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Research Triangle Park NC 27711

Research and Development

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Project Summary

Microwaves, Hyperthermia, and Human Leukocyte Function

Norbert J. Roberts, Jr., Shin-Tsu Lu, and Sol M. Michaelson

The objective of this study is to determine whether exposure to microwaves (2450 MHz) affects the function of human leukocytes in the resting state and during antigenic or mitogenic challenge. This publication is a summary report of the construction and calibration of a waveguide exposure system for the exposure of human mononuclear leukocytes to 2450 MHz (CW) microwave energy. A description of the dual vial waveguide exposure facility for *in vitro* irradiation of human leukocytes is presented. Calorimetric determinations of specific absorption rates (SAR) were made using heating curves measured with a microwave transparent Vitek 101 Electrothermia Monitor. The correlation between SAR and forward power was highly significant ($r = 0.95$). At a forward power of 0.55 W, the averaged SAR was approximately 33 mW/ml. However, inhomogeneity and significant resonance absorption were noted in the dual vial waveguide exposure facility. A 30-point measurement of SAR distribution revealed that the SAR at any of the measured points could range between 0.12- and 3.94-fold of the average SAR within the given vial. Measurements indicated that this variability in SAR values did not create significant thermal gradients within the vials when external agitation was applied.

This Project Summary was developed by EPA's Health Effects Research Laboratory, Research Triangle Park, NC, to announce key findings of the research project that is fully documented in a separate report of the same title (see Project Report ordering information at back).

Introduction

Microwave radiation has many current uses that result in public exposure, with very little information available on the effects of microwaves on man. Investigators have reported increased spontaneous transformation of lymphocytes from animals that have been exposed to microwaves. These effects are still of unknown functional significance. Quantitation of thermal variables is difficult but it is critical to understanding these effects. This study will determine whether microwave exposure of human mononuclear leukocytes *in vitro* will similarly affect these cells, and will determine whether such effects are beneficial or detrimental and finally, will determine the influence of thermal flux in these reactions. In addition, the studies will explore the effects of microwave-induced hyperthermia on the function of human leukocytes in host defenses that are pertinent when challenged by bacteria, viruses, toxic foreign material and neoplastic tissue.

Human mononuclear leukocytes will be exposed *in vitro* to microwaves in a 37°C environment to effect no change in temperature and to attain temperatures in the range of 37 to 42°C, to provide a definition of temperature-response relationship. Low equivalent

power densities (<0.5-10 mW/ml) will be specifically examined. Exposure without temperature increase will be studied initially. The function of these cells, measured by transformation response to mitogen or antigen, will be assayed and compared to that of cells treated concurrently in a like fashion with the exception of microwave exposure. The latter cells, in studies of temperatures >37°C, would have their temperature set by exposure to appropriate ambient temperature conditions.

This report details the construction and calibration of the dual vial waveguide system to be used for the *in vitro* exposure of human leukocytes at 2450 MHz.

Technical Discussion

The study reached these objectives: (1) design, acquisition and construction of the microwave dual vial exposure system; and (2) dosimetry analysis of the system. Analysis of dosimetric and thermal characteristics constituted the major scientific effort after system procurement and construction.

Figure 1 shows the block diagram of the waveguide exposure facility for cell exposure to microwaves. The waveguide exposure chamber dimensions are shown in Figure 2.

Calorimetric determination of specific absorption rate (SAR) was made using a microwave transparent Vitek 101 Electrothermia Monitor. SAR values were determined using heating curves at steady state [Ln(ΔTss-ΔT) = LnΔTss-k·t]. Heating analysis was employed for the following reasons: (1) deviation from linearity occurs consistently earlier in the cooling curve than in the heating curve; and (2) a slower and larger deviation is noted in the cooling constant determined by cooling analysis than by heating analysis. Table 1 shows the calorimetric determination of SAR using heating analysis. Specific absorption rates were also determined from the power reading sampled by the bidirectional coupler. SAR determinations of the dual tube waveguide exposure facility are shown in Table 2.

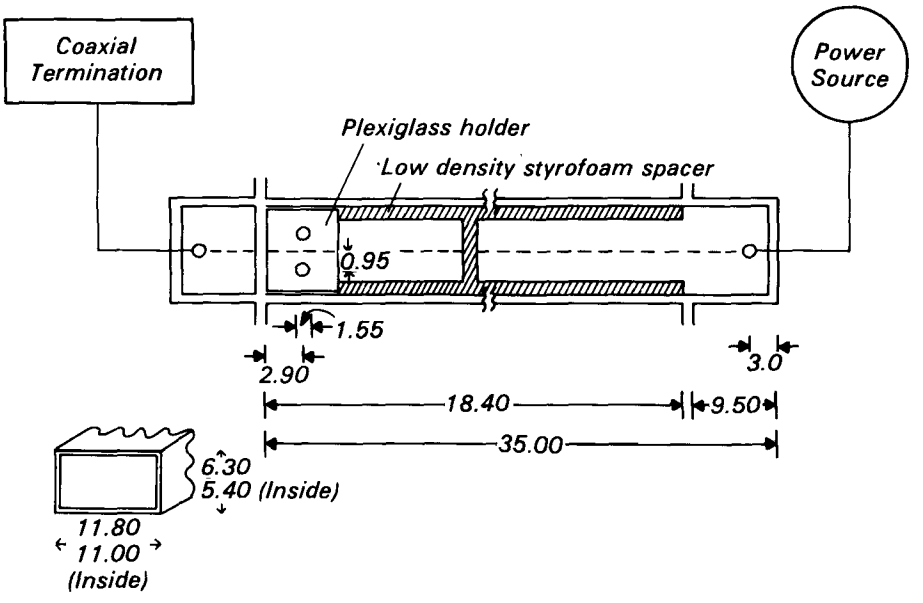

Figure 2. Dual vial waveguide exposure chamber.

Determination of SAR under different dosimetric procedures is shown in Table 3. SAR determinations using muscle phantom material in the vials and medium in the vials with agitation but no insulation and under non-steady-state conditions gave the highest SAR values. A 30-point measurement of SAR distribution in the vials using muscle phantom material showed 0.12 to 3.94-fold variation from the averaged SAR for the vial.

Conclusions

Inhomogeneity and significant resonance absorption were noted in the dual vial waveguide exposure facility. A 30-point measurement of SAR distribution revealed that the SAR at any of the measured points could range between 0.12- and 3.94-fold of the average SAR within the given vial. However, such variable SARs did not create significant thermal gradients within vials when external agitation was applied. The differences in averaged SAR between vials of the present dual-vial waveguide system were not significant, irrespective of the method of quantitation used. This, as well as the fact that much lower averaged SAR values are planned for

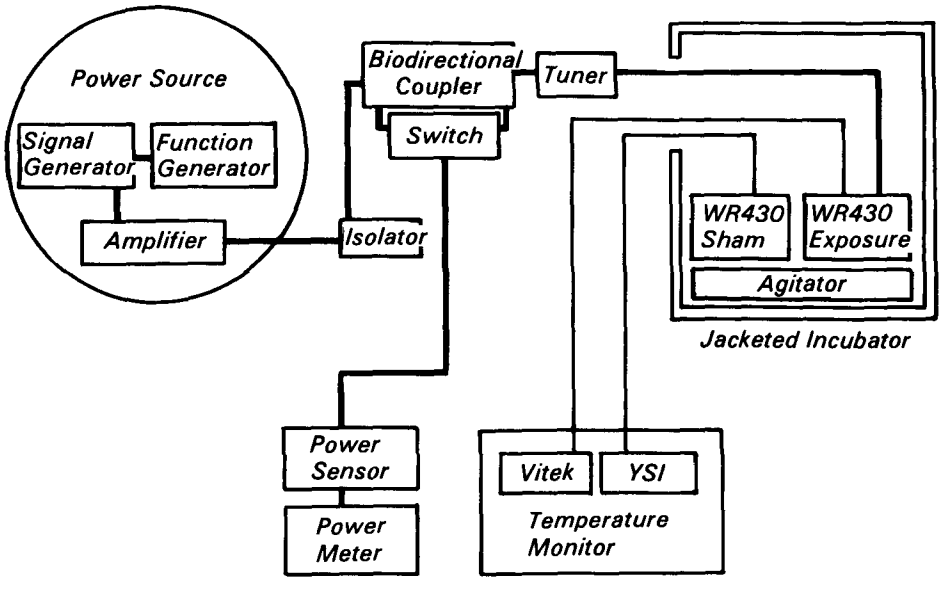

Figure 1. Microwave exposure system

Table 1. *Calorimetric Determination of SAR Using Heating Analysis*

Forward Power (W)	ΔTss (°C)[a]	k (min^{-1})[b]	SAR (mW/ml)[c]
0.22	2.28	-0.0617	9.54
0.33	3.04	-0.0928	15.96
0.45	3.47	-0.0710	16.70
0.55	4.91	-0.0794	26.49
0.55	4.53	-0.0961	29.57
0.67	4.79	-0.0751	24.45
0.67	4.57	-0.0921	28.59
0.77	6.98	-0.0763	35.68
0.78	6.44	-0.0856	37.89
0.78	5.63	-0.0824	31.48
0.79	5.10	-0.0864	29.92
0.89	7.24	-0.0798	39.22
0.89	6.40	-0.0841	36.54
1.00	6.60	-0.0783	35.12
1.01	7.03	-0.0882	42.10
1.01	7.43	-0.0942	47.54
1.10	6.40	-0.0902	39.20
1.13	8.10	-0.0896	49.26
1.18	9.24	-0.0809	50.78
1.28	9.39	-0.0909	57.95
		-0.0838	
		±0.0087 (mean ± S.D.)	

[a] *ΔTss = steady state temperature increment.*
[b] *k = cooling constant.*
[c] *SAR: specific absorption rate.*

Table 2. *Comparison of SAR's for Right and Left Vials*

Forward Power (mW -20.4 dB)	SAR, Left Vial	SAR, Right Vial
0.1	0.93	0.93
0.5	4.70	4.69
0.8	7.51	7.50
1.0	9.40	9.38
1.5	14.09	14.08
1.8	16.92	16.88
2.0	18.80	18.78
2.5	23.51	23.46
2.8	—	26.30
2.85	26.80	—
3.0	28.21	28.17
3.5	32.91	32.89
3.8	35.74	35.71
4.0	37.61	37.60
5.0	—	47.03
5.1	47.97	—
6.0	—	65.43
6.1	57.38	—
7.0	65.84	—
7.2	—	67.73
8.3	—	78.07
8.4	78.98	—
9.2	86.48	86.54
10.0	93.98	94.06

the biological work, indicates that this exposure system can provide an assessment of the importance of inhomogeneous SAR in the absence of substantial compromise by thermal mechanisms.

Recommendations

The construction and dosimetry measurement phase of this project has gone well. The dosimetry should go a long way in evaluating the data of human leukocytes exposed to microwaves. It is recommended that this project proceed to the evaluation of the effects of microwaves on human leukocytes exposed at 2450 MHz in this exposure system.

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Table 3. *Determinations of SAR with Different Dosimetric Procedures*

Procedure	Right Vial	Left Vial
Muscle phantom,[a] Lim d/dt (ΔT) t→0	*58.7 ± 46.2 (30)[b] 63.4 ± 45.4 (29)*	*76.1 ± 63.9 (30)[b]*
Culture medium, agitated, non-insulated, non-steady-state	*80.0 ± 23.1 (4)*	*72.9 ± 9.2 (4)*
Culture medium, agitated, insulated, linear heating rate	*34.1 ± 2.9 (4)*	*31.3 ± 3.2 (4)*
Culture medium, agitated, non-insulated, steady-state	*26.4 ± 4.4 (4)*	*28.8 ± 0.7 (4)*

[a]*Multiple points measured within the vial.*
[b]*Mean ± S.D. (no. of determinations).*

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***Ralph J. Smialowicz** is the EPA Project Officer (see below).*
The complete report, entitled "Microwaves, Hyperthermia, and Human Leukocyte Function," (Order No. PB 81-208 951; Cost: $6.50, subject to change) will be available only from:
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Project Summary

Determinants of Cancer and Cardiovascular Disease Mortality in Mining Counties of California

R. A. Ziskind, D. F. Smith, J. L. Hahn, and G. Spivey

The purpose of this research effort was to design an epidemiological study protocol to evaluate the influence of environmental asbestos exposure on mortality from lung cancer, mesothelioma, and cardiovascular disease in the asbestos mining areas of California. Mortality data (1968-1978) and emissions data (both anthropogenic) were reviewed in an effort to determine the most preferable study area. The area selected for future study was Western Calaveras and Tuolumne Counties which contain the Calaveras serpentine deposit. Selection criteria included suitable population base, sufficient number of deaths, evidence of elevated airborne and waterborne asbestos concentrations, and the existence of archives containing ambient air sampler filters for preceding years. A questionnaire was developed for obtaining information from next-of-kin of decedents in the study area though interviewing was not attempted. Next-of-kin interviews are expected to be a component of future studies. Necessary elements of quality assurance were identified and documented as part of protocol design.

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Introduction

This epidemiological study evaluates the hypothesis that asbestos-related health effects have been observed among populations not occupationally exposed. The study was divided into four conceptual tasks:

Epidemiological protocol design. In this segment, alternative study approaches were evaluated. The mortality data base, the sources, and the exposure to asbestos were considered.

Questionnaire development. In concert with protocol design and exposure findings, the primary data-gathering mechanism for obtaining subject information from survivors was drafted, pretested, revised, and submitted.

Source inventory and exposure characterization. All anthropogenic and natural emission sources of asbestos were delineated and quantified in each California study area. Existing occupational and ambient data were reviewed to establish inhalation and ingestion population exposure.

Quality assurance. Elements of quality assurance were to be identified and documented as part of the protocol design.

The initial components of this study were the source inventory and exposure characterization. A summary of the

principal findings are given here.

Two distinct California asbestos mining and milling areas were researched. One is associated with a serpentine deposit running through the junction of Fresno and San Benito Counties (herein referred to as the New Idria Deposit). The second is located throughout the western sections of Calaveras and Tuolumne Counties (the Calaveras Deposit). The preferable study area was determined to be that associated with the Calaveras Deposit. Selection criteria included greatest population base, evidence of elevated airborne and waterborne concentrations of asbestos, and the existence of archives of useful ambient air sampler filters dating back over seven years.

For the case of the New Idria Deposit, the mining areas are sufficiently remote to make it unlikely that any population center will be affected. One mill is located near a community and limited airborne asbestos measurements point to significant concentrations there at the time taken.

By contrast, the Calaveras Deposit area has a greater at-risk population as a result of mining and milling of asbestos and other minerals. In addition, airborne background ambient levels taken upwind or remote from known sources are elevated. No waterborne asbestos measurements were made specifically for the water distribution systems serving the Calaveras Deposit area; however, measurements on San Francisco Bay water district reservoirs located in western Calaveras and Tuolumne Counties show higher than average concentrations for those with supplies passing through serpentine formations. The oldest ambient data uncovered for the Calaveras Deposit area was reported in the California Department of Health Study of 1965-1967. Asbestos concentration was measured by dust sample collection through impingers. Quantification was by optical microscopy. Measured ambient levels (upwind at a large mine site, etc.) on two separate occasions ranged between 0.1 and 2 million particles per cubic foot of air. A federal study at about the same time of the area "Environmental Survey of Asbestos Mining and Milling in California" December, 1966, Public Health Service Division of Occupational Health, suggests the equivalence 10 total fibers/cc $\equiv$ 1 mppcf by impinger. In the cited ambient concentrations (from the NIOSH Recommended Asbestos Standards), the levels across the country are summarized as generally < 10 ng/m^3 with occasional peaks as high as 100 ng/m^3 (by electron microscopy). Using optical microscopy, ambient levels are generally less than 0.01 fibers > 5 μm/cc with peak values as high as 0.03 fibers > 5 μm/cc. Use of the Public Health Service equivalence 6 fibers > 5 μm/cc $\equiv$ 1 mmpcf by impinger yields the mine area ambient (upwind) concentration range 0.6-12 fibers/cc.* Further, use of the NIOSH suggested equivalent 20 fibers > 5 μm in length (as determined by optical microscopy) per nanogram of asbestos yields the mine ambient range 12-240 ng/m^3. Thus, the ambient levels detected at upwind locations in the vicinity of a Calaveras mine/mill are at the extreme high end of the surveyed range.

High volume air sampler filters from the Calaveras Deposit area population centers have been located in the California Air Resources Board archives dating back to the early 1970s. They can be utilized to quantify airborne asbestos concentration and they therefore approximate exposure data. Coupled with the water assay, they will establish the quantitative relationship among population centers in the serpentine area and the other areas of Calaveras and Tuolumne Counties. Also, they will provide the basis for stratifying the populations according to inhalation and ingestion exposure.

Based upon the source and exposure information available to this study, the potential study group was defined as those people who died in Calaveras and Tuolumne Counties during the last ten years. Approximately 4,300 people will be included. Exposure of the preliminarily identified group is expected to be significant; principally due to general ambient sources rather than a dominant single point source. Exposure may be differentiated among the group members between air and water, with either predominating in particular residential segments. This approach will permit investigation of the relative importance of different exposure routes and will facilitate interpretation of possible dose-effect relationships. Water distribution systems for the area through the last ten years were described.

*Note: The current NIOSH recommended standard is 0.1 fiber/cc for an 8-hour time-weighted average.

Conclusions

There are two principal areas of California in which asbestos mining and milling activities are conducted. This study investigated both areas and surveyed the anthropogenic and natural sources of asbestos emissions into the environment. The county areas which constitute both regions are principally rural; the cities generally contain less than 6,000 people. The only large cities in Calaveras, Fresno, Monterey, San Benito, and Tuolumne Counties are located apart from the serpentine areas. The coincidence of asbestos mining and milling with such less-urbanized county areas is a favorable factor; people in more populous urban centers are exposed to a number of toxic substances in their ambient environment.

Based upon the synthesis of published literature, a field survey, and the review of the limited asbestos monitoring information available, the study concluded that airborne and waterborne asbestos levels in particular areas of Calaveras and Tuolumne Counties may be elevated with respect to background. In the other principal serpentine area (San Benito, Fresno, Monterey), insufficient information is available to estimate exposure. In these latter areas, mining activities are relatively isolated from population areas. However, ore transport and milling are in the King City-San Lucas areas. Isolated airborne data taken in King City showed elevated concentrations; more extensive mill site data (provided by the mill management) appears somewhat lower. The single piece of waterborne assay information from the Coalinga vicinity is insufficiently documented to be definitive.

Upwind data taken at Calaveras asbestos during 1965-1967 range from 12-240 ng/m^3 extrapolated to electron microscope concentrations from optical microscopy counts of fibers greater than 5 μm. Ambient concentrations across the country are generally below 10 ng/m^3.

High volume air quality sampler filters were located in the archives of the California Air Resources Board for a number of sites in Calaveras and Tuolumne Counties. Samples of 24- and 48-hour duration date back to the early 1970s. These asbestos analyses are practical and may be utilized to provide an exposure mapping of the areas of interest.

Water distribution systems in Calaveras and Tuolumne Counties have been identified. Sources, routes, and

reatment differ throughout the area. No ;pecific asbestos analyses of the water ɹsed for local supply was found. Based ɹpon several available measurements ɔf elevated asbestos content in serpen- ine deposit area reservoirs (which ;erve San Francisco Bay communities), water sampling and analysis should be ɔerformed for chrysotile asbestos.

Based upon available air and water ɗata, elevated asbestos exposure to the ɟeneral population may have occurred n areas of Calaveras and Tuolumne Counties.

Recommendations

Water sampling and air/water anal-ysis should be conducted to define ex-ɔosure to the population by place of ·esidence. Parallel with that effort, nformation from the California death ape rolls can be initially extracted on an ınnual basis for both counties. These apes can be processed according to ɔause of death (ICD system) with case ınd control groups extracted, and dis-ıase mortality rates compiled. The ɨtatistical adequacy of all cause-of-ɗeath categories of interest would then ɔe determined. All diseases associated with occupational exposure to asbestos would be considered. In addition, all ɨtatistically adequate death category ɔopulations can be contrasted as a unction of exposure. The product of this ıffort is the delineation of the range of ɔorrelation of mortality categories with ıxposure. This may suggest additional ɔause-of-death categories. These steps will be followed by the final study ɔomponents which will include the ɗetailed data gathering by survivor ɋuestionnaire and medical records and he comprehensive data analyses.

R. A. Ziskind, D. F. Smith, J. L. Hahn, and G. Spivey are with Science Applications, Inc., Los Angeles, CA 90067.

***John Acquavella** is the EPA Project Officer (see below).*

The complete report, entitled "Determinants of Cancer and Cardiovascular Disease Mortality in Asbestos Mining Counties of California," (Order No. PB 81-208 985; Cost: $11.00, subject to change) will be available only from:

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