arterial pressure
	1	chronic (12—14 weeks)	60	rats	
2. Chronotropic effect (Presman 1968)	1—10	—	20	rabbits	bradycardia or tachycardia
IV. *Biochemical changes*					
1. Cholinesterase					
— in the blood serum	10	chronic (20 weeks)	60	rabbits	lowered activity
— in the brain stem		(13 weeks)	60	rats	
— in the liver and heart (Nikogosjan 1960, 1964)		(23 weeks)	60	rats	

Tab. 2

Investigated functions	Radiation intensity (mW/cm²)	Type of experiment	Duration of each irradiation (min)	Animal species	Character of the changes
2. Catalase in blood (Nikogosjan 1960, 1964)	10	chronic (3 weeks)	60	rabbits	lowered activity
3. Acetylcholine					
— in the brain hemispheres	10	chronic (5 weeks)	60	rats	increased content
— in the brain stem	10	chronic (1 week)	60	rats	increased content
4. Histamine in the blood (Gelfon, 1964)	10	chronic (0.5 week)	60	rabbits	increased content
5. Aminoacid metabolism					
— protein fractions in the serum	10	chronic (20 weeks)	60	rabbits	increased content of albumins, decreased content of α, β and γ-globulins
— nonprotein nitrogen in the blood	10	chronic (20 weeks)	60	rats	increase in nonprotein nitrogen
— aminoacids in the urine	10	chronic (20 weeks)	60	rats	increased content
6. RNA (in the organs)					
— spleen	10	chronic (7—10 weeks)	60	rabbits	increased content
— brain and liver (Nikogosjan, 1964 a, b and c)	10	chronic (13 weeks)	60	rabbits	
7. Ascorbic acid (Nikogosjan, 1968)	10	chronic (22 weeks)	60	rabbits	increased content

Tab. 2

Investigated functions	Radiation intensity (mW/cm^2)	Type of experiment	Duration of each irradiation (min)	Animal species	Character of the changes
V. *Reproductive function*					
1. Effects on gonads	10	chronic (20 weeks)	120	mice of both sexes	disturbances of the estrus cycle; changes in functional status of spermatozoids; slight evidence of degenerative changes in the gonads
2. Effects on fetal development	10	chronic (2.5—48 weeks)	120	mice	increased intrauterine lethality and frequent anomalies in fetal development
3. Effects on fertility	10	chronic (20 weeks)	120	mice (females)	decrease in number of successful crosses, reduced litter size
	10	chronic (20 weeks)	120	mice (males)	increased percentage of abnormal offspring
	10	chronic (48 weeks)	120	mice (females)	decreased number of gestations and births, inferiority of the offspring (particularly of the first and subsequent gestations), premature cessation of reproductive function
	0.250	chronic (48 weeks)	240	mice (females)	
	10	chronic (48 weeks)	120	mice (males)	decreased fecundity and litter size; premature cessation of reproductive function
	0.250	chronic	240		
VI. *Nonspecific reactivity*					
1. Immunologic effects	0.5	chronic (40 weeks)	60	rats	lovere natural resistance (inhibition of natural immunity)

WHO - Biologic EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION 1974

Upon cessation of irradiation some of its sequelae may disappear but a prolonged action results in destructive, irreversible pathologic lesions.

Attention is drawn to the fact that, as can be seen in Table 2, even at intensities that are extremely low by comparison with those considered above (e.g., 500—250 $\mu W/cm^2$), certain biologic effects occur (bioelectric phenomena with resetting to a new level of activity of the brain systems, changes in immunobiologic resistance), including definite pathologic effects (reproductive functions).

When speaking about criteria of significance of reactions, one should keep in mind that not all reactions are of importance but some, while lacking pathologic traits under certain conditions, should nevertheless be given attention when possible harmful consequences are considered. It is therefore necessary to introduce the term "potentially harmful reaction" as a main criterion of importance of a symptom, as opposed to either a threshold biologic (regulatory) reaction in general or a threshold pathologic reaction.

Studies of qualitative and quantitative indicators of the biologic action of microwaves have yielded data which not only allowed assessment of the biologic effects of microwave irradiation of various parameters but also showed main directions for research aimed at elucidation of a whole range of pathogenic mechanisms, from the molecular level up to system and intersystem relationships.

Our investigations of primary mechanisms of the biologic action of microwaves have been directed in particular towards studying the possibility of a direct action of microwaves upon the activity of some physiologically important enzymes (catalase, cholinesterase, actinomyosin). We have also tried to influence permeability of ions across cell membranes by microwave exposure.

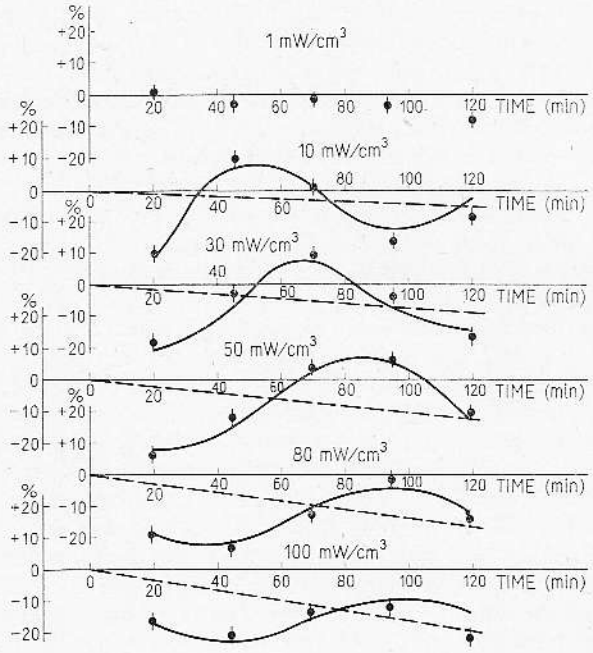
Studies on the influence of microwave irradiation of the range of 10 cm on catalase and cholinesterase activities *in vitro* using various conditions gave negative results. Attempts to demonstrate *in vitro* any direct influence of the field upon the enzyme molecules which would result in changes of enzymatic activity have failed. At the same time our *in vivo* investigations have shown that activity of a whole range of enzymes in the tissues of irradiated animals, including cholinesterase, changes markedly at intensities significantly lower (by at least one order of magnitude, down to 1 mW/cm^2) than those used in *in vitro* experiments (14, 15, 19, 30). It was possible to show, by means of a simple method and taking as an example nonspecific serum cholinesterase, that changes in tissue activity of the enzyme following whole body irradiation result not from a direct action on molecular structures but from changes in enzyme concentration in the tissues, apparently related to disturbances in the neurohormonal regulation of metabolic processes.

It has been possible to demonstrate a direct action of microwaves upon enzyme activity using preparations of rabbit muscle actinomyosin which possesses a more complex level of biologic organization than catalase and cholinesterase and is distinguished by a highly labile conformation. Irradiation of actinomyosin gel at 350 MHz frequency with the density of the absorbed energy of about 5 mW/cm^2 resulted a reduction in ATP-ase activity.

In another series of biophysical investigations the influence of microwaves upon cell membranes was studied, and particularly on their selective permeability to the ions which influence the membrane electric potential, K^+ and Na^+. Isolated human blood erythrocytes provided the biologic model for studies of microwave influence on membrane permeability. Changes in influx rates of radiolabelled K^+ and Na^+ into red blood cells were determined during and after microwave irradiation within the dose range of 900 to 2340 MHz, and compared with respective heat controls. Relationships between irradiation parameters (frequency, intensity and duration) and changes in ion transport into erythrocytes were investigated.

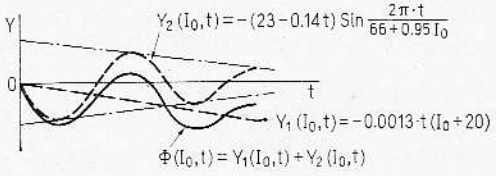
The results revealed statistically significant changes in the rates of transport of K^+ and Na^+ ions across membranes not related to a rise in temperature of the suspension. These changes did not depend on radiation frequency within the range investigated (31, 32). The threshold microwave intensity leading to a significant change in the rates of ion transport following irradiation for two hours approximated 1 mW/cm². The relationship between intensity and duration of irradiation and its effects was of a multiphasic character and did not follow a linear dose-effect relationship with regard to absorbed energy.

The above experimental data were used to develop a mathematical model showing how changes in K^+ influx rate depend on intensity and duration of irradiation. Within



a

$$\Phi(I,t) = -0.0013 \cdot t\,(I+20) - (23 - 0.14t)\,\mathrm{Sin}\,\frac{2\pi \cdot t}{66 + 0.95\,I}$$



b

Fig. 3 a. The dependence of changes in the rate of entry of potassium into erythrocytes upon duration of irradiation at fixed intensities. The solid lines show the estimated functions of the dependence of effect on the time of irradiation, as obtained from a mathematical model of the process. The broken lines represent the linear component. b. The graphic and analytical presentations of the process as a resultant of two components.

WHO – Biologic effects & health hazards of microwave radiation 1974

the constraints of the model, the observed effect is interpreted as a resultant of two processes: linear decline in K^+ entry rate with increasing dose of absorbed energy and change of the rate of transport under conditions of diminishing adaptation possibility (Fig. 3 a and b). These processes account for the multiphasic oscillatory character of the effect during the course of the experiment.

It is important to emphasize that even in such relatively simple objects as erythrocytes, the regulatory processes contribute significantly to the ultimate biologic effect (changes in the rate of ion transport). Indeed, it has been shown that the primary effect, depending linearly on the dose of energy, has a triggering effect on cell regulatory phenomena. The overlapping of regulatory processes and the primary effect determines the complex, non-linear character of the relationship between intensity and duration of irradiation (i.e., the dose of energy) and biologic effects. It appears that it is even more so when we deal with reactions of much more complex systems, such as the whole organism, to irradiation of relatively low intensity, or prolonged exposure at intensities which do not evoke pathologic lesions during short-term exposures. In such cases external evidence of the biologic effects is limited, as a rule, to reflections of changes in complex regulatory processes, only indirectly connected with the action of electromagnetic energy. This is presumably why, particularly within the range of low intensities (up to 10 mW/cm²), it proves impossible to obtain a simple quantitative relationship between intensity and duration of irradiation, on the one hand, and the biologic effect on the other. It has been shown (3) that, apart from the depolarizing action of microwaves upon excitable membranes, hyperpolarizing effects occur (rise in membrane potential of muscle fibres).

Electrophysiologic investigations of elementary excitable structures (3) at an extremely low intensity of irradiation (5 μW/cm²) have revealed changes in a number of functional parameters and characteristics, namely, a slowed conduction of impulses, an increased synaptic delay, lengthening of latent and refractory periods, changes in action potential (all in isolated nerve and muscle fibres of the frog), inhibition of the impulse

Table 3

Changes in the amplitude of action potentials (stimulation frequency, 20 Hz), optimal and maximal rhythms of the frog muscle fibre

	Amplitude of action potentials			Optimal rhythms			Maximal rhythms		
	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance
Control group	100 (99—103)			10			20		
Experimental group	79 (51—86)	< 0.01	Wilcoxon's	58	0.025	Fisher's	84	< 0.025	Fisher's

WHO – Biologic effects & health hazards of microwave radiation 1974

Table 4

Changes in the rate of conduction of impulses and absolute refractory period in the frog muscle fiber

Group	Rate of conduction			Refractory period		
	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance
Control	100 (98—102)	0.01		99 (97—102)		
Experimental	75 (64—85)	0.01	Wilcoxon's	150 (94—176)	0.05	Wilcoxon's

activity of single ganglionic neurons (the medicinal leech). Some of these results are presented in Tables 3 to 5.

Table 5

Changes in synaptic delay (myoneural transmission in the frog)

Group	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance
Control	103 (90—110)		
Experimental	140 (100—167)	< 0.01	Wilcoxon's

Results of studies on red blood cell membranes coupled with data on the influence of microwave irradiation on isolated excitable structures (2, 6, 9, 10, 13, 32) make it possible to hypothesize that the influence of microwaves on excitable cells is connected with alterations in the permeability of the cell membranes brought about by changes in transport of ions, which influence the membrane potential.

Unfortunately, we do not have at present data on the precise physicochemical nature of the processes leading to changes in ion transport across membranes of the irradiated cells. Undoubtedly, these processes would be worth studying in greater detail.

Consideration of the possibility of a selective absorption of microwave energy at interfaces of heterogeneous biologic systems led to the assumption that the single physical mechanism — a selective absorption of electromagnetic field energy at the surfaces of colloid molecules, membranes and other cell constituents — underlies the various "non-thermal" biologic effects of electromagnetic fields. This may be true since the surface conductivity is increased within the double electric layer at the interfaces of biologic objects. Biophysical studies aiming at experimental testing of this assumption are being planned.

WHO – Biologic effects & health hazards of microwave radiation 1974

Finally, at the system and organism levels, particular attention has been paid to the mechanisms of biologic effects in the central nervous system. As a result of neurophysiologic investigations, CNS effects have been observed at intensities up to 1 mW/cm². These effects are determined by both a direct action on the brain and the reflex component and intersystem relations within the brain (3, 4, 5).

Particularly interesting in the pathogenesis of radiation sickness are the intersystem relations. These include processes in such systems as a) the reticular formation of the brain stem, the hypothalamus and the cortex of the cerebral hemispheres and b) the cortex and thalamus.

Changes in the nervous system are characterized first of all by a marked contribution from nonspecific subcortical and stem structures superimposed upon cortex effects. This is particularly true of the hypothalamus, where changes at low intensities (30—100 μW/cm²), taking place in both acute and chronic experiments, are of exceptional interest because the hypothalamus constitutes the structure connecting nervous and humoral means of regulation (hypothalamic — hypophyseal — suprarenal system).

The most characteristic syndrome shown by the system reticular formation of the brain stem — hypothalamus — cortex is the syndrome of generalized inactivation (Fig. 4). Disruption of the integrating activities of the specific and nonspecific afferent systems of the brain (thalamo-cortico-thalamic cycle) takes place simultaneously. Experimental investigations (11, 12) show that, following microwave irradiation, the ascending activating influence of the reticular formation on the brain cortex is blocked.

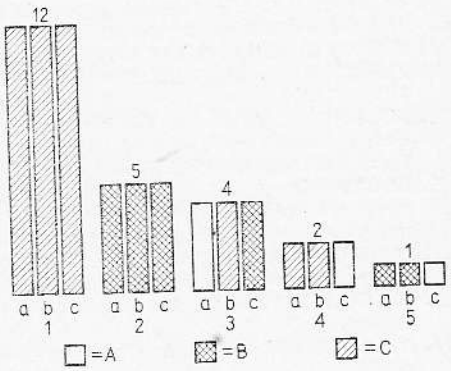


Fig. 4. The variants of relations between shifts in the cortex of hemispheres, posterior hypothalamus and reticular formation of the brain stem accompanying the exposure to SHF fields. The numbers at the top indicate the number of rabbits demonstrating a given effect. The numbers at the bottom correspond to sequential numbers of the variants. Symbols: *A* — Lack of effect of SHF, *B* — Activation, *C* — Deactivation, *a* — The cortex of hemispheres, *b* — Posterior hypothalamus, *c* — The reticular formation of the brain stem.

Changes in the regulatory activities of the hypothalamic region due to microwave irradiation of nonthermogenic intensities also result in shifts in cholinergic processes (19, 26), participation of choline-reactive (5, 11) and adrenergic (5) structures of the brain, as well as biphasic changes in vascular tonus (8, 25) with accompanying changes in accumulation of neurosecretion within the nervous cells and tissues of the hypothalamic region (27, 28).

At low intensities (of the order of 1 mW/cm²) microwave-induced disturbances of adaptation to various factors have also been observed (25).

All the above findings taken together bring us closer to understanding the pathogenesis of the neurologic manifestations of microwave sickness by showing clearly that in human beings the astheno-vegetative shifts and psychophysiologic symptoms are mainly of a mesencephalo-diencephalic nature, and are elicited by microwave action of low intensity.

WHO – Biologic effects & health hazards of microwave radiation 1974

The program of further investigations envisages elucidation of new aspects of the mechanism of biologic action of microwaves, of late sequelae of this action, and of the restoration period. Particular attention will be paid to the combined action of microwaves and other physical factors of the working environment, various exposure conditions, threshold significance of biologic effects depending upon wave-range and modulation characteristics, and the reliability of forecasting of possible harmful effects.

REFERENCES

1. BELOVA, S. F., GORDON, Z. V.: *Bjull. eksp. biol. med.*, 1956, **41**, 4, 59.
2. BOGAČ, P. G., MIRUTENKO, V. S., DOLGI, N. L.: In: *Puti powyšenija produktivnosti selsko-hazajskih životnych i pticy*. Odessa, 1972, p. 3.
3. BYČKOV, M. S.: *Problemy neirokibernetiki*. Referaty dokladov 3 Vsesojuznoj konferenci po neirokibernetike. A. V. Kogan (Ed.). Izdatelstvo Rostovskogo Universiteta. Rostov na Donu, 1967, p. 17.
4. BYČKOV, M. S.: In: *Bioničeskie principy samoorganizacii*. Trudy vsesojuznogo simpozjuma po kibernetike, vol. 1. Izdatelstvo Instituta kibernetiki AN Gruzinskoj SSR, Tbilisi, 1970, p. 90.
5. BYČKOV, M. S. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot*. Sbornik materialov 4 Vsesojuznogo simpoziuma. Izdatelstvo gigieny truda i profzabolevani AMN SSSR, Moskva, 1972, p. 46.
6. BYČKOV. M. S., MOREVA, Z. E. In: *Trudy Leningradskogo obščestva ispytatelei prirody*, 1960, **71**, 1, 78.
7. GELFON, I. A. In: O biologičeskom deistvii elektromagnitnyh polei radiočastot, 1964, **2**, 68.
8. GORDON, Z. V.: *Voprosy gigieny truda i bilogičeskogo deistvia elektromagnitnyh častot*. Izdatelstvo Medicina, Leningrad, 1966.
9. ZUBKOVA, S. M., NIKONOVA, V. A.: *Trudy CNII kurortologi i fizioterapi*, 1969, **14**, 34.
10. ZUBKOVA, S. M., NIKONOVA, V. A.: *Trudy Moskovskogo obščestva ispytatelei prirody*, 1970, **45**, 79.
11. LOBANOVA, A. E. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot*. Sbornik materialov 4 Vsesojuznogo simpoziuma. Izdatelstvo Instituta gigieny truda i profzabolevani AMN SSSR. Moskva, 1972, p. 44.
12. LOBANOVA, A. E., SUDAKOV, K. V. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot*. Sbornik materialov 4 Vsesojuznogo simpoziuma. Izdatelstwo Instituta gigieny truda i profzabolevani AMN SSSR. Moskva, 1972, p. 42.
13. MIRUTENKO, V. I., BOGAČ, P. G. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot*. Moskva, 1972, p. 60.
14. NIKOGOSJAN, S. V. In: *O biologičeskom vozdeistvii sverhvysokih častot*, vol. 1. Moskva, 1960, p. 43.
15. NIKOGOSJAN, S. V. In: *O biologičeskom deistvii EMP radiočastot*, vol. 2. Moskva, 1964, p. 43.
16. NIKOGOSJAN, S. V. In: *O biologičeskom deistvii elektromagnitnyh polei radiočastot*, vol. 2. Moskva 1964, 66.
17. NIKOGOSJAN, S. V. In: *Tezisy dokladov Vsesojuznoj konferenci po medicinskoj radioelektronike*. 1964, 15.
18. NIKOGOSJAN, S. V. In: *Gigiena truda i professionalnye zabolevanija*. 1964, **9**, 56.
19. NIKOGOSJAN, S. V. In: *O biologičeskom deistvii EMP radiočastot*, vol. 3. Moskva 1968, p. 97.
20. NIKOGOSJAN, S. V. In: *O biologičeskom deistvii elektromagnitnyh polei radiočastot*, vol. 3. Moskva, 1968, p. 107.
21. NIKOGOSJAN, S. V. In: *O biologičeskom deistvii elektromagnitnyh polei radiočastot*, vol. 3. Moskva, 1968, p. 120.
22. PETROV, N. R. (Ed.): *Vlijanie SVČ — izlučeni na organizm životnyh i čeloveka*. Izdatelstvo Medicina, Leningrad, 1970, p. 151.
23. PRESMAN, A. S.: *Elektromagnitnye polja i živaja priroda*. Izdatelstvo Nauka. Moskva, 1968, p. 109.
24. RAMZEN, I. G., SOROKIN, V. A. In: *Vlijanie SVČ — Izlučeni na organizm životnyh i čeloveka*. I. R. Petrov (Ed.), Izdatelstvo Medicina, Leningrad, 1970, p. 130.
25. SUBBOTA, A. G. In: *Vlijanie SVČ — izlučeni na organizm životnyh i čeloveka*. I. R. Petrov (Ed.), Izdatelstvo Medicina, Leningrad, 1970, p. 70 and 151.

WHO – Biologic effects & health hazards of microwave radiation 1974

26. SYNGAEVSKAJA, V. A. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln rediočastot.* Izdatelstvo Instituta gigieny truda i profzabolevani AMN SSSR, Moskva, 1968, p. 150.
27. TOLGSKAJA, M. S., GORDON, Z. V. In: *O biologičeskom deistvie elektromagnitnyh polej radiočastot.* Trudy laboratori elektromagnitnyh polej radiočastot Instituta gigieny truda i profzabolevani AMN SSSR, Moskva, 1968, **3**, 87.
28. TOLGSKAJA, M. S., GORDON, Z. V.: *Morfologičeskie izmienenia pri deistvii elektromagnitnyh voln radiočastot.* Izdatelstvo Medicina, Moskva, 1971.
29. TJAGIN, N. V.: *Kliničeskie aspekty oblučeni SVČ-diapazona.* Izdatelstvo Medicina, Leningrad 1971.
30. ŠTEMLER, V. M. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Moskva, 1968, p. 175.
31. ŠTEMLER, V. M. In: *Sbornik materialov 4 Vsesojuznogo simpoziuma.* Izdatelstwo Instituta gigieny truda i profzabolevani AMN SSSR. Moskva, 1972, p. 62.
32. ŠTEMLER, V. M. In: *Sbornik Bionika 1973.* Materialy 4 Vsesojuznoj konferenci po bionike. Moskva, 1973, **3**, 87.

WHO – Biologic effects & health hazards of microwave radiation 1974

PHARMACOLOGIC EFFECTS OF A PULSED MICROWAVE FIELD

B. Servantie, G. Bertharion*, R. Joly*, A. M. Servantie, J. Etienne, P. Dreyfus and P. Escoubet*

Postgraduate School of the Navy Medical Service; Center of Biophysiologic Studies and Research Applied to the Navy; Military Hospital for Postgraduate Study, Sainte Anne, Toulon — Naval, France

For a few years, we have been studying the effects of prolonged microwave exposures of laboratory animals. Systematically, we used low mean power densities, looking for biologic effects which are not obviously of thermal origin. Our aim is to present certain pharmacologic observations made by us.

DESCRIPTION OF THE EQUIPMENT**

1. **Generators.** We have used navy generators, which are more fitted for biologic research. These generators produced a pulsed hyperfrequency field of 10 cm wavelength (S band: 3000 MHz) with a maximum peak power of 600 kW. The pulse duration is 1 microsecond, variable between 0.9 and 1.2 μs depending on the magnetron used, with a pulse repetition rate of 525 Hz, variable between 450 and 650. The maximum mean power is consequently 350 W. Usually we employed long-term exposures of many weeks, sometimes many months. Two identical generators which can be exchanged were used.

2. **Anechoic chamber.** The emitted field was transmitted through a wave guide to a 15 dB horn. This horn was fixed on the wall of a 20 m³ anechoic chamber in which animals could be irradiated in free space and far field conditions; the experimental subjects, in specially designed Plexiglass cages, were placed at more than two meters from the horn, the Rayleigh distance being of one meter; in the exposure region, the mean power density, measured in the absence of animals, was 5 ± 1 mW/cm².

3. **Measurements.** Power densities were measured by means of a Hewlett-Packard 432 A milliwatt-meter connected to a 478 A thermistor mount. To determine frequencies (except hyperfrequency) and duration, we used a Hewlett-Packard 5326 B timer-counter. Our measurements were made either directly at the generator output by a coupler-attenuator, or in the anechoic chamber with a tuned dipole or a calibrated horn.

FIELD EFFECT ON SENSITIVITY TO PENTETRAZOL

1. **Techniques.** Our experiments were carried out on 300 albino CD-1 mice of the Charles River strain; the body weight ranged between 30 and 35 g. Experimental and control groups were selected at random, in equal numbers.

---

* Military Medical Corps.

** We thank the Office for Research and Experimental Facilities (D.R.M.E., French Ministry of Defence) for its assistance.

WHO – Biologic effects & health hazards of microwave radiation 1974

The experimental animals were exposed to microwaves for periods of 8, 15, 20, 27 and 36 days, according to the above-described conditions. Normal mice were maintained under the same environmental conditions, outside the anechoic chamber. Each experiment was repeated three times.

At the end of the exposure period, 50 mg/kg of pentetrazol were administered intraperitoneally to each mouse; the time interval from the injection to the beginning of the convulsive fit was measured. At the end of each experiment the mortality of the mice was determined.

2. **Results.** It was found that exposures to microwave fields affected the convulsion times and the mortality.

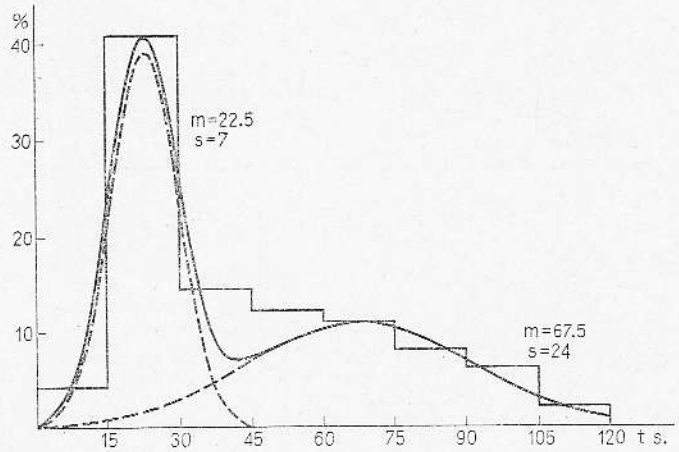


Fig. 1. Pentetrazol convulsion times — controls.

Table 1

Pentetrazol convulsion time ratios

Exposure times	Less susceptible / More susceptible	Experimental / Controls
Controls	1.13	—
8 days	1.29	1.14
15 days	0.64	0.56
20 days	1.66	1.47
27 days	1.81	1.60
36 days	1.44	1.27

a. **Convulsion times.** Histograms of the time intervals between the injection and the beginning of the fit were drawn for each experimental and control group. There is no statistically significant difference between the various control groups; we can treat them together as one normal population (see Fig. 1). As a matter of fact, this normal population can be assigned a sum of two gaussian distributions, with a probability ranging between 0.99 and 0.975. The parameters (mean and standard deviation) of these two distributions were: 22.5 s and 7 s for the first, 67.5 s and 24 s for the second.

This represents a good approximation to the distribution of the convulsion times for normal mice, which vary from 7 to 120 seconds. Consequently, it appears that, in the strain of mice with which we have worked, there are animals which are more susceptible than others to the convulsive action of pentetrazol: the two types were represented in approximately equal numbers.

For irradiated mice, all groups, except the 8-day group, differ significantly from the control population. The individual groups were too small to permit calculation of the theoretical distribution; nevertheless, the "more susceptible" and "less susceptible" cate-

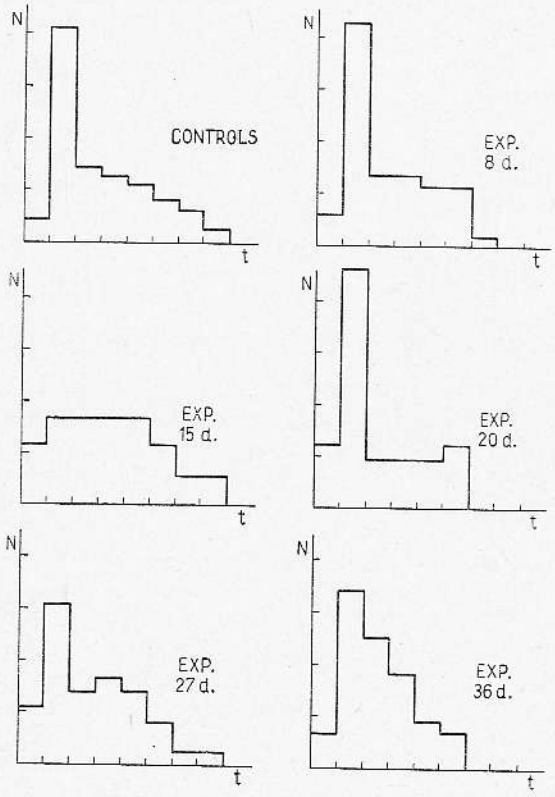


Fig. 2. Pentetrazol convulsion times.

Table 2

Pentetrazol percentage mortalities

Exposure times	Experimental animals	Normals
8 days	20.0	20.0
15 days	16.67	6.25
20 days	20.0	6.67
27 days	15.62	14.28
36 days	33.0	14.0

WHO – Biologic effects & health hazards of microwave radiation 1974

gories are found again on the histograms (see Fig. 2). It was assumed that a good evaluation of the microwave field action would be obtained from the ratio between these two categories. To compute this ratio, the time corresponding to the intersection of the two theoretical curves on Figure 1 (broken line) representing the distribution of convulsion times within the two theoretical normal populations, that is 36.75 seconds, was taken.

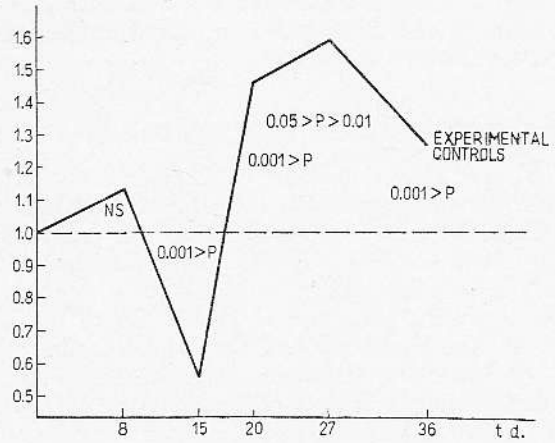


Fig. 3. Pentetrazol: ratio of "more susceptible" to "less susceptible" animals in the experimental groups as compared to the controls, as a function of exposure time.

The values obtained are summarized in Table 1. The convulsion time ratios for experimental animals compared to controls were plotted against exposure times (see Fig. 3): for 8 days' exposure, there was no difference between experimental and control groups; after 15 days, the number of "less susceptible" animals increased: the exposure to microwaves delays the appearance of the fit. For longer exposures, on the contrary, the number of "more susceptible" animals increases: the exposure to the fields tends to hasten the onset of the fit, particularly after 27 days of exposure.

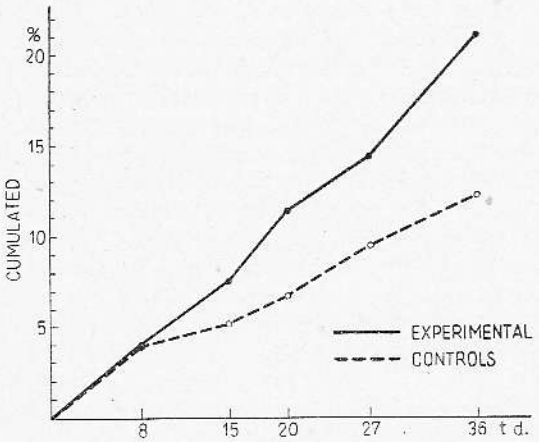


Fig. 4. Pentetrazol mortality.

WHO – Biologic effects & health hazards of microwave radiation 1974

b. **Mortality.** In each test, the animals which died after the fit were counted. The results are shown in Table 2, for control and experimental groups. There is a statistically significant difference (p between 0.005 and 0.001) between control and experimental populations. This difference is seen more clearly in Figure 4 with cumulated percentages plotted along the abscissae: it is non-exstent for the 8-day exposure, it appears for the 15-day exposure and increases for longer exposures.

Consequently it appears that in mice under our experimental conditions the effect of microwave exposure on convulsion times and mortality becomes perceptible only after a period longer than 8 days.

FIELD EFFECT ON SENSITIVITY TO CURARE-LIKE DRUGS

1. **Techniques.** To study the susceptibility of animals to curare-like drugs, we have used three different methods: Experiments on the intact animal, on an "*in situ*" neuromuscular preparation, and on an isolated neuromuscular preparation. All experimental animals were irradiated for 10 to 15 days: the control animals were held during the same time under the same environmental conditions.

a. **Intact animals:** 64 control and 78 experimental rats of the Charles River strain were used. In each rat, after anesthesia with Nembutal, a catheter was introduced into the jugular vein, following which the tested drug (Gallamin, suxamethonium) was injected at the rate of 1 mg/min; the time required for the disappearance of all movements, particularly respiratory movements was measured and from this we computed the amount in mg/kg necessary to obtain complete paralysis.

b. *In situ* preparation: 16 control and 24 experimental rats were used. In each rat, after anesthesia with Nembutal, a jugalar vein catheter, a tracheal cannula for assisted respiration and a rectal thermistor were introduced; the tendon of the left gastrocnemium muscle was set free, and then fastened to an isometric transducer which was connected to a paper recorder; the left sciatic nerve, after central tying, was stimulated by 6 volts 0.5 millisecond rectangular electric shocks with 0.1 Hz frequency; after a 10-minute waiting time for attainment of the steady state of the preparation, we gave a quick injection of 0.1 mg/kg of the tested drug (Pancuronium bromide); the amplitude in percentages of the initial value was computed from the recording.

c. **Isolated preparation.** 166 control and 166 experimental rats were used; each animal was decapitated without anesthesia; the left half of the diaphragm with the left phrenic nerve was taken out and placed in an oxygenated Tyrode bath at laboratory temperature; the nerve was stimulated by electric shocks identical with those of the *in situ* preparation; a glass pen fastened to the muscle recorded the twitches on a smoked drum; one normal and one experimental preparation were prepared simultaneously; after attaining a steady state, the tested drug (decamethonium: 146.3 μg/ml; suxamethonium: 3 μg/ml; tubocurarin: 3 μg/ml; diallylnortoxiferin; 5 μg/ml) was added to the bath and left undisturbed for three minutes; then the preparation was washed with uniform Tyrode flow of 4 000 ml/h for 10 minutes; the percentage decrease in amplitude per minute was computed from the recordings.

2. **Results.** All these experiments demonstrated that irradiated rats appear to be less susceptible to paralysing drugs than normal rats.

a. **Intact animal:** Table 3 shows a comparison between the numbers of animals which were paralysed by less than a threshold dose: 6 mg/kg for gallamin, 1.5 mg/kg for suxamethonium: there is a very significant difference (p lower than 0.001) between experimental and control animals, the former requiring higher doses for paralysis.

b. *In situ* **preparation:** the averaged curves from records were plotted (see Fig. 5) as for the intact animal technique; the experimental rats were paralysed to a lesser

Table 3

Gallamine — 6 mg/kg

	Control	Experimental animals
Paralysed rats	45	32
Non-paralysed rats	19	44
Total	64	76

(χ^2 = 15.93)
$p<0.001$

Suxamethonium — 1.5 mg/kg

	Control	Experimental animals
Paralysed rats	21	6
Non-paralysed rats	6	18
Total	27	24

(χ^2 = 12.17)
$p<0.001$

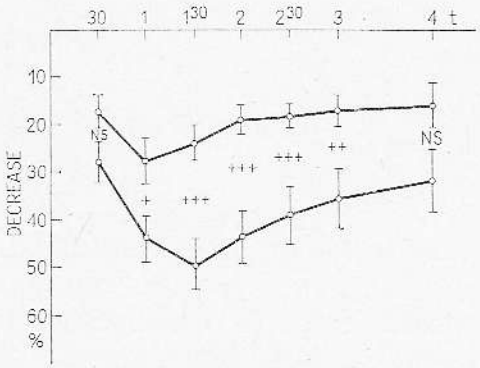


Fig. 5. Amplitude decrease after Pancuronium. NS = not significant; + = significant.

Table 4

Pancuronium

	30s	1 min	1 min 30 s	2 min	2 min 30 s	3 min	4 min
Difference %	10.65	16.53	25.6	24.8	21.12	18.44	15.92
t	1.94	2.38	4.08	4.35	3.54	2.76	1.80
	NS	0.025>P >0.02	0.001>P_o	0.001>P_o	0.005>P_o >0.001	0.01>P_o >0.005	NS

NS = not significant

WHO – Biologic effects & health hazards of microwave radiation 1974

extent than control rats. With this technique, we obtained an additional result: the recovery was faster for irradiated animals than for controls; the difference between the averaged curves, not statistically significant for 30 seconds, was very significant from 1 to 3 minutes (see Tab. 4).

c. **Isolated preparation**: four drugs were tested: two (decamethonium and suxamethonium) are leptocurares which stabilize the depolarization of the membrane, and two

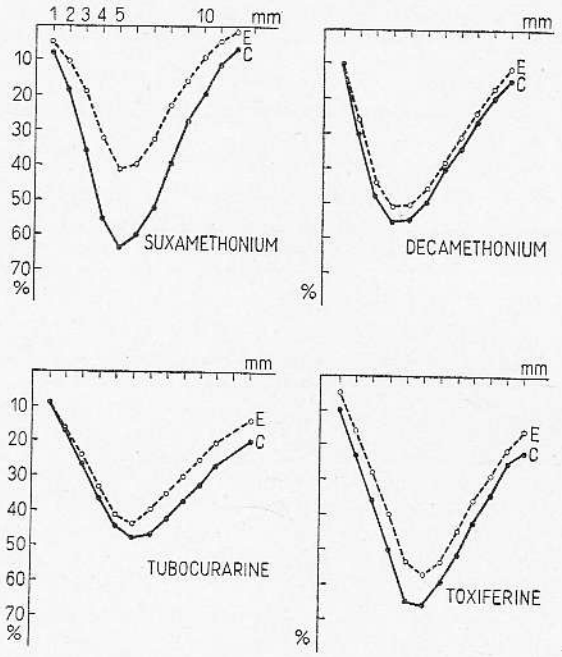


Fig. 6. Isolated preparations.

Table 5

Suxamethonium

		1	2	3	4	5	6	7	8	9	10	11	12
N	m	8.3 ±0.89	18.7 ±1.19	36.6 ±4.12	55.5 ±5.03	64.7 ±4.92	61.3 ±5.75	53.0 ±6.47	40.1 ±6.58	27.9 ±6.26	19.5 ±5.71	11.9 ±4.88	6.8 ±4.36
	n	19	19	19	19	19	19	19	19	19	18	18	18
E	m	4.7 ±0.58	10.6 ±1.13	19.2 ±2.12	33.2 ±3.50	41.7 ±5.06	40.3 ±5,82	33.0 ±5.91	23.1 ±5.30	16.3 ±4.50	9.4 ±3.74	4.6 ±3.24	1.6 ±2.70
	n	26	26	26	26	26	26	26	26	25	24	23	22
	d%	43.4	43.3	47.5	40.2	35.5	34.3	37.7	42.4	41.6	51.8	61.3	76.5
	t	3.53	4.85	4.06	3.77	3.17	2.50	2.26	2.03	1.54	1.53	1.29	1.06
		P<0.001	P<0.001	P<0.001	P<0.001	P<0.005	P<0.02	P<0.05	P<0.05	NS	NS	NS	NS

WHO – Biologic effects & health hazards of microwave radiation 1974

Table 6

Decamethonium

		1	2	3	4	5	6	7	8	9	10	11
N	m	10.3 ±0.95	29.6 ±1.68	27.7 ±1.80	55.7 ±1.77	54.9 1.86	49.5 ±1.93	42.5 ±2.03	34.4 ±1.95	26.2 ±2.02	19.5 ±1.95	14.5 ±1.80
	n	78	78	78	78	78	78	78	78	78	78	76
E	m	9.3 ±0.82	26.6 ±1.55	44.0 ±1.96	51.5 ±1.75	50.7 ±1.76	46.1 ±1.87	38.9 ±2.08	30.9 ±2.10	23.2 ±1.91	17.0 ±1.67	11.5 ±1.49
	n	70	70	70	70	70	70	70	70	70	70	68
d%		9.7	10.1	7.8	7.5	6.7	6.9	8.5	10.2	11.5	12.8	20.7
t		0.79	1.31	1.39	1.68	1.63	1.26	1.24				
		NS	(P<0.2) NS	(P<0.2) NS	(P<0.1) NS	(P<0.1) NS	NS	NS	NS	NS	NS	NS

Table 7

Tubocurarine

		1	2	3	4	5	6	7	8	9	10	11	12	13
N	m	8.8 ±0.57	17.6 ±0.86	27.0 ±1.32	37.1 ±2.02	45.0 ±2.35	48.5 ±2.55	47.9 ±2.58	43.3 ±2.59	38.1 ±2.72	33.2 ±2.59	27.8 ±2.47	24.0 ±2.34	20.4 ±2.26
	n	46	46	46	45	45	45	45	45	45	45	45	45	45
E	m	9.4	17.7	25.4	34.8	42.7	44.7	40.9	35.4	30.8	25.9	20.8	17.2	14.2
	n	45	45	45	44	44	44	44	44	44	44	44	44	44
d%		—6.8	—0.6	4.8	6.2	5.7	7.8	14.6	17.8	19.2	22.0	25.2	28.3	30.4
t		0.57	0.07	0.72	0.91	0.89	1.19	2.10	2.29	2.09	2.10	2.32	2.36	2.25
		NS	NS	NS	NS	NS	NS	P<0.05	P<0.025	P<0.05	P<0.05	P<0.025	P<0.025	P<0.05

others (tubocurarine and toxiferin) are pachycurares which stabilize the polarization of the membrane; for both kinds, the results (see Fig. 6 and Tab. 5, 6, 7, and 8) are similar: the preparations obtained from irradiated rats are paralysed to a lesser extent and recover sooner than those from normal rats; the difference is evident and very significant for suxamethonium and toxiferin; less evident or not significant for the two other drugs.

Table 8

Toxiferin

		1	2	3	4	5	6	7	8	9	10	11	12
N	m	9.6 ±0.88	23.2 ±2.14	37.1 ±3.24	52.7 ±4.01	65.6 ±4.13	66.8 ±4.00	60.2 ±4.30	52.1 ±4.62	42.3 ±4.47	34.4 ±4.55	27.7 ±4.61	22.4 ±4.44
	n	23	23	23	23	23	23	23	23	23	23	22	22
E	m	4.9 ±0.93	16.4 ±1.70	23.4 ±2.53	40.9 ±2.95	54.4 ±3.03	58.2 ±3.00	54.7 ±3.30	45.4 ±3.63	36.6 ±3.72	29.5 ±3.83	22.1 ±3.51	16.6 ±3.01
	n	25	25	25	25	25	25	25	25	25	24	24	24
d%		49.0	29.3	36.9	22.4	17.1	12.9	9.1	12.9	13.5	14.2	20.2	25.9
t		3.58	2.50	2.14	2.40	2.22	1.73	—	—	—	—	—	—
		P<0.001	P<0.02	P<0.05	P<0.02	P<0.05	NS	NS	NS	NS	NS	NS	NS

DISCUSSION

These results show that exposure to a microwave field of a 5 mW/cm² mean power density for a few days alters the susceptibility of animals to certain drugs.

Our experiments with pentetrazol were begun following our observations of the alterations in the rat EEG (2) following exposure to a microwave field; at that time, we were unaware of the work of Barański and Edelwejn (1). The EEG records of rats which we had irradiated with microwaves in the above-described conditions (2) showed alterations analogous to those which are found in an epileptic fit. We supposed that the susceptibility to a convulsant should be increased in a parallel way to EEG alterations, but Figure 3 shows a biphasic variation in susceptibility which cannot be explained at this time.

We were led to study the susceptibility to curare-like drugs by an accidental observation, also during our work on the EEG. Even more than our experiments with pentetrazol, these drugs have permitted us to begin to understand the way in which the microwave field acts.

Many hypotheses to explain a decrease in susceptibility to a drug could be advanced:

1) the absorption decreases;

2) the excretion is increased;

3) the distribution volume is increased, or modifications of the blood distribution occur;

4) the binding between the drug and the carrier protein increases;

5) the enzymatic mechanism is modified, either by a decrease in the quantity of the enzyme or by a modification in the enzyme itself.

Our experiments, and particularly the isolated diaphragm trials, lead us to localize the action of the field at the level of the neuromuscular synapse; consequently, we can exclude the first four hypotheses.

We have measured neuromuscular excitability, which is identical for normal and

WHO – Biologic effects & health hazards of microwave radiation 1974

irradiated rats; we have also tried to titrate the enzyme acetylcholinesterase in the muscle without finding any difference between normal and irradiated animals.

For all these reasons, it seems to us that the microwave field, acting on the muscular level of the neuromuscular synapse, creates a decrease in the binding energy between the drug molecule and the enzyme molecule; such a decrease could explain the difference between the susceptibility to curare of normal and irradiated animals. We shall now try to check this hypothesis.

CONCLUSION

We have shown that albino rats, after a few days of exposure to a microwave field, do not react in the same way to certain drugs as normal animals do. For curare-like products, we can locate the site of action of the field at the neuromuscular synapse, and more precisely at the post-synaptic membrane; the mechanism is an alteration of the acetylcholinesterase molecule by the field, probably by a decrease of the binding energy.

It is unlikely that this mechanism is the only one by which a microwave field is able to act on living matter. Among the numerous biological effects of microwaves which are quoted in the literature, we shall certainly find many other mechanisms operative.

As a matter of fact, many of these biological effects of microwaves are probably parts of a "psychologic disease" which is not generally apparent by itself, but is revealed by some external agents.

REFERENCES

1. BARAŃSKI S., EDELWEJN Z.: *Acta Physiol. Polon.*, 1968, **19**, 31.
2. BERTHARION G., SERVANTIE B., JOLY R.: *J. Microwave Power*. 1971, 6, 62.
3. SERVANTIE B., BERTHARION G., JOLY R.: *J. Microwave Power*, 1971, 6, 59.

WHO – Biologic effects & health hazards of microwave radiation 1974

MICROWAVE IRRADIATION AND ENDOCRINE FUNCTIONS

H. J. Mikołajczyk

Institute of Occupational Medicine, Łódź, Poland

During investigations on the biologic effects of microwaves attention should be paid to the endocrine functions. This is because of the following reasons:

1. The transformation of electromagnetic energy into heat within living tissues justifies research on pituitary-thyroid functions because of the physiologic role of the thyroid hormones for heat production in the animal body.
2. Microwave irradiation can be an environmental stress factor and thus it is reasonable to investigate the pituitary-adrenocortical system because of its major importance in the stress reaction of the animal organism.
3. The function of male gonads shows a natural sensitivity to the harmful effect of excessive heating; this provides the logical background for studies of the pituitary-gonadal system in the case of microwave irradiation.
4. Such hormones as acetylcholine and adrenaline are mediators between the nervous system and tissues. It seems possible that microwave radiation may modify the activity of these mediators.

The question of whether there is general or selective reactivity of the endocrine system in an organism exposed to microwaves cannot be answered definitively. So for there have been no complex endocrinological investigations in animals or in men exposed to this kind of radiation. Among over 130 biological changes described following electromagnetic irradiation and listed in Report No. 2 from the Naval Medical Research Institute (9) some fourteen changes are of endocrinologic character.

In spite of the use of various classical and modern endocrinologic methods not all results obtained in different laboratories are in agreement. It seems that for studies of this kind on microwave irradiation control investigations and experimental procedure are of prime significance.

THE PITUITARY-THYROID AXIS

Convenient and sensitive tests for the functional evaluation of the pituitary-thyroid axis consist in the uptake of radioiodine by the thyroid gland under standard conditions and after its stimulation with thyroid-stimulating hormone (TSH).

The results obtained in groups of subjects professionally exposed to microwave radiation did not reveal any significant changes in radioiodine tests in comparison with similar tests in control groups (6, 7).

Recently Barański et al. (1) showed the stimulating influence of microwaves at 5 mW/cm² on the trapping and secretory functions of the thyroid gland in rabbits. These functional changes have been found to be in agreement with the histology of the thyroid tissue.

The simultaneously published results of Milroy and Michaelson (14) of their experiments on rats exposed to microwaves using power densities ranging from 100 mW/cm²

WHO – BIOLOGIC EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION
1974

in acute experiments to 10 mW/cm² or 1 mW/cm² in chronic experiments did not reveal any essential changes of the thyroid function.

It seems that it was the experimental procedure and conditions rather than the difference in animal species that might have been responsible for the discrepancies in the above-mentioned results.

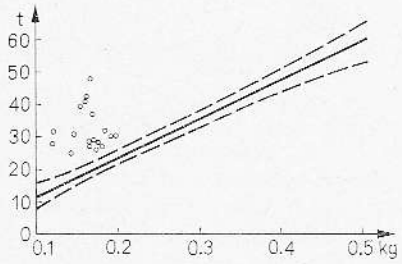


Fig. 1. The relation between body weight m in kg and survival time t in minutes. Continuous and interrupted lines denote the function $t : m$ and 95% confidence limits, respectively, for 37 normal rats. The survival times of 18 hypophysectomized rats are denoted by circles which are non-linearly dispersed above the upper confidence limit of survival time for normal rats.

Conditions of irradiation: Frequency 2860—2880 MHz; far field in an anechoic chamber. Continuous plane wave with power density 120 mW/cm². The rats were irradiated individually in perforated cages made from polymethacrylate.

Table 1

Corticosterone determined fluorometrically in the adrenals and in blood plasma of male rats which had been accustomed for a fortnight to experimental procedures before their exposure to microwave radiation compared to rats that had not been so accustomed. Conditions of irradiation:

Frequency 2860—2880 MHz; far field in an anechoic chamber.

Continuous plane wave with power density 10 mW/cm². $\bar{X} \pm$ S. D. — mean and standard devision.

Experimental procedure	Group of animals (in parentheses number of animals)	Corticosterone in	
		Adrenals µg/100 mg $\bar{X} \pm$ S. D.	µg/100 mg $\bar{X} \pm$ S. D.
Male rats unaccustomed to experimental procedures	Control (2)	14.2 — 15.4	28.8 — 29.0
	Irradiated during 15 minutes (2)	14.9 — 16.4	26.4 — 28.8
Male rats accustomed during a fortnight to experimental procedures before irradiation	Control (4)	5.6 ± 0.45	18.5 ± 3.3
	Irradiated during 15 minutes (4)	4.8 ± 1.10	22.2 ± 3.0
	Control (4)	4.5 ± 1.04	29.0 ± 2.3
	Irradiated during 30 minutes (4)	4.3 ± 1.70	

WHO - Biologic effects & health hazards of microwave radiation 1974

Indirect evidence has been obtained that the lowered general and tissue metabolic rate following hypophysectomy exerts some protective influence on the time-related lethal exposure of rats to microwave radiation. It was found that the survival period of normal rats exposed to microwaves was largely a function of body mass. Survival period per unit of body weight was significantly longer in hypophysectomized than in normal rats (Fig. 1).

THE PITUITARY-ADRENOCORTICAL AXIS

The functional relation between these two endocrine glands under normal conditions shows clearly a circadian rhythm. Numerous environmental factors potentiate the activity of this axis, inducing what is known as a stress reaction. It has been shown that excessive heat can be a powerful stress factor activating the pituitary-adrenocortical axis. Heat stress due to a high power density of microwaves may also be such an activating factor. However, moderate or low power densities of microwaves, being insufficient to produce a thermal effect, probably cannot elicit a stress reaction.

In short-term experimental procedures, especially in the investigation of the pituitary — adrenocortical axis, the need to adapt the animals to new environmental conditions before a proper experiment is obvious. The rats accustomed to experimental procedures did not show a stress reaction following short-term exposure to microwave irradiation (Tab. 1).

THE PITUITARY-GONADAL AXIS

The external localization of the male gonads, the high rate of cell divisions and differentiation, and the fact that the main route of heat dissipation is through the blood vessels of the scrotal skin are probably the principal factors responsible for the high sensitivity of these organs to microwave irradiation.

At various power densities of microwaves histologic and functional changes in the testes have been observed in experimental animals (4, 11) and in men (16, 17).

In the course of chronic microwave irradiation of different animal species both normal reproduction (5, 12, 15) and seriously disturbed reproduction have been described (2).

Gunn et al. (11) suggested that the androgenic hypofunction of interstitial gonadal tissue (Leydig cells) in rats exposed to microwaves could be of extragonadal origin, due to a diminished reactivity of these cells to LH or to reduced LH in the hypophysis.

From the results presented in Tables 2, 3 and 4 it is evident that there were no consistent pathologic changes in the amounts of gonadotropins (LH and FSH) after chronic or short-term exposure of rats to nonthermal doses of microwaves. However, single or repeated exposure of rats to such power densities induced detectable shifts of hypophyseal gonadotropic activities. In general, the content of LH and FSH in the hypophysis was augmented in animals killed immediately and was diminished in animals killed 18—20 h after irradiation.

In the hypophysis of animals exposed to lethal power density levels (2880 MHz, 150 mW/cm^2) the content of FSH, LH and GH was unchanged in comparison to that in control animals (unpublished data).

WHO – Biologic effects & health hazards of microwave radiation 1974

Table 2

The amounts of gonadotropins (LH and FSH) in the anterior pituitary gland of control male rats and of male rats exposed to microwaves 2 hours daily between April 23 and May 27, 1971. The pituitary gland has been excised at autopsy 18—20 hours after the last irradiation of animals. LH and FSH were assayed at one dose level by the ventral prostate augmentation test (Christiansen, 1968) and by the ovarian augmentation test (Evans et al., 1939) in hypophysectomized immature male and female rats, respectively. The standards, i. e. NIH-LH-S15 and NIH-FSH-S7, were assayed at three dose levels (these standards were obtained from the National Institute of Health, Endocrinology Study Section, Bethesda, USA). Conditions of irradiation:

Frequency 2860—2880 MHz; far field in an anechoic chamber. a) continuous wave with power density of 10 mW/cm²; b) pulsed wave repetition rate of 800 Hz and average power density of 10 mW/cm².

$\bar{X} \pm$ S. D. $\pm$ S. E. — mean and standard deviation or standard error.

Group of animals	Body weight in g $\bar{X} \pm$ S. D.		µg/pituitary	
	initial	final	LH $\bar{X} \pm$ S. E. (limits)	FSH $\bar{X} \pm$ S. E. (limits)
I. Control rats 10 ♂♂ kept all the time in plastic cages in the animal house	39 ± 11	171 ± 11	480 ± 56+ (390 — 700)	800 ± 24+ (730 — 840)
II. Control rats 10 ♂♂ kept 2 h daily in wire cages in a sound-proof chamber	32 ± 5	177 ± 7	444 ± 20+ (390 — 510)	740 ± 55 (620 — 810)
III. Irradiated rats 10 ♂♂ exposed 2 h daily, 10 mW/cm², continuous wave	35 ± 5	181 ± 10	368 ± 11+ (340 — 390)	870 ± 114 (680 — 1200)
IV. Irradiated rats 10 ♂♂ exposed 2 h daily, 10 mW/cm², pulsed wave	39 ± 5	177 ± 14	298 ± 33+ (230 — 380)	700 ± 11+ (680 — 720)

Difference significant at $p = 0.05$

OTHER HORMONAL CHANGES

The quantity of growth hormone estimated at the same time as LH and FSH tests showed no clear changes. Some experiments revealed a stimulatory effect of microwave irradiation on the amounts of GH in the hypophysis of rats whereas others showed an inhibitory influence (unpublished data). GH was estimated by the method of Greenspan et al. (10).

Rats injected with acetylcholine survived longer, whereas those injected with adrenaline survived for a shorter time than control animals during acute microwave irradiation (2880 MHz, 150 mW/cm²) (unpublished data). Such an irradiation of adrenaline in solution accelerated its transformation into chromogenic derivatives, e.g. adrenochrome. This process has been shown to be indistinguishable from that after conventional heating of adrenaline solutions (13).

Table 3

The amounts of gonadotropins (LH and FSH) in the anterior pituitary gland of control male rats and of male rats exposed once during 6 hours to microwave radiation. The pituitary gland was excised at autopsy made immediately after exposure of the animals. Conditions of irradiation, assays of gonadotropins and other indications the same as described in Table 2.

Group of animals	Body weight in g $\bar{X} \pm$ S. D.	µg/pituitary	
		LH $\bar{X} \pm$ S. E. (limits)	FSH $\bar{X} \pm$ S. E. (limits)
I. Control rats 10 ♂♂ kept all the time in plastic cages in the animal house	270 ± 23	246 ± 20 (190 — 310)	493 ± 25 (430 — 540)
II. Control rats 10 ♂♂ kept from 7.00 a. m. to 1.00 p.m. in wire cages in a sound-proof chamber	244 ± 14	292 ± 27 (230 — 390)	510 ± 59 (370 — 660)
III. Irradiated rats 10 ♂♂ exposed, from 7.00 a. m. to 1.00 p. m., to 10 mW/cm², continuous wave	262 ± 18	428 ± 44 (300 — 500)	702 ± 53 (600 — 800)

Difference significant at p = 0.05 for FSH group I : III

Table 4

The amounts of gonadotropins (LH and FSH) in the anterior pituitary gland of control male rats and of male rats exposed to microwave radiation 2 hours daily from Dec. 14, 1972 to Jan. 10, 1973. The pituitary gland was excised at autopsy made immediately after the last irradiation of animals.

Conditions of irradiation, assays of gonadotropins and other indications are the same as described in Table 2.

Group of animals	Body weight in gm $\bar{X} \pm$ S. D.	µg/pituitary	
		LH $\bar{X} \pm$ S. E. (limits)	FSH $\bar{X} \pm$ S. E. (limits)
I. Control rats 10 ♂♂ kept 2 h daily in double screened cage placed near the anechoic chamber	207 ± 21	408 ± 32 (310 — 470)	805 ± 55 (670 — 940)
II. Irradiated rats 10 ♂♂ exposed 2 h daily to 5 mW/cm², continuous wave	220 ± 22	520 ± 47 (400 — 630)	1306 ± 92 (1000 — 1720)

Difference significant at p = 0.05 for FSH group I : II

WHO – Biologic effects & health hazards of microwave radiation 1974

COMMENTS

The links between nervous and endocrine systems are multiregional in the body, but the main one is situated in the hypothalamus. Going down from the hypothalamic centers through the hypophysis to peripheral glands a stepwise amplification of hormonal stimuli may be observed. Thus the whole endocrine system displays some characteristics of a biological amplifier with the hypothalamus as the most sensitive and crucial region.

Unpublished preliminary results obtained with hypothalamic extracts from control and irradiated rats indicate that the time-related quantitative changes of hypophyseal gonadotropins described above can depend on the blocking or inhibitory effects of microwaves on the secretion of releasing hormones in hypothalamic centers. This assumption is consistent with the observed quantitative changes in neurosecretory granules in cells of hypothalamic centers of animals exposed to electromagnetic radiation (18, 19).

The harmful effects of microwave radiation on testicular and perhaps on other endocrine functions could be of both local and central (hypothalamic) origin.

REFERENCES

1. BARAŃSKI, S., OSTROWSKI, K., STODOLNIK-BARAŃSKA, W.: *Acta Physiol. Polon.*, 1972, **23**, 6, 997.
2. BEREZNICKAJA, A. N.: *Gigiena Truda*, 1968, **9**, 33.
3. CHRISTIANSEN, P.: *Acta Endocrinol.*, 1968, **59**, 622.
4. CIECIURA, L., MINECKI, L.: *Histological changes in testicles of rats exposed to the action of microwave radiation under conditions of hypothermia.* Proceedings of the XVth International Congress of Occupational Health. Vienna, 1966, p. 881.
5. DEICHMANN, W. B., BERNAL, E., STEPHENS, F., LANDEEN, K.: *J. of Occup. Med.* 1963, **5**, 9, 418.
6. DENISIEWICZ, R., DZIUK, E., SIEKIERZYŃSKI, M.: *Pol. Arch. Med. Wewn.*, 1970, **45**, 1(7), 19.
7. DIAČENKO, N. A.: *Gigiena Truda*, 1970, 7, 51.
8. EVANS, H. M., SIMPSON, M. E., TOLKSDORF, S., JENSEN, H.: *Endocrinology*, 1939, **25**, 529.
9. GLASER, Z. R.: *Bibliography of reported biological phenomena ("effects") and clinical manifestations attributed to microwave and radio-frequency radiation.* Project MF12.524.015. Report No 2. NMRI, National Naval Medical Center. Bethesda, Maryland. Second printing, 20 April, 1972.
10. GREENSPAN, F. S., LI, CH. H., SIMPSON, M. E., EVANS, H. M.: *Endocrinology*, 1949, **45**, 455.
11. GUNN, S. A., GOULD, T. C., ANDERSON, W. A. D.: *Lab. Investig.*, 1961, **10**, 2, 301.
12. MICHAELSON, S. M., HOWLAND, J. W., DEICHMANN, W. B.: *Industr. Med.*, 1971, **40**, 18.
13. MIKOŁAJCZYK, H.: *Medycyna Lotnicza*, 1972, **39**, 89.
14. MILROY, W. C., MICHAELSON, S. M.: *Aerospace Med.*, 1972, **43**, 10, 1126.
15. MIRO, L., LOUBIERE, R., PFISTER, A.: *Revue de Médecine Aéronautique* (Paris), 1965, **4**, 37.
16. ROSE, V. E., GELLIN, G. A., POWELL, CH. H., BOURNE, H. G.: *American Industr. Hyg. Assoc. J.*, 1969, **30**, 137.
17. ROSENTHAL, D. S., BEERING, S. C.: *J. of Med. Assoc.*, 1968, **205**, 4, 245.
18. TOLGSKAJA, M. S., GORDON, Z. V.: *Morfologičeskie izmenenia pri deistvii elektromagnitnyh voln radiočastot.* Izdatelstvo Medicina, Moskva, 1971.
19. ZUBKOVA-MIHAILOVA, E. I., ALEKSEEV, JU. H.: *Bjul. Eksp. Biol. i Med.* 1968, **33**, 1, 115.

WHO – BIOLOGIC EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION 1974

BIOLOGIC EFFECTS OF RADIATION IN THE 30—300 MHZ RANGE

T. V. Kalada, P. P. Fukalova and N. N. Gončarova

Institute of Industrial Hygiene and Occupational Diseases, Leningrad; Institute for Scientific Research on Industrial Hygiene and Occupational Diseases of the Academy of Medical Sciences of the USSR, Moscow, and Institute of Industrial Hygiene and Occupational Diseases, Harkov, USSR

This communication presents some general results of investigations conducted during many years on the biologic action of continuously generated electromagnetic fields of non-thermal intensity within the range of 40—200 MHz. The studies were directed at hygienic, clinico-physiologic and experimental aspects.

A complex clinical examination of a large number of specialists working with generators of ultra-high-frequency energy made it possible to define various health deviations in these workers (2, 3, 5, 14). The examination of this group of people aged under 40 years with a history of occupational exposure of over 5 years demonstrated the frequent occurrence of functional changes in the central nervous system (52%). No organic lesions were found. A vegetative dysfunction was the principal form of neurodynamic disturbances. The symptoms included hyperhidrosis, persistent red dermographism and enhancement of the pilomotor reflex, all of a mild degree. However, examination of the functional status of higher vegetative centers by means of special diencephalic tests disclosed quite frequently various anomalies of the thermoregulatory reflexes (distortion, inhibition, lack). Thermoasymmetry and isothermy were sharply expressed. Disturbances of photoreactivity of the skin took the predominant form of a lowered threshold sensitivity to ultraviolet radiation. The vegetative dysfunction was accompanied by neurasthenic (hypersthenic) symptoms in 14% of cases. In no case were well-developed forms of asthenia observed. The relationship between the frequency of neurodynamic disturbances and the length of work was clear-cut. The nervous pathology was somewhat more frequent in women (54%) than in men (48%). Circulatory pathology (hypertension, myocardiodystrophy, cardiosclerosis) was found in 24% of those examined. The histories of these patients did not reveal any factors which might have led to lesions of the heart muscle. A number of functional shifts of predominantly sympathicotonic nature were disclosed. Oscillographic data revealed raised hemodynamic parameters. Capillaroscopy visualized spastic and spastic-atonic pictures of the capillaries. Electrocardiographic examinations established a high frequency of moderate impairment of oxygenation of the heart muscle (in 42 out of 50 patients under 40 years of age, with negative histories). Cholesterol metabolism was investigated in the whole group and included measurements of total cholesterol, protein-bound cholesterol and total phospholipids. The level of loosely protein-bound cholesterol was elevated, and the ratio of phospholipids to cholesterol was lowered. In those working for over 5 years, also the total cholesterol content was elevated.

The combination of the two interdependent factors — neurocirculatory and metabolic disturbances which accompanied long exposures to electromagnetic fields of the meter range — played a significant role in the development of circulatory pathology.

Changes in the gastrointestinal tract were found in 14% of cases (chronic gastritis,

WHO - BIOLOGIC EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION
1974

12%; ulcers, 2%). In half of the cases, gastritis was diagnosed in young patients. It should be noted that in all patients gastric lesions developed against a background of neurasthenia syndrome and vegetative dysfunction. No quantitative changes in the peripheral blood were found. Some deviations in the physicochemical and functional properties of the erythrocytes and leukocytes were observed. A lowered osmotic resistance of the leukocytes of those examined occurred six times more frequently than in controls. The phagocytic reaction was also lowered and led to a weakened immunobiological reactivity of the organism. The increase in functional disturbances with longer periods of work in electromagnetic fields, taken together with sharp differences in health status between those working with sources of electromagnetic fields and their controls, point to a link between the changes and the occupational factors.

Analysis of data of experimental investigations conducted both in factories (7, 13) and under laboratory conditions on workers and volunteers (8, 9, 10, 11, 12) showed that electromagnetic fields of non-thermogenic intensity are indeed harmful and may produce cumulative effects.

Accumulation of biological effects is reflected in resetting of functional systems of the organism to a new level of activities.

In this way statistically significant phasic changes in the initial level of the functional status of the thermic skin analyser, and of circulatory and central nervous systems in those working for various lengths of time were ascertained. Figure 1 may serve as an illustration.

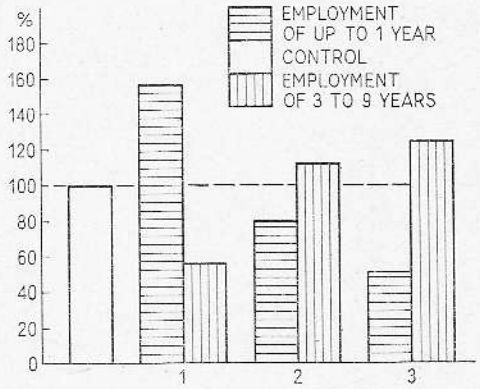


Fig. 1. Changes in the level of activity of thermal receptors (1), threshold temperature sensitivity (2) and threshold excitability of the visual analyser (3) in workers with various duration of employment, as compared with the control group taken as 100%.

Figure 1 shows that electromagnetic fields had an activiting influence on those working for less than 1 year as manifested by changes in the pattern of thermal receptors as compared with the control group. With increasing length of work under conditions including irradiation with electromagnetic waves, the level of active thermal receptors sharply declined. The adjustment of thermal perception changed correspondingly. In those with a shorter length of work the threshold of heat perception was much lower than in controls, and in those working longer it was higher.

Phasic changes in the initial level of functional activity were recorded on investigating other analytical systems. Shortening of the latent period of reflexes to sound and light stimuli and a lowered value of the optical chronaxy in early periods of work were disclosed. These parameters lengthened with increasing length of work. Hemody-

WHO – Biologic effects & health hazards of microwave radiation 1974

namic parameters reflected hypo- and hypertensive fluctuations during the working day and an increase of hypertensive states with lengthening occupational exposure.

On comparing results of physiologic investigations with physico-hygienic parameters of irradiation of workers, a clearcut relationship was noted between the character and level of reactions and intensity of the factor acting in the industrial environment.

Experimental data obtained in volunteers under laboratory conditions of irradiation mimicking industrial variants revealed certain principles concerning general physiologic responses of the human body towards electromagnetic fields. The thermoregulatory system, some systems of hemodynamics and thermal, optical and auditory analysers proved most functionally reactive and sensitive to the influence of experimental irradiation. The dynamics of functional deviations were compared with those accompanying the presumed action of the factor. The irradiation was systematic with daily 15 min exposures and the 30 days' duration of each series of treatments. The ambient temperature ranged from 22.6 to 23.4°C with relative humidity of 40—46%.

The results showed that some functional deviations took place during irradiation, while others followed it. The skin temperature of distal parts of the body (hands, feet) was elevated during the whole period of actual irradiation with simultaneous intensification of heat loss through emission and demobilization of heat receptors. The number of active cold receptors sharply increased.

Figure 2 presents the levels of the hand skin temperature, heat emission, and changes in the pattern of heat and cold receptors during simulated and actual irradiation.

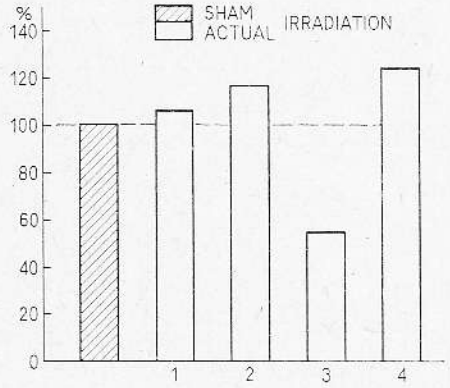


Fig. 2. The levels of indices of the hand skin temperature (1), heat emission (2) and changes in numbers of heat (3) and cold (4) receptors during actual and sham irradiation, the latter taken as 100%.

For assessment of the status of the temperature analyser, duration of the latent periods of the reflex to contact and radiated heat were measured. The visual and auditory analysers were also assessed. It was found that after irradiation, as well as during the whole period of the actual action of the stimulus, the duration of the reflexes was shortened. Thus the excitability of the analysers was increased. The initial values of hemodynamic parameters and of the pulse rate had a tendency to increase, apparently due to the irritation of the sympathetic nervous system by the field.

Results of investigations of regional blood circulation showed active vasomotor reactions not only during irradiation but also following it. Figure 3 illustrates fluctu-

WHO – Biologic effects & health hazards of microwave radiation 1974

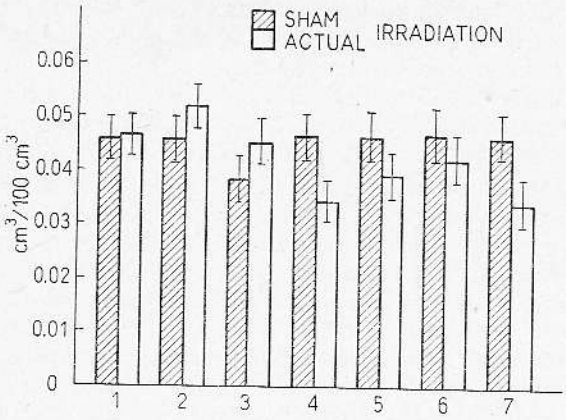


Fig. 3. Fluctuations in pulse volume during sham and actual irradiations. Symbols: 1 — initial readings, 2 — switching on of the generator, 3 and 4 — 15 and 30 min of irradiation, 5 — switching off of the generator, 6 and 7 — 15 and 30 min of recovery.

ations in pulse volume as recorded plethysmographically during simulated and actual irradiation. Switching on of the generator, as well as cessation of irradiation, were accompanied by an increase in pulse volume. Towards the end of irradiation and during the 30 min recovery period this value was lowered. In the conditions of the experiments the tonus of peripheral blood vessels was increased during the entire irradiation period with partial normalization following irradiation.

An analysis of the data showed that the initial increase in tonus resulted from an increase in pulse pressure, while in the process of irradiation it was due to spastic status of the peripheral vessels.

From the point of view of contemporary physiology, such shifts in physiologic systems from one functional level to another are regarded in some cases as adaptive responses to the action of exogenous irritants, and in others as exhaustion or functional weakening.

The experimental results obtained showed that the level of activity of the functions under investigation was changed; these changes may be regarded as adaptive responses.

However, repeated radiowave irradiation over a long period of time led to more serious functional disturbances, as evident from clinical symptoms. It follows that adaptive responses taking place during the initial stages of irradiation should be regarded in some instances as transient states with a potential for becoming pathologic.

The influence of electromagnetic fields upon the organism of animals was investigated in both acute and chronic experiments (5—8 months' irradiation), using thermal and non-thermal intensities, respectively (1, 4, 6, 15, 16, 17). The functional status of the central nervous system (electroencephalography, conditioned reflex activity, the threshold of neuromuscular stimulation, and others), hemodynamics, biochemical processes in the animal nervous tissue directly connected with its function (acetylcholine metabolism, some aspects of carbohydrate and nitrogen metabolism), protein metabolism and immunobiologic reactivity were all assessed. The morphology of various organs and tissues was studied.

The results of these investigations showed a definite dependence of biologic effects in the functional systems under study on the length of action of the irradiation and physical parameters of the latter (intensity, frequency and components of the field). The

WHO – BIOLOGIC EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION 1974

effects of thermogenic intensities were connected with evident disturbances of the nervous regulation and functional impairment of the hypophysis and suprarenal cortex. Functional disturbances of the nervous system were clearly connected with the exhausting influence of the causative factor (EM field) upon nervous cells with progressive inhibition, in some cases extremely severe. Sequelae of irradiation with nonthermogenic intensities were of the same character, though milder.

Investigations aimed at elucidation of animal brain metabolism were conducted to gain insight into some aspects of the mechanism of functional disturbances of the nervous system. The results of exposure to electric fields showed that glycogen hydrolysis was more intense and that oxidation of its intermediates was impaired (low glycogen and high lactic and pyruvic acid content). Chronic irradiation with magnetic fields led to glycogen accumulation in the tissues without changes in concentration of the other compounds under study. The findings were regarded as a result of lowered activity of the processes of glycogen utilization by the nervous tissue due to functional inhibition, as was established by physiologic investigations. The processes of carbohydrate metabolism in the brain were still abnormal one month after electromagnetic field action, indicating the long-lasting nature of the changes and, perhaps, the cumulative nature of bioeffects. Deviations of ammonia formation in the brain tissue were found to be a similar in character.

The functional status of the nervous system depends to a certain extent upon the acetylcholine level in the brain tissue. It was shown experimentally that, as a result of prolonged action with electromagnetic fields, the level of acetylcholine increased conspicuously and cholinesterase activity decreased. The former was evidently connected with disturbed processes of acetylcholine synthesis and binding to brain proteins. A lowered cholinesterase activity was of a compensatory-adaptive character.

Changes in immunobiologic reactivity had a phasic character, with periods of suppression of phagocytic and bactericidal blood functions alternating with increased activity.

Morphologic investigations showed hemodynamic disturbances and mild dystrophic changes in the parenchymatous organs (particularly in the liver), heart muscle and nervous system. In the central nervous system, changes in the ganglionic cells of the cortex and of subcortical nuclei were found; in the skin receptors there was partial fragmentation of nervous fibers with clearly visible swelling.

Thus the complex clinico-physiologic and experimental studies on the biologic action of electromagnetic fields made it possible to establish some general biologic trends in reactions of the human and animal organism, to elucidate some aspects of pathogenesis of functional deviations, and to prove their cumulative character.

REFERENCES

1. VOLKOVA, A. P., FUKALOVA, P. P. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Sbornik materialov simpoziuma. Moskva, 1972.
2. VOLFOVSKAJA, R. N., ASANOVA, T. P., SEMENOVSKAJA, N. A., ŠČEGLOVA, A. V., KONIKOVA, G. S. In: *Voprosy gigieny truda i vliania elektromagnitnyh polei na organizm čeloveka.* Leningrad, 1968.
3. VOLFOVSKAJA, R. N., ASANOVA, T. P., SEMENOVSKAJA, N. A., KONIKOVA, G. S.: *Voprosy serdečno-sosudistoi potologi v klinike professionalnyh bolezni.* Leningrad, 1969.
4. GONČAROVA, N. N., KARAMYŠEV, V. B., MAKSIMENKO, N. V., OSTROVSKAJA, I. S., JAŠINA, L. N. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Sbornik materialov simpoziuma. Moskva, 1968.

WHO – BIOLOGIC EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION 1974

5. GONČAROVA, N. N., MIŠČENKO, L. I.: *Gigiena truda,* 1973, 7, 22.
6. GORDON, Z. V., FUKALOVA, P. P., KICOVSKAJA, I. A., BEREZINSKAJA, A. N., PONKIN, A. A.: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Sbornik materialov simpoziuma. Moskva, 1968.
7. KALADA, T. V. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Sbornik materialov simpoziuma. Moskva, 1968.
8. KALADA, T. V. In: *Voprosy gigieny truda i vlianie elektromagnitnyh polei na organizm čeloveka.* Leningrad, 1968.
9. KALADA, T. V.: *Temperaturnaja recepcija. Izdatelstvo Nauka,* Leningrad, 1969.
10. KALADA, T. V.: *Teploobrazovanie i termoregulacja organizma v norme i patologičeskih sostojaniah.* Kiev, 1971.
11. KALADA, T. V., NIKITINA, V. N., SVERDLINA, N. T. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Sbornik materialov simpoziuma, 1972.
12. KALADA, T. V.: *Fizičeskoe faktory proizvodstviennoi sredy i ih vlianie na sostojanie zdrovia rabotajuščih.* Moskva, 1973.
13. OSIPOV, J. A., KALADA, T. V. In: *Voprosy gigieny truda i vlianie elektromagnitnyh polei na organizm čeloveka.* Leningrad, 1968.
14. SADČIKOVA, M. N., GLOTOVA, K. V., ČULINA, N. A. In: *O biologičeskom deistvii elektromagnitnyh polei radiočastot.* Moskva, 1968.
15. FUKALOVA, P. P., TOLGSKAJA, M. S. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Sbornik materialov simpoziuma. Moskva, 1968.
16. FUKALOVA, P. P., BYČKOV, M. S., TOLGSKAJA, M. S., KICOVSKAJA, I. A., VOLKOVA, A. P., DEMOKIDOVA, N. K., VORONCOV, R. S. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Sbornik materialov simpoziuma. Moskva, 1972.
17. JAŠINA, L. N., OSTROVSKAJA, I. S., GONČAROVA, N. N., KARAMYŠEV, V. B. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Sbornik materialov simpoziuma. Moskva, 1969.

WHO – Biologic effects & health hazards of microwave radiation 1974

THE CHARACTERISTICS OF BIOLOGIC EFFECTS OF MICROWAVES COMBINED WITH THE ACTION OF SOFT X-RAY IRRADIATION AND HEAT

K.V. Nikonova and I.P. Sokolova

Labor Order of the Red Banner Institute for Scientific Research Industrial Hygiene and Occupational Diseases Academy of Medical Sciences of the USSR, Moscow, USSR

Under natural conditions, microwave irradiation is often accompanied by other factors in the industrial environment, such as X-ray irradiation, unfavourable weather conditions, noise and toxic compounds.

Studies on the character of the biological effects resulting from such combined influences are important for the solution of a number of hygienic questions, and for elucidation of the role played by the accompanying factors in the etiology of pathological processes occurring in those working with SHF generators.

The first publications on the combined action of microwaves and ionizing radiation appeared in the early sixties (4, 9, 14, 13, 17).

Experimental studies by American authors (13, 14, 17) provided interesting data on changes in sensitivity of the organism to microwave and gamma-irradiation, depending on the sequence of action of these factors.

The present communication presents the results of experimental studies on the combined action of microwaves and low energy (soft) X-ray irradiation, since earlier investigations (7, 15) showed that electronic equipment with an effective voltage of at least 10 kV, used in SHF installations, could be a source of X-rays.

Biological effects of the combined action of 10 cm microwaves and X-ray irradiation with $E_{ef} = 13 \times 5$ keV were studied.

In our work an RUM-7 (RUT 60—20—I) instrument was the source of X-rays with an anode voltage of 30 kV and 0.3 mm Al + 0.5 mm organic glass (the bottom of a cage) filtration. The dose rate was regulated by means of changes in current, and dosimetry was carried out with a KD-IM condensor dosimeter. Irradiation of animals was performed essentially from the abdominal side.

A 10 cm wavelength pulsed microwave generator was used. The power density of irradiation was controlled with a PO-I apparatus.

Investigations carried out at various power densities of SHF currents and different doses of soft X-ray irradiation made it possible to establish a relationship between the character of biological effects and intensity of action.

It was found that the combined action of high intensities of microwaves and of soft X-rays was synergistic (by synergism we mean the effect close to, or somewhat exceeding, summation). At the same time in the clinical picture lesions caused by X-rays were predominant. Thus, upon combined action of a single dose of 2500 r of X-rays and 15 min daily irradiations with 40 mW/cm² microwaves for 6 weeks, the clinical picture of the affected mice was that of developing radiation sickness, as manifest

WHO - BIOLOGIC EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION
1974

by changes in body weight, low leukocyte count in the peripheral blood, progressive skin lesions, and decreased weight of the testes.

The histological examination of the testicles revealed severe morphological changes testifying to atrophy and dystrophy of the seminiferous epithelium. According to a number of parameters, the lesions following the combined action were more severe than those resulting from X-rays or microwaves applied singly. Thus, with the combined action, the death rate of animals was higher, the loss of body weight was more marked, the skin lesions occurred earlier and were more evident, and the decline in number of leukocytes in the peripheral blood was more pronounced (Tab. 1, Fig. 1). This enabled the conclusion to be drawn that the action of high intensities of microwaves coupled with that of soft X-ray irradiation was synergistic.

Table 1

Reaction of white blood cells and mortality during the experimental period (2500 r, 40 mW/cm²)

Type of action	Leukocyte number		Died during 6 weeks (%)
	Background	3rd day	
Microwaves	10886 ± 412	8071 ± 588	5.0 ± 4.0
X-rays	10844 ± 410	7350 ± 514	5.5 ± 5.3
Combined	11814 ± 521	5300 ± 226	36.4 ± 10.2
Control	11190 ± 443	12514 ± 994	0 ± 4.5

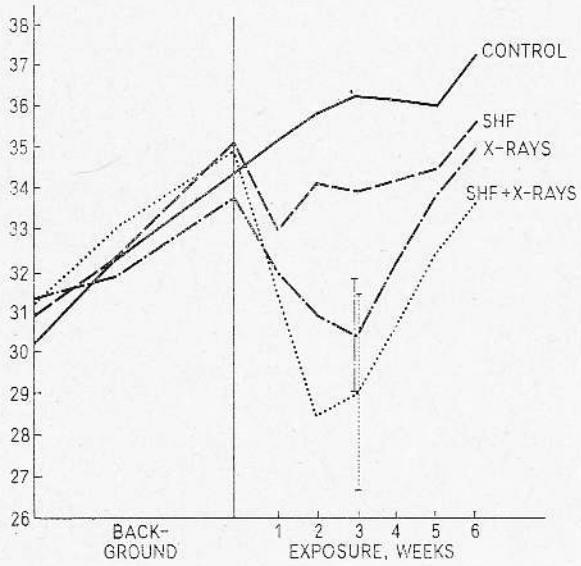


Fig. 1. Changes in body weight of white mice (2500 r, 40 mW/cm²).

However, of the greatest practical interest were the characteristics of those biological effects which resulted from low intensities of action, close to those of actual industrial conditions.

WHO – Biologic effects & health hazards of microwave radiation 1974

It should be noted that with the change to low intensities, the role of microwaves became more conspicuous and the manifestation and reproducibility of the "amplification" effect declined.

The following are results of studies on biological effects accompanying the combined action of 1 mW/cm² for 1 h daily and 25 r weekly. Under conditions of repeated, long-lasting, chronic experiments, investigations were made of the changes in body weight of the animals, the peripheral blood, permeability of the blood vessels, immunobiolo-

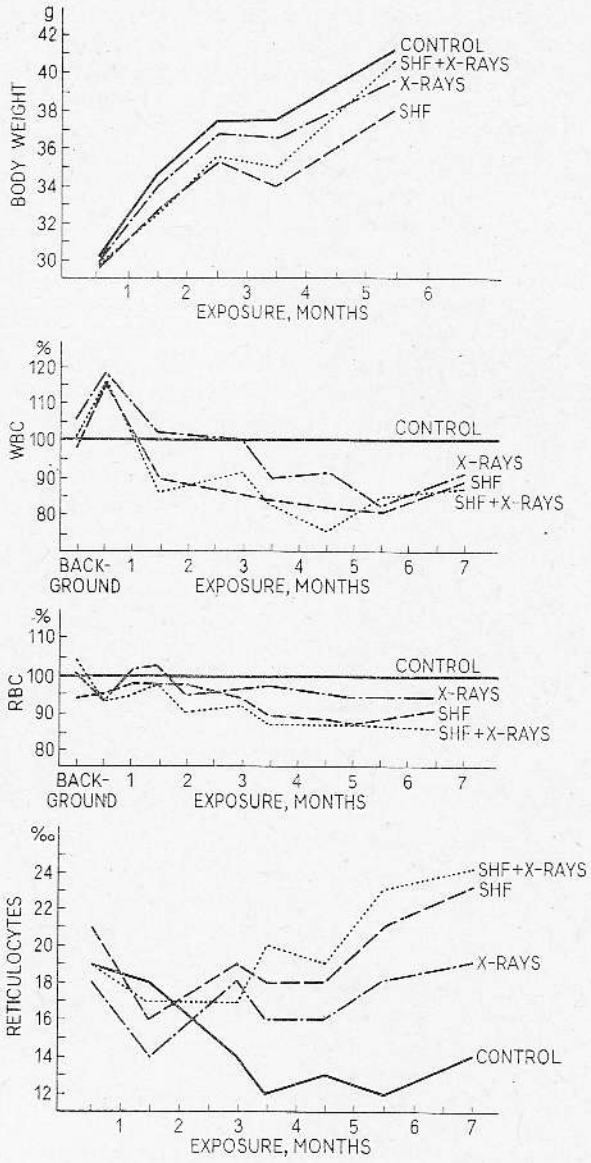


Fig. 2. Changes in body weight of white mice and in peripheral blood parameters of white rats (1 mW/cm², 25 r per week).

WHO – Biologic effects & health hazards of microwave radiation 1974

gical reactivity, functional status of the central nervous system (the labyrinth and EEG methods), weight of the testicles, reproductive function of males, as well as histological pictures of the organs and tissues of the irradiated animals.

Analysis of the collected data showed that the combined action of microwaves and soft X-ray irradiation at the level of low intensities was governed by biological laws which differed from those prevailing at high intensities.

Under conditions of the combined action of low intensities no well-defined intensification of biological effects was observed. According to a number of parameters the observed extent of the changes was close to that characteristic of the factors applied singly.

The pattern of the reactions in different organs and systems was defined in some cases by the action of radiowaves, and in others by X-rays.

According to weight changes and the peripheral blood picture the groups of animals acted upon with the combined agents behaved in a way analogous to those subjected to microwave irradiation alone (Fig. 2).

Following the combined action, in a number of experiments during separate periods of observation the animals lagged behind in weight gain. We could observe an analogous effect also with isolated radiofrequency irradiation, and in none of the experiments were significant differences noted in this parameter between the groups.

In the peripheral blood of animals changes were found following the combined action of microwaves and soft X-rays and took the form of lowered leukocyte and erythrocyte counts and increased reticulocyte numbers, very much like those accompanying isolated microwave irradiation. Some differences noted between these groups in individual cases were, as a rule, transient and poorly reproducible in repeated experiments.

Related to the action of microwaves was a marked hyperplasia of reticuloendothelial elements in the liver and spleen, of lymphoid elements in the lungs, and of microglia in the brain, as well as manifestations of irritation of the receptor apparatus of the skin and a decrease in ribonucleoproteins of the epidermis and its derivatives.

The second factor of the combination, X-ray irradiation, determined the lowered weight of the testicles, increased vascular permeability and, as consequences of the latter detectable upon histological examination, an increased content of mast cells and plasmocytes in the subcutaneous tissue, of mast cells in the connective tissue surrounding the spleen, and of iron-containing pigment in the pulmonary lymph nodes and spleen (Tab. 2, Fig. 3).

Finally, the reactions of a number of organs and systems under conditions of combined action were determined by both microwave and X-ray irradiation.

Table 2

Weight of testicles in percentages of body weight of mice (1 mW/cm², 25 r per week)

Type of radiation	Duration of action	
	4 months	11 months
Microwaves	0.61 ± 0.03	0.53 ± 0.02
X-rays	0.47 ± 0.03	0.46 ± 0.015
Combined	0.51 ± 0.02	0.45 ± 0.02
Control	0.61 ± 0.02	0.58 ± 0.034

WHO – Biologic effects & health hazards of microwave radiation 1974

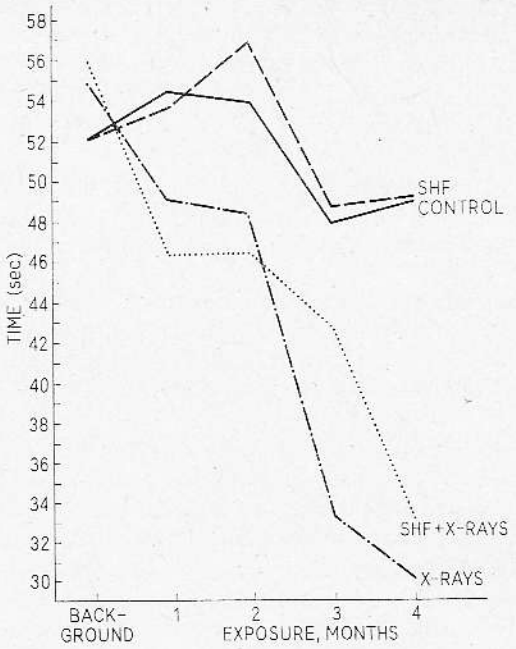


Fig. 3. The state of vascular permeability (1 mW/cm², 25 r per week).

Thus, during studies of immunobiological reactivity over a period of 6 months, various changes in the phagocytic and digestive functions of neutrophils, and also in the bactericidal power of plasma, were observed. During different periods of the study, the consequences of one or the other factor predominated. As to their intensity, the

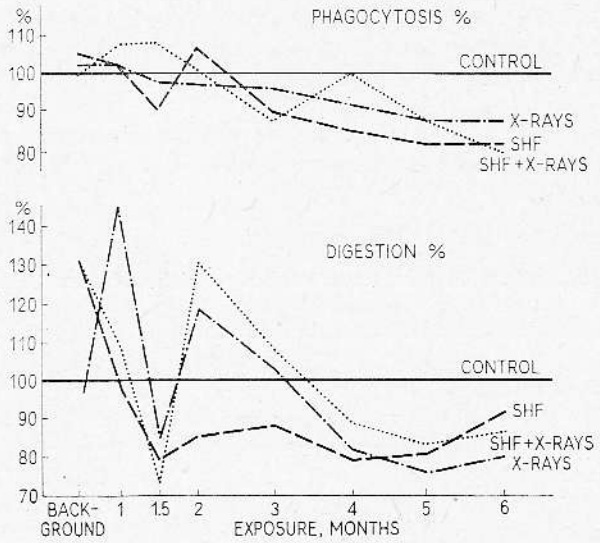


Fig. 4. Changes in indicators of immunobiological reactivity (1 mW/cm², 25 r per week).

WHO - Biologic effects & health hazards of microwave radiation 1974

changes due to the combined action were indistinguishable from those observed following exposure to the separate factors (Fig. 4). In the testes, following long periods of action, marked dystrophic changes in the seminiferous epithelium were detected as elicited predominantly by X-rays. They were accompanied by homogenization and interstitial edema beneath the capsule and proliferation of the interstitial elements due to microwave irradiation. The process was focal in character which might apparently explain the lack of more pronounced changes in reproductive capacity of the animals by comparison with the influence of a single factor.

Thus, the biological effects of the combined action of low-intensity microwaves and soft X-ray irradiation were characteristic of both the former and the latter factor. No clear-cut intensification of the biological effects by comparison with those induced by the separate factors was observed.

Other investigators (5) came to analogous conclusions while studying the combined action of microwaves of 12.6 cm wavelength and X-ray irradiation of E_{ef} of 73 and 10 keV.

It is true that some authors have reported that functional changes of the central nervous and circulatory systems were somewhat more pronounced in people working under conditions of the combined action of SHF and X-ray irradiation than in workers subjected mainly to the action of microwaves. At the same time these authors noted that the changes did not exceed the range of physiological fluctuations.

Another combination of factors — microwaves and heat — is equally interesting from both the theoretical and practical points of view.

There are data in the literature about more pronounced changes in the health status of people subjected to microwave irradiation under conditions of tropical climate (6, 10). American investigators (12) observed that, following the combined action of microwaves and heat, weight loss and susceptibility to microwave irradiation in dogs were more pronounced. Some authors (16) deem it necessary to differentiate the safe exposure levels taking into account a temperature factor.

We studied the biologic effects of the combined action of 10 cm microwaves and high air temperature. To create the temperature conditions needed, use was made of a chamber with hot air supplied by a heater.

As in the case of combination with ionizing radiation, biologic effects were found to depend on levels of exposure.

Table 3

Survival of animals in SHF fields as a function of ambient temperature

Type of animal	SHF power density (mW/cm^2)	Air temperature (°C)	Mean survival time (min)
Mice	80	40	28.3 ± 1.8
	80	22	63.3 ± 7.6
	80	14	106.5 ± 4.5
Rats	60	40	43.3 ± 3.2
	60	20	111.5 ± 4.7

Investigations of the survival rate of white mice and rats showed that the higher the ambient temperature the more rapid was the death of the animals in SHF fields (Tab. 3).

WHO – Biologic effects & health hazards of microwave radiation 1974

Thus, with a reduction in temperature from 40°C to 14°C, the duration of life of white mice irradiated at a power density of 80 mW/cm² increased from 28.3 ± 1.8 to 106.5 ± 4.5. An analogous result was obtained in rats. A similar observation has been recorded in the literature (11).

An analysis of the thermal reactions of white rats with changes in irradiation conditions showed that, under conditions of impaired heat emission due to failure of compensatory mechanisms, the body temperature increased faster under the combined action and caused an earlier death of the animals.

The synergism of action of microwaves and heat was clearly evidenced at the intensity level of 10—15 mW/cm² and 38—40°C. Experiments performed on mice showed that a single exposure to the combined action at these intensities led to a more pronounced loss of physical endurance than following exposure to microwaves or temperature alone. During chronic experiments, the highest number of reinforcements for attaining the criterion of strengthening the previously elaborated conditioned defence reflexes of "escaping" was required following exposure to both factors.

In rats under chronic exposure conditions a stronger biological effect was noted with the combined action according to such indicators as weight changes and vascular tonus.

Studies of the bioelectric activity of rabbit brain showed that EEG effects following the combined action o SHF and heat were of the same character as those caused by SHF or heat alone, but exceeded the latter in severity.

We now move on to the combined action of heat and lower intensities of microwaves. Results of investigations on the combined action of microwaves and heat of 5 mW/cm² and 40°C intensities, respectively, under conditions of chronic exposure have been reported (2).

The author found that previous microwave irradiation increased the sensitivity of white rats to thermal exposure as evidenced by a greater rise in rectal temperature, a tendency towards increased numbers of erythrocytes, lowered viscosity of the blood, decreased percentage of pregnant rats and average size of the litter, and lowered weight coefficients of the liver and spleen.

In rats exposed daily for 1 h simultaneously to the combined action of microwaves and heat at intensity levels of 1 mW/cm² and 35—38°C we investigated the following indicators: thermal reaction, weight changes, immunobiological reactivity, blood pressure and cholinesterase activity of blood erythrocytes.

Analysis of the results showed that the combined action at low intensities was characterized by the absence of clear-cut intensification of biologic effects by comparison with exposure to microwaves or heat alone, and the presence of symptoms characteristic of either of the factors.

An increase in body temperature of white rats following the combined exposure did not exceed that resulting from heat exposure alone. At the same time, return to the initial temperature after cooling at 4—6°C for 1 h was faster than in animals submitted to microwave irradiation alone, while the prolonged influence of heat resulted in some slowing of the process of recovery.

Investigations of immunobiological functions (phagocytic and digestive activity of neutrophils, bactericidal properties of plasma, the course of inflammatory processes) lasted for 6 months and showed that at various times and according to different indicators the changes following the combined action were either of a "microwave" type or analogous to the "thermal" type. At the same time no significant differences from data on the isolated action of each of the factors were detected.

An interesting result was obtained upon investigating the blood pressure. Simultaneous combined exposure elicited increased arterial pressure analogous to that observ-

WHO – BIOLOGIC EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION 1974

ed with thermal exposure alone. However, functional loading in the form of intraperitoneal injection of 0.1% adrenalin solution (1 mg per kg body weight) enabled detection of a more pronounced increase in vascular tonus in the case of combined exposures (Fig. 5). Thus, according to increase in blood pressure 45 and 60 min after injection, the latter group differed significantly from the "thermal" one ($p < 0.05$).

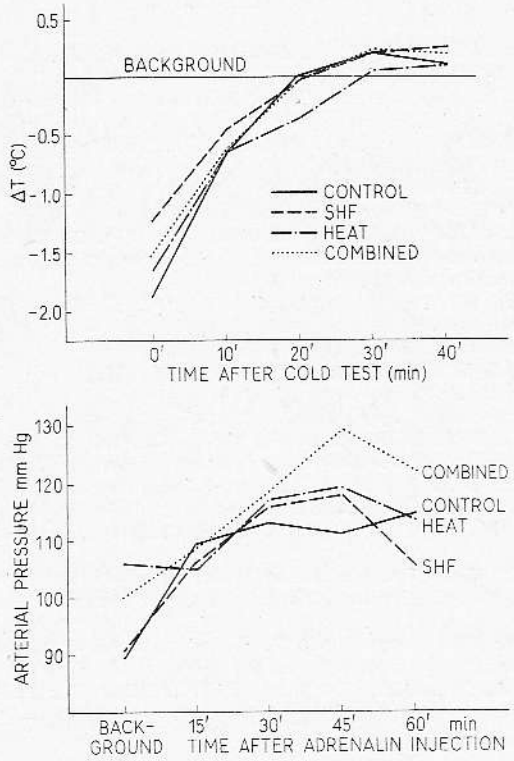


Fig. 5. Results of functional tests (1 mW/cm², 38°C): a) restoration of body temperature after cold test, b) changes in arterial pressure upon adrenalin injection.

More pronounced changes in vascular tonus following combined action of microwaves and heat were validated by data (8) on breakdown of adaptation to infrared rays and elevated ambient temperature under the influence of microwaves (wavelength, 12.6 cm; power density, 1 mW/cm²): thermal exposure following microwave irradiation resulted in changes of arterial pressure irrespective of the number for such tests.

The presence of such effects points to the necessity for further accumulation of experimental materials. Particular attention should be paid to those systems providing for regulatory and adaptive functions of the organism (central nervous, cardiovascular and endocrine-humoral systems).

Dependence of the character and severity of biologic effects upon the intensity and sequence of action of factors has been described in the literature for combinations of microwaves with reduced air pressure (8), and also for joint action of other physical and chemical factors (1, 3). This suggests that in order to elucidate the character of

the combined action of factors one should not limit oneself to a single level of action. Intensities employed in experiments should be determined by practical problems, the solution of which was the aim of the present study.

REFERENCES

1. GALANIN, N. F., MOSTOVA, R. S., SVIDERSKAJA, T. A., TIUKOV, D. M.: *Vestnik akad. med. nauk SSSR*, 1966, **8**, 45.
2. ŽURAVLEV, V. A. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Moskva, 1972, p. 39.
3. KAGAN, J. S., DIUBLINA, E. I., SANOCKI, I. V. In: *Materialy XV Vsesojuznogo sjezda gigienistov i sanitarnyh vračei.* Kiev, 1967.
4. KLJAČINA, K. N., STOLUBIN, B. M., OKONIŠNIKOVA, I. E. et al. In: *Gigiena truda pri rabote z radioaktivnymi veščestvami i istočnikami ioniziruiščih izlučeni.* Moskva, 1961, p. 32.
5. LIBERMAN, A. N., SOKOVSKAJA, M. S., BRONSTEIN, I. E., OROBEJ, V. V. In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Moskva 1972, p. 10.
6. LOŠAK, A. J.: *Gigiena i sanitarja*, 1965, **6**, 18.
7. NIKONOVA, K. V., HRAMOVA, N. D., KARTAŠOV, N. V. In: *O biologičeskom deistvii elektromagnitnyh polej radiočastot.* Moskva, 1968, p. 12.
8. PETROV, I. R.: *Vojenno-medicinskij žurnal*, 1968, **5**, 21.
9. PRESMAN, A. S., LEVITINA, N. A.: *Radiobiologia*, 1962, **21**, 170.
10. BOITEAN, H.: *Medicin de Reserve Sante.*, 1963, 1.
11. DEICHMANN, W.: *Ind. Med. Surg.*, 1959, **28**, 12, 535.
12. HOWLAND, J. W., THOMSON, R. A. E., MICHAELSON, S. M.: *Biomedical Aspects of Microwave Irradiation of Mammals.* Proc. 4-annual Tri-Service Conf. Biological Effects of Microwave Irradiation. M. F. Peyton, N. Y., 1961, p. 261.
13. HOWLAND, J., MICHAELSON, S. M.: *Ind. Med. Surg.*, 1964, **33**, 500.
14. MICHAELSON, S. M., THOMSON, R. A. E., HOWLAND, J. W.: *Aerospace Med.*, 1963, **34**, 2, 111.
15. DE MINKO, A. P.: *Generation and Detection of Pulsed X-Rays from Microwaves Sources.* Proc. 4-annual Tri-Service Conference Biological Effects of Microwave Radiation, M. F. Peyton, N. Y., 1963, p. 3.
16. MUMFORD, W. W.: Heat Stress Clue to R. F. Radiation. In: *Effects and Health Implications of Microwave Radiation.* Symposium Proceedings. Richmond, Virginia, 1969, p. 21.
17. THOMSON, R. A. E., MICHAELSON, S. M., HOWLAND, J. W.: *Radiat. Res.*, 1965, **24**, 631.

WHO – Biologic effects & health hazards of microwave radiation 1974

INFLUENCE OF MICROWAVE RADIATION ON THE HEMATOPOIETIC SYSTEM

P. Czerski, E. Paprocka-Słonka, M. Siekierzyński and A. Stolarska

Department of Human Genetics, National Research Institute of Mother and Child, Warsaw; Military Institute of Aviation Medicine, Warsaw, and Institute for Postgraduate Study of the Military Medical Academy, Warsaw, Poland

A review of the literature (see 3, 8, 12 for bibliographies) demonstrates that acute microwave exposure may induce transient changes in the peripheral blood picture dependent on exposure conditions (field intensity, duration etc.) and animal species. Such effects may be explained by displacement of blood cells between the blood stream and tissues, as well as by displacement of body water. Divergent reports on the effects of repeated exposure exist. In the case of long-term, low-dose exposure most authors stress a tendency to a slight decrease in RBC counts and a peripheral lymphocytosis (1, 2, 3, 5, 6). Nevertheless negative reports stressing the lack of effects of exposure exist (5, 12, 14).

Only a few reports concerning microwave effects on the hematopoietic tissue itself and hematopoietic function exist. Those of Michaelson (10, 11), Barański (1, 2), Miro (this volume) and Yagi (this volume) should be mentioned. Barański found that

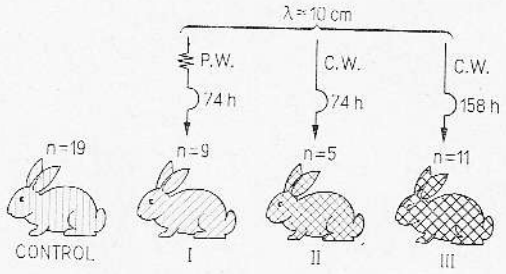


Fig. 1. The experimental system used in the first series of experiments: animal groups and irradiation conditions.

long-term, low-dose exposure induces stimulation of lymphopoiesis in the bone marrow, lymph nodes and spleen of rabbits and guinea pigs. Moreover this author described nuclear structure anomalies and aberrations of mitosis in the lymphocytic and erythroblastic cell lines of long-term irradiated animals. Michaelson described disturbances in iron metabolism of repeatedly exposed dogs and shortening of red cell life time.

In view of this it seemed interesting to investigate microwave effects in the lymphocytic and red cell systems. The aim of this work is to present briefly the principal findings of several series of experiments designed to examine such effects.

WHO - Biologic effects & health hazards of microwave radiation 1974

In the first series of experiments 3 groups of rabbits were exposed in an anechoic chamber to 2950 MHz pulsed (1200 MHz, 1 μs) or CW microwaves at 3 mW/cm² 2 h daily for a total of 74 or 158 h, a 4th group of animals serving as controls (Fig. 1). The irradiated animals were restrained in plastic cages and placed with head directed to the source (horn-antenna) in the far field zone. Control temperature measurements at various points of the body in yet another group of animals did not demonstrate a temperature rise over 0.5°C after irradiation. At the end of the irradiation period 1.5 μCi/kg body weight of ^{59}Fe citrate was introduced into the marginal vein of the ear and 100 minutes later the first blood sample was withdrawn for hematologic and radioactivity determination (Fig. 2). Using routine methods ferrokinetic indices were calculated. The results obtained are described in more detail elsewhere (5, 13), but the principal findings are illustrated on Figures 3—7. Significant differences between the control group and the experimental groups were demonstrated.

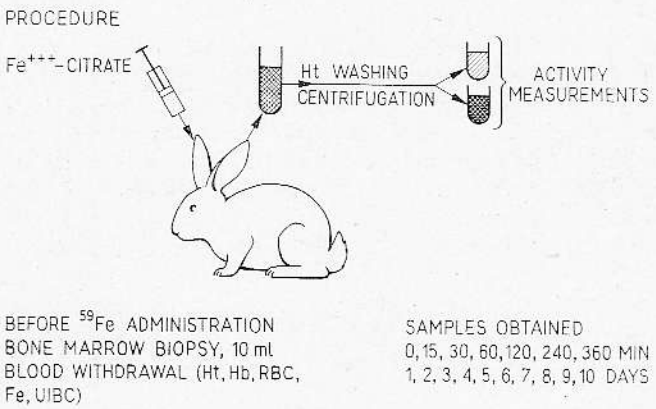


Fig. 3. Radioactivity half-time.

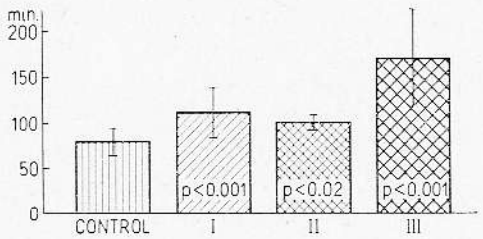


Fig. 3. Radioactivity half-time.

Perhaps the most interesting finding is that 74 h of exposure to pulsed microwaves (group I) induced much more pronounced effects than exposure to CW (group II) of the same duration, the differences between both these groups being highly significant. On the other hand 158 h exposure to CW microwaves (group III) induced very similar effects to those of exposure to pulsed microwaves of half that duration.

WHO – Biologic effects & health hazards of microwave radiation 1974

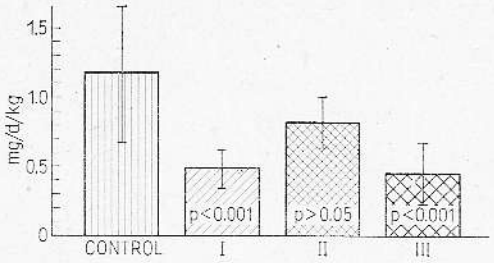


Fig. 4. Iron transport rate.

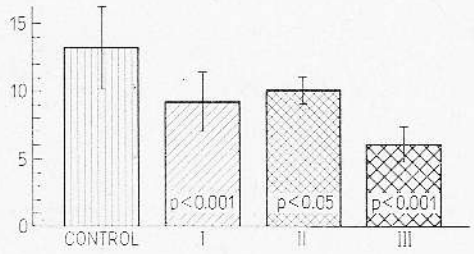


Fig. 5. Iron turnover rate.

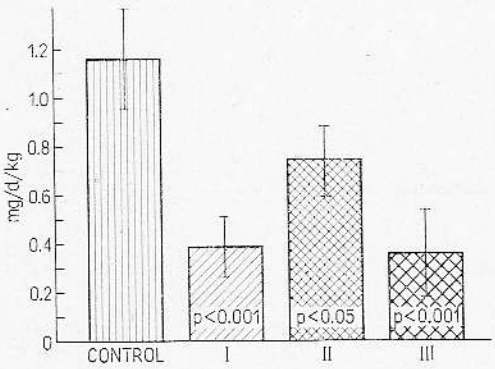


Fig. 6. Quantity of iron incorporated into erythrocytes.

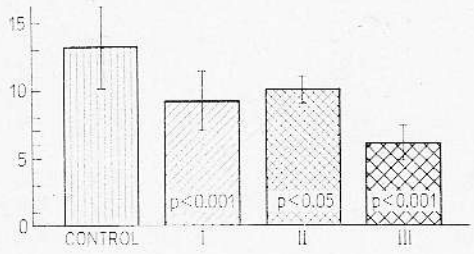


Fig. 7. Percent erythrocyte production.

WHO – Biologic effects & health hazards of microwave radiation
1974

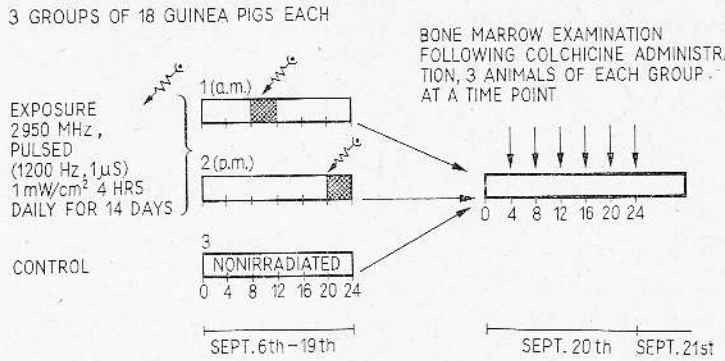


Fig. 8. Experimental system used in the second series of experiments (guinea pigs).

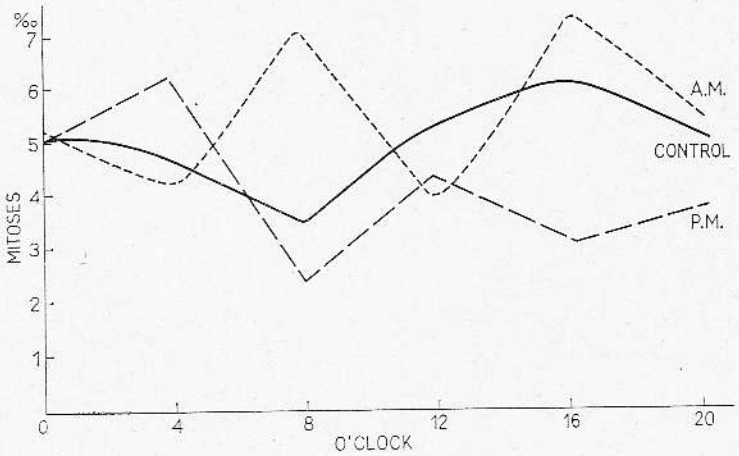


Fig. 9. Rhythm of mitoses in bone marrow cells (stem cells) of control and a. m. or p. m. irradiated guinea pigs.

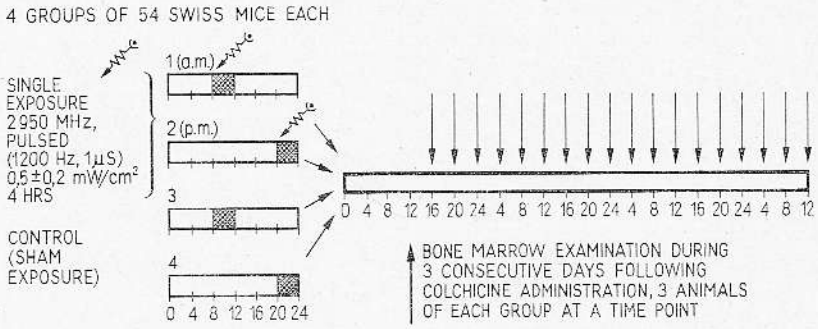


Fig. 10. Experimental system used in the second series of experiments (mice).

WHO – Biologic effects & health hazards of microwave radiation 1974

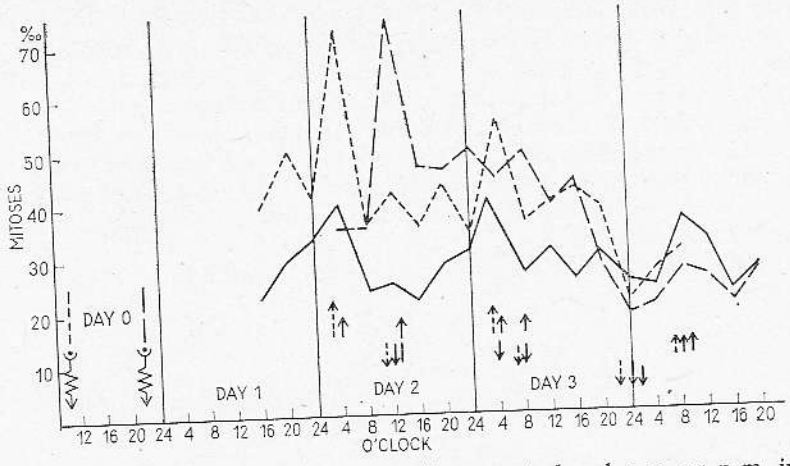


Fig. 11. Total mitotic index of bone marrow cells in control and a. m. or p. m. irradiated mice.

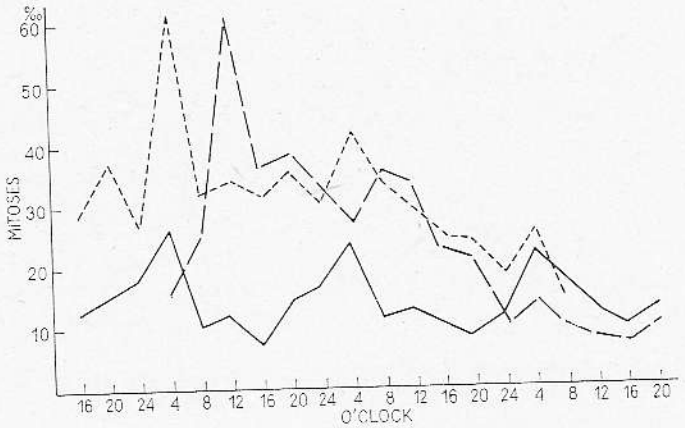


Fig. 12. The mitotic index of stem cells (undifferentiated and lymphocyte-like cells) in the bone marrow of control and a. m. or p. m. irradiated mice.

The second series of experiments concerned effects of microwave exposure at various times of the day on the circadian rhythm of bone marrow cell mitoses. Once more the full details are described elsewhere (4, 7). In one of these experiments repeatedly exposed guinea pigs were used (4). The experimental system is presented in Figure 8. No marked differences between control animals and irradiated ones were seen in the circadian rhythm of recognizable precursors of granulocytes and erythroblasts. In the cell category classed as bone marrow stem cells (early erythroblasts, myeloblasts, hemopoietic stem cells and probably lymphocytes) a distinct change both in amplitude and phase of the circadian rhythm of cellular divisions was noted in animals irradiated in the evening or in the morning, as compared with one another and with the control group (Fig. 9). The statistical significance of these findings may be questioned, because of both the short observation period and the small number of animals. In view of this

WHO – Biologic effects & health hazards of microwave radiation 1974

syngeneic mice were subjected to a single exposure (a.m. or p.m.) and examined during 3 consecutive days beginning 28 h after the termination of irradiation (Fig. 10). It was reasoned that if in reality microwave exposure induced changes in the circadian rhythm of bone marrow cell mitoses, a disturbance resembling a decaying oscillation should be obtained. The results confirmed the expectation (Fig. 11), a disturbance in the amplitude and phase of the mitotic rhythm of cells belonging to the "stem cell" category being responsible for the observed phenomena (Fig. 12). Once more significant differences could be detected in the rhythm of cellular divisions in the precursors of granulocytes and red cells.

The third series of experiments was aimed at quantitation of the reaction of the lymphocytic system.

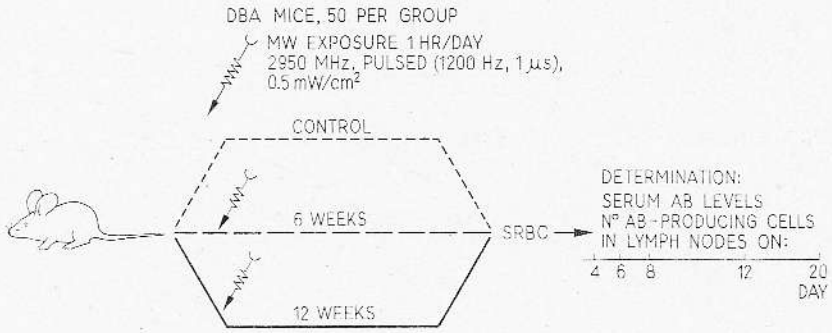


Fig. 13. The experimental system used in the third series of experiments.

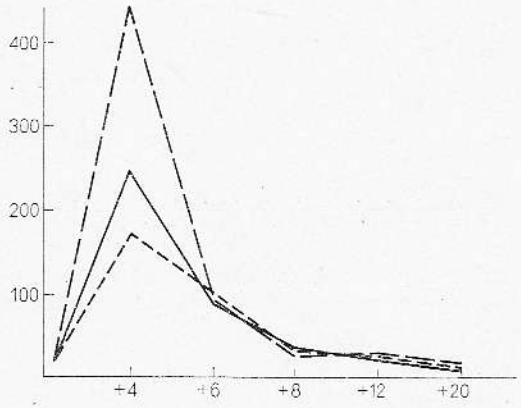


Fig. 14. The number of antibody producing cells in the lymph nodes of control and irradiated mice (direct Jerne's plaque technique).

Syngeneic mice were irradiated for 6 or 12 weeks, immunized with sheep red blood cells and the serum hemagglutinin level, as well as the number of antibody producing cells in lymph node homogenates, determined using Jerne's direct and indirect plaque techniques (9). The experimental system is presented in Figure 13, the results — in Figures 14 to 16. Differences between the control group and both irradiated groups in the course of the immunologic reaction are clearly seen. This indicates that the microwave exposure affected the lymphocytic system of immunocompetent cells. Additionally,

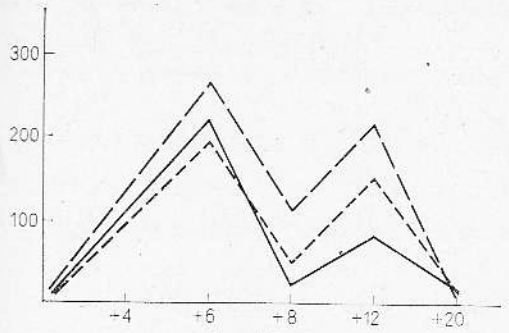


Fig. 15

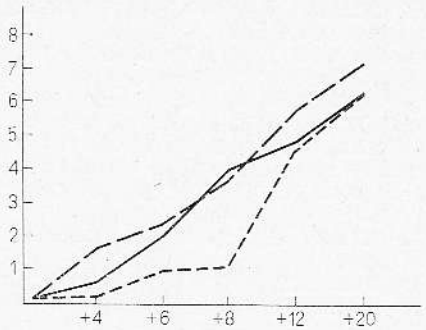


Fig. 16

Fig. 15. The number of antibody producing cells in the lymph nodes of control and irradiated mice (indirect Jerne's plaque technique).

Fig. 16. Hemagglutinins in the serum of control and irradiated mice.

it should be stressed that peripheral blood lymphocytes of long-term, low-dose irradiated rabbits undergo "spontaneous lymphoblastoid transformation" when cultured *in vitro* in a proportion dependent on the total exposure time (6). All these observations, as well as those of Stodolnik-Barańska (this volume) seem to indicate a peculiar susceptibility of the lymphocytes and the lymphocytic system to microwave radiation.

No explanation of the observed phenomena may be offered at this time. The most significant findings should, however, be pointed out:

1. Differences between CW and pulsed microwave effects at the same wavelength and average power density in strictly comparable exposure conditions were demonstrated by iron metabolism studies.

2. Differences between microwave effects on the circadian rhythm of mitoses of cells belonging to various hematopoietic cell lines were demonstrated; this may serve to stress the importance of taking into account the physiologic properties of cells, tissues and organs, when investigating microwave bioeffects and the danger of generalizations.

3. The above results and numerous reports in the literature point to the existence of easily demonstrable and easily quantified microwave effects on the lymphocyte and the lymphocytic system. It is the authors' feeling that this cell is a convenient model for further studies of microwave effects at the cellular level. Possibly reactions of the lymphocytic system could be used to develop a biologic comparative index to assess microwave bioeffects in various tissues and organs, as well as under various exposure conditions.

REFERENCES

1. BARAŃSKI, S.: *Acta Physiol. Pol.* 1972, **23**, 685.
2. BARAŃSKI, S.: *Aerospace* Med., 1971, **42**, 1196.
3. BARAŃSKI, S., CZERSKI, P.: *Biological Effects of Microwaves.* Polish Medical Publishers (to be published 1975).
4. BARAŃSKI, S., CZERSKI, P., JANICKA, U., SZMIGIELSKI, S.: *Medycyna Lotnicza*, 1972, **39**, 67.
5. CZERSKI, P.: In: *Gigiena truda i biologičeskoe deistvie elektromagnitnyh voln radiočastot.* Symp. Abstr, Moskva 1972 p. 56.

WHO – BIOLOGIC EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION 1974

6. CZERSKI, P., BARAŃSKI, S., SIEKIERZYŃSKI, M.: *IIIrd International Conference Medical Physics.* Göteborg 1972 Abstr. 39, 9.
7. CZERSKI, P., PAPROCKA-SŁONKA, E., STOLARSKA, A.: *J. Microwave Power,* 1974, **9**, 32.
8. GORDON, Z. V.: *Voprosy gigieny truda i biologičeskogo deistvia elektromagnitnyh polei sverhvysokih častot.* Medicina, Moskva 1966.
9. MACKIEWICZ, U., CZERSKI, P.: *In preparation for press.*
10. MICHAELSON, S. M., THOMSON, R. A. E., TOMAMI, M. Y. E., SETH, H. S., HOWLAND, J. W.: *Aerospace Med.,* 1964, **35**, 824.
11. MICHAELSON, S. M., THOMSON, R. A. E., QUINLAN, W. J.: *Aerospace Med.,* 1967, **38**, 293.
12. PETROV, I. R.: *Vlijanie SVČ-izlučenii na organizm čeloveka i životnyh.* Medicina, Leningrad 1970.
13. SIEKIERZYŃSKI, M.: *Medycyna Lotnicza,* 1972, **39**, 53.
14. SPALDING, J. F., FREYMAN, R. W., HOLLAND, L. M.: *Health Physics,* 1971, **20**, 421.

WHO – Biologic effects & health hazards of microwave radiation
1974

HARMFUL EFFECTS OF MICROWAVE RADIATION ON THE BONE MARROW

K. Yagi, R. Ueyama, S. Kurohane, N. Hiramine, H. Ito and S. Umehara

IIIrd Department of Internal Medicine, Tokyo Medical College, Tokyo, Japan

During the second world war, the Japanese army studied the biologic effects of microwaves for use as a death ray and many harmful effects were observed (9), but all the results of the studies were destroyed by fire immediately after the end of the war. After the war, Inoue and Fujino (3) studied the effects of microwave radiation on peripheral blood cells. Umehara (11), one of the co-authors of this report, studied the biologic effects of microwave radiation on several organs of guinea pigs and reported that microwave radiation induced a serous allergic-like inflammation in many organs, such as the liver, lungs, kidneys, heart and gastrointestinal tract. These results were reported in "Nippon Acta Radiologica" in 1950.

On the basis of the results of the studies, Umehara recently speculated that microwave radiation might induce a serous inflammation in the bone marrow and result in aplastic bone marrow. In order to prove this speculation, the author performed an experiment to observe what changes occurred in the bone marrow after irradiating one femur of rabbits with microwaves (12).

It was proved by this experiment that an aplastic bone marrow developed after the microwave exposure. Furthermore, Ueyama designed an experiment to find out whether cortisone would prevent the development of aplastic bone marrow after the microwave exposure or not. These results are the subject of this report.

MATERIALS AND METHODS

Young white male rabbits weighing about 1.6 kg were used in these experiments (Tab. 1).

The microwave source was a 2450 MHz (12 cm) continuous microwave generator and the power density was 1.3 W/cm^2. The generator used was an ITO-200 Model therapy unit.

The rabbit was secured in a special wooden cage with a hole provided for one leg to be stretched out through it. The whole body except the left leg was completely shielded with a metal mesh. The distance between the antenna and the leg was 14 cm.

One irradiation session lasted 30 minutes and it was repeated 5 times a day for 7 consecutive days. The histologic changes in the irradiated bone marrow were examined during 6 weeks after the irradiation.

In the group in which the effectiveness of cortisone was observed, a 60-minute weak irradiation was made once daily for 2 weeks. 4 mg/kg of hydrocortisone were injected daily for 6 weeks from the beginning of the irradiation period or were terminated immediately after the exposures.

WHO - BIOLOGIC EFFECTS & HEALTH HAZARDS OF MICROWAVE RADIATION
1974

Table 1

Materials and Methods

1. Laboratory Animals
   Young White Male Rabbits weighing 1.6 kg
2. Microwave Generator
   (Microradar MR-200)
   manufactured by Itoh Electro Co.
   Output: 150 W
   Frequency: 2450 Mc/sec
   Wavelength: 12 cm
3. Irradiation Method
   Distance: 4 cm
4. Irradiation Time

	1st week			2nd week			3rd week			4th week			5th week	
Intensity	S	W	Rest	S	W	Rest	S	W	Rest	S	W	Rest	S	W
Exp. Time	5	25	30	5	25	30	5	25	30	5	25	30	5	25

Intensity: S (strong). Output: 150 W, Volt — 1700 V, Am — 200 mA
Intensity: W (weak), Output: 50 W, Volt — 1300 V, Am — 100 mA

The tissue temperature was measured by an electric thermometer.

Hematologic, histologic and histochemical studies were performed using routine techniques.

WHO - Biologic effects & health hazards of microwave radiation 1974

Table 2

Effect of microwaves on peripheral blood cells

	Hb %	RBC ×10⁴	WBC	Hemogram														Ht %
				N		E		Ba		Mo		Ly		L—Ly		S—Ly		
Pre Exp.	95	522	10 360	3 977	38.6	123	1.1	9	0.1	68	0.6	6 183	59.6	496	4.7	5 687	54.9	42
During Exp.	95	499	13 888	8 178	58.9	97	0.7	67	0.5	78	0.6	5 468	39.3	2 666	19.2	2 802	20.1	43
Post Exp.	93	464	12 237	6 608	54.0	68	0.7	39	0.5	69	0.6	5 453	44.5	4 387	35.8	1 066	8.7	45
1	95	485	12 227	6 984	57.1	133	1.1	36	0.3	230	1.9	4 844	39.6	2 841	23.2	2 003	16.4	48
2	95	507	10 481	5 830	55.6	178	1.8	80	1.8	43	0.4	4 492	41.4	1 837	16.1	2 655	25.3	52
3	96	520	11 661	5 650	51.2	223	2.0	135	1.2	96	0.8	4 949	45.8	1 746	15.8	3 203	30.0	52
4	98	542	11 950	6 369	53.3	250	2.1	79	0.6	113	0.9	5 139	43.1	1 527	12.8	3 612	30.3	52
5	103	552	12 500	5 380	43.0	357	2.8	121	1.0	174	1.4	6 468	51.8	1 149	9.2	5 319	42.6	55
6 weeks after Exp.	105	552	12 175	5 273	41.3	407	3.2	78	0.6	118	0.9	6 899	54.0	831	6.5	6 068	47.5	49

RESULTS

1. Changes in body weight: The body weight of the animals decreased gradually and was lowest from the 2nd to 4th week after the termination of the irradiation period. The average decrement of the body weight was 0.4 kg (Fig. 1).

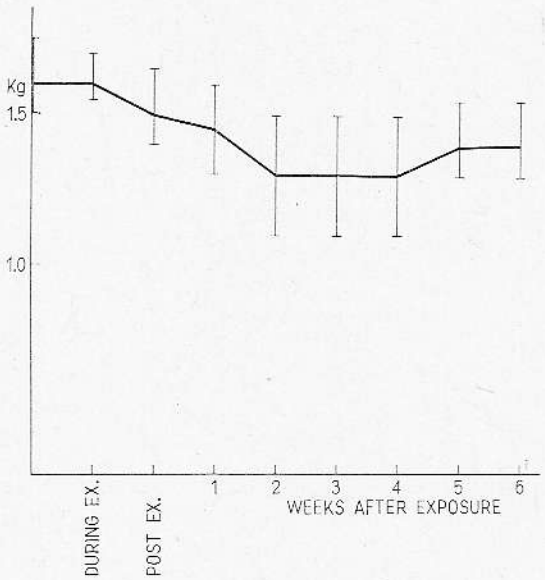


Fig. 1. Effect of microwaves on body weight.

2. Changes in tissue temperature: The temperature of the femoral tissue rose to 39°C within the first 5 minutes of irradiation and maintained a level of 42°C during the next 30 minutes (Fig. 2).

3. Changes in peripheral blood: A slight decrease in hemoglobin content and red cell count were found immediately after the irradiation period was terminated, but

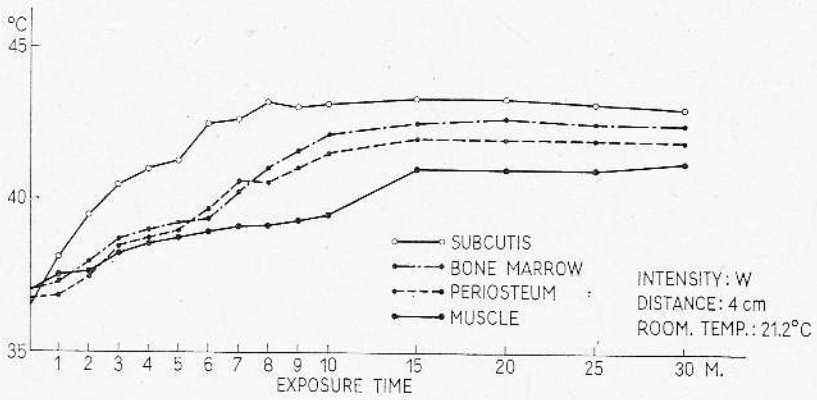


Fig. 2. Femoral tissue temperature during exposure.

WHO - Biologic effects & health hazards of microwave radiation 1974

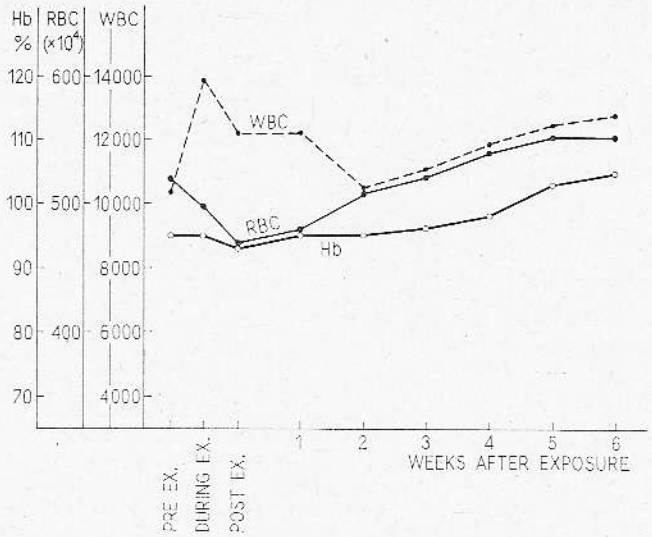


Fig. 3. Peripheral blood changes after exposure.

disappeared in the 4th to 6th week after the end of the irradiation period (Tab. 3, Fig. 3).

Moderate leukocytosis was observed during the irradiation (7) and slight leukocytosis continued for 6 weeks after the exposure was terminated. A moderate increase in neutrophilic leukocytes was seen during the irradiation and thereafter a slight neutrophilia continued during the whole course of the experiment. The lymphocytes, especially the small lymphocytes, decreased remarkably at the end of the irradiation (1, 6), but large lymphocytes increased to 900% of the initial value during the same period (Fig. 4).

Eosinophilic leukocytes also decreased during the irradiation, but increased to 400% of the initial value by the 6th week after the end of the irradiation period.

A progressive decrease of basophilic leukocytes was found. The changes in the monocytes were not significant.

4. Bone marrow findings.

a. Macroscopic findings: The colour of the bone marrow was fresh red and strong bleeding was seen during and immediately after the irradiation was terminated. The colour changed to yellowish red in the 1st to 3rd week after the end of the irradiation period. At that time, the bone marrow was jelly-like. The colour of the bone marrow changed further to gray in the 4th to 6th week after the irradiation period was terminated.

b. Histologic findings: The changes in the hemopoietic cells were not very remarkable the first 3 or 4 days after the irradiation was initiated (5). The most specific and characteristic finding at that time was the appearance of plasma-like substances coloured pinkish with hematoxylin-eosin staining. The plasma-like substances had a tendency to develop around the fat cells, though they were also found in the center of the parenchyma. This state was named "sand bay formation" by us. It was suggested that the plasma-like substances seemed to be an exudate (Fig. 5).

Seven days after the irradiation was begun, the exudate increased gradually in the parenchyma and surrounding fat cells. This finding was called "perilipocytic edema". The sinuses were filled with the plasma-like substance and dilated (Fig. 6). Degenera-

Table 3

Staining of the exudate, megakaryocytes and blood vessels

		During Exp.	Post Exp.	Time after Exposure						
				2—6 Days	1	2	3	4	5	6 Weeks
Exudate	H. E.	±	+	+++	+++	+++	++	++	+	±
	PAS	±	+	++	++	+	±	±	±	±
	Mucicarmine		+	++	+	+++	+	+	±	±
	Best's Carmine		—	—	±	±	++	±	±	
	Van Gieson's	±	++	++	+++	++	++	++	++	+
	Silver Nitrate	—	+	++	+	++	++	+++	++	±
	T. B. M.		++	++	++	+	—	—	±	—
	Azan Mallory's		—	—	±	±	++	+++	+++	++
Megakaryocytes	PAS	+	+	+	+	±	±	—	±	±
	Mucicarmine		—	—	—	+	±	±	±	+
	Best's Carmine		—	—	—	—	—	—	±	—
	Van Gieson's	+	++	++	++	+	+	+	—	±
	Silver Nitrate	+	+	++	+	+	+	+	++	++
Blood vessels	PAS	±	+	++	++	++	+	—	—	±
	Mucicarmine	+	—	—	—	—	—	—	—	—
	Best's Carmine			+++	+	±	—	±	—	—
	Van Gieson's	+	++	++	+++	++	++	++	+	++
	Silver Nitrate		—	+	+	+	++	+++	++	±
	Azan Mallory's	—	—	±	+	++	+++	+++	++	++

tion of the hemopoietic cells began to occur and bleeding into the parenchyma was seen. However, in some cases, a diffuse proliferation of hemocytoblasts was seen (Fig. 7). Vascular changes such as fibrinoid swelling and desquamation of the endothelium were observed.

2 or 3 days after the irradiation period was terminated, the hemocytoblasts and the fat cells decreased; this was associated with an increase of the exudate in the parenchyma. The cell arrangement of the parenchyma was disturbed, and degeneration of the hemocytoblasts and the blood vessels progressed. Karyorrhexis and vacuolization of the megakaryocytes were seen (Fig. 8). Follicular lymphoid cell infiltration became