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EPIDEMIOLOGIC APPROACH TO THE STUDY OF MICROWAVE EFFECTS*

CHARLOTTE SILVERMAN, M.D., Dr. P.H.

Deputy Director, Division of Biological Effects
Bureau of Radiological Health
Food and Drug Administration
Department of Health, Education and Welfare
Rockville, Maryland

I was asked to include in this presentation a report of a recently concluded epidemiologic study of occupational exposure to radar during the Korean War.¹ Before getting to the study, I shall give a brief account of the objectives and methods of epidemiology and their application to the investigation of microwave radiation effects.

GENERAL EPIDEMIOLOGY

Ever since epidemiology became broader than the study of epidemics, a simple definition has failed to convey the nature and scope of the field. It is the study of both the distribution and the determinants of disease (or any health-related condition) in defined groups of individuals or the population.² The study of the distribution of disease in terms of age, sex, race, geography, environment, occupation, socioeconomic status, and other characteristics is essentially descriptive; investigation of the influence of these and other factors on disease patterns is analytic, a search for causes.

Epidemiology is one of many disciplines that search, each in its own fashion, for causal factors in health and disease. Because many levels of influence lead to disease, and disorders rarely are due to one cause alone, many types of knowledge are needed. In epidemiology, a science basic to public health and important to medicine, the search is for determinants that can be modified to prevent disease or ill health. Interest covers the whole spectrum of disease from an inapparent or subclinical state through frank illness to death. Epidemiologic evidence about etiology may be incomplete

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Address for reprint requests: BRH, FDA (HFX-101), 5600 Fishers Lane, Rockville, Md. 20857.

TABLE I. EPIDEMIOLOGIC STUDIES

Characteristics of data

- Defined groups of individuals or the population
- All cases in a defined population
- Rates of observations
- Same information for cases and controls

Types of studies (observational)

- Demographic
 - Cross-sectional (prevalence)
 - Cohort (prospective, longitudinal)
 - start with population and seek cases over time
 - Case-control (retrospective)
 - start with cases and refer back to populations
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or inconclusive but may still provide a reasonable basis for preventive action as well as for further study aimed at improvement of our understanding of causation.

Some features of epidemiologic studies are shown in Table I. In contrast to clinical medicine, which deals with individual cases or a series of cases, epidemiology is concerned with all cases, or a representative sample of them, in defined groups of individuals. Cases are related to the population group and the time period in which they occur; the reference population is as necessary as the cases of interest. Several basic rates measure the frequency of disease and deaths. For example, morbidity rates, in terms of occurrence (incidence) or prevailing frequency at a particular time (prevalence), and mortality rates make it possible to compare the health experience of different groups of individuals. And, of great importance in epidemiologic studies, the same quality of information is needed for cases and controls.

In the main, methods used in search of etiologic factors are those of observational rather than experimental studies. A study may be suggested by the findings of descriptive epidemiology, clinical investigation, experimental work, or other sources. A tentative hypothesis is followed by demonstrating a statistical relation between the condition under study and certain individual or group characteristics. Then, the meaning of the relation must be established. If causal inferences are derived, they are tested in studies of individuals with the condition or characteristic compared to those without it. Two principal approaches are used: studies can start either with a given population in which cases are sought over time (cohort, prospective) or with cases which are referred back to their popula-

tion groups (case-control, retrospective). There are advantages and disadvantages to both types of studies, as well as different indications for their use and differences in the type and quality of information produced.

The strength of epidemiology is its ability to provide a direct measure of risk in humans. Risk estimates from nonhuman experimental studies may require epidemiologic confirmation and for some diseases experimental studies cannot be done at all because there are no suitable animal models. Adequate risk information cannot be furnished by clinical medicine alone.

The limitations of epidemiology are those of a population-based life science. Information must come from many other disciplines such as clinical medicine, pathology, environmental sciences, and statistical and social sciences. More often than not, data sources have been developed for other purposes. There can be considerable variation not only in the quality and quantity of data but also in the availability and completeness of records. And the epidemiologic method may be impractical to detect some low-level risks because of large sample-size requirements and problems of identifying and controlling confounding variables.

Epidemiologic Studies of Microwave Effects

Epidemiologic studies of microwave effects have been few in number and limited in scope; two recently completed cohort studies will be reported at this session of the symposium.^{1,3} People occupationally exposed in the military services or in industrial settings have been the principal groups studied. A few other populations living or working near generating sources or exposed to medical diathermy have been or are being investigated.

Information about health status has come from medical records, questionnaires, physical and laboratory examinations, and vital statistics. Sources of exposure data include personnel records, questionnaires, environmental measurements, equipment emission measurements, and (assumed adherence to) established exposure limits. Microwave dosimetry presents formidable problems in assessment. There is at present no practical way to determine exposure to large numbers of individuals or to determine absorption or distribution of absorbed energy in humans. Epidemiologic approaches to some reported or suspected adverse effects, none of which appears pathognomonic for microwave radiation, will be presented.

OCULAR EFFECTS

Many surveys of ocular effects in man have been made, especially in the United States. Most investigations have involved service personnel and civilian workers at military bases and in industrial settings. The principal subject of interest has been the significance of minor lens changes in the cataractogenic process; cataracts (opacities impairing vision) have been infrequently investigated, and only recently have retinal changes been looked for.

Minor lens changes. Lenticular defects too minor to affect visual acuity have been studied as possible early markers of microwave exposure or precursors of cataracts. Studies have been mainly prevalence surveys, although the time periods are often variable or not specified; re-examination data rarely permit estimates of incidence. These occupational studies have generally emphasized careful clinical eye examinations, including the use of slitlamp biomicroscopy and photographs, without comparable attention to study design and follow-up plans for exposed and comparison groups.

The following generalizations can be made about observations of lens changes in microwave workers and comparison groups:

- 1) Lens imperfections occur normally and increase markedly with age among all employed men studied. There is evidence that lens changes increase with age even during the childhood years.⁴ By about age 50, lens defects have been reported in most comparison subjects. This is illustrated in the scatter diagrams (Figure 1) based on data from various studies.

- 2) Although a few suggestive differences have been reported,⁴⁻⁶ there is no clear indication that minor lens defects are a marker for microwave exposure in terms of type or frequency of changes, exposure factors, or occupation. Inspection of Figure 1 suggests possible earlier appearance of lens defects among microwave workers than among comparison groups, but there is considerable variation in the type, number, and size of defects recorded, in the scoring methods used by different observers, and in the numbers examined.

- 3) Clinically significant lens changes, which would permit selection of individuals to be followed, have not been identified.⁷

- 4) There is to date no evidence from ophthalmic surveys that minor lens opacities are precursors of clinical cataracts.

Cataracts. Although there has been much interest in the cataractogenic

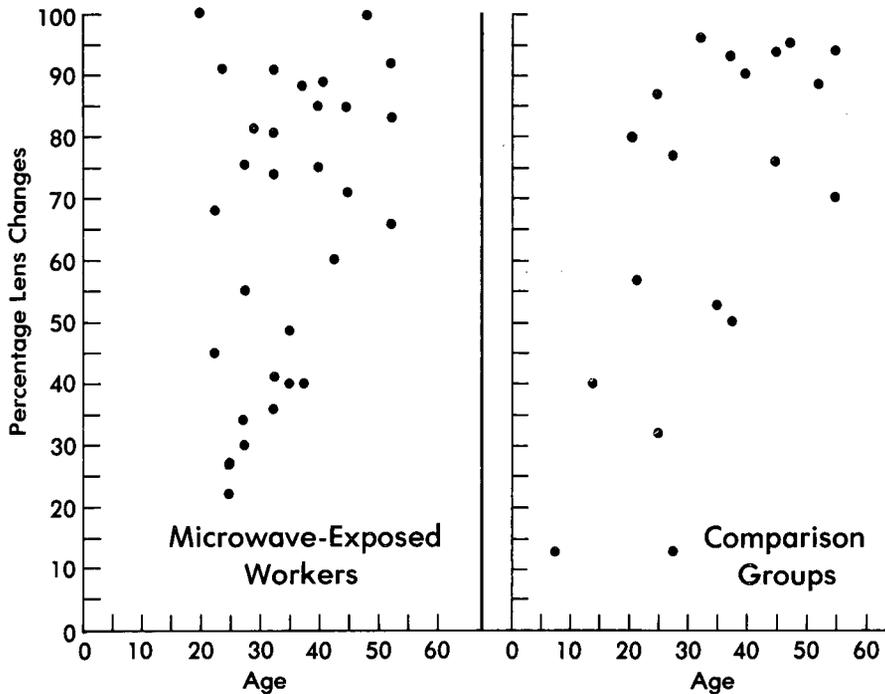


Fig. 1. Percentage lens changes (all types) by age: various studies

effect of microwave radiation, only minimal effort has been made to investigate cataracts as such, as distinct from their precursors. The only epidemiologic study of cataracts in microwave workers, a case-control study of World War II and Korean War veterans with negative findings, was reported in 1965.⁸ A recent statement that "not one epidemiologic study... suggests even a slight excess of cataracts in microwave workers"⁹ is certainly true because there has been only one study.

Neither definitions nor methods of detection of cataract are standardized. The common meaning of cataract, a lens opacity that interferes with visual acuity, is open to many interpretations as to degree and nature of the opacity and loss of visual acuity. Specific disorders, physical agents, and injuries are known to cause cataracts, but many cataracts are loosely called senile when they occur after middle age, implying they result solely from aging of the lens. Microwave cataracts are, in the opinion of most observers, not distinguishable from other cataracts.

The most prominent characteristic of cataracts is their age distribution.

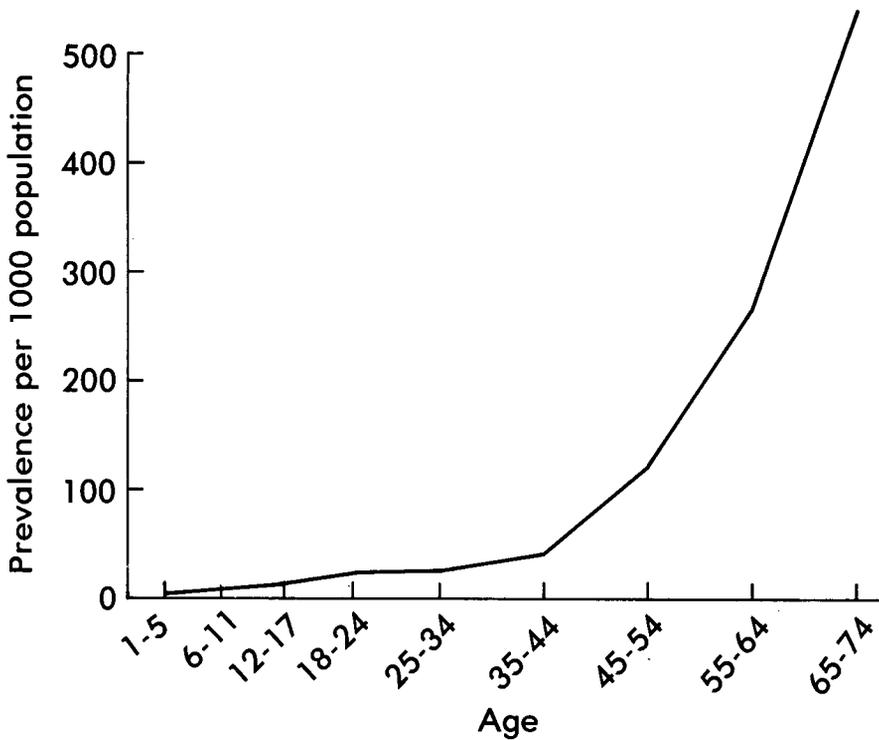


Fig. 2. Prevalence by age of one or more types of cataracts among persons 1 to 74 years of age, United States, 1971-1972. Preliminary national estimates. Source: National Center for Health Statistics, Division of Health Examination Statistics, Medical Statistics Branch, March 2, 1979.

Although estimates of frequency are not comparable because of differences in population groups surveyed, as well as nonuniform methods of detection and definition, all point to low frequencies until about the fifth decade of life when sharp increases occur.

Preliminary national estimates by age of the total prevalence of cataracts in the civilian noninstitutionalized population 1 to 74 years of age in the United States have recently been made available by the National Center for Health Statistics.¹⁰ They are based on diagnoses by ophthalmologist examiners in the Health and Nutrition Examination Survey of 1971-1972 and are shown in Figure 2.

One or more cataract conditions were found in 9% of the population. For the various age groups under 45, frequency increases gradually from 0.4% in those 1 to 5 years of age to 4% in the 35-to-44-year age group. The marked increase that occurs after age 45 reaches a maximum in the

oldest group examined: of those 65 to 74 years of age, more than half had cataracts.

Cataract data for personnel on active duty in the armed services (who are mainly healthy, relatively young men) are available as incidence rates which show similar age dependence up to about age 55. Although not comparable with general population figures, recorded mean annual incidence rates are extremely low, of the order of two per 100,000.¹¹

In the one case-control study of cataracts mentioned earlier,⁸ armed services personnel with cataracts ascribable to a nonmicrowave factor were eliminated from the sampling plan, that is, all congenital, traumatic, diabetic, and other specified types. The sampling plan also eliminated veterans 55 years of age and over to minimize dilution of the study group by senile cataracts.

Studies of microwave workers have been designed to find out whether cataract formation is accelerated in younger people. It may be necessary to look at possible increases in all cataracts by age to detect possible heightened microwave-induced susceptibility. The determinants of the microwave cataractogenic effect are not fully understood¹² and the epidemiology of cataracts has been inadequately studied.¹³

Retinal lesions. Until recently, retinal lesions have not been considered a possible microwave effect. There is some reason to think that oculists examining microwave workers have observed but not reported retinal changes, because no relation to microwave exposure was known.¹⁴ A small Swedish study reported in 1975,¹⁵ which included examinations for retinal as well as lens changes, was prompted by preliminary findings of paramacular and macular disease among industrial radar workers. A significantly higher proportion of retinal lesions was found among microwave workers aged 26 to 40 years than in controls. The retinal lesions had resulted in decreased vision in two cases. No further reports are available.

NERVOUS AND BEHAVIORAL EFFECTS

The many clinical and laboratory studies from the USSR and other Eastern European countries provide important information but no firm evidence of specific microwave effects on neurologic, mental, or behavioral performance.^{14,16,17} Clinical studies of groups employed in the operation, testing, maintenance, and manufacture of microwave-generating equipment have involved mainly low-level (microwatts or a few milliwatts) and

long-term exposures. With few exceptions, functional disturbances of the central nervous system have been described as a typical kind of radiowave sickness, the neurasthenic or asthenic syndrome. The symptoms and signs include headache, fatigability, irritability, loss of appetite, sleepiness, sweating, thyroid gland enlargement, difficulties in concentration or memory, depression, and emotional instability. This clinical syndrome is generally reversible if exposure is discontinued. Another frequently described manifestation is a set of labile functional cardiovascular changes including bradycardia (or occasional tachycardia), arterial hypertension (or hypotension), and changes in cardiac conduction. This form of neurocirculatory asthenia is also attributed to nervous system influence. More serious but less frequent neurologic or neuropsychiatric disturbances have occasionally been described as a diencephalic syndrome.

The only American epidemiologic study thus far of some of these effects is the cohort study of American embassy employees in Moscow and comparable groups in embassies of other Eastern European capitals³ which will be reported by Dr. Herbert Pollack. No differences were attributable to microwave exposure at the intensities measured outside the Moscow embassy (1-18 $\mu\text{W}/\text{cm}^2$). These levels, however, were even lower than exposures reported in the Russian occupational studies (microwatts up to about 4 mW/cm^2).

The identification and assessment of poorly defined, nonspecific complaints, symptom complexes, and illnesses is extremely difficult.^{18,19} In addition to medical examinations, consultation with specialists in the behavioral sciences is needed. The use of health questionnaires designed to detect emotional ill health and objective psychologic tests for specific types of symptoms can provide relevant information. Useful data may also come from attendance rates at clinics or physicians' offices, absentee rates due to illness, accident liability, and job performance.

CONGENITAL ANOMALIES

A case-control study of Down's syndrome in Baltimore²⁰ yielded an unexpected finding regarding paternal exposure to microwave radiation. Fathers of children with mongolism more frequently gave unsolicited histories of occupational exposure to radar during military service than did fathers of unaffected children, a difference that was of borderline statistical significance. Exposure during military service occurred prior to the birth of

the index child. After publication of the first report in 1965, expansion of the study group, follow-up of all fathers to obtain more detailed information about radar exposure, and search of available armed forces records were undertaken. The suggestive excess of radar exposure of fathers of Down's syndrome cases was not confirmed on further study but occupational exposures were difficult to document.²¹ A chromosome study of peripheral blood of exposed and unexposed fathers showed some suggestive but inconclusive changes; the findings are to be reported.

A study of congenital anomalies in Alabama²² showed that during the three-year period 1968-1971 the adjoining counties of Dale and Coffee, in which Fort Rucker was located, had a reported number of clubfoot cases among white babies that greatly exceeded the expected number (based on birth certificate notifications for the state). More detailed investigation revealed that in the six-county area surrounding Fort Rucker there was, during the same time period, a considerably higher rate of anomalies (diagnosed within 24 hours after birth) among births to military personnel than in the state as a whole. Fort Rucker was a training base for fixed wing and helicopter aircraft, situated within 35 miles of dozens of radar stations. Errors in malformation data on birth certificates and probable over-reporting from Fort Rucker led to the conclusion that convincing evidence was lacking that radar exposure was related to congenital malformations.²³ The high malformation rate across a group of counties of the state was presumably environmentally induced but no specific agent was suggested. It was not possible to do a more detailed study at this or at another military base.

The use of microwave heating as diathermy to relieve the pain of uterine contractions during labor was reported from Belgium in 1973.²⁴ The analgesic effect was helpful in 1,000 selected patients without obstetric disease, and the babies were born healthy with good circulation. By 1976²⁵ 2,000 microwave-exposed patients and 2,000 controls had been observed. No untoward immediate or long-term effects on the fetus are known from such exposure shortly before delivery. The only possible congenital defect so late in gestation would involve the central nervous system. Systematic follow-up examinations have not yet been made.

CANCER

Microwave-induced cancer has not been reported experimentally or suspected in medical surveillance examinations of microwave workers or

military service personnel. Only the two recently completed prospective epidemiologic studies^{1,3} to be reported at this session have looked into the question systematically. Neither has revealed an excess of any form of cancer thus far that can be interpreted as microwave-induced. A description of the occupational study of Navy servicemen follows.

Study of Occupational Exposure to Radar in the Navy¹

In 1970-71 we did a pilot study to determine the requirements and feasibility of a cohort study of health risks from microwave radiation. The study was to make use of differences in levels of occupational exposure and of medical information recorded during military service and after discharge. We proposed to study Navy enlisted men and to investigate their total mortality and morbidity experience, reproductive performance, and the health of their children.

The pilot work was done in collaboration with the Medical Follow-up Agency of the National Academy of Sciences and with the assistance of various Navy specialists. We found the proposed investigation feasible but the cost of studying all factors of interest very high. After several modifications of the study plan to conform with available funds, a protocol was developed which involved the use of largely automated military and veterans' records to analyze a limited number of endpoints: mortality, hospitalized illness in naval and veterans' hospitals, and disability. The study, recently completed under contract with the National Academy of Sciences, is being prepared for publication.

Selection of study population. Since World War II the Navy has maintained technical schools where thousands of enlisted men have been trained in the use and maintenance of radar equipment for navigation and gunfire control. Large numbers of servicemen similarly selected for educational achievement, general intelligence, and aptitude have also graduated from other technical schools, thus offering the possibility of selecting valid comparison groups. The records of the technical schools, available at the Military Personnel Records Center in St. Louis, identify graduates of specific training programs; these graduates were used to construct rosters of study subjects. Men selected for this study graduated during the period 1950 through 1954. The Korean War period was chosen for two reasons: wartime service ensured virtually complete ascertainment of deaths, and exposure during the 1950s provided a sufficient time for long-term effects.

Measurements made by the Navy offered a guide for selecting the most

TABLE II. NUMBER OF STUDY SUBJECTS BY NAVAL ENLISTED CLASSIFICATION OF OCCUPATIONS AND EXPOSURE CLASS

<i>Potential high exposure (equipment repair)</i>	
Electronics technician	13,078
Fire control technician	3,298
Aircraft electronics technician	3,733
	20,109
<i>Potential low exposure (equipment operation)</i>	
Radioman	9,253
Radarman	10,116
Aircraft electrician's mate	1,412
	20,781

highly exposed occupations. On the basis of a consensus decision by Navy personnel involved in training and operations, occupational groups were classified as probably maximally exposed (those repairing radar equipment) and probably minimally exposed (those operating radar equipment). Technical occupational groups probably nonexposed (such as engine-room personnel) were considered unsuitable because of their exposure to heat and humidity stress. Men selected for the study were drawn from six Naval Enlisted Classifications of occupations as shown in Table II.

The high-exposure cohort is made up of electronics technicians, fire-control technicians, and aircraft electronics technicians. The low-exposure cohort, consisting of men trained in equipment operations, are classified as radioman, radarman, and aircraft electrician's mate. Of a study population of approximately 40,000, there are about 20,000 in each of the two cohorts. The groups were composed predominantly but not exclusively of young men who entered service shortly after graduating from high school. The mean age of the total low-exposure men was 20.7, whereas the average of the high-exposure group was 22.1 years.

Medical information. Follow-up medical information was derived from search and linkage of Navy and Veterans Administration records. The death of almost every war veteran is a matter of record in Veterans Administration files, because applications for burial benefits are made for about 98% of war veterans. The application usually includes a copy of the death certificate, from which the certified cause of death may be obtained. The Navy's records of hospital admissions were searched, and records of admissions to Veterans' Administration hospitals were available for com-

puter search, as were current awards for disability compensation. The cohorts of more than 40,000 men were followed through extant records for the following endpoints and time periods of ascertainment:

Mortality	1955-1974
Morbidity (in-service hospitalization)	1950-1959 (excl. 1955)
Morbidity (VA hospitalization)	1963-1976
Disability compensation	1976

Assessment of exposure. It is unfortunate that the lack of dosimetry for occupational exposure has not permitted assignment of exposure doses to any individuals in this study. The only measurements possible are environmental, or arise out of efforts to reconstruct the circumstances of accidental overexposure. There have been enough accidental exposures at estimated levels exceeding 100 mW/cm^2 to indicate that there are occupations in which some men at some times on certain classes of ships have been exposed well in excess of the 10 mW/cm^2 limit.²⁶ Shipboard monitoring programs in the Navy since 1957 show that men in other occupations rarely, if ever, were exposed to doses in excess of this limit.²⁷ Radiomen and radar operators (our low-exposure group), whose duties keep them far from radar pulse generators and antennae, were generally exposed to levels well below 1 mW/cm^2 , whereas gunfire control technicians and electronics technicians (our high exposure group) were exposed to higher levels in the course of their duties.

In addition to occupation per se, other relevant elements of exposure were included in the analysis, namely, length of time in the occupation, class of ship, and power of equipment on the ship at the time of exposure. To obtain information on these items, it was necessary to review individual personnel records. Because this procedure was both costly and time consuming, it was done only for men in the high exposure occupations who died from nonaccidental deaths and for a randomly selected 5% sample of living men in the same occupations.

An index of *potential* microwave exposure to individuals, called the Hazard Number, was constructed for those men whose individual records were reviewed. This consisted of the sum of the power ratings of all gunfire-control radars aboard the ship or search radars aboard the aircraft to which the technician was assigned, multiplied by the number of months of assignment. To create the Hazard Number for an individual it was necessary to trace his service assignments from ship to ship or squadron to squadron. The Navy made available information concerning the radar

TABLE III. PERCENTAGE DISTRIBUTION OF NAVAL ENLISTED PERSONNEL IN OCCUPATIONS IN THE HIGH EXPOSURE GROUP BY EXPOSURE HAZARD NUMBER

<i>Hazard number</i>	<i>Electronics technician</i>	<i>Fire control technician</i>	<i>Aircraft electronics technician</i>
-0-	28.0	6.6	13.0
1-2,000	28.4	23.8	16.9
2,001-5,000	19.9	30.9	18.0
5,000+	10.8	26.6	48.3
Unknown	12.9	12.1	3.8
Total	100.0	100.0	100.0

equipment in service on each ship or patrol aircraft type at various times.

The Hazard Number, then, is a measure not of actual, but of potential exposure. A technician with a low Hazard Number had little opportunity for substantial exposure to microwaves, while men with large Hazard Numbers may have had substantial opportunity for such exposure. The distribution of Hazard Numbers by specified occupational rating in the high exposure group is shown in Table III. It is evident that within the high exposure group the fire control technicians and the aircraft electronics technicians had much larger proportions of men with large Hazard Numbers than did the electronics technician group.

Results. Differential health risks associated with potential occupational exposure to radar in the Navy more than 20 years ago are not apparent with respect to long-term mortality patterns or hospitalized illness around the period of exposure, two endpoints for which there is virtually complete information for the total study group. Later hospitalization (in Veterans Administration facilities only) and awards for service-connected disability, the two other endpoints examined, provide incomplete information. While some significant differences among the occupational groups classified by level of potential exposure have been found with respect to all the endpoints studied, the differences could not be interpreted as a direct result of microwave exposure.

Because no measures of *actual* as opposed to *potential* exposure were available, the so-called "high exposure" rosters were made up of a mixture, in unknown proportions, of men whose actual exposures varied from high to negligible. If a large proportion of the men had, in fact, very small exposures, the consequence would have been to obscure by dilution any differences which might have been found had it been possible to study

a large group of men who actually received high exposures. Further, it is possible that effects involving the cardiovascular, endocrine, and central nervous systems are transient, disappearing with the termination of exposure or soon thereafter, or are not perceived to be of sufficient consequence to result in admission to hospital.

It was not possible in this study to determine hospitalization outside the Navy and Veterans Administration systems, nonhospitalized medical conditions during and after service, reproductive performance and health of offspring, or employment history after discharge from service. A subsample of living men with high and low exposure patterns during service, however, can be identified for intensive individual followup. This would make it possible to obtain additional information about occupational exposure by reviewing individual service files and by making direct inquiries of the men.

Suggestions for Further Research

In view of the exceptional difficulty in extrapolating microwave effects from experimental animals to man, epidemiologic studies, including appropriate clinical and laboratory examinations, are essential to improve our understanding of possible hazards to health.

1) Studies of identified populations should be improved, continued, or expanded wherever possible and useful. It is difficult to identify exposed populations, to select suitable controls, and to obtain exposure data. Some study groups already characterized can be improved by the acquisition of additional exposure data, some groups should be followed for longer periods of time, and some should be investigated for additional endpoints.

2) Additional study populations should be sought. Exposure to microwave radiation has been experienced increasingly for more than three decades. A careful search should be made for exposed groups not yet investigated or considered for study. In epidemiologic studies, as in experimental or clinical work, there is rarely a single study, positive or negative, that can be accepted as definitive. Replication and validation are needed at all exposure levels.

3) Some specific endpoints should be studied further:

- a) Cataracts. It is reasonable to hypothesize and feasible to investigate a synergistic or additive action of microwaves in cataract formation. Comparative frequencies of cataracts from all causes in exposed and nonexposed occupational groups can be investigated

by following study subjects into the older age periods, when cataracts increase in frequency.

- b) Mental and behavioral changes. The numerous reports from Eastern Europe of a wide variety of functional changes and possible nervous system effects have yet to be confirmed or rejected. In appropriate epidemiologic studies, medical reports should be augmented to include assessment of emotional and psychological status.
- c) Congenital anomalies. There have been two preliminary and inconclusive epidemiologic investigations of the effect of paternal exposure to radar on the occurrence of congenital anomalies in their offspring. The subject needs more intensive investigation to assess possible genetic effects.
- d) Malignancies. There is no direct evidence that microwaves are carcinogenic, but the possibility has not been excluded experimentally. More intensive and extended morbidity monitoring may provide pertinent information.

To clarify the complexities of the biologic and health effects of microwave radiation, all possible study approaches are needed. Epidemiologic research, which is in an early state of development, should be broadened. As noted²⁸ "...as far ahead as one can see, medicine must be building, as a central part of its scientific base, a solid underpinning of biostatistical and epidemiological knowledge. ...impressions are essential for getting the work started, but it is only through the quality of the numbers at the end that the truth can be told."

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