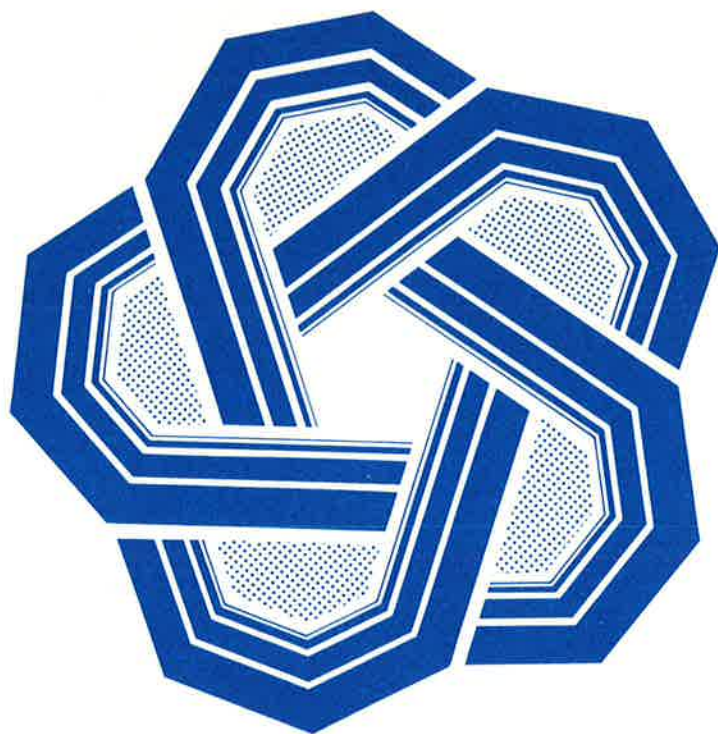


Proceedings of a Workshop on Thermal Physiology

Sponsored by the Radiofrequency
and Microwave Committee of the
Interagency Regulatory Liaison Group



Interagency Regulatory Liaison Group

U.S. Consumer Product Safety Commission

U.S. Environmental Protection Agency

Food and Drug Administration, U.S. Department of Health, Education, and Welfare

Food Safety and Quality Service, U.S. Department of Agriculture

Occupational Safety and Health Administration, U.S. Department of Labor

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Held in Rockville, Maryland
March 29, 1979

Edited by
T. Whit Athey, Ph.D.
Bureau of Radiological Health



Interagency
Regulatory Liaison
Group

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March 1980

Published by

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service
Food and Drug Administration
Bureau of Radiological Health
Rockville, Maryland 20857

The opinions and statements contained in this report are those of the authors and may not reflect the views of the Department of Health, Education, and Welfare (HEW).

FOREWORD

The Interagency Regulatory Liaison Group (IRLG) was formed to coordinate the activities of the five regulatory agencies, FDA, EPA, OSHA, Consumer Product Safety Commission (CPSC), and the Food and Consumer Services Division of the Department of Agriculture, pertaining to hazardous materials. In August 1978, the Commissioner of FDA wrote the other agency heads and suggested that the IRLG concept be extended to cover radiofrequency and microwave radiation. As a result the Radiofrequency and Microwave Committee was formed. Two other agencies, the FCC and NIOSH also have representatives on the committee because of their interest and activities in this area.

The objectives of this committee are: (1) to develop a consistent radiation protection philosophy for radiofrequency and microwaves; (2) to coordinate the development of a comprehensive biological effects survey report on published experimental and epidemiological studies considering the efforts of all agencies; (3) to identify and classify radiofrequency and microwave emitters and the populations exposed to identify significant sources; (4) to identify common research needs and to coordinate a biological and physical research program; and (5) to develop a coordinated control and corrective action plan in areas of overlapping jurisdiction.



Mays L. Swicord
Chairman
IRLG Radiofrequency and
Microwave Committee

PREFACE

Upon its formation in October 1978, the IRLG Radiofrequency and Microwave Committee identified the radiation from RF heat sealers operating at 17 MHz as the most pressing immediate concern requiring coordinated action by the member agencies. Field studies have found levels which the Committee felt were too high, but then the problem becomes, what is an acceptable level?

In any discussion of RF safety the question of the mechanism of interaction for any health effect is always prominent. However, the Committee felt that resolution of this question was not likely in the near future, while timely action was needed. At a minimum a safety guide must protect against thermal injury, the one mode of interaction which is clearly demonstrable. However, the basic question remains, albeit in a slightly different form: what is an acceptable (thermal) insult?

This Workshop on Thermal Physiology was organized to help clarify this question. Our participants were asked to address the effects of heat deposition in the body, regardless of the source of the heat, but allowing for the possibility of nonuniform distribution.

This publication is an edited transcript of the workshop, and is intended only as a record of the proceedings. However, because of the general interest in this question, it was decided to make these proceedings available to a wider audience.

The discussions of the workshop were illustrated with slides and viewgraphs and these are referred to in the text. With the exception of the illustrations for the presentation by Dr. Adair, few of the figures were available for inclusion in this publication. Even those which are included are mostly made from copies of journal articles, resulting in poor quality reproductions. However, it was felt that these would be better than nothing, and so they are included.

In 1968 an international symposium on Physiological and Behavioral Temperature Regulations was held at the John B. Pierce Foundation Laboratory in New Haven, Connecticut. Those with an interest in this subject should be aware that the Proceedings of this symposium have been published (Hardy, J.D., A.P. Gagge, and J.A.J. Stolwijk, editors, Charles C. Thomas, Springfield, Illinois, 1970).



T. Whit Athey
Editor
Bureau of Radiological Health

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ACKNOWLEDGMENTS

Special thanks are due to Dr. Eleanor Adair of the Pierce Foundation Laboratory for her help in organizing this workshop.

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RADIOFREQUENCY AND MICROWAVE COMMITTEE WORKSHOP ON THERMAL PHYSIOLOGY

INTRODUCTION

MR. SWICORD: I wish to welcome you to this workshop on Thermal Physiology sponsored by the Radiofrequency and Microwave Committee of the Interagency Regulatory Liaison Group (IRLG). I would like to take a few moments to explain what this Committee is, what its objectives are, and how this workshop relates to those objectives.

First, the (IRLG) is currently composed of the heads or their designate surrogates of five regulatory agencies: the EPA, FDA, OSHA, Consumer Product Safety Commission, and the Food and Consumer Services Division of the Department of Agriculture. The last is a recent addition to this organization.

Initially, the major role of this IRLG liaison group was to coordinate regulatory and related activities pertaining to hazardous materials. Originally, eight work groups and a number of subcommittees were formed under the liaison group to coordinate the various aspects of this objective.

In August 1978, Dr. Kennedy, Commissioner of the FDA, wrote to the other agency heads and suggested that the IRLG concept be extended to cover radiofrequency and microwave exposure hazards. As a result, this Committee, the Radiofrequency and Microwave Committee, was formed.

I would like to introduce at this time the participants of this Committee and the agency designees:

Mr. Dave Janes from EPA; Dr. Fred Hodge from EPA; Mr. Bob Curtis from OSHA; Dr. Richard Boggs from NIOSH; Dr. Joe Elder from EPA; Mr. Frank Tipton from OSHA; and Jack Monahan from the Bureau of Radiological Health, FDA. Mr. Will McGibbon of the FCC; Alan Andersen and Moris Shore from the Bureau of Radiological Health. Zory Glaser from NIOSH is a special case. He was a representative from NIOSH, but he is now a BRH employee. We hope that his participation in the Committee can continue, although his agency representation may cease to exist.

The agencies that are named are not necessarily the same agencies that I named in relationship to the umbrella IRLG organization. Only three of those original agencies were concerned with regulation of radiofrequency and microwave emissions. These are the Food and Drug Administration, the Environmental Protection Agency, and the Occupational Safety and Health Administration. We have been asked to add to this Committee the FCC and NIOSH.

The objectives of this Committee are: (1) to develop a consistent radiation protection philosophy for radiofrequency and microwaves; (2) to coordinate the development of a comprehensive biological effects survey report on published experimental and epidemiological studies considering the efforts of all agencies; (3) to identify radiofrequency and microwave emitters and the populations exposed, to identify significant sources and to

categorize them; (4) to identify common research needs and to coordinate a biological and physical research program; and (5) to develop a coordinated control and corrective action plan in areas of overlapping jurisdiction.

The Committee has been working on most of these objectives. The most pressing concern under the last objective, which was to develop a coordinated control and corrective action plan in areas of overlapping jurisdiction, was determined to be the control of radiation from RF sealers operating at 27 MHz. Extremely high fields, greater than 5 amps/m and greater than 100 volts/m were measured at the location of the operator of these machines. The Committee came to the conclusion that these fields are too high and were a risk to the health of the operator. The question then posed was if these levels are too high, what is an acceptable level?

The available information on biological effects at 27 MHz is scarce. The small amount of data collected in this country indicates effects in animals at rather high electric field strengths, and the data from the Eastern European countries is several orders of magnitude below the Western results.

Several alternative bases for judgment were offered and examined by the Committee:

- (1) Use the small amount of 27 MHz data taken on animals and apply engineering scaling to determine the acceptable level for humans;
- (2) Use as a guide existing or proposed standards; and
- (3) Assume that the mechanism or cause of the effect or hazard is thermal and thus not frequency-specific at the microscopic level. Frequency would only play a role in the distribution of energy on the macroscopic level. With this assumption, the data taken at 2450 MHz, of which there is a great deal more, with proper scaling considerations would be applicable at 27 megahertz.

If we adopt the third alternative then we may examine the experimental animal data taken at 2450 MHz. Dr. Don Galloway of BRH has collected the reported effects on the basis of the incident power density.

Among the effects above 100 mW/cm^2 are subcutaneous burns and death--effects which clearly can be related to a health hazard. Most of them are thermally related.

The effects which fall in the range from 25 to 100 mW/cm^2 include cardiovascular function changes, decreased serum growth, etc., as well as teratological effects. This certainly indicates a hazard for certain segments of the population, the young and the old with cardiovascular problems, although it is not a clear hazard for the general population. It is probably a thermally significant level.

Table 1 shows the different types of effects observed below 25 mW/cm^2 : hematological effects, behavior changes, EEG disturbances, systemic effects, cellular effects, and several subcategories under those. This brings into question whether the effect is a hazard. It also is not clear whether this area is thermal or not. Dr. Galloway has made the arbitrary distinction of saying above the 100 mW/cm^2 level is hyperthermic, but the rate of temperature elevation is certainly not great; below 25 mW/cm^2 nothing is very clear. It is not clear that the effect is a hazard and whether this is a thermally significant level at local points.

We are faced, as far as the regulatory agencies are concerned, with two major uncertainties. First, are these reported effects the results of elevated local or whole-body temperature, allowing scaling to other frequencies, or is there a direct interaction of the field with the membrane, molecule, etc.? Second, is the observed effect significant in terms of human health, or is it a transient phenomenon having no short-term significance? Overall, does an apparently insignificant effect cause stress to the system, resulting in a hazard from long-term occupational exposure?

Table 1

Power density mW/cm ²	Character of effects	EEG disturbance from power densities less than 25 mW/cm ²			
> 100	Clearly associated with hyperthermia, rapid rate of temperature increase	Animal	Frequency MHz	Power density mW/cm ²	Duration min
25 - 100	Hyperthermic, but rate of temperature increase less rapid	Rabbit	2950	5-30	Up to 120/day for 120 days
		Rat	3000	5	10*
< 25	May be subtle and not clearly related to acute exposure regimes	Rabbit	9300	0.7-2.3	5
		Mouse	3000	5	Up to 36*

Hematological changes from power densities less than 25 mW/cm ²				Systemic effects of power densities less than 25 mW/cm ²			
Type of effect: animal	Frequency MHz	Power density mW/cm ²	Duration min	Type of effect: animal/specimen	Frequency MHz	Power density mW/cm ²	Duration min
Increased lymphocytes:				Altered thyroid function:			
Dog	1285	2.0	28*	Rat	2450	15	360
Guinea pig	3000	3.5	90*	Rat	2450	20	240
Rabbits, guinea pig	3000	3.5	90*	Morphological change:			
Increased blast transforms:				Mouse	3000	2	145
Hamster	2450,9000	5-30	75	Rat	3000	10,20	60/day for 220 days
Rat	2950	0.5					
Immunological effects:				Altered blood-brain barrier:			
Mouse	2450	12 mW/g	90	Hamster	2450	10	120

Behavioral changes from power densities less than 25 mW/cm ²				Cellular effects of power densities less than 25 mW/cm ²			
Type of effect: animal	Frequency MHz	Power density mW/cm ²	Duration min	Type of effect: animal/specimen	Frequency MHz	Power density mW/cm ²	Duration min
Decreased stimulus control:				Metabolic disturbances:			
Rat	2860,9600	5-20	30	Wish cells	3000	5	30
				Rat	2700	0.005-0.01	10(10 exp)
				Rabbit	2950	3.5	Up to 120/day for 120 days
Avoidance:				Cell membrane changes:			
Rat	1200	0.2	120	Rabbit			
Mouse	2450	0.5 mW/gm	120	Granulocytes	3000	5	60
Decreased behavioral output:				Rabbit granulocytes & erythrocytes	3000	1,5,10	5-60
Rat	2450	15	900	Chromosome effects:			
Rat	2450	5	6600	Hamster & human	2450	20	
Monkey	1000	3&8	10-95	Human lymphocytes	2950	7.20	Up to 240
Increased behavioral output:							
Rat	3000	5	60				

*Exposure duration reported in days

This workshop has been organized to address this dilemma. The individual responsible for doing much of the work of the organization has been Dr. Whit Athey of the Bureau of Radiological Health.

DR. ATHEY: I would like to elaborate on the effects that have been reported, and give an example of one type of question with which we are concerned. Several investigators have exposed mice and other animals to microwave levels of 10 mW/cm² and observed an increase in responsiveness to mitogen stimulation of lymphocytes, and other immunological effects. The levels that were used did not seem to significantly increase the core temperature, although it was also clear that it was not an insignificant thermal load that was being placed on the system. We are faced with the question: is this an electric field effect or is it a thermal effect? Similar effects using other stressors such as sound have been observed. Could this type of effect be a general response to stress? Navy researchers may have found that this particular effect, increased responsiveness to mitogen stimulation, is strain-specific for mice. Although this is not a clear indication, it suggests that something more fundamental than a general stress response might be taking place.

It is probably true that in examining any microwave effects research one of the first things to be considered is how well the temperature was controlled. However, even if all microwave effects were found to have a thermal basis, should this make us feel any more comfortable from a safety standpoint when microwaves clearly can deposit thermal energy in ways not easily duplicated? We have asked our participants to share their knowledge and experience in thermal physiology. We want to know what effects we can expect from heat alone, regardless of the source. One microwave modification to this charge we asked of them is consideration of the possibility that the thermal energy be nonuniformly deposited.

We have two guests from the John B. Pierce Foundation Laboratory in New Haven. Dr. Eleanor Adair did her undergraduate work at Mount Holyoke and her doctoral work in psychology and physics at the University of Wisconsin. She is an Associate Fellow at the Pierce Lab and is also a Senior Research Associate at Yale University. She has been active in the area of behavioral thermal regulation.

Dr. Jan Stolwijk is the Associate Director of the Pierce Laboratory. He studied at the universities at Utrecht and Wageningen in Holland. He has worked in the area of modeling and in some experimental areas as well.

Dr. Steve Horvath is Director of the Institute of Environmental Stress at the University of California at Santa Barbara. Dr. Horvath received his doctorate at Harvard in medical sciences and has been interested in all aspects of stress.

Dr. Richard Dassler received his doctorate at Michigan State University in physiology. He is Special Assistant to the (Navy) Surgeon General for Environmental Physiology and Surface Medicine. He also heads the Fleet Occupational Safety and Health under the President's Board of Inspection and Survey.

Dr. Francis Dukes-Dobos is from the NIOSH lab in Cincinnati where he is the Chief of the Physiology and Ergonomics Branch.

We will begin with a tutorial on thermal physiology led by Dr. Stolwijk and Dr. Adair. Later, Dr. Adair will discuss the question of local versus generalized heating. Dr. Dukes-Dobos will speak on philosophies of standard setting for hot environments and his experiences in working on the NIOSH recommendations to OSHA of standards for thermal stress. However, the fundamental question - what level of thermal stress is significant for safety and health considerations - will take into consideration the fact that thermal stress might not be uniformly applied.

filling amount to do it, and, that is like a hemorrhage in terms of losing it. The blood does not return to the heart, and, the heart responds negatively. There are systems, and this flattening system that Dr. Dukes-Dobos discussed is the most easily available in the gut. One can get 300 - 400 ml of blood out of the system without too much difficulty. It will close down the circulation some, but normally it is excess circulation anyway. But eventually the excess will be used up and then difficulties may result.

If one stands and becomes too hot, fainting and falling will occur making the blood redistribute itself, and reviving the individual. There are a number of different mechanisms. We are normally used to redistributing blood all the time, and drinking enough to make sure we do not dehydrate. Dehydration would be just as bad. From the point of view of blood redistribution, dehydration due to sweating and not drinking is as bad as anything that could happen due to redistribution or local heating.

MR. CURTIS: What sort of tissue recovery time is necessary if one fractionates the thermal dose? What period of time should you allow for the tissue to recover before insulting it again with another thermal dose?

DR. STOLWIJK: That would break down into two categories. One would be if you stay within physiological temperatures up to 42 °C or so. If you go at 45 °C and denature something, the repair process takes longer and is uncertain. I think that would be a factor that would depend on how high you went, how long, and how much damage was actually done.

There is something to be learned from the few cases that have been worked up rather carefully from heat stroke deaths. There was an article in Aerospace Medicine not too long ago, concerning several cases and the circumstances of people in heat stroke deaths, and what damages were found after death. In the case of heat stroke, the kidney and liver were almost always the places where the greatest damage occurred. Then, even if they were cooled down, they would often not recover because some of the repair mechanism would not return.

When cancer specialists do fever therapy, essentially, they go to 42 °C. One of the theories by which they explain this is that enzymes that repair single DNA breaks are inactivated. If these are inactivated, then the breaks do not get repaired and there is much more damage and less radiation is needed. The 42 °C would be necessary for one-half hour to inactivate the repair enzymes. If that is so, several other enzymes are probably being hurt.

Our knowledge of that range of temperature is very poor. When somebody goes into a heat stroke death, that is a medical emergency and no one measures anything. When fever therapy was conducted, other signs were also observed. Most of the people who conducted the therapy are now retired. So we are faced with developing a new generation who know about how to raise a patient's body temperature to 42 °C, and bring them back safely.

If it is at all possible, we should be learning from these experiences because there are going to be mishaps and we at least ought to learn from them. These people will be very carefully followed-up when they go into the hyperthermia before or after irradiation, and it would be unfortunate if we did not learn a little more about the dangers of these hyperthermic temperatures. I am attempting to work something out in that direction. However, most of the people who are responsible in hyperthermic therapy are either physicists who work for the radiologists, or they are radiologists and their prime objective is not this kind of research, or they are surgeons.

DR. GLASER: Is stimulation of the immunologic system another area of concern?

DR. STOLWIJK: We do not know much about it. However, it is quite clear that the host defense mechanisms do not benefit from a close call with heat stroke.

DR. DASSLER: This is absolutely true, although the data have not been published as yet. In animal studies where controls unfortunately had a form of heat stroke, it was found that after the animals supposedly recovered from the stroke they had lost their immune response.

DR. STOLWIJK: But generalized infection is not an unusual sequel to heat stroke either.

DR. DASSLER: That is correct. But this could be very important for other purposes.

DR. ELDER: I read recently that in some studies where cancer patients' temperatures are increased, that there is a spread of the cancer rather than a beneficial effect. Whether or not that is a result of compromised immunodefense system or because more cells sloughed off due to higher temperature, I don't know.

DR. DASSLER: If you are thinking whole body, you can think of massive vasodilation.

DR. STOLWIJK: But, the vasodilation that is seen in individual tissues when you heat them up to 42 °C is accompanied by an enormous increase in blood flow locally. If the whole body is heated, one cannot get that much. Something else breaks down, and I do not know what does not get enough. That is probably one of the reasons why 42 °C is a very unhappy temperature to be at.

DR. ELDER: In Dr. Adair's experiment the monkey is perceiving and responding to 6 to 8 mW/cm². Can you extrapolate any health hazard or can you extrapolate from that data?

DR. STOLWIJK: Almost anything will make that monkey want to change the temperature nuance. For 5 mW/cm² I think he changed his preferred ambient temperature by 1 °C or so. He will do the same thing if he gets excited. If he moves around a lot, he will change it more. It is within the range of physiological variability. But the fact that it is there does not indict it yet because if it is thermal, then it is indistinguishable from many other ways of inducing a thermal load for which the organism is equipped. The 10 mW/cm² is within the range of normal experience. I feel that it is a good thing to have and probably leaves quite a large margin of safety for uncertainties.

DR. GLASER: At 2450 MHz?

DR. STOLWIJK: No. If it has been concentrated somewhere in funny ways, I have not heard about it.

MR. CURTIS: One of the things that are available in OSHA are case studies, workers' particular complaints, or physician complaints telling workers they should not work in certain places because of the RF exposure. Maybe I can give you a couple of these symptoms and maybe you could comment on whether or not they could possibly be attributed to a thermal mechanism: ovarian cysts, micarriages, a funny taste in the mouth, tingling sensation in the eyes.

DR. DASSLER: Eyes?

MR. CURTIS: In the eyes. Now again, we may be talking about extremely high levels here.

DR. STOLWIJK: Did the individual with the bad taste in the mouth have a lot of dental bridgework?

MR. CURTIS: That would have to be verified. These are guys climbing radio towers while they are energized. They reported their eyes "didn't feel funny anymore," but the bad taste in the mouth remained.

DR. GLASER: Sandy eyes, or sand in the eyes, a feeling of dry eyes.

DR. STOLWIJK: This is something that also occurs in workers with infrared and is related to a defect in the lacrimal glands. It is a dry eye phenomenon and is cause to remove workers from that sort of environment. They are going to be very displeased with that environment and continue complaining, and there is nothing that can be done about it. There is some small number of workers that has a problem with insufficient tearing. If they do not get enough tearing, they become sensitive to a fireplace or similar things.

MR. CURTIS: That could possibly be a thermal effect.

DR. STOLWIJK: Yes.

MR. CURTIS: Some of these workers actually feel very hot where they might have a metal pin implanted in their leg or something of that nature.

DR. STOLWIJK: Yes.

MR. CURTIS: Or an implanted copper IUD.

DR. STOLWIJK: Yes. At that frequency you would expect anomalies of that nature around metals. That could easily happen. At that frequency pacemakers and similar things are even more likely to develop serious problems.

MR. CURTIS: If a man can actually feel his legs getting warmed up, are we talking about the sensing mechanism? Would that also be internal besides being external?

DR. STOLWIJK: The sensing mechanisms are not only in the skin, but also subcutaneous. There may also be sensing mechanisms in the veins that drain the legs. People have found sensitivities there. It could be in a number of different ways. If it is a metal pin the entire length of the pin would get warm due to its own very high conductivity. So any sensors anywhere along the way would signal that.

MR. SWICORD: It might be interesting to hear your ideas about the investigations that are needed to answer some of the questions raised today.

DR. STOLWIJK: I think that some description of the biochemical and enzymatic changes that result from temperatures that are above physiological would be useful. Unless this activity becomes the client for it, I do not think it is going to get done because there is no other client for it and it does not pose sufficient fundamental challenge so that the basic research operations would be interested. It is also quite clear that if theoretical models report that there are heavy concentrations at lower frequencies, then experimental confirmation of that would be heavily indicative because those are troublesome. We are much more used to having high levels of that in various places. It has been around longer. If these concentrations really do occur, why did we not get complaints around induction heating and capacitive heating units which must have leaked?

DR. DUKES-DUBOS: We did get those.

DR. STOLWIJK: Oh, do you get those?

DR. DUKES-DOBOS: Particularly sexual libido.

DR. STOLWIJK: But, you should have received those complaints in the 1950's before any of this became controversial. You should have had these complaints and they must be on record somewhere.

MR. JANES: It is apparently a geometrical resonance phenomenon, so it occurs roughly at frequencies or wavelengths that are about half the body length.

DR. STOLWIJK: It is a standing wave problem.

MR. JANES: It is an antenna problem.

MR. SWICORD: Three have been complaints. Many of them read "I get warm around this," "I feel warmth in my knees or in my ankles," this type of thing.

DR. STOLWIJK: I think that probably calls for reexamination of the entire diathermy situation from that point of view because wasn't there a lot of diathermy in the 1940's and 1950's that was at 40 Mc?

MR. SWICORD: 27.13 MHz.

DR. DUKES-DOBOS: It is known how much of the power of RF radiation is converted to heat if it is absorbed in the body, the tissue?

MR. SWICORD: There are theoretical models that give some indication.

DR. DUKES-DOBOS: Has it been absolutely measured in tissues?

MR. SWICORD: Yes, in phantom models.

DR. GLASER: Carcasses?

MR. SWICORD: Yes. But I have been thinking in terms of Lehman's data on diathermy exposure in which he actually inserted temperature probes into volunteers' legs and measured the temperature.

DR. STOLWIJK: In general, one must be very careful of measurements in phantoms and carcasses because blood flow is such a major factor.

DR. DUKES-DOBOS: Are there data on how fast the heat is eliminated or spread into the body when it is concentrated in one spot? If you have radiation on one part of the body, what is the speed of distribution of this heat in the whole body?

MR. SWICORD: That is one area about which we know very little.

DR. DUKES-DOBOS: This is a critical question because one knows that this heat is spreading faster in the body than most current measurements which are done with oral temperature, which is not an intolerable idea. The dehydration is nothing but weighing the body before and after work.

MR. JANES: Almost all of this work is done either on phantoms or animal surrogates. Outside of just looking at medical diathermy and these case studies, no one is doing any work on humans at all that I am aware of. Are you?

MR. SWICORD: No.

DR. GLASER: Many of the animal experiments were done with anesthetized animals in which the circulatory system has been altered.

DR. STOLWIJK: It is still better than not having any circulatory system at all. There is an enormous amount of heat transport within the body that occurs even without any adaptive change. There is much more motion or potential motion. Of course, the gradients are not very high, so the amount of heat transported in the body is not very high. However, the minute that a gradient is raised, the amount of heat that can be transported, that always is potentially transported, suddenly increases with the gradient and one becomes aware that there is an enormous amount of heat moving around. That is the kind of thing with which

one needs to be concerned. I would specifically worry about those tissues that act like your phantoms and do not have perfusion.

MR. JANES: The phantom has been done to identify sites of absorption and give an input distribution. Then the heat input is handled by model systems.

DR. DUKES-DUBOS: It is important to clarify the point that if a person is exercising at a certain level in a certain environment of heat and then microwave radiation is added to that person whether this would alter the inflection point or the upper limit of prescriptive zone.

MR. CURTIS: The man climbing a 900-foot tower has a lot of exercise involved plus a lot of exposure.

DR. DUKES-DUBOS: But there is no experimental evidence of how much this phenomenon would change. It may be that the person's perspiration is increased and he may be able to maintain thermoregulation. Yet, it may also be that if this heat is added by microwave into the deep tissues, such a maintenance of deep-body temperature will not occur because immediately the body temperature will increase. That is a very important consideration because it would nullify the concept which assumes that up to a certain level, man is able to maintain equilibrium.

MR. JANES: It would be a very interesting calculation to take the data presented today concerning the zones in terms of units that are convertible to watts per kilogram, and substitute that as a radiofrequency or radio wave load and see what is computed in terms of watts per kilogram for zones. Then one might ask the question of whether that is analogous to an environmental heat load or to a deep tissue load, and where it stands with respect to standards.

DR. STOLWIJK: The loads we were showing you by comparison, are enormous. They are many hundreds of watts.

MR. JANES: But roughly, in watts per kilogram?

DR. STOLWIJK: Five watts per kilogram, concentrated in the muscle mass first and then distributed over to the rest of the body.

MR. JANES: Is it prescriptive zone?

DR. STOLWIJK: Yes.

DR. DUKES-DOBOS: This is because the basic metabolism is raised as much as 3 to 5 times.

DR. DASSLER: In the case of your pole climbers, or the outside worker, be very careful with the laboratory data because one may forget the thermal radiation effect that exists outdoors. This can be rather extensive in an industrial setting as well. It has to be included, and indoors in a blast furnace type situation, it could be a very serious thing.

MR. JANES: I don't think this discussion should be ended with the workshop.

DR. ATHEY: I think you are right. This dialogue between the disciplines should continue.

(The meeting was concluded)

DR. JAN A. J. STOLWIJK

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I think it was only 2 weeks ago that I was, in another context, talking to people who wanted to heat particular tissues, using microwaves and ultrasound, and reminding them about the difficulties of doing so. I guess we are taking the opposite tack here and trying to see to what extent this can happen inadvertently.

Man is a homeotherm who is equipped with behavioral and physiological mechanisms to maintain his body temperature within very narrow ranges. The most normal stress that he will encounter is twofold -- through differing environmental temperatures and different internal heat productions due to metabolic effects.

The range of temperatures over which man can actually deal with his thermal environment is very wide indeed (Fig. 1). As the NASA people have shown, man can operate in temperatures between -200 to $+150$ $^{\circ}\text{C}$. We see only a very narrow range where straightforward physiological responses, involuntary responses, can deal with the effects of these temperatures. There are also a number of behavioral adjustments that go outside this

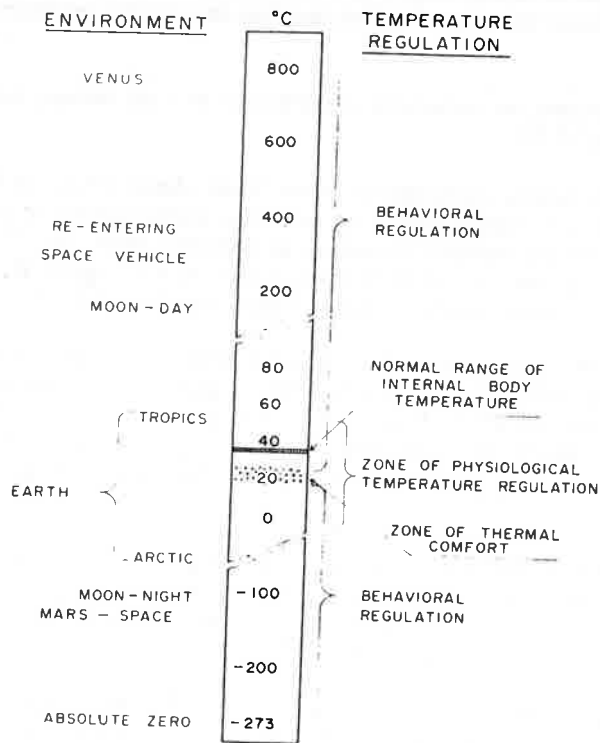


Figure 1. Environmental temperatures and corresponding zones of human thermoregulatory activity indicating the limited capacities of physiological thermoregulation ($0-50$ $^{\circ}\text{C}$) relative to behavioral control. Environments with extreme temperatures (left) and human responses (right).

range. There is a very narrow range, indeed, described as the zone of thermal comfort, in which neither behavioral nor physiological adjustment is necessary and where no voluntary or involuntary responses are needed. It is a temperature that we prefer. We can go on either side of that temperature relying on physiological mechanisms, involuntary mechanisms which are always seen as unpleasant and which we try to avoid as much as possible. We try to avoid this by means of behavior adjustments such as changes in clothing or changes in thermostat settings or in other means by which we affect the microclimate immediately around us. But man is able for short periods, and with the expenditure of lots of energy, to exist in a very wide range of temperatures.

The temperatures that we find inside the body - the central temperature, the deep-body temperature - fall into this category. Skin temperatures are usually lower than these by several degrees Celsius. During any one day the deep-body temperature might be at any one position between 36.3 and 37.3 °C. There is actually a diurnal variation which is built-in. In most people this means that their central temperature ranges from a high point in the afternoon or the early evening which is as much as .9 degrees higher than the lowest temperature that would occur early in the morning. This is not a result of a normal drift, but is actually a result of the system wanting to be at different temperatures, and regulating the body temperature at different temperatures.

As we exercise and produce large amounts of heat, or enter into very hot environments, there will be a tendency for this temperature to go up. The control system will limit this rise as much as possible to levels that are somewhere between 38 and 39 °C. It is relatively unusual to go much above that for we also develop increasing problems when the strain goes over 39 °C.

In heavy cold exposure, or exposure underwater in cold water, internal temperature can go down to 36 or even 35 °C.

Skin temperatures rarely increase to more than about 37 or 38 °C. The reason is that this temperature rise will cause sweating, and the evaporation of sweat will tend to limit the skin temperature on the outside to ranges somewhere between 37 and 38 °C. Local temperature, of course, can be raised to temperatures much higher than this by immersion in hot water, by exposure to radiation, or by contact with hot objects.

Another very important limit to remember is that a temperature of 45 °C always elicits pain. This is a very uniform value, and elicits pain in any tissue that you heat to that temperature. The value of 45 °C begins in either the skin or in tissues other than skin. The 45 °C is also a point where thermal denaturation begins to become serious and, as a result, thermal pain is also a very good protective mechanism against local tissue destruction through heating.

People who do not have pain sensation - and there are some who lack pain sensation in the skin - very routinely and very easily accumulate lots of burns over a lifetime and will look very scarred. It is a very necessary thing for us to be able to reflexively withdraw from contact with surfaces that are hotter than 45 °C.

If you expose nude individuals to ambient temperatures in the range of 12 to 48 °C over a period of time such that more or less these quasi-states are achieved, responses are obtained as indicated in (figure unavailable). The figure shows a large number of subjects that have been exposed to this, and the mean skin temperature at 12 °C ambient temperature will be down in the 26 °C range. As the ambient temperature increases, the steady-state skin temperature acquired at equilibrium will rise. This also shows that at an ambient temperature of 48 °C, which corresponds to about 120 °F, the skin temperature is 36 °C. The flattening here is due to extensive sweating which tends to keep the skin temperature down if the sweat can evaporate.

(Figures for the remainder of Dr. Stolwijk's opening remarks are unavailable.)

There are a number of internal locations where deep-body temperature can be conveniently measured. The rectal temperature is a convenient one for that, although it has some disadvantages because it is a relatively slowly varying one. It does not respond very rapidly to changes in body-heat content. The tympanic membrane has been advocated because it is relatively accessible, is deep in the ear canal, and is rapidly responding to a change in the state of body-heat content. The tympanic temperature over this ambient temperature range, varies from about 36.6 °C up to perhaps about 37.2 °C. All these experiments are in the resting state. Similarly, the rectal temperature tends to be a little higher than a tympanic temperature, and lies somewhere between 37.7 and 36.6 °C, depending on the particular individual and the particular experiment. However, there is no particular pattern recognizable. The rectal temperature stays remarkably constant over this entire range of ambient temperatures for people who are at rest.

If all the individual points are disregarded and we look at a more generalized version, the core temperature does not vary a great deal for the range of ambient temperature from 20 to 38 °C. It tends downward a little while we see that the skin temperature now goes down as low as 29 °C, and you can see these average responses to this.

You can also see how the body actually manages to maintain this constant temperature because three of the effector systems, three of the involuntary systems that are used by the body to maintain the body temperature, are actually shown in the way they express themselves in these environments. For a nude individual, thermal neutrality occurs somewhere between 28 and 30 °C, about 85 °F. This is the most comfortable temperature for a nude individual and the metabolic rate, which is constant at temperatures above this, begins to increase very slightly at ambient temperatures below. This is due to increased tensing of the muscles, and shivering, which is an involuntary way of increasing your own metabolic heat production to compensate for the increased heat loss that takes place at temperatures below thermal neutrality. In the temperatures above thermal neutrality, there is an increase in the evaporation rate, which means that the body begins to sweat and the evaporative heat loss that results from the evaporating sweat that is secreted over most or almost all of the skin area now compensates for the heat gain that occurs in temperatures above thermal neutrality. This also is a precisely graded response so that, in fact, the temperatures stay remarkably constant throughout.

There is yet a third mechanism which deals with the method by which the body rids itself of the metabolic heat that it produces even at rest. The average body at rest produces about 100 watts of heat, which must be eliminated. Much of that heat is produced in the brain, about 20 percent of the heat production. In other words, somewhere between 15 and 20 watts are being produced in the brain continuously, a little bit more when you are asleep than when you are awake. Most of the remainder is in the vital organs, the heart and the liver and other highly active organs in the trunk core. The 100 watts must be eliminated by conduction from the interior to the skin. That conduction is modulated by a convective factor which results from the blood bringing heat from the center of the core out to the skin. To the extent that there is skin-blood flow, it serves to take heat from the center, by-passing a conduction mechanism, directly out to the skin. If this skin-blood flow is increased, the efferent conductance of the effective heat conductance between the core and the skin can increase very rapidly. Here it is at a relatively low level; but above 28 °C (thermal neutrality), it begins to increase. As the central and skin temperatures rise, the conductance can reach very high values, although of course it is at a cost of having to produce the cardiac output to carry this heat around.

The mechanisms that are involved are diagrammatically presented. If the whole-body heat capacitance in an extremely schematic form is assumed, then this body temperature is sensed by thermal receptors. These thermal receptors are integrated in different places compared with some form of reference. Out of that integration sets of command signals are produced that reach out to the periphery from the brain. This integration occurs in the hypothalamus. Signals arise that either cause the muscles to go into shivering and increase the heat production, cause the sweat glands to secrete sweat, or cause the peripheral blood

vessels to change their caliber and, as a result, increase or decrease the blood flow to the skin. This changes the internal heat transfer, and the evaporative heat loss, or it might change the heat production.

There are two external stresses or exogenous stresses to the system. One is produced by exercise, which introduces an additional amount of heat production into the muscles, which now must be entered into the body heat capacitance. Or it is due to changes in the environmental temperature which can affect the system and stress it.

Here we see an example of an experiment that we use to study the effect of cold exposure on shivering. It is an attempt to study how much shivering we get for how much loss in central or skin temperature. Here is a subject who is in an environment of 10 °C. Because he is nude, his skin temperature drops substantially below the initial value of 35 °C here. The internal temperature is measured as the esophageal temperature. That is also a favorite quick-responding temperature, and, probably the best measure of internal temperature that one can have. A thermocouple is introduced into the esophagus and placed as close to but opposite the heat in the esophagus. As a result, it measures the temperature of the blood, a value very closely approximating the temperature leaving the heart in the aorta. Thus, we have a very rapidly responding temperature which can give very quick responses.

Now this subject is left for 60 minutes in this cold environment. He begins to shiver a little bit all through this, increasing somewhat at this point. But in the meantime, his legs and his arms are cooling down, and a lot of the tissues directly under the skin are cooling down. His peripheral blood flow during this period is very low because the skin circulation is almost completely closed down in an attempt by the body to conserve heat.

At this point, the situation changes because we make him do a little exercise. We could leave him at rest, which is what the present exposure is, or we could set him into free pedaling on a bicycle, or we can make him actually do a little work on a bicycle, 30 or 60 watts of external work. Under those conditions, the cooled-down muscles ask to be perfused with warm blood. Of course, the blood that returns ultimately from these cold muscles is cooled down substantially, and there are rapid decreases in the internal temperature, the esophageal temperature, that occur as a result of the onset of the exercise. As a result of the decrease in temperature, we can also see that the shivering activity here increases substantially. As the internal temperature begins to rise, especially during the heavy exercise, the shivering activity diminishes quite rapidly. This is the sort of experiment conducted to study cold.

This is an attempt to find out what the relationship is between the internal temperature and the level of shivering by doing such experiments with the mean skin temperature here shown as a fixed value. In other words, all of these points were taken at the same identical skin temperature. By dropping the internal temperature, the involuntary heat production greatly increases as a result of shivering.

If this process can be reversed, the internal temperature can be maintained at a relatively constant value. You see here the same subject, and his heat production as a function of skin temperature. All these points have a corresponding value here; and you can see that even at a relatively elevated central temperature, if the skin temperature is lowered enough the involuntary heat production will increase.

Another example of measurements that can and have been made, and that can now satisfactorily be predicted is that if we look at the central temperature and integrate it with the appropriate response, which in man we can do because we know the relative ratio and the relative sensitivity for the skin receptors and the central receptors, and, if we calculate what that central drive is at any one time, we can see how much sweating and how much evaporative heat loss corresponds to a given increase in the central drive or in what amounts to the mean body temperature or the body's method of determining what the mean body temperature is.

Here we show what the response looks like for a group of men and a group of women. This gives you an idea that we have gone fairly far in determining which physiological outcomes are from rises in temperature in different parts of the body. The parts that we are particularly interested in here, of course, are the receptors in the brain and the receptors in the skin. Under specialized circumstances, sensors in other parts of the body also participate in this undertaking. But most of these experiments are conducted with animals.

Using another measurement from such experiments, the plot of the forearm blood flow, which is done by a method which basically, in part, occludes the arm and allows the arterial inflow to occur but temporarily stops the venous outflow, one can find that the total volume of the arm increases over a short period of time, and can measure this increase in volume by means of a strain gauge. This provides a method to measure how much skin-blood flow and muscle-blood flow actually goes into the arm in terms of milliliters, 100 ml/min. At relatively low temperatures or normal temperatures, this blood flow is very low. Either one of these can be used at the moment for the difference between these two is irrelevant. As this temperature increases, there is considerable increase in the amount of arm-blood flow, so that ultimately it reaches 5 l/min and can reach a fairly high level, if the body temperatures go up.

As an example, the normal blood flow to the skin for the whole body is somewhere on the order of 250 ml/min. In extreme forms of heating of the entire body, the total skin-blood flow can reach 3 or 4 l/min a level which is approaching the whole cardiac output in the resting state (nearly 5 l/min). It is, on the other hand, not possible to increase the skin-blood flow to much more than 4 l/min because of special problems that arise concerning pooling and loss of venous return. The blood goes out to the skin, but a lot of it does not return. It then appears as if there is a loss in total blood volume. As a result, there is a limit to how much blood can actually be sent out to the skin. Normally, it does not exceed 4 l/min. If you try to do more than that, then you will find that people will faint or develop other problems.

Another experiment highlights another form of exposure that can reach very high levels. We have here three bouts of exercise done by an individual. In the three bouts of exercise, we measured primarily the metabolic rate, the heat loss due to evaporation of sweat. The bouts of exercise were about 30 minutes in each case with the experiment conducted at 10 °C. Thus, before we start the exercise, the subject is cooled down substantially. He is shivering and he has a total heat production of about 120 W/m², which is fairly severe shivering because the normal heat production is about 40 W/m², and is reduced after the bouts of exercise. The bout of exercise requires an extra heat production and an extra metabolic expenditure. As the body warms up, the total level of heat production decreases because the shivering component diminishes. At this point, the body has warmed up enough so that the subject is beginning to sweat a little bit. He is trying to dump heat now instead of trying to make more heat. During the remainder of this period, he cools down over this rest period so that he begins to shiver again. Now he is working at a much higher level. Note that the level at which he is now working is somewhere on the order of 200 W/m², a reasonably high level of power. This rise again accounts for the work being done. There is a decrease in work as well as a simultaneous decrease in sweating. The subject returns to basal, and has warmed up to such an extent that he remains at basal even in this cold period in between. Next, he is asked to work at a total metabolic rate of 500 W/m². Because the subject is a man with a surface area of 2 m², he is now producing heat at the rate of 1000 W. At the end of the 30-minute bout, he is actually losing heat at the rate of 250 W/m² through the evaporation of sweat, although he is nude in an environment of 10 °C.

All through these various experiences, the subject is able to maintain his body temperature within a very narrow range.

People will not voluntarily seek these exposures unless they are somehow rewarded because there are some discomforts associated with them. One way to determine how

people react to such exposure is by measuring the conductance of the palm of their hand. The palm conductance is a sensitive indicator of the blood flow that occurs to the skin. When exposed to the cold, the palm conductance drops, there is no inherent heat production in the hand. When the palm conductance drops, the hand very quickly adopts the ambient temperature. Because exposure to the cold causes the loss of blood flow the hand temperature very quickly goes to ambient and at 10 °C is a very unpleasant experience.

The subjects were asked for a proportional discomfort estimate as a function of palm conductance. One set of individuals feels one level as uncomfortable. Another set of individuals has only a very narrow range of palm conductance which is seen as comfortable. At this point, with high palm conductances, the discomfort is no longer due to the particular feeling in the hand, but to the fact that there is an associated level of sweating that causes the discomfort to occur.

If we examine how people regard the differences in central temperature, in central drive (integrated body temperature), we see that a group of males that was exposed to a series of environments at rest, state they are essentially comfortable or have a low level of discomfort anywhere but in this range. Women, characteristically, object more to a lowering of the body temperature and object less to a raising of the body temperature than men do. This is a characteristic response that is found very widely and has a number of reasons that are not relevant here. Whenever one experiences Level 2 or Level 3 discomfort, people attempt to relieve themselves of it. If they can escape it by halting activity, they will tend to do that. If they can get out of it by turning on the air conditioning or turning on the heat, then they will do that also. There is a considerable motivation to avoid anything that goes above this. So there is a built-in mechanism that through behavioral adjustment attempts to reduce the exposure.

There is another anticipatory kind of recognition of this. This diagram shows comfort reports as a function of internal and skin temperature - and any position on the diagram represents an average body heat content. People were exposed to varying transients of different temperatures. In other words they were moved from a very hot environment to a very cold environment. So the thing that is relevant about this whole slide is that if you have somebody in this zone here he almost finds himself to be comfortable since you find all these open circles here. You find, however, there are also open circles all the way out here, which is a very cool internal temperature and also a relatively cool skin temperature. All of a sudden, going from this point and moving a person to another position you find that they vote themselves comfortable. The reason is that the only way this can happen is by moving them into a warmer environment. Even if one is cold, once one is moved into a warmer environment the tendency is to over-report the comfort resulting from it and to under-report how uncomfortable you were before. There is a similar mechanism that operates out here. If a person is forced to move in order to raise his internal temperature, thus elevating skin temperature, the minute he is exposed to a cool environment which drops his skin temperature but not his internal temperature, he immediately reports comfort because he is moving toward the center of this overall graph. There is a very clear anticipatory reporting that adjusts for how we are going to feel in a little while rather than how we happen to be feeling right at the very moment.

One of the ways in which the strain can be measured is by considering the effect of body temperature on the heart rate, keeping all other things constant. A set of experiments were conducted in which people exercised at 25 percent of their maximum aerobic capacity, working reasonably hard but not terribly hard, in a variety of different environments. If this is done in a relatively cool environment - as measured by an effective temperature index combining the total effective temperature of the environment, including the radiant, and the convective and the conductive components as well as the air velocity - one can see that when the same amount of work, 25 percent of the maximum aerobic capacity, is done in a range of different environmental temperatures, it results in an increased heart rate. Because, depending on the individual, 160 or 180 is an undesirable heart rate, only a limited strain can actually be accommodated.

Similarly, an attempt to actually account for that heart rate as a function of the mean body temperature is prevented. As mean body temperature begins to approach 39 °C heart rates become relatively high and approach a limit as to what can actually be accommodated. However, this is at a relatively high level of internal body temperature and effective temperature. These increases in heart rate are, of course, also associated with a relatively higher level of sweating, and a relatively increased wetness of the skin, which is also recognized as contributing to discomfort. The warm discomfort increases more or less with the effective ambient temperature, and is also predictably related to the mean body temperature.

These are results of the experiments that we do with man. Dr. Adair will go into some detail on animal experimentation as well as behavioral experimentation in animals. Then we will discuss mathematical modeling, the physiological responses for whole-body heating and cooling as well as for local heating and cooling.

DR. JUSTESEN: You indicated that pain thresholds, presumably referent to the human are near 45 °C. This is contrary to my experience in terms of a well-tuned thermistor, running water over my own hands and increasing the temperature. But I realize I may have an aberrant subject here. It also is contrary to what I have read about cat skin temperature pain thresholds existing at about 56 or 57 °C. Would you comment on that please?

DR. STOLWIJK: The difficulty one faces when running water over the skin, is that you can measure the water temperature but not your skin temperature. Thus, one will find what seems to be a higher threshold under those conditions than if you actually measured skin temperature.

In the case of the cat or any animal, it depends on how you heat it, how long you heat it, and how anesthetized the cat is or how you have otherwise persuaded the cat to sit still for this.

DR. JUSTESEN: I am referring to Kenshalow's study which involved living, awake animals.

DR. STOLWIJK: The pain threshold in animals, as far as it has been looked at in manners where the skin temperature is known, the 45 °C holds. But, if one has relatively short exposures with heat transfers that are not precisely described, then you can get quite wide variations in terms of the temperatures.

DR. JUSTESEN: Would you characterize then, the differences in the zone of discomfort? Is that, somewhere between 37 and 45 °C? And then above 45 °C one comes into the zone of pain?

DR. STOLWIJK: No, pain is a very different kind - you will never report discomfort from having your hand alone at a temperature anywhere between 30 and 44 °C. You note that it has a temperature, but it does not particularly produce a discomfort. But the discomfort sensation that you get from your thermal state is quite diffuse and really requires that you have an integrated response that involves the whole skin. Pain, on the other hand, can be produced on 1 mm² of skin and it is just as effective as if it affected a much larger area. So it has a different quality to it.

DR. GLASER: I was struck by the differences in the behavior or the responses between the sexes. Is it relevant perhaps to our interpretation of other experiments that might be felt to be thermal-stress related?

DR. STOLWIJK: Well, the difference between individuals in general, quite apart from male and female, in the appreciation of discomfort is fairly substantial. So are, by the way, the ability of individuals to respond physiologically to a rise in temperature or to increased workloads.

The major factor that you probably need to consider is the state of physical fitness of the individual. If one can generalize to that extent, I would say that anybody who is physically fit will be more likely to object to the heat and heat exposures, and be more tolerant of cold exposures. Anybody who is physically not fit will tolerate relatively high temperatures and will be very intolerant of a reduction in temperature.

DR. HORVATH: But that is only at rest.

DR. STOLWIJK: Yes.

DR. HORVATH: I think the distinction has to be made that this does not apply to people who are working in those environments. The more fit individual does better in the hot environment working.

DR. STOLWIJK: What basically occurs is that the people who are not very physically fit tend to need a relatively high body temperature rise to produce the necessary sweat level that they need in order to dissipate the heat they produce. Associated with that are other consequences that make one not feel well. People who are not very physically fit tend to vasoconstrict very quickly when placed in a cool environment. Of course, that means that some segments of their body temperature will go down; some parts of the skin temperature will go down very rapidly and will seem painful and unpleasant. Whereas, people who are physically fit tend to not vasoconstrict very much or very quickly when they are exposed to a cool environment.

But these are generalizations and are somewhat different when you work. Of course, there is also a level of preferring not to be in a particular environment, and one's ability to cope with it is another factor. In other words, if one begins to sweat very quickly in a warm environment after a little bit of work, then your clothes begin to stick very quickly, more quickly than somebody who doesn't begin to sweat so soon. There are a number of other factors that can create the whole gestalt of being uncomfortable.

DR. GLASER: Are there significant differences between the ratio of surface area to height or mass between sexes?

DR. STOLWIJK: The surface area-to-mass ratios are not radically different. There is, of course, a difference in the total mass which is not noticeable.

DR. HORVATH: The major difference, actually, is in the amount of fat. Females, adult females, vary in fat from 24 to 35 percent; whereas, a male in the same age range will vary from about 14 to about 18 percent. So one of the major factors is the amount of subcutaneous and other fat. It is unknown what the distribution of fat has done to this response. But certainly we do know that there is a difference in the amount of fat.

Probably the more important difference is the remarkable difference in terms of the age of the individual. So far, of course, we have considered the young-adult, college male who has nothing much else to do since he has to spend 4 years in college and serve as a subject. But, in actuality, the biggest problem resides in those women who are premenarche and post-menopausal and probably the same is true for males although not as much is known about males. However, this is probably the major factor.

There is another point that should be brought out. In actuality, we have exposed humans to much more severe environments than Dr. Stolwijk is talking about. I have put them down as low as -60 °F without any clothes to see how long they tolerate it. I have put them as high as 180 °F to see what happens there. So I think we have evidence on a lot of other temperatures besides the relatively small range of temperatures that we are talking about now, and I think that should definitely be kept in mind. Our information on the ability of the human being to respond to extremes of temperature is fairly well-known, although we tend to emphasize this normal pattern of difference which is hardly significant, I think. All we have to do is put on some more clothes or take off some at these normal temperatures. But it is at extremes where we see the way in which the organism responds.

DR. STOLWIJK: The body heat storage, of course, gets one over these very extreme humps that Dr. Horvath is dealing with. In other words, if you go to very low temperatures, if you limit the amount of time, then you can deal with that. Depending on how well you insulate, or whether you insulate or not, the relationship between your immediate environment and the body temperature is due to changes in body heat content, and can be accommodated in a variety of different configurations.

DR. BOGGS: Thus, other considerations such as age that we have just been talking about are more significant than male/female difference?

DR. STOLWIJK: I think I mentioned there is a great deal of variability in the whole population. We found there is another form of self-selection that takes place when acquiring subjects for experiments because they tend to be fitter. You tend to self-select fitter individuals. We did find, however, not too long ago one young woman, a medical student, who was essentially poikilothermic, with no ability to have any involuntary responses at all. She just basically did not react and had relied on behavioral regulation and on storage practically all her life. She also was, of course, not particularly active in sports or any thing like that. One finds that with age, change in physical activity, and other physiological adaptations, changes and deficits, there is a wide variety of responses. We would undoubtedly have to consider some of those that are lacking a lot of responses that we consider normal. The people that you see here are among the people who are best able to deal with thermal and exercise stresses of any you will encounter.

DR. HORVATH: I think the differences between males and females are not really as great as anybody wishes to imagine. The main trouble previously has been that the investigators, before our group, who started studying females made a serious mistake. We probably know more about females, at least in their reactions to hot and cold environments, than anybody. The absolute working capacity of a female is about 20 percent less than that of a male. Most investigators, having inadequate tools available to them, worked all subjects at the same rate, so that a poor female was not working at 26 percent but probably at 50 percent of her capacity. Therefore, much of the early work, I would say 99 percent, until about 1973 was worthless in terms of evaluating the responses of males versus females. But, now that we have apparently fully appreciated the fact that things need to be considered in a relative way instead of at an absolute, constant level, I think it is quite obvious that there is not any real difference between males and females. In fact, I think females do better than males. I believe the evidence is accumulating to indicate that males are not really as accomplished as they think they are.

DR. NEUDER: One of the slides shows that an individual was producing about 1000 watts over a period of 40 minutes. That is 5 times the metabolic rate, is that correct?

DR. STOLWIJK: No, it is about 12 times the basal - 12 to 15 times.

DR. NEUDER: Could you describe the reaction of that individual in doing that?

DR. STOLWIJK: He is tired.

DR. NEUDER: Other than just being physically exhausted.

DR. STOLWIJK: Thirty minutes later he feels fine.

DR. HORVATH: We have run people at 20 times their level. Twelve is a minimal amount of work for somebody in good condition, for that is only 50 percent of his capacity for 8 hours, and at 50 percent you can work for 6 to 7 hours without any trouble. For those of us sitting in chairs, it is a great effort. But for people who are accustomed to this, it is nothing at all.

MR. SWICORD: I am a little confused concerning the internal temperatures, particularly during the periods of extreme cold and heat. Are we still regulating within a fairly reasonable temperature?

DR. STOLWIJK: In general, one would find that internal temperatures that, without fever, are going to 41 or 42 °C would be very difficult to deal with for almost all individuals - would be dangerous, for that matter - and temperatures below 34 to 35 °C would be difficult to recover from without help from the outside.

DR. DASSLER: Over the range that you are talking about, he is regulating.

DR. STOLWIJK: Yes, the things Dr. Horvath describes, with very low or very high temperatures, are things one will not tolerate in a steady state kind of adaptation. One now relies on thermal mass to deal with that. In other words, it is a tolerance problem and there is not a steady state. There is no attempt or capability for dealing with it when you go very far out.

DR. ADAIR: You are then outside the zone of physiological adaptation.

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Many experiments are conducted on animals because, obviously, there are many procedures that one cannot perform on human subjects. The neurophysiology and neuro-anatomy underlying the basic thermoregulatory system will be discussed. I will also include a discussion of how neurophysiological knowledge has aided in the study of some of the underlying thermoregulatory mechanisms in animals and, therefore, in men. The neuro-physiological experiments have provided a cue in that they have led to the appropriate portions of the central nervous system to investigate, as far as their import for thermoregulatory capability is concerned.

I will spend a good deal of time discussing localized heat deposition in various parts of the body, primarily in locations in the central nervous system and elsewhere, and what we have learned about the functioning of the organism that allows it to regulate its body temperature in response to such local heat deposition.

Finally, I will, with a type of local heating device, return to the human subject. Figures 1 and 2 are of paintings that used to hang on the wall in Dr. James Hardy's laboratory at the Pierce Foundation. Figure 1 refers to the control systems for human temperature regulation. It depicts the temperature sensation on the skin and the impulses going up the spinothalamic tracts to the brain stem. It shows the major cold and warmth sensing areas in the anterior portion of the brain stem as well as the mechanisms for the various effector responses (shivering, vasomotor, sudomotor) and the control centers for respiration and vasomotion. The hormonal influences are diagrammed here as well.

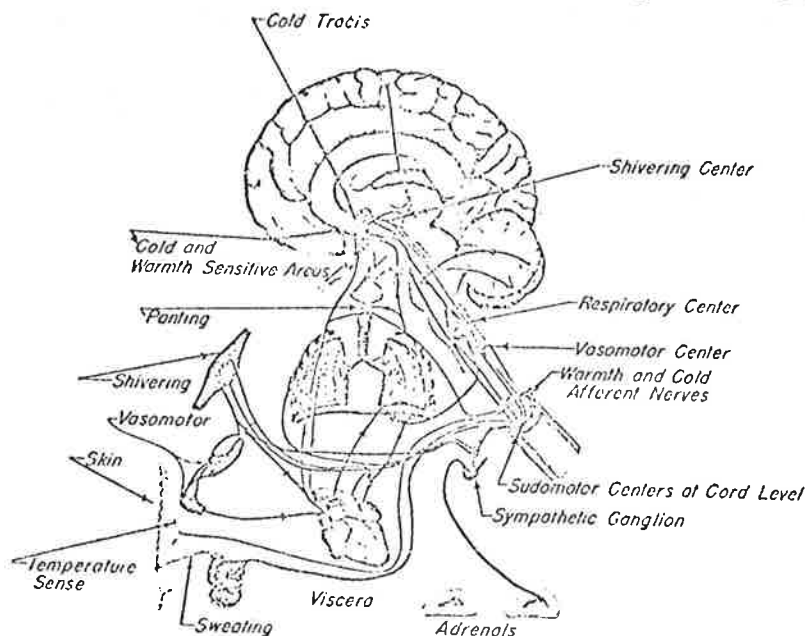


Figure 1. Schematic diagram of the temperature regulating system. (From Hardy: Les Concepts de Cl. Bernard sur le milieu interieur. Copyright: College de France, Place Marcelin Berthelot, 75005 Paris - Permission granted to reprint.)

Figure 2 (not available) refers to a few historical matters. In the last century physiologists began to realize that certain kinds of lesions in the central nervous system, particularly in the brain, had rather strong import on the ability of the animal to regulate its body temperature when exposed to cold or warm environments. Over the years, through careful lesion experiments, physiologists were able to determine that a portion of the anterior hypothalamus seemed to act as a central thermostat. Around 1915, Barbour, working in Germany, implanted a rather primitive device in this anterior hypothalamic area by which he could locally heat and cool the tissue there. He made some observations that we still make today. If you heat this anterior portion of the brain stem, the organism will respond as though it is hot all over. The organism will vasodilate, it will pant if it is a panting animal, or sweat if it is a sweating animal. In effect, it will immediately begin to lose body heat to the environment. On the other hand, if you cool this anterior hypothalamic area, the opposite will occur. The animal will vasoconstrict, piloerect, and will begin to shiver if the cooling is maintained long enough.

This kind of experimental result led the neurophysiologists to suspect that there must be some kind of special neurons, at least in this part of the central nervous system and perhaps in others, that might respond to temperature changes in their immediate vicinity. The first and now classic experiments were done at the Pierce Foundation by Dr. Terno Nakayama, and his first results are shown in Figure 3.

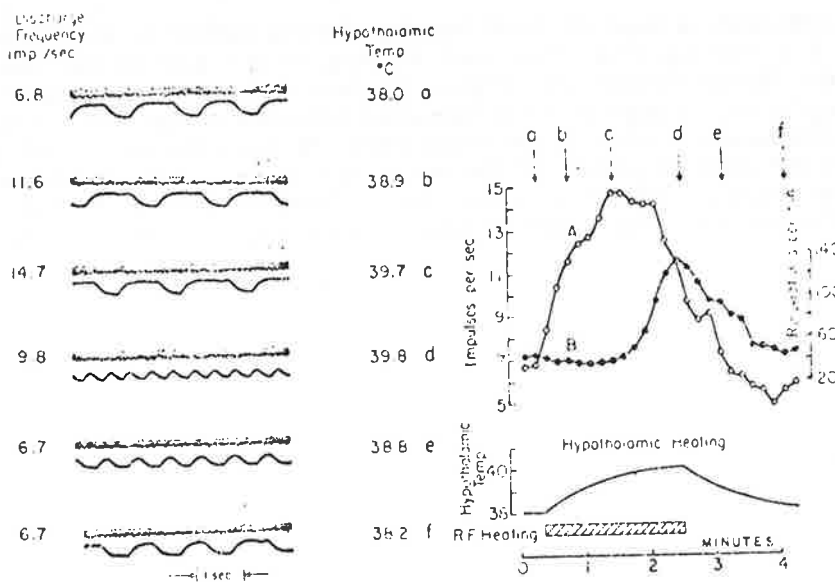


Figure 3. Changes in frequency of discharge of neuron in preoptic region and respiration rate with 3 mc heating. Effect of local rf heating of anterior hypothalamus on A: electric activity of single neuron; B: respiration. (From: Nakayama, Eisenman, and Hardy: Single Unit Activity of Anterior Hypothalamus During Local Heating, Science 134:560-561 (March 25, 1961). Copyright 1961 by the American Association for the Advancement of Science.)

Here we have a cat who has in his anterior brain an implanted radiofrequency device which we call a thermode by which Nakayama could alter the temperature of the tissue locally. Microelectrodes were implanted in this same vicinity, along with a thermocouple device for measuring the changes in the tissue temperature. Nakayama then measured the

firing rate of individual neurons in this area as a function of the local temperature produced by the tissue thermode.

This depicts the basic experiment. Once Nakayama had located a neuron that was firing at a regular rate, he produced a temperature rise in the anterior hypothalamic tissue for 2 or 3 minutes. A change in the rate of firing of this particular neuron was directly related to the temperature imposed upon the area. To the left are sample tracings, discharge frequency of the neurons at specific hypothalamic temperatures. This indicates how the records were taken. To the right is a summary of the impulses per second from this neuron as a function of the temperature of the local tissue.

Nakayama also measured the respiratory frequency of the animal and saw that it also varied in a regular manner. As the tissue heated up and the neuron began to fire maximally, the respiratory frequency increased (which, of course, would begin to rid the body of excess heat).

Nakayama and others have made many measurements of such neurons and described a wide variety of such neural elements. Figure 4 shows recordings of neurons taken from the anterior hypothalamic preoptic area of the dog by Hellon. Shown are temperature response functions for many different heat-sensitive neurons. These neurons are all regarded as temperature sensors. The firing rate is directly related to the increase in temperature of the tissue in which they are located. We believe, then, that these are the direct sensors of temperature change in the brain as it reflects changes in the central blood temperature.

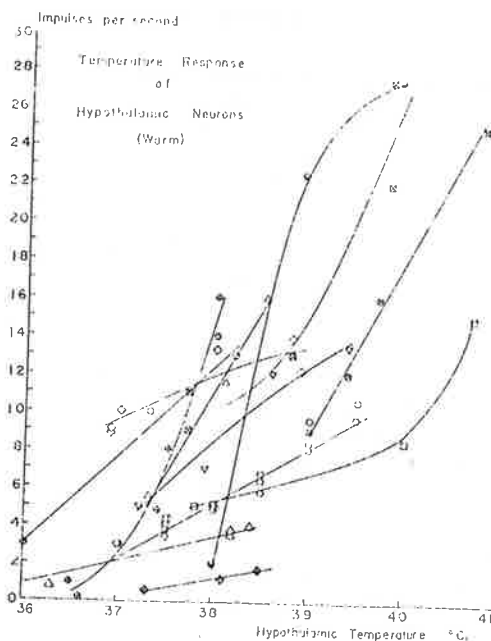


Figure 4. Impulse versus hypothalamic temperature for thermally responsive <<Warm>> units of the preoptic region of the dog. (From: Hardy, Hellon, Sutherland: *J Physiol (Lond)* 175:242-253 (1964). Permission granted to reprint.)

These neurons are usually described in terms of their Q_{10} , which is an index of the change in response rate or rate of firing over a 10 °C temperature interval. Ordinarily, a

neuron that has a Q_{10} of greater than 2 is considered to be temperature sensitive. Any neuron that has a Q_{10} of less than 2 would be essentially temperature insensitive. One has to make sure that one knows not only the Q_{10} of such an event but also the context in which it was measured. For example, if one has a neuron that fires at 30 °C at 2 impulses per second, and at 40 °C fires at 6 impulses per second, it has a Q_{10} of 3. But that is not really very temperature sensitive. This neuron is "down in the mud" and may not even be functioning properly. On the other hand, if a neuron is located that is firing at 20 impulses per second at 30 °C, and 60 impulses per second at 40 °C, it also has a Q_{10} of 3 but is truly temperature sensitive. That is one " Q_{10} caution." Another " Q_{10} caution" would be to observe that the index is determined over a 10 °C temperature range. Some investigators take a rate change over less than a 10 °C temperature range and then extrapolate on the basis of presumed linearity of response, which may not necessarily be the case.

Figure 5 shows some examples of cold-sensitive neurons also taken from the anterior hypothalamus of the dog. There are many more warm-sensitive neurons and this tends to parallel the functions one derives from cold and warm sensors on the skin. Much of the cutaneous work has been done by Dr. Hensel and Dr. Kenshalo. We find that warm-sensitive neurons have a much higher slope than those that are sensitive to cold. This seems to be generally true throughout the nervous system.

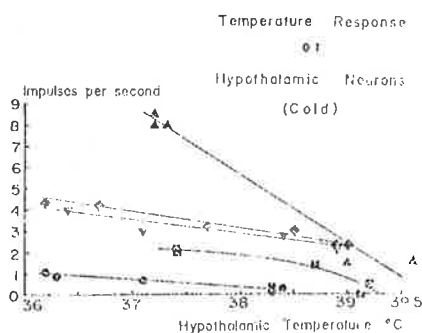


Figure 5. Steady-state firing rates and hypothalamic temperatures of <<cold>> cells of the preoptic region. Each symbol represents one neuron. (From: Hardy, Hellon, Sutherland: J Physiol (Lond) 175: 242-253 (1964). Permission granted to reprint.)

The anterior hypothalamus is by no means the only area where such temperature-sensitive neurons exist. Although it is probably the primary temperature-sensing area in the central nervous system, such temperature-sensitive neurons have been found in many other areas: in the posterior hypothalamus, the septum, in the motor cortex, in the midbrain reticular formation, the medulla, the full length of the spinal cord, and in various parts of the deep viscera. It turns out that these sensors in the various areas interact, as is shown in Figure 6 which shows an experiment recording the temperature of a neuron in the anterior hypothalamic area and measuring its firing rate over time. During the experiment, temperature was changed not only in the preoptic area, but also in the posterior hypothalamus by means of a tube running the length of the cord and perfused with water of controlled temperature. The neuron in Figure 6 responds to temperature changes, particularly in the preoptic area. It is sensitive to warming in the preoptic area, but it also even more sensitive to cooling of the posterior hypothalamus and warming of the spinal cord.

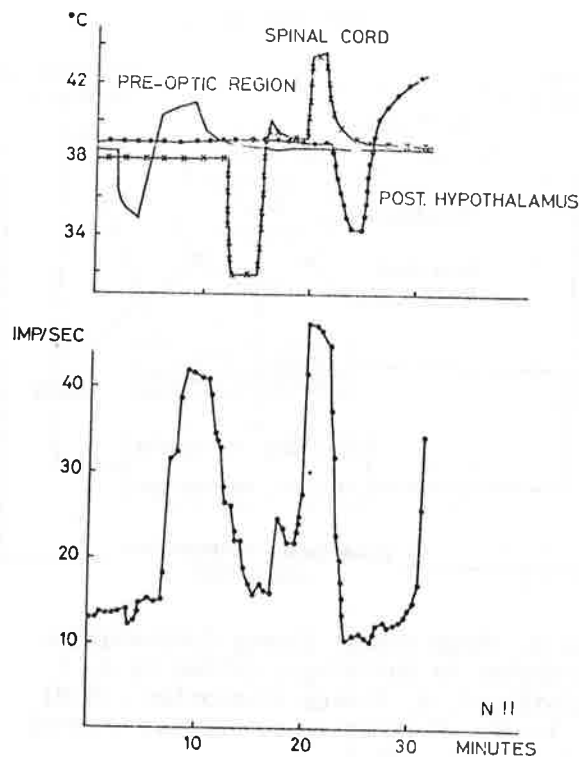


Figure 6. Units (no. 11) responding to local heating in preoptic region posterior hypothalamus and spinal canal. (From: Wunnenberg and Hardy: J Appl Physiol 33:547-552 (1972). Permission granted to reprint-The American Physiological Society.)

Figure 7 (not available) gives a quick view of the kinds of neurons that have been recorded from the anterior hypothalamic preoptic area and the detected influence of these three areas on the response rate of these various kinds of neurons. It is difficult to make sense out of such a complex system, but it is very clear that the main point is that many different temperature-sensitive areas throughout the central nervous system may have input into this anterior hypothalamic controlling or integrating center.

Figure 8 shows Dr. Hardy's most recent flow diagram of thermoregulatory control. It displays, primarily, the input sites to the central integrator that gives the command signal for thermoregulation. The skin has direct input and also provides information to the sensory cortex about the sensations of warmth and cold in the periphery. Also indicated are some of the specific regions in the interior of the body that are probably most important for the generation of afferent signals into this integrating system. We have then the integrated signal or command signal for thermoregulation, and the various physiological responses. We also have a second loop in this system that relates to the behavior of the organism that regulates the skin/air interface or the microclimate within which the organism lives. Temperature sensations derived from the skin and the body core will lead to behavioral regulation of the environmental temperature. Also sensations of discomfort that arise from the physiological reactions, as well as from the integrated signal, will lead to thermal motivation which in turn will involve behavioral thermoregulatory responses.

Physiologists and psychologists have used this experimental information to investigate the properties of the input signals to these two kinds of effector responses. The strategy

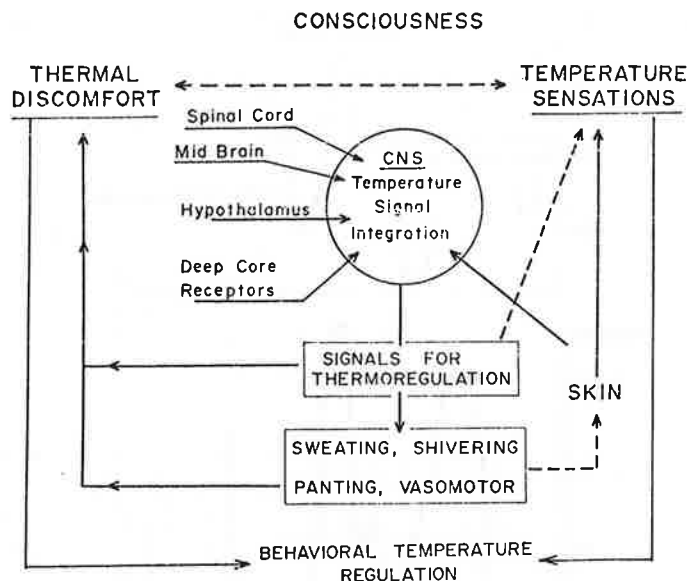


Figure 8. (From Hardy: Energy Conservation Strategies in Buildings; Edited by J. A. Stolwijk, J. B. Pierce Foundation (1978) pp. 14-37. Permission to reprint granted by J. A. Stolwijk.)

has been to invent small devices that can be implanted in various parts of the body in experimental animals, such that the local temperature in these areas can be raised or lowered at will. Dr. Ted Hammel devised one of the best of these devices, a thermode for implantation in the brain of experimental animals. The thermode is of the same character as an electrode or a chemitrode: it will heat or cool the tissue in which it is implanted. Basically, it consists of a sealed stainless steel tube lowered into the brain tissue under stereotaxic guidance to a specific structure. Then, during the experiment, a second concentric inner tube is inserted into the implanted one, and a temperature controlled fluid, usually water, is flushed through this system, forced into the inner tube and aspirated out the outer tube so that a rapid flow rate of the fluid through the system is achieved and thereby changes the temperature of this device most particularly at the tip. Hammel's original thermode system (Fig. 9) also included a special water circulator which is mounted on the head in his experimental animals. This provides for the appropriate distribution of the temperature controlled fluid through the thermode system.

In a large animal such as a dog, one of these devices certainly will not suffice to clamp the temperature of the tissue under investigation; usually 6 or 8 are needed. Also incorporated into the system are additional tubes which are not perfused with water but into which one can insert a very fine thermocouple to measure the changes in tissue temperature produced by the thermode array.

The thermode system arrangement of tubes and how the circulator system works is seen in Figure 10. Temperature controlled water is flushed into the circulator under pressure and is forced through the inner tube which is inserted in the implanted thermode. The fluid is then aspirated through a vacuum system out the outer tube and away. With such a system as this under 15 psi pressure, one can obtain a flow rate of fluid of 10 to 12 ml/min and thereby change the temperature of the tissue 6 or 7 °C/min.

I have brought with me a sample thermode system with the circulator and an implant from one of my monkeys. Visible are not only the connections from the circulator to the thermode but also connections to a second tube, a reentrant tube, into which we place a fine

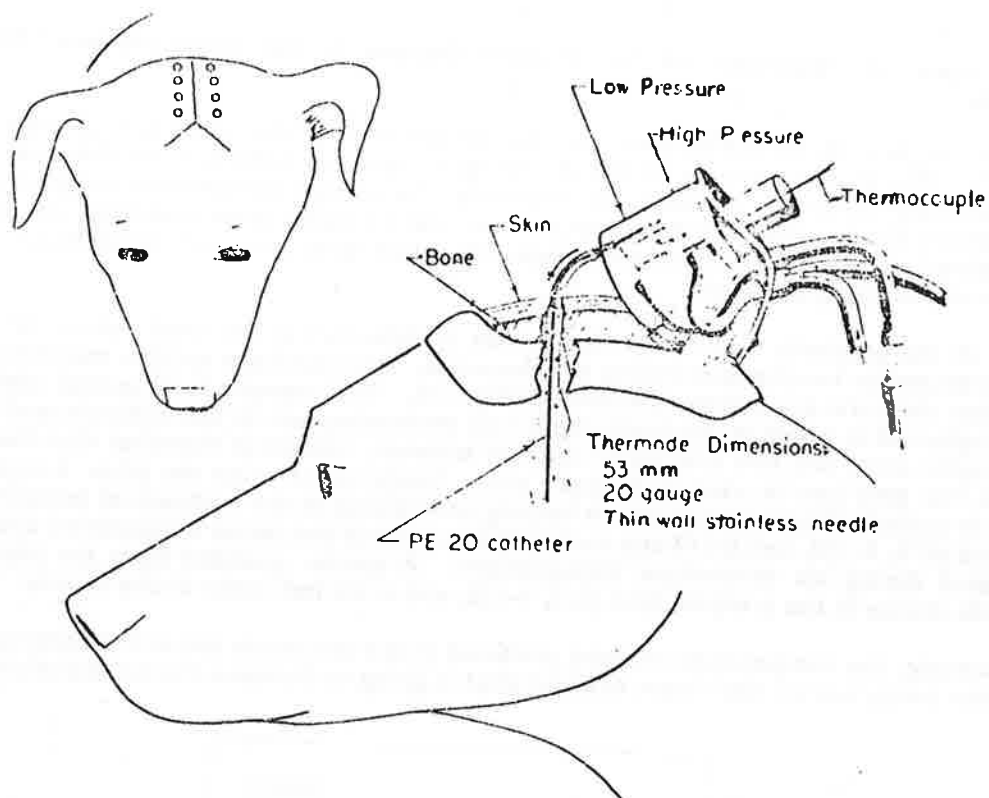


Figure 9. (From: Hammel, Andersen, Jackson, Hardy; ASD Technical Report 61-489 (December 1961) - Biomedical Laboratory, Aerospace Medical Laboratory, Aeronautical Systems Division, Air Force Systems Command, USAF, Wright-Patterson Air Force Base, Ohio.)

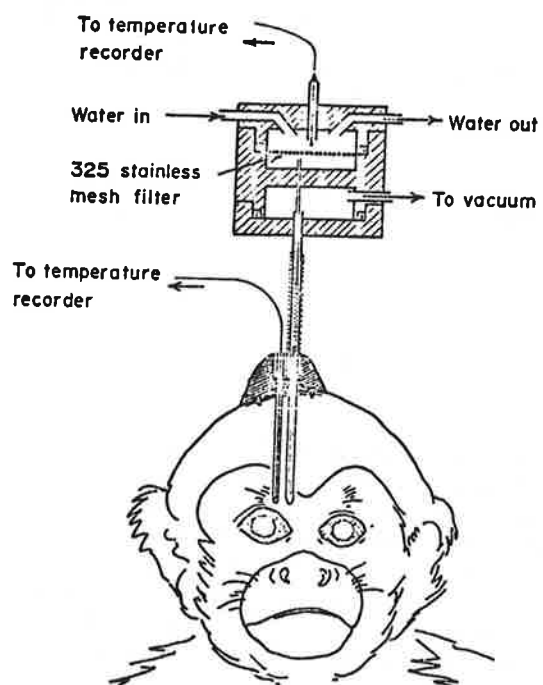


Figure 10.

thermocouple for measuring the temperature changes in the tissue produced by the thermode.

Normally, in such applications we vary the temperature of the tissue over a range of 34 to 43 °C. This extends outside of the physiological range of temperatures that the tissue would normally undergo. However, by extending the normal temperature range one can better derive the functional relationship between the variables under investigation. If one just confined oneself to a very narrow range, one might miss unique characteristics of the function one is trying to obtain.

One of the problems with such a device lies in determining the total volume of tissue that is affected by heating and cooling the thermode. One can make specific measurements at a given distance away from the device (Fig. 11). This represents an animal with four tubes implanted in a line in the brain stem; two thermodes, one in the midbrain and one in the preoptic area; and two additional tubes in between, spaced as shown so that the thermode in one area can be used to measure tissue temperature when the other thermode is heated or cooled. Figure 11 also shows heating and cooling of the midbrain at temperatures measured at 2, 4-1/2, and 6-1/2 mm away. It also depicts the rectal temperature change in the animal during his temperature displacement. A similar gradient from the implanted thermode device in the preoptic area at 2, 4-1/2, and 6-1/2 mm away is also shown.

Obviously, the temperature changes produced in the thermode are still affecting tissue 6-1/2 mm away, but we don't know exactly what is going on between the measured points.

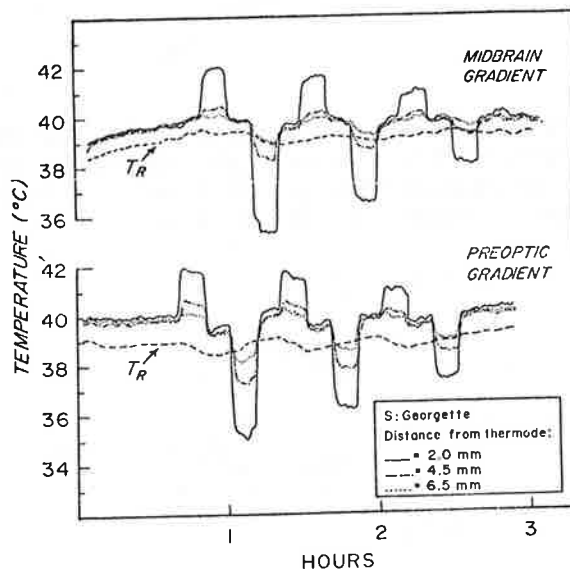


Figure 11.

Figure 12 gives the location of these two thermodes together with the other tubes in midsagittal brain section. Below you will see some simulated thermal gradients that we have computed based upon what we know about the tissues involved, their characteristics, the blood flow, their heat production, and so on. We have derived functional gradients that would be anticipated when, for example, the temperature of the thermode is increased 10 °C above the normal tissue temperature. One would not produce such a temperature change ordinarily in an experimental animal, but in a computerized simulation one derives some feeling for the steepness of the gradient in this manner.

SPEAKER: What is the scale?

DR. ADAIR: This is a millimeter scale. This figure shows a cross section through a squirrel monkey brain, and these are distances in millimeters from zero reference. This is from Emmers and Akert's stereotaxic atlas. The preoptic thermode is implanted here in the medial preoptic area, and the second thermode is in the midbrain. The vertical scale in the insert is the temperature of the brain tissue ($^{\circ}\text{C}$) in the computer simulation.

But, it is extremely difficult to make measurements of the volume of tissue affected and the exact extent or shape of the thermal gradient away from such a device.

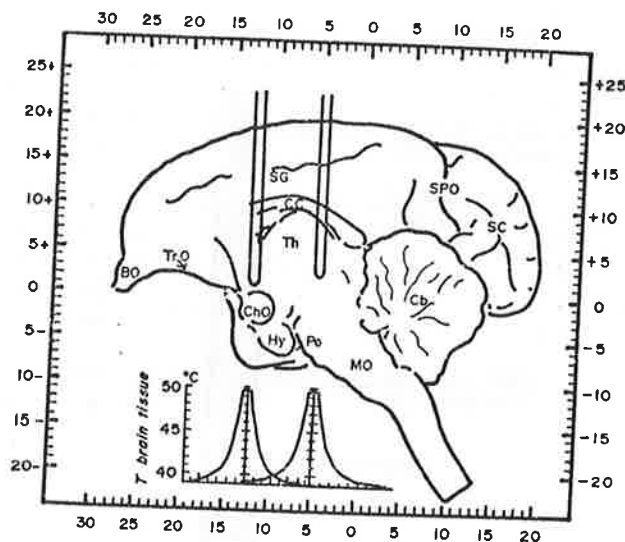


Figure 12.

Another variation on a thermode is the one shown in Figure 13 that we have used in our laboratory. It consists of a miniature electric heater built into a 26-gauge needle which then fits inside of a thermode implanted in the experimental animal. It is a replacement for the inner thermode system with the water perfusion.

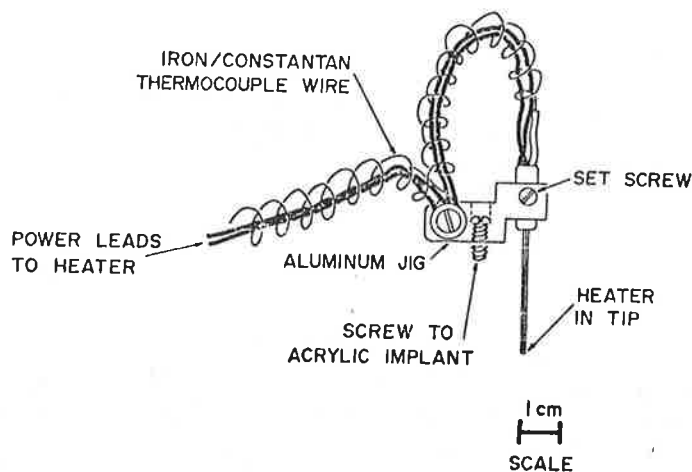


Figure 13.

Figure 14 is a diagram of the construction of the heater and the scale of the device. The heater itself is wound around a 16-gauge thermocouple. It consists of about 50 turns of high-resistance wire wound under a microscope and then imbedded in epoxy inside a .032-inch thin-

walled tube and the leads then carried out. At the time of the experiment the heater is slipped into the implanted thermode tube. With the little aluminum jig it is screwed down to the implant on the surface of the skull and held tightly in place. Of course, this can only be used for heating, and not cooling. We built this originally for some experiments in which we attempted to train experimental animals to turn the heat off when we turned it on. It is much easier and faster to do this electrically than with a water perfusion system.

MICROHEATER DESIGN

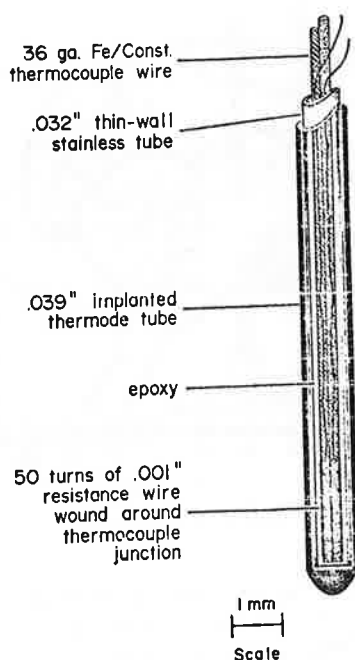


Figure 14.

Figure 15 gives some idea of the temperature changes on the surface of the implanted thermode tube. The abscissa represents the thermode going from its tip (left) to its top (right); and the bar shows the location of the heater within that tube. We welded thermocouple junctions on the outside of a thermode tube at the tip and at 5-mm intervals above that, so that we can measure a total of four temperatures.

We implanted this special thermode tube in an acute animal preparation. We then raised the temperature of the heater by specific amounts and measured the surface temperature of the thermode tube which was adjacent to the tissue. Those are the profiles in this figure, drawn in terms of the delta-T - that is, the displacement of the microheater temperature above the baseline level. The microheater is the thermocouple around which the heater coil is wound. Shown are functions for three temperature differences. These, then, are the thermode surface temperatures measured at the tip and at 5-mm intervals above the tip.

Figure 16 shows a step chart of the same devices set to about 53 °C. This is the temperature of the heater coil. The temperature of the preoptic tissue is measured 2 millimeters away by a thermocouple in a reentrant tube. One can see the rapid response of the preoptic tissue temperature to each heating and cooling segment of the record.

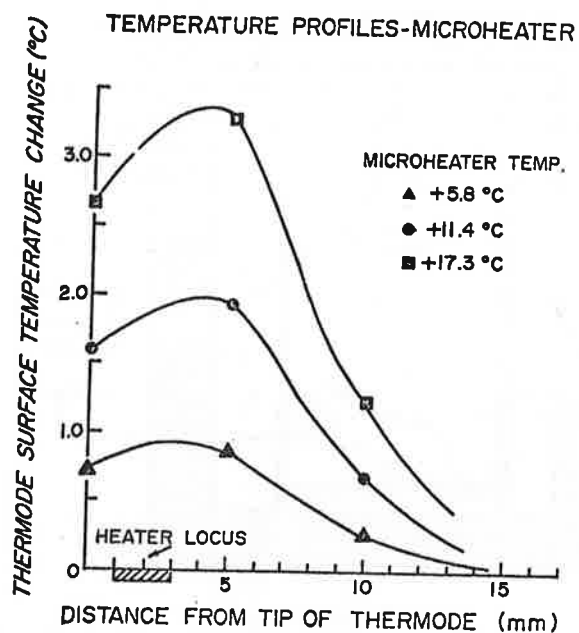


Figure 15.

These devices have been used in various experiments and next, I will discuss what we have been able to learn through localized heating and cooling of the junction of the anterior hypothalamic area of the brain in normal thermoregulation.

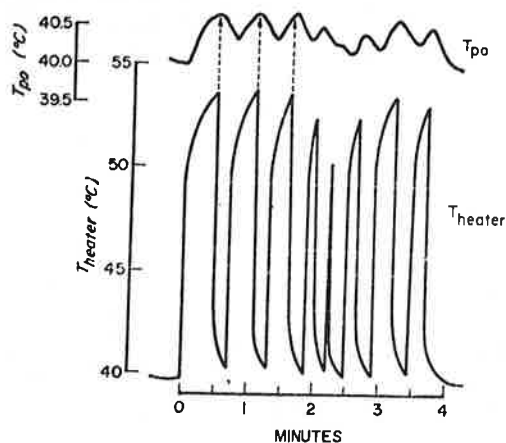


Figure 16.

Figure 17 shows the kind of apparatus that was first used by Weiss and Laties to study behavioral thermoregulation in rats. They trained an animal who was in a refrigerated chamber to press a lever (on some schedule) to obtain short bursts of radiant heat provided by an infrared heat lamp. Weiss and Laties did not heat or cool the brain tissue, but many other people have. Dorothy Murgatroyd at the Pierce Foundation did some of the earlier experiments in which she implanted thermodes in the anterior brain stem of rats and measured the number of times the animal would press the lever for infrared heat or cool air as a function of the temperature imposed upon the preoptic area by means of the thermode.

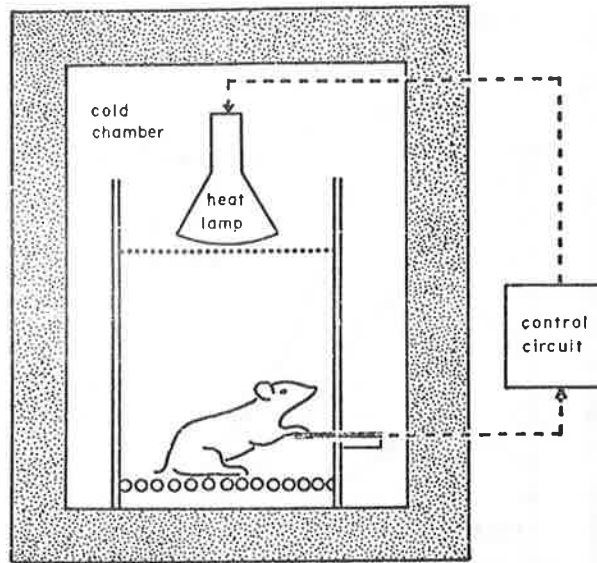


Figure 17.

We see in Figure 18 that when the animal is working for infrared heat, when the temperature of the hypothalamus is lowered below its normal level by about half a degree, the animal begins to work for more external heating. The animal behaves as though he is cold all over, while only a very small portion of his anterior hypothalamus is being cooled. We see an essentially linear functional relationship here between the temperature of the preoptic area and the rate at which the animal works for heat.

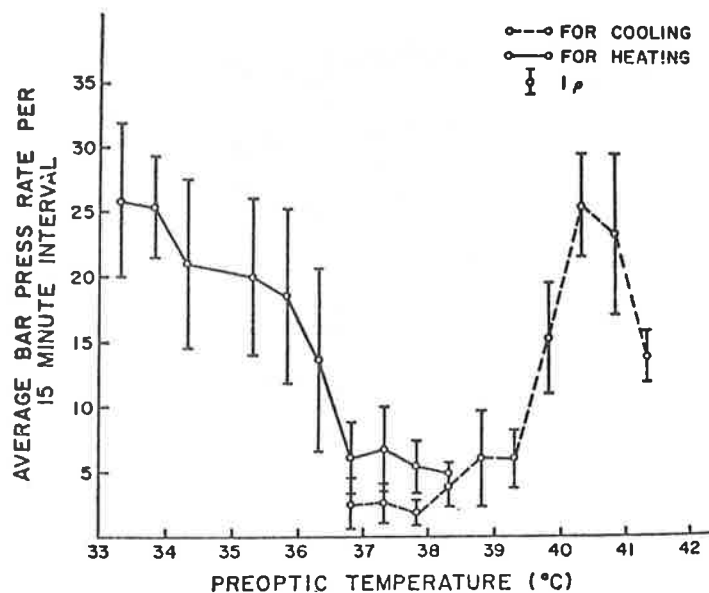


Figure 18. Average bar-press rate as a function of preoptic temperature. $N = 10$ animals. (From: Murgatroyd and Hardy; Physiological and Behavioral Temperature Regulation, Edited by Hardy, Gagge, and Stolwijk (1970) p. 880. Reprinted by courtesy of Charles C. Thomas, Publishers, Springfield, Ill.)

DR. JUSTESEN: What was the rate of payoff here?

DR. ADAIR: I believe it was 5 seconds of radiant heat.

DR. JUSTESEN: Per lever press?

DR. ADAIR: Per lever press, right. Lever presses that occurred during the heating interval did nothing.

For environmental cooling, Dr. Murgatroyd had an arrangement whereby the animal could receive a blast of cold air which, I believe, lasted 2 seconds for each lever press. It was a bit noxious and she had some problems with the cooling. But at any rate, the animal would then work for external cooling when the temperature of the preoptic area was heated essentially about the same, one-half a degree above the rat's normal preoptic temperature.

A great deal of my work at the Pierce Foundation has been this kind of study in which I have investigated, with a nonhuman primate, the same kind of functional relationships, and also probed various parts of the central nervous system, not just the preoptic area. I have a slightly different kind of test system. I was anxious not to become involved with the radiation-convection problem that Dr. Murgatroyd had, so I designed a complete convective system.

Figure 19 shows my original test chamber in which the animal is restrained in the small space and sits in a moving airstream. Temperature controlled air enters at the inlet by the feet, flows over the body, and exits behind the head. We have two air source chambers that provide the temperature controlled air that ventilates the chamber. One is set at a

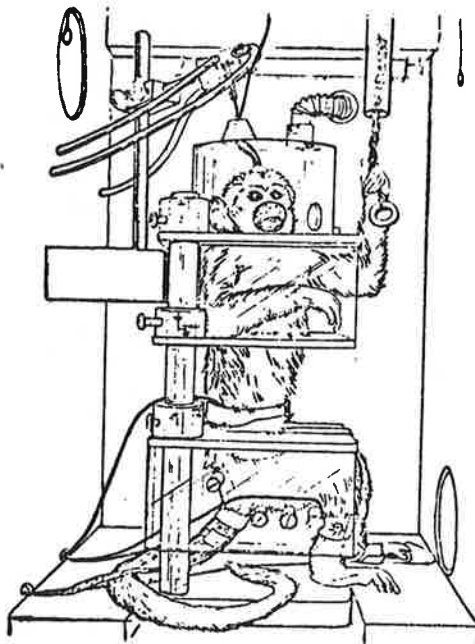


Figure 19. Diagram of a monkey in experimental apparatus. (From: Adair, J. Appl Physiol 40:694-700 (1976). Permission granted to reprint - The American Physiological Society.)

noxiously high level of about 55 °C, and the other at a noxiously low level of about 10 °C. The animal is trained either to work for timed reinforcements of one air temperature when he is exposed to the other, or is given complete control over the situation in such a way that every response he makes produces the other air temperature that is not at the moment flowing over his body. The animal's response is to pull the chain that hangs from above, and squirrel monkeys learn this very readily. After a few months of training, they will very accurately focus in on a time-averaged, preferred ambient temperature of about 35 or 36 °C. When an animal is so trained, we then implant it stereotaxically with thermodes in various parts of the brain stem.

This animal shows an implant and the connection to the circulator and the thermocouple to measure brain temperature changes.

One experiment involves an animal who is selecting his environmental temperature behaviorally (Fig. 20). Each time he pulls the chain, he operates valves in these air sources that change the temperature of the air that blows through his chamber. During the experiment we measure four skin temperatures: the abdomen, tail, leg and foot. We measure the rectal temperature, and the temperature of the hypothalamus as we change it by means of the thermode.

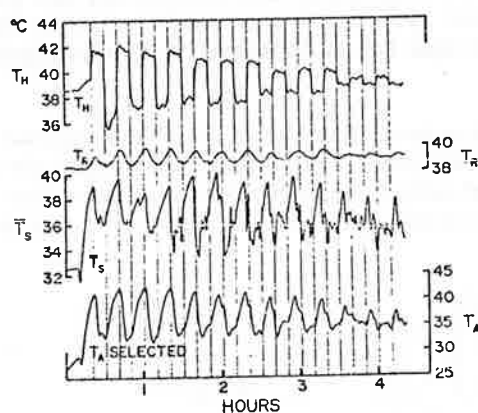


Figure 20. Typical experiment using Procedure A. (Records show changes in rectal temperature (T_R), mean skin temperature ($\bar{T}_S$), and air temperature (T_A) selected by one monkey when the hypothalamus (T_H) is heated and cooled every 10 min.) (From: Adair et al., *J Comp Physiol Psychol* 72:17-27 (1970) -Copyright (1970) by the American Psychological Association. Reprinted by permission.)

When the thermode is heated in the preoptic area, the animal immediately selects a cooler environment and his skin and rectal temperatures fall. Conversely, when we cool this area of the brain stem, the animal immediately selects a warmer environment, driving his skin and rectal temperatures up. This kind of relationship holds even though the displacements we make every 10 minutes in his preoptic temperature become of smaller and smaller magnitude.

A more quantitative way of looking at this relationship is shown in Figure 21 in which we plot the percentage of each of these 10-minute intervals - the animal selected the warmer of the two airstreams - as a function of the temperature of his anterior hypothalamus. We see that for brief (10 minute) displacements of preoptic temperature, there is a linear relationship between the percentage of time the animal sits in the warm air and his hypothalamic temperature. The second ordinate gives you the average temperature of the environment produced by the animal's behavioral change.

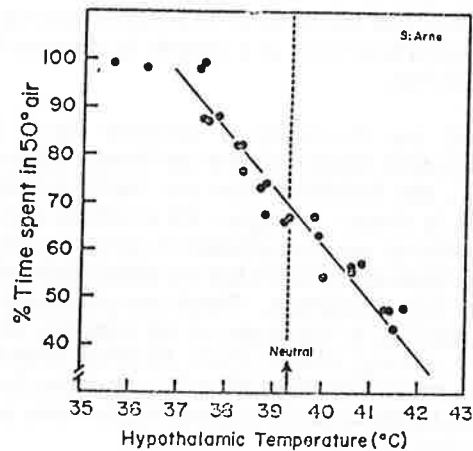


Figure 21. Behavioral analysis of experiment shown in Figure 20. (Percentage of each 10-min. interval 50° C. air was chosen is plotted as a function of hypothalamic temperature.) (From: Adair et al., J Comp Physiol Psychol 72:17-27 (1970) - Copyright (1970) by the American Psychological Association. Reprinted by permission.)

This becomes a little more complicated when we maintain a displaced hypothalamic temperature longer than for just a brief interval. We then begin to see some additional adjustments shown in Figure 22.

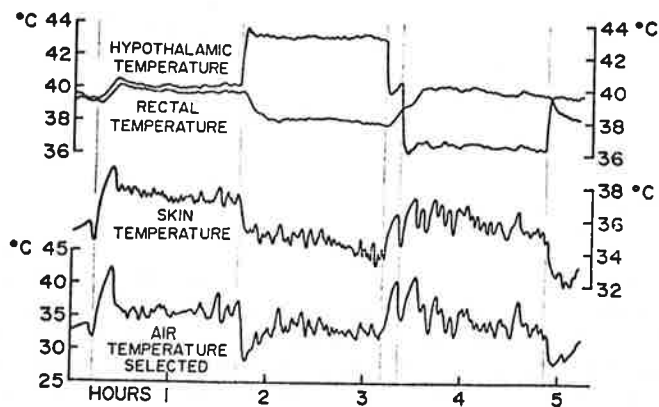


Figure 22.

Once again, the animal is selecting the temperature of his environment behaviorally, and we measure skin and rectal temperatures as well as the temperature of the hypothalamus. The initial "warm-up" is simply the animal elevating the air temperature when he first comes to the test chamber and this results from the fact that our colony room is kept at about 23 °C. The animal's preference is for a temperature of 35 °C. In the second segment we heat the thermode to about 43 °C and maintain that temperature for 90 minutes. The animal immediately lowers his chamber air temperature such that his skin temperatures fall, and his rectal temperature is driven to a new regulated level. This is maintained essentially constant throughout the duration of this hypothalamic temperature clamp. Note that the environmental temperature here is a couple of degrees below the level that he had chosen during the baseline period.

Now the temperature of the thermode is lowered for a 90-minute period to about 36.5 °C. The animal immediately warms up the air temperature, driving his skin and rectal temperatures up. However, the behavior does not hold up quite as well as it did for the hypothalamic heating. This is shown in Figure 23 which is a summary. This figure represents data from many experiments on five animals in terms of the mean rectal temperature, skin temperature, and air temperature selected by these animals as a function of temperature imposed in the anterior hypothalamus. These are all steady-state measurements taken at the end of an extended period, a minimum of 60 minutes, and after 90 minutes or even 2 hours. There is a very strong effect from heating above the normal hypothalamic temperature, which is in the region of 39 to 39.5 °C. But the function is not nearly so steep on the cold side. So, clearly, hypothalamic heating has a more potent effect than cooling on the behavioral thermoregulatory response.

There are many temperature-sensitive sites within the central nervous system, most particularly at the neuronal level, as well as interactions between these various sites on the signals that may be generated in the anterior hypothalamus. The effects of heating and cooling some of these other sites affects thermoregulatory behavior.

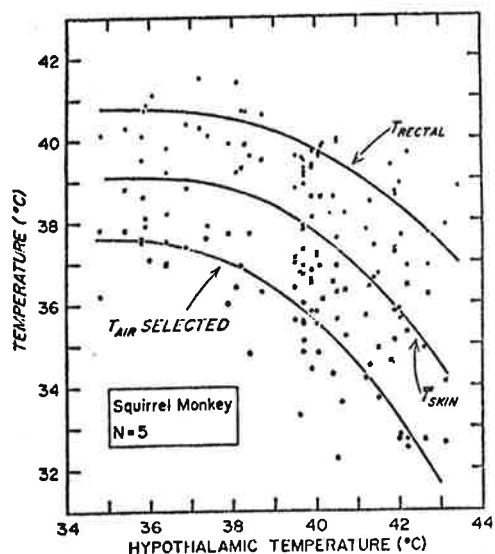


Figure 23. Steady-state functions representing the rectal temperature (●), weighted mean skin temperature (x), and air temperature selected (o) when the preoptic-hypothalamic temperature of 5 monkeys was displaced from neutral for 90 min. Each point is the mean temperature for the final 30 min. of the period. (From: Adair, E. Reprinted with permission from *Physiol Behav* 7:21-26 (1971), Copyright (1971) Pergamon Press, Ltd.)

Figure 24 is an example of what happens when you heat one or both of the preoptic areas. (We are still just dealing with the preoptic area in this experiment.) This animal is implanted bilaterally with thermodes and we change the temperature of one or the other, and then both. From the tracings to the left, one can see that when the right thermode is heated, the animal selects the cooler environment. When the left thermode is cooled, the animal selects a warm environment. When we oppose the two, the animal does nothing; the stimuli essentially cancel each other out.

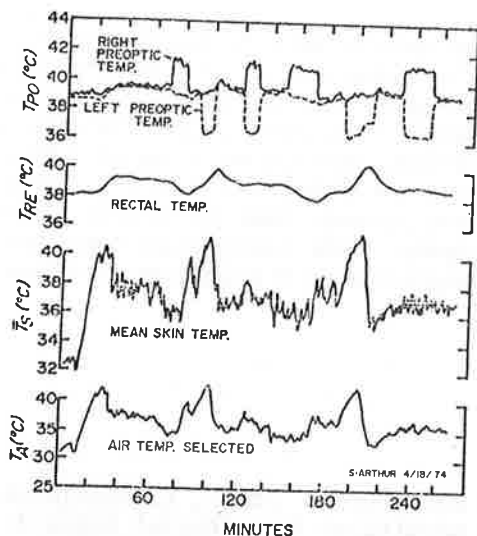


Figure 24. Simultaneous right preoptic heating and left preoptic cooling produces no change in the air temperature selected by one squirrel monkey, although either stimulus applied alone strongly affects the rectal and mean skin temperatures and the air temperature selected. (From: Adair and Rawson, *Pfluegers Arch* 352:91-103 (1974). Reprinted with permission of Springer-Verlag, New York, New York.)

The same is true in the right panel. For example, when both areas are being manipulated in opposite directions, the rectal temperature stabilizes and the skin temperature stabilizes because the animal does not make any change in his normally preferred environment.

DR. JUSTESEN: Was there a true absence of lateralized dominance?

DR. ADAIR: Not completely, in this preparation. We have done similar experiments in sheep, studying effects of unilateral versus bilateral temperature stimulation of the preoptic area on physiological responses. In the sheep, these devices are the same size as the ones we implant in the monkey, but they are much further apart, about 8 mm. The results are similar.

Figure 25 shows an experiment on an animal implanted with thermodes in the preoptic area and in the midbrain reticular formation. The midbrain is one of the areas Nakayama investigated, and he found many temperature-sensitive neurons there. However, it was not clear exactly what the function of these neurons might be. When we heat and cool the thermode in the midbrain, doing our best to keep the temperature of the preoptic thermode constant, we see no change in the animal's behavior or in its body temperatures. When we change the temperature of the anterior hypothalamus, keeping the midbrain temperature as close as possible to its neutral level, we see the strong behavioral responses. Thus, while the midbrain reticular formation has many temperature-sensitive neurons, their importance for the behavioral responses that regulate the body temperature has not been detected. Nor, I believe, do they have much effect upon the physiological responses.

Figure 25. Changes in rectal temperature, mean skin temperature, and air temperature selected when either midbrain or hypothalamic temperature is displaced at 10-min intervals around the neutral level. (From: Adair et al., *J Physiol* (Paris) 63:191-194 (1971). Permission granted to reprint by Masson, Editeur, Paris 75280 France.)

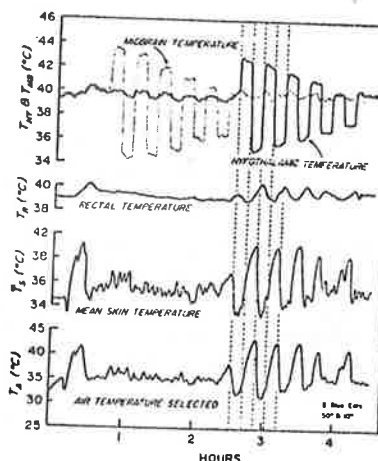


Figure 26 shows an experiment in which we have inserted a rectal or colonic thermode in an animal. This device was a flexible, sealed, polyvinyl tube, a set of concentric tubes arranged similar to a hypothalamic thermode system, complete with circulator, whereby we could introduce heat into the abdominal cavity of the animal through the colon. There have been reports of temperature-sensitive units in the cat jejunum, and it is not clear what their role in thermoregulation may be. However, somewhere in the abdominal cavity or the deep viscera there must be some sensors that influence behavior because when the colon is cooled the animal will select a slightly warmer environment again. These responses are not nearly as dramatic, however, as those that occur from temperature changes in a highly temperature-sensitive area such as the preoptic area.

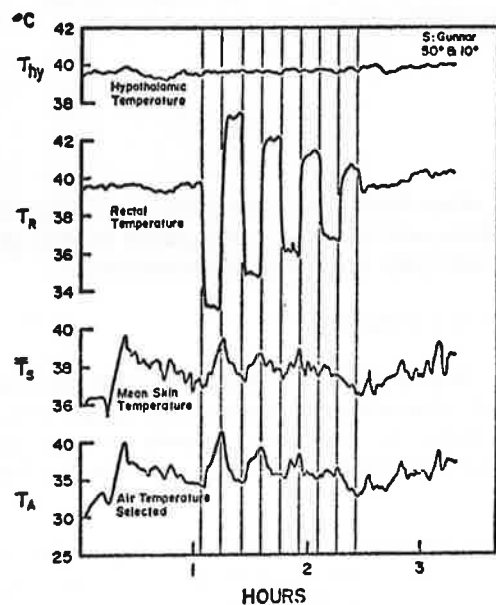
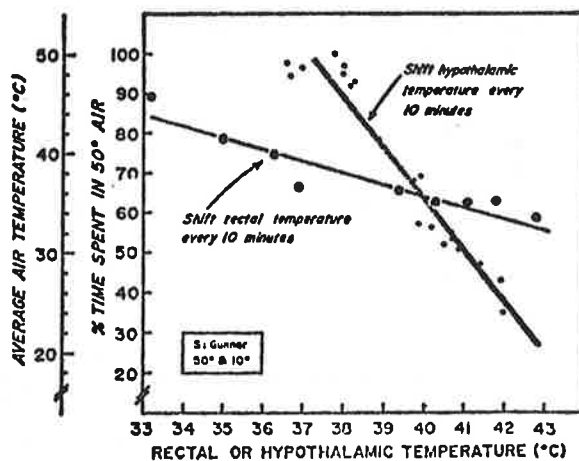


Figure 26. (From: Adair, E. Reprinted with permission from *Physiol Behav* 7: 21-26 (1971), Copyright (1971) Pergamon Press, Ltd.)

Figure 27 shows a summary of results for the same animal (implanted with a thermode in the preoptic area) for heating and cooling the colon versus heating and cooling the preoptic area. The ratio of these slopes is about 3:1. It is not clear whether we are just not in the region of temperature-sensitive units in the abdomen, whether they are much fewer in number or have different output characteristics. However, one can get an idea of the relative input from the two areas into the behavioral effector system from an experiment of this kind.

Figure 27. Behavioral analysis of experiment. Percentage of each 10-min interval 50° air was chosen (and time-averaged air temperature produced) is plotted as a function of rectal temperature (large dot, solid line). (From: Adair, E., *Int J Biometeorol* 15:121-125 (1971). Permission granted to reprint figure by Swets Publishing Service, Lisse, The Netherlands.)



Physiological response changes were observed in the squirrel monkey. Figure 28 shows an experiment done by my colleague, Dr. Wesley Lynch, in which the temperature of the dorsal surface of the monkey's tail was measured as a function of the environmental temperature. As the animal is exposed to a warmer and warmer environment, the tail temperature rises rather regularly until a point which is about 26.5 °C ambient temperature. Here there is a great shift in level of the tail temperature. This is an indication of the vasodilation of the tail vessels. Tail skin temperature then continues to rise at higher ambient temperatures. We would classify this ambient of 26.5 °C as the vasodilation threshold for the tail subcutaneous vascular bed. There is another area that one can measure that is vasoactive, and one can obtain a threshold similar to this one. This is the foot or hand of the animal. Dr. Lynch proceeded to determine in an implanted animal how the vasodilation threshold for the foot depends not only upon the environmental temperature (or the skin temperature it produces) but also the temperature of the preoptic area. This is a criterion vasodilation of the foot skin specified in terms of a given skin temperature increment.

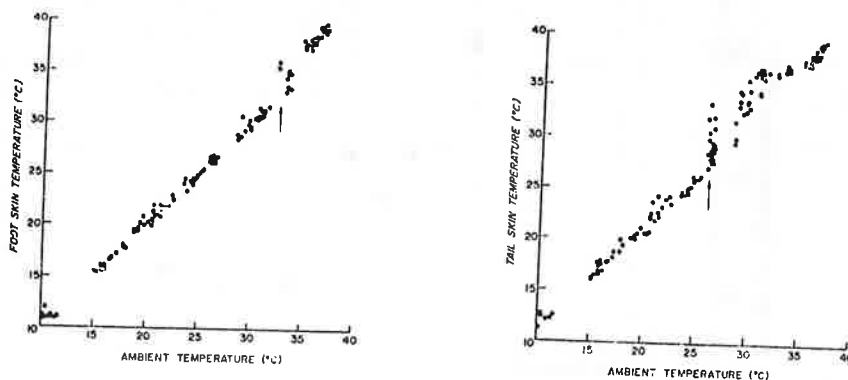


Figure 28. Skin temperature versus ambient. (From: Lynch, et al. J Appl Physiol (in press) (1980). Permission granted to reprint by the American Physiological Society.)

Lynch found (Fig. 29) that when the animal has a foot skin temperature of about 36 or 37 °C, the foot will vasodilate of its own accord. This represents an ambient temperature of roughly 33 °C. But as the animal is exposed to cooler and cooler environments, his foot can be induced to vasodilate by heating the thermode implanted in the brain. The relationship shown here is probably linear although we are not quite sure at this time.

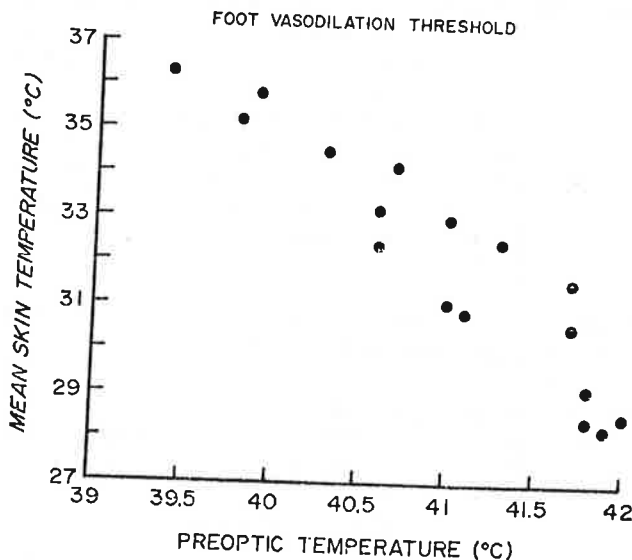


Figure 29. Foot vasodilation threshold. (From: Lynch, et al. J Appl Physiol (in press) (1980). Permission granted to reprint by the American Physiological Society.)

These data apply to the determination of a similar kind of threshold in current experiments involving the exposure of animals to 2450 MHz CW microwaves in an anechoic chamber. The temperature of the monkey's tail is measured with a very fine copper thermocouple, and a change in the threshold for vasodilation of the tail has been derived as a function of the incident power density to which the animal is exposed. These are 5-second exposures and a criterion vasodilation of the tail is determined by a specific increase in tail skin temperature. Figure 30 has as ordinate the ambient temperature in which the animal sits. At 26.5 °C, the tail will vasodilate by itself and, therefore, no microwave energy is necessary to induce this response. However, at slightly lower ambient temperatures, vasodilation in the tail can be produced by a 5-minute exposure at 6 to 8 mW/cm² incident power density. As the animal is put into cooler and cooler environments, the incident power density necessary to induce vasodilation is shown to be a linear function of ambient temperature. These experiments are currently in progress in my laboratory.

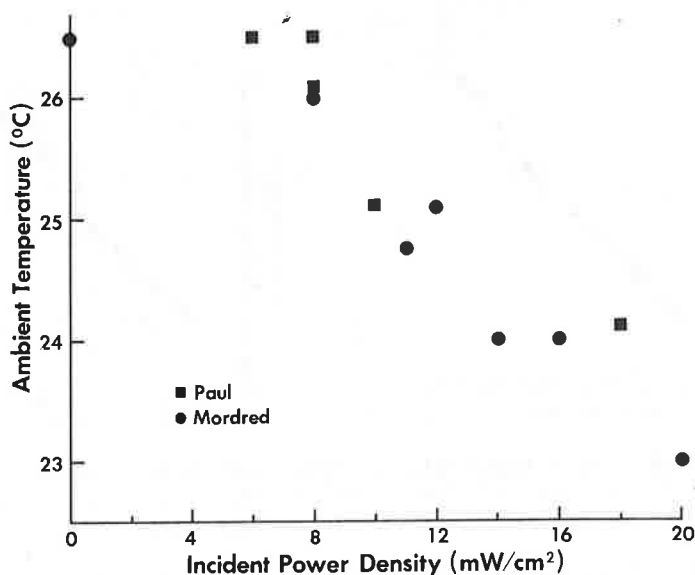


Figure 30. Threshold for tail vasodilation ~ 5-minute exposures to 2450 MHz CW microwaves.

Let me turn to another kind of heat source that has been used in the Pierce Foundation Laboratory. Figure 31 shows heaters that have been surgically implanted in the abdominal cavity of sheep by Dr. Robert Rawson. These are coils of high resistance wire molded in epoxy then surgically implanted and sutured to the abdominal wall. This research project was originally undertaken as part of the artificial heart program in an attempt to determine the thermoregulatory effects of additional endogenous heat that might be introduced through an artificial heart or its power source. After the coils were implanted in sheep and dogs, they were energized chronically 24 hours a day. After about 18 days, if the heater surface temperatures were kept to about 45 °C, some vascularized scar tissue capsules formed.

Figure 32 shows the location of the heaters in the sheep. Rawson usually implanted either two or four heaters which were powered through externalized wire leads.

Figure 33 (not available) shows a micrograph of scar tissue in a capsule formed around an implanted heater when the heater was not energized (a control capsule). On the other side of the animal (Fig. 34, not available) is the scar tissue around the heater when it was continuously energized to a surface temperature of 45 °C for 18 days or more. The presence of large vessels indicates that the scar tissue has become highly vascularized. This

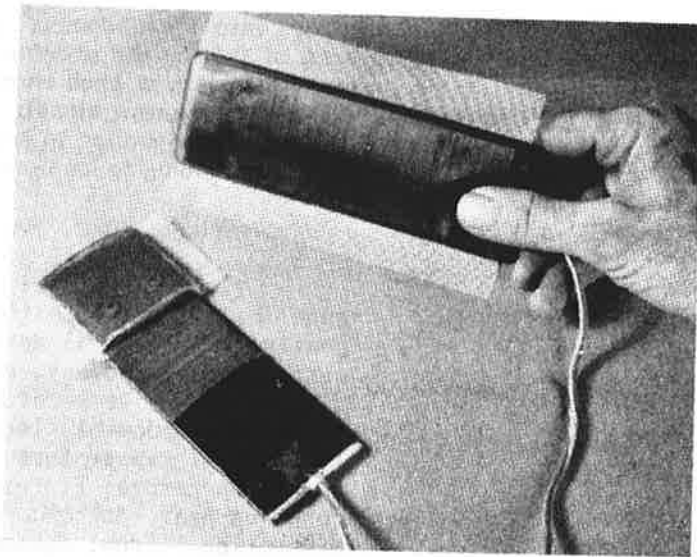


Figure 31. An implantable electric heat source used to administer intra-abdominal heat to sheep. Flat concentric coils of copper wire, thinly coated with silicone rubber, were cast in a mold to give a smooth, uniform layer of medical-grade epoxy. Dacron skirts were sutured to the body wall, and became incorporated with fibrous scar tissue. A cut-away model is on the left. (From: Rawson and Quick, J Appl Physiol 28:813-820 (1970). Permission granted to reprint - The American Physiological Society.)

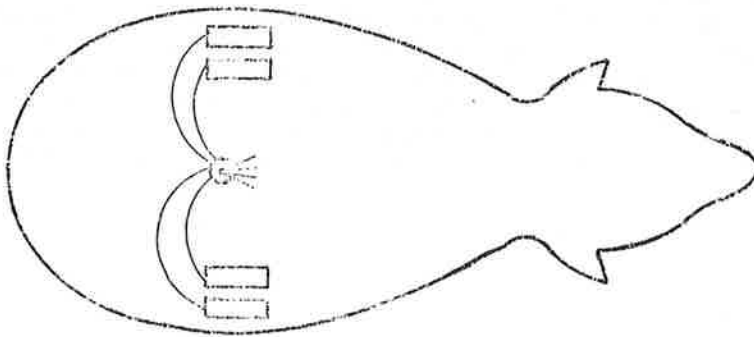


Figure 32. Sheep strip heater placement.

then is a mechanism for removing the chronic heat introduced into this part of the abdominal cavity.

Figure 35 shows a sheep in a neutral environment implanted with four of these heaters. The heaters are energized at the point marked "endo" to .5 W/Kg total heat input. This heat stimulates an increase in respiratory evaporative heat loss and produces a drop in hypothalamic temperature. This figure is a measurement of the temperature of the skin on the abdomen, overlying the implanted heaters, as well as respiratory frequency increases.

The animal begins to pant as heat is introduced into the abdomen. However, when an external heating pad placed over the same area of skin on the abdomen is energized such that the temperature of the skin itself is higher than it was when energized with internal heaters, we see none of these response changes (to skin heating alone). However, when the heaters in the abdomen are energized, we see a response similar to those before. This is additional evidence for internal thermal receptors responding to localized heating that have import for the total thermoregulatory system.

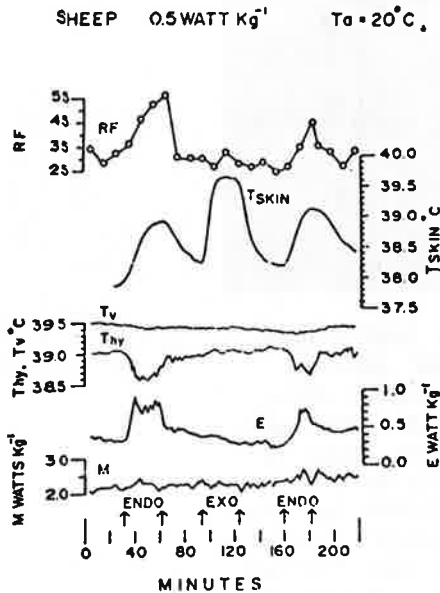
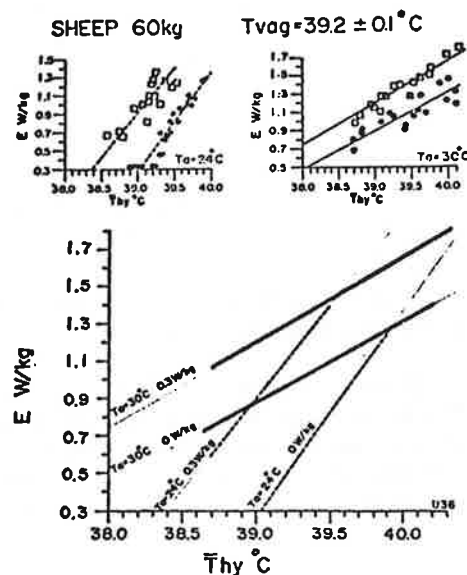


Figure 35. Response to intra-abdominal heating in a neutral environment. RF: respiratory frequency, breaths per minute; T_{skin}: temperature of skin overlaying abdominal locus of heaters; T_v: vaginal temperature; T_{hy}: preoptic area temperature; E: respiratory evaporative heat loss; M: metabolic heat production. (From: Rawson, Quick, and Coughlin; Thermoregulatory Responses to Intra-Abdominal Heating of Sheep. Science 165:919-920 (August 1969). Copyright (1969) by the American Association for the Advancement of Science.)

Figure 36 shows an experiment performed on an animal implanted with such abdominal heaters and thermodes in the anterior hypothalamus. The interaction of the hypothalamic heating and cooling and two different levels of heat deposited in the abdominal cavity are evident here. The animal is in a warm environment and his respiratory evaporative heat loss is being measured. The sheep is exposed to two levels of ambient temperature, and the temperature of the hypothalamus is being changed. One function depicts no heating and one depicts .3 W/Kg introduced into the abdomen at the two environmental temperatures. Not only does the abdominal heat increase the magnitude of the response output, but there is

Figure 36. (From: Rawson and Quick, Isr J Med Sci 12:1040-1043 (1976). Permission granted to reprint by Israel Journal of Medical Sciences, Jerusalem, Israel.)



also a change in slope or gain produced by the change in the environmental or skin temperature. This is a rather generalized finding that internal thermosensitive sites, when they are simultaneously energized, will change the effector response in more or less an additive manner; but when a thermal change is made in the periphery (that is, in the skin) it is more likely to be a multiplicative effect.

Figure 37 shows an experiment on a sheep restrained in a cool environment with vasoconstricted ear vessels produced by lowered hypothalamic temperature. This response was overridden by applying endogenous heat in the abdomen of the animal. This is an example of hypothalamically induced vasoconstriction in this animal, overridden by abdominal heat.

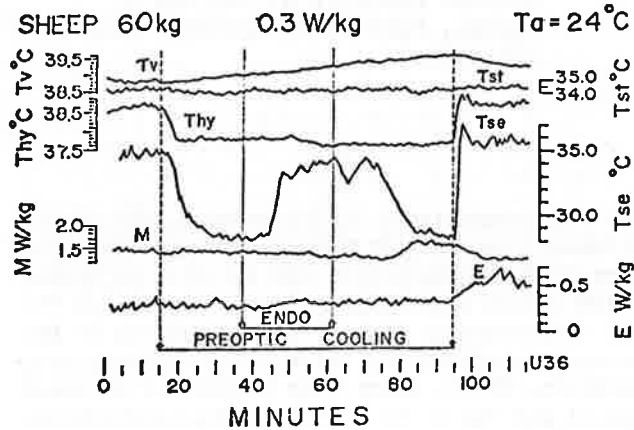


Figure 37. (From: Rawson, et al. Isr J Med Sci 12:1040-1043 (1976). Permission granted to reprint by Israel Journal of Medical Sciences, Jerusalem, Israel.)

Figure 38 shows examples of experiments comparable to those mentioned previously, but now we have right and left abdominal heaters demonstrating the additivity of response first to heating the left heater then superimposing upon that the right heater. The experiment demonstrates how the metabolic heat production of the animal in the cold environment is selectively reduced or additively reduced thereby.

Concluding with a discussion of humans, Figure 39 shows a thermoregulatory experiment with a device similar to a thermode that has been used to measure skin conductance in humans on the forearm and on the palm by Drs. Cunningham and Stolwijk. It is a water-perfused applicator, and copper disc and a guard ring. On the left is a frontal view and on

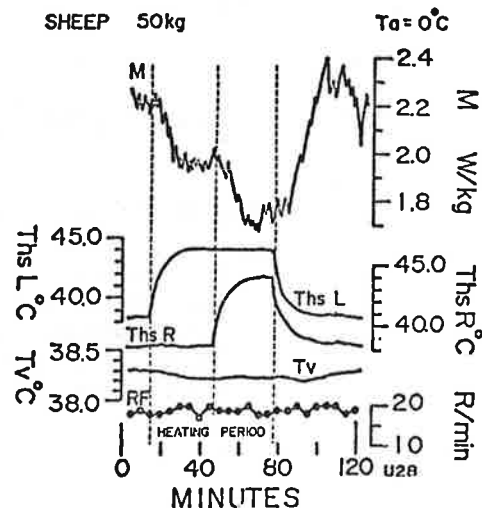


Figure 38. (From: Rawson, et al. Isr J Med Sci 12:1040-1043 (1976). Permission granted to reprint by Israel Journal of Medical Sciences, Jerusalem, Israel.)

the right, a side view showing the applicator surface that contacts the skin and the direction of water flow through the system. The temperature of the applicator disc itself is measured by a thermocouple embedded in the disc. A differential thermocouple in the inlet and outlet sides of this water-perfused disc system measures the change in water temperature (positive-negative) produced by the heat gained or lost from the skin on which the applicator is placed.

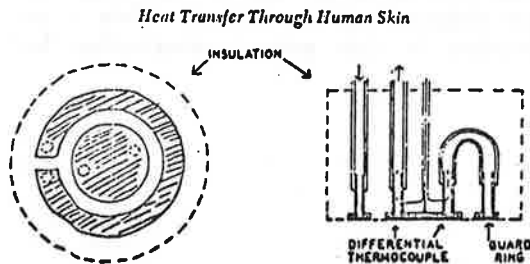


Figure 39. (From: Cunningham, *Physiol Behav Temp Reg.* Edited by Hardy, Gagge, and Stolwijk (1970). Reprinted courtesy of Charles C. Thomas, Publisher, Springfield, Illinois.)

Figure 40 shows a function relating the skin conductance to the temperature of the applicator. The applicator determines the blood flow through the area in question. The conductance was measured at a steady state when the applicator was set at a particular temperature. The arm was then occluded with a cuff above the applicator to remove the blood flow from the system. This provides a measure of change in conductance or the conduction change from the occluded to the non-occluded state. At very low temperatures and up to very close to normal skin temperature, 38 °C, there is no effect due to blood flow but there is a great effect above this point and this is the portion of the conductance that is due to greatly increased blood flow through the area.

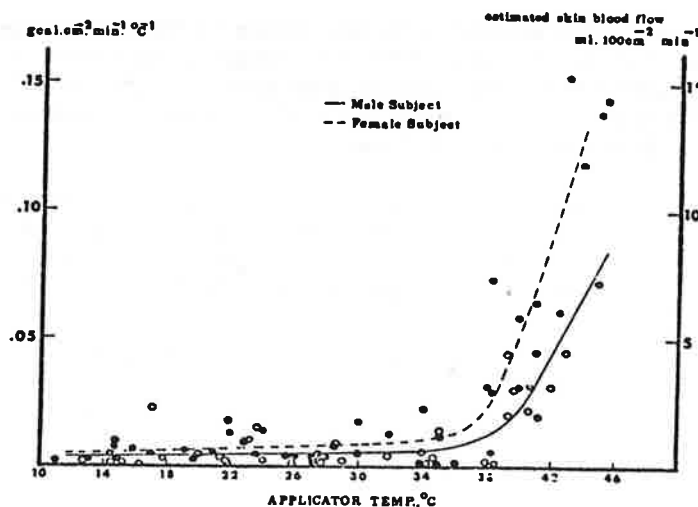


Figure 40. Difference between nonoccluded and occluded forearm conductance at applicator temperatures ranging from 10 to 45 °C. (From: Cunningham, *Physiol Behav Temp Reg.* Edited by Hardy, Gagge, and Stolwijk (1970). Reprinted courtesy of Charles C. Thomas, Publisher, Springfield, Illinois.)

MR. JANES: In your radiofrequency studies, the 2450 studies, can you either experimentally or by inference relate the exposure under the conditions that you are using to watts per kilogram in brain tissue and to temperature excursions?

DR. ADAIR: Not in terms of brain tissue alone. I have done some whole-body dosimetry using saline-filled cylindrical phantom models that are most representative of the size and shape of my animals. But nothing yet can be said about the deposition of energy in the animal. I wish I could answer your question. Obviously, the heat is being deposited all over the animal's body and whatever effects seen are certainly due to the stimulation of multiple temperature-sensitive sites. It is important to emphasize that there are many such sites in the body, that they pool their information into the integrator, and that internal sites may well be additive in the way they affect the command signal.

But, if an effect is seen, for example, at 10 mW/cm^2 incident energy, I would never assume that this was all affecting the brain stem thermal sensors. It is obviously affecting the whole body.

MR. JANES: So these are whole-body irradiations?

DR. ADAIR: Yes.

MR. CURTIS: When you alter the animal's response by inducing, elevating the temperature, occluding the temperature with these probes, have you found any chronic effect to the animal after they have been treated this way?

DR. ADAIR: No, we have some animals not currently being used in the microwave field, but we have some animals that have been chronically implanted with thermodes of this type for 5 to 6 years. The animals still give the same response as they did the first day we tested them after the surgical implantation, and there is no evidence of any change in basic thermoregulation, either behavioral or physiological. Longitudinal studies are done on many of our animals and we use these in a variety of different kinds of experiments.

DR. KANTOR: Are you aware of miniaturized applicators at microwave frequencies that can be used for internal heating? Professor Taylor at the University of Maryland has just developed such a device similar to the dimensions of your thermode.

DR. ADAIR: I would be delighted to have the opportunity to test such a device.

DR. GLASER: With regard to the sensor in the gut of the cat that enables some behavioral modification, I guess that I have been under the impression that in the human animal, the only sensors of temperature are in the skin. Therefore, radiofrequency energy that is able to penetrate deeply into the body may do so without the subject being aware of it.

Would you care to speculate on the possibility that there might be some sensor of that sort in the human animal?

DR. ADAIR: I am sure there are sensors all over the human interior. The fact that these sensors are stimulated does not necessarily mean that this stimulation is appreciated or sensed directly. Let me give an example, several people, including myself - this is why we built that little electric brain heater - have tried to train animals to regulate the temperature of their hypothalamus directly. It is an extremely difficult experiment and I am not sure that it can be performed. I have agonized for 2 years trying to demonstrate this phenomenon. If an animal appears to be trained, he loses his training by the following week. I think it is because the hypothalamus does not normally get hot, and there is no built-in connection to the sensorium to tell an animal that his brain is hot and that he should do something about it. Nevertheless, if I use that little brain heater as a thermal stimulus, the animal will behaviorally regulate the temperature of his environment as I have demonstrated to you. The information from the warm hypothalamus is getting through to the "regulator," but it is not necessarily being sensed in the way temperature change on the skin is sensed.

MR. MONAHAN: You had mentioned that internal temperature sensors appear to be additive as they have an input to the hypothalamus. Would you care to speculate on what sort of temperature increase would be necessary in some relatively small, localized areas such as the liver or abdominal cavity to produce an effect, a regulatory effect?

DR. ADAIR: There are no experimental data that would allow me to answer that question. I am not aware that anyone has put a heating device on the liver, or the immediate vicinity of the heart. That is one of the problems with the current research in this area. Research has been directed toward understanding the thermoregulatory system, thus we have concentrated on putting our devices in those areas that are known to be thermosensitive. There is certainly considerable need for research of the kind that you are asking me about. What does happen to the liver when you heat it experimentally? I don't know, do you, Dr. Horvath?

DR. HORVATH: Sure. We have measured temperature in both human and animal livers and temperature in the liver can get up to 44 °C.

I don't think anyone is worried about it from the standpoint of thermoregulation except for the fact that it does produce extra heat. Depending on the animal's size, you can get an appreciable amount of heat produced by that mechanism. Whether the animal reacts to this extra heat is only incidental. As long as the blood temperature is increased, it will go up to the hypothalamus, and the response there will be appropriate.

DR. ADAIR: Or the spinal cord. The spinal cord is somewhat secondary because there is a big cooling device coming up the spinal cord, a huge mass of venous plexus which originates way down at the base of the cord and goes all the way up. This mass modifies that temperature - considerably, as far as the arterial temperature is concerned.

We have tried several different things in the liver. But, as far as I know, nothing specifically occurs there except as a secondary effect on the blood temperature.

DR. STOLWIJK: There is some indirect evidence for the relative sensitivity or the relative contribution from different systems. If you change the hypothalamic temperature by 1 °C in the animal, then you are going to produce a change in the opposite direction of all other tissues because if you raise the temperature, it is going to drop heat. At some point the new signals come from all other areas as well as that part of the hypothalamus that was not touched by the thermode. An opposing signal will be brought in, and, as a result, there will be no further change and the body temperature will achieve a new steady-state. The relative displacements of the various tissues from this give one some idea as to where most of the sensitivity lies.

DR. HORVATH: But in actuality those differences are very, very small because the total amount of heat that is necessary in most of the animals studied is not really a great deal. A few calories is hardly significant.

DR. STOLWIJK: However, after one has done this and a new steady-state has been achieved, part of the hypothalamus is at an elevated temperature and produces a signal. The rest of the body is in the new steady-state at a temperature somewhat below what it used to be and that produces an opposite effect. If one wants to weigh the relative worth of the signals contributed by these two systems, some kind of estimate can be made concerning the relative contributions. On that basis, one can say that in man we know the relative contribution for central versus skin temperature, which is usually a ratio of about 10:1, central temperatures being 10 times more important or having 10 times as many sensors contributing than the skin does. One degree Celsius skin temperature is equivalent to one-tenth of a degree central temperature.

In animals where we have differential temperatures in the hypothalamus and the rest of the body, one often finds that the hypothalamus has at least, even at very small volume, one-half of all the sensing that goes on. But where it is, and how it might contribute is very difficult to know, unless pursued through specific studies.

DR. JAN A. STOLWIJK

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The information that thermophysiological experimentation has actually produced, both from man and animals, needs to be organized in a manner that can aid in answering questions on research or in raising questions that fall into the range of experimentation but for which the actual experiment has not been done. We have developed a number of models for this over the years that gradually became more complex and accounted for more and more of the sorts of responses that go on.

The simplest representation that one can make is to imagine that the human body consists of a cylinder which is 2 meters in length and which has a mass-to-area ratio of 40 kg/m^2 with these layers: the skin layer, the muscle layer, and a core layer. That is not a very pleasant-looking representation of man. A model this simple can only account for the grossest kind of heat transfer, heat production localizations and responses that may occur.

A description from about 1965 looks a little bit more human. It consists of a head and trunk, and all the extremities are presented by one other cylinder; that head has skin and a core; the trunk has skin, and a muscle layer and a core, and also a central blood compartment; the extremities are represented by a core which is primarily muscle, and a skin layer. We are careful that the surface-to-volume ratios for each of these elements becomes a closer representation of what man might look like. We deal with the heat transfer to each of these surfaces, the heat conductance between these layers, the convective heat transport from the central blood and its communications with all the various layers, the heat production in the trunk core and in the brain, the respiratory heat loss out of the trunk core and then the head core, and the heat production in the muscular layers, assigned to each of these compartments in the appropriate manner. This is the passive part of the model. There is an active part or a controller part.

Wissler, at the Department of Chemical Engineering, University of Texas at Austin, developed almost simultaneously a much more elaborate model which was graphically represented this way. It consisted of a great many more nodes, about 250. It did not have, however, any ability to respond to the thermoregulatory stresses. It was completely a passive model which accounts very well for convective and conductive heat transfer and heat exchange with the environment, as well as for countercurrent heat exchange that can occur especially in the extremities. Where arteries and veins run relatively close together with relatively low blood flow rates, there can be appreciable amounts of countercurrent heat exchange, which he also represented in this model.

The current model, shown in Figure 1, consists of six cylindrical compartments with a central blood compartment. You can see the arrangement of the nodes here for one of these cylinders in Figure 2. The trunk has a core, the muscle, a subcutaneous fat layer and a skin layer. The conductive heat transfer occurs between these via resistance symbols. There is heat production which is carefully entered as the best approximation of the local heat production for each of these layers. Each of these layers communicates with an amount of blood flow from the central blood compartment. As that blood flows, it also obviously moves oxygen, waste products and heat between these various layers. This becomes a passive model, not as complicated as Wissler's, but probably articulated enough for the interests in thermal physiology. It might not be well-enough articulated for some specific problems, but in general, via these different methods, it is not difficult to provide further articulation and to provide more layers.

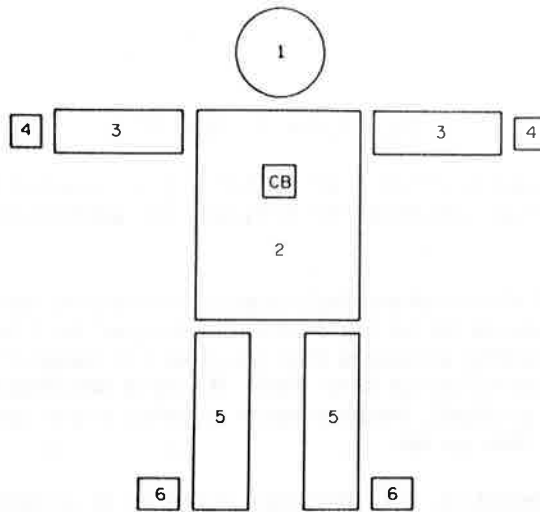


Figure 1. Representation of passive model of six segments indicating method of identification: (1) head; (2) trunk; (3) arms; (4) hands; (5) legs; and (6) feet.

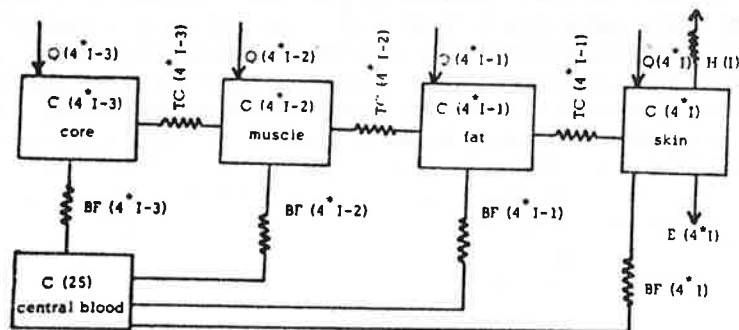


Figure 2. Schematic representation of heat exchange for the four compartments of Segment (1).

In this model the temperature for each of these compartments can be determined relatively easily. We can imagine that there are receptors there and what these receptors might be telling the central integrator. The integrator must accept these thermal receptor signals in a weighting which is the best estimate of the relative weighting of input from all thermal receptors from all areas. This goes into an integrator, and from there command signals are released that are distributed over the various layers as well as possible. We know that the shivering command goes primarily to trunk muscles, and there is not very much in the way of shivering commands that go to leg muscles. On the other hand, the work goes to a great extent to the muscles - we have large muscles on the legs - depending on the kind of work being done. One can see that each of these heat productions and each of these effector actions must now be assigned to physiologically appropriate distributions over the various layers. The connections for the environment are taken care of passively in the model of the control system.

For each of these relationships now, we must rely on experimental data to tell us how much sweating is going to be produced and where, on the basis of a 1 degree increase in the

central receptors in the brain. We must then also specify how much a 1 degree change in skin temperature is going to contribute to the control of that sweating. This puts an enormous demand on our physiological knowledge because we don't know nearly as much as we would like to. In addition, there are a large number of complicating factors that are not represented in this model. As one adds more and more to the model, it becomes more like the real thing and becomes more difficult to run.

Here is an example of the results of using such a model in comparison with an actual experiment. These models are more highly tested by simulating dynamic responses than by the simulation of steady-state responses. Steady-state responses are somewhat implicit in what one builds into the control coefficients, and they are relatively easily satisfied. It is much more difficult and much more critical to satisfy the dynamic responses.

In Figure 3 one sees the dynamic responses of subjects moved from a 30 °C environment to into a 48 °C environment -- in other words from 85 °F to 120 °F, and back down to 85 °F. The total rate of sweating and the time response of sweating are indicated where the broken lines represent the model response, and the solid lines represent the actual measurements that were made on a number of subjects.

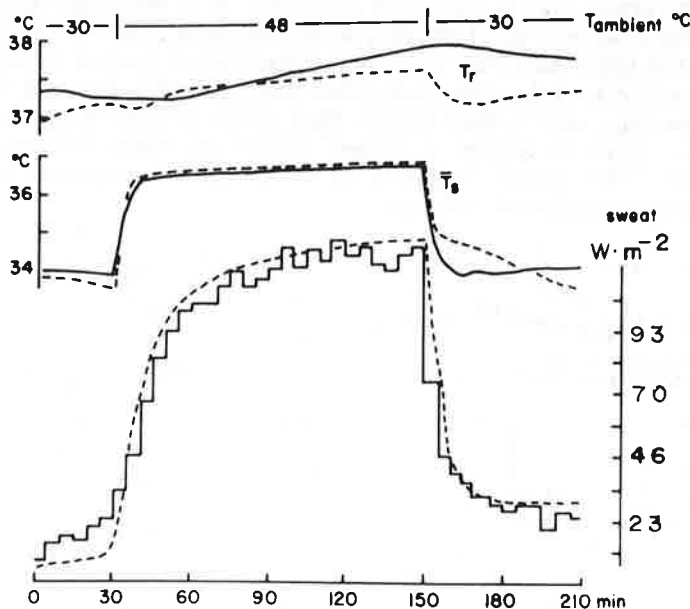


Figure 3. Comparison of physiological data with theoretical values derived from model. Subject clad in shorts sat for 30 min in a neutral environment, 30 °C, and transferred quickly to a room at 48 °C for 2 hours. A final hour was spent at 30 °C. Solid lines, experimental data; dashed lines, computed values.

In Figure 4 one moves from 43 °C down to 17 °C, which is cold for a nude subject, and back up to 43 °C. This represents the onset of the sweating, the off-transient of the sweating, then the delayed onset after the cooling. The model represents the skin temperatures reasonably well, and also represents the back-on-transient of the sweating in both size and timing.

One can do experiments with a model of this kind that couldn't be done easily with people. This experiment deals with low heat deposited in particular locations, what its effect might be, and how much one might get. This is the effect this model would predict

when putting 100 watts of heating, presumably radiofrequency or ultrasound heating, into the brain. The brain normally would have a heat production of about 15 or 17 watts which one suddenly increases to 100 watts. Here is the temperature rise that one would expect in the brain from 100 watts of heating, and these are the physiological responses that this model would also predict. This heating of the brain heats a relatively high concentration of sensors. As a result, one gets a relatively high increase in sweat output. In fact, it is more than 100 watts. That shows that you have been hitting one of the sensors and you have sort of interfered with the loop now. The result of sweating more than the heat you are trying to eliminate, is that the total body temperature begins to drop and now a slight decline in the skin temperature associated with the sweating is detected as well as a decline of the supplying blood temperature to the brain, with a much higher gradient. As this blood temperature decreases, the sweating also decreases, and the brain temperature itself goes down a little bit more, and a new, essentially steady state is achieved. When you relax that and take the flap off, you see the brain temperature goes down to below where you started because the supplying blood temperature quickly brings it down. Then, after a while things slowly return to normal conditions.

One has an idea of the power of the convective heat transfer that blood is capable of because the brain is an organ that is very well perfused. It is relatively difficult to raise its temperature by putting heat into it. This, of course, assumes that the heat is uniformly distributed throughout the brain and that no other organs were heated in this experiment. It also assumed gain coefficients for the controller that are of a level of the people in the experiment. It is possible, and indeed likely, that other people would have a lower gain coefficient and would have to accept a higher degree of brain heating than one would predict in this model. The model is based on very highly competent thermoregulatory responses in young and self-selected subjects.

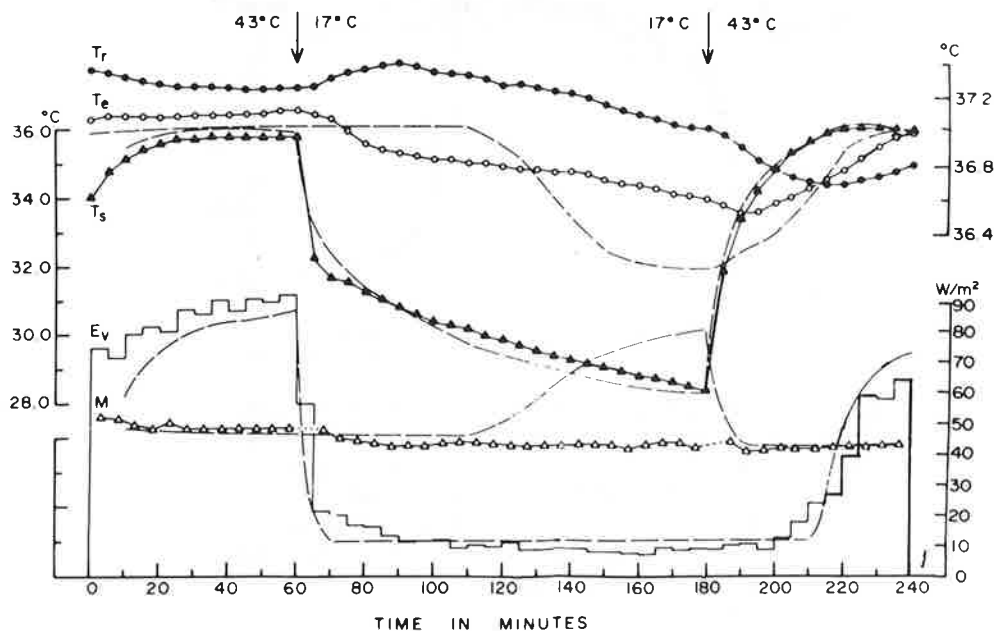


Figure 4. Experiment in which subject clad in shorts sat for 1 hour in a 43 °C environment followed by 2 hours at 18 °C and 1 hour at 43 °C. Solid line, experimental data; dashed line, model calculations; T_r , rectal temperature; T_e , tympanic membrane temperature; E_v , evaporative heat loss; $W \cdot m^{-2}$; M , metabolic rate, $W \cdot m^{-2}$.

In another kind of experiment I conducted for the NCI, I placed 500 watts of heating in the trunk core and prevented any evaporation of sweat. In other words, the subject could be imagined to be covered with a plastic layer so that although he might secrete sweat he

cannot evaporate it. The rectal temperature, the trunk core temperature, goes up relatively rapidly while the hypothalamic temperature is lagging somewhat. The skin temperature ultimately also goes up.

One also notes that after 30 minutes one reaches overall body temperatures of around 41°C due to the absence of sweating. Sweating is prevented from evaporation, and the body becomes very much better stirred. In fact, serious heating of any specific tissue, using local deposition of heat is really not a very simple matter because the body defends itself through a very high convective component which actually increases at this temperature. This is due to the fact that there is a very rapid increase in any tissue as the tissue is heated more than about 40°C . The tissue spontaneously and locally increases its circulation dramatically and to much higher values than normal. As a result, it is difficult to heat tissues locally as the body quickly tries to take whatever excessive heat there is and mix it in with all the other body tissues.

SPEAKER: What is the body mass here?

DR. STOLWIJK: The model is based on a 70-kilogram man.

One other form of heating, infrared heating, does go into the skin, at least at a wavelength of 1.2 microns where it has its highest penetrating power. It goes in and at a depth of 1.4 mm there is still 30 percent of the original flux. This differs at different wavelengths. The absorption coefficient also differs and changes. Fairly complicated situations can also be simulated by appropriate modeling of the skin. Here one notes the comparison of theoretical and experimental results for skin heating by thermal radiation. We can do the surface skin temperature measurements, very carefully using radiometers for the purpose so that we know precisely what a skin surface temperature is. We put in a certain amount of heating -- in this case, 200 kcal/cm/min . As the skin is exposed over a period of 20 seconds, one notes that the skin temperature rises as a result. The points are the observed measurements. The lines are the calculated temperatures at various depths in the skin.

DR. GLASER: What form of thermal radiation are you using?

DR. STOLWIJK: This is the high temperature incandescent at about 2800 or 2900 $^{\circ}\text{K}$. This is a kind of modeling that can be accomplished and some of this is available and can be utilized.

Dr. Schwan and Dr. Kritikos have a student who is involved in combining models of thermoregulation as well as of radiofrequency energy deposition. One may find there has also been some work in this area going on in Philadelphia.

The models that deal with this are in the literature, with the complete source programs and input data files so that one can rather easily adopt and adapt them for use.

DR. ATHEY: Could you discuss the nature of the signals from the integrator in the brain to the rest of the body? Is this chemically mediated or is it through the nervous system?

DR. STOLWIJK: It is almost all nerve-mediated. These measurements are not easily made because one has to make them in a closed-loop control system that is operating all the time. One has to use different tricks to try to open the loops, or at least observe as many variables in a dynamic state as possible. The only effective way one has of opening the loop is by imposing heavy transients of various types which allows different combinations of temperature, and measure the outputs from the control system at a wide range of combinations of various temperatures of skin and core. That is basically how quite a few of them have been separated.

We then make an assumption, based on one set of experiments, that we understand how the integration of the incoming signals works. Once you have satisfied yourself of that, you

then should know what the outgoing signal looks like. If the assumption can be made that the outgoing signal is understood, one can examine the assignment to different parts of the body and see how the most reasonable estimates of weights can be made.

(Note: Much of the material in this presentation is covered in "Control of body temperature" by J.A.J. Stolwijk and J.D. Hardy in Handbook of Physiology - Reactions to Environmental Agents. American Physiological Society, Bethesda, Maryland, 1977.)

DR. ATHEY: Are there other systems that might produce similar signals which might be confused in some cases? And, conversely, are these signals used by other portions of the body for different purposes?

DR. STOLWIJK: In the hierarchy of control systems, the thermoregulatory system is fairly senior. For instance, it gives command signals to the cardiovascular control system and in animals it gives command signals to the respiratory control system. However, the opposite doesn't happen very often. There are very few cases where other physiological systems seem to displace set point or control variables. If one places demands on the cardiovascular system that can not be met, obviously, it is not going to get it. Similarly, if one asks the sweat secretion mechanism to secrete sweat when there is not enough fluid to go around, or when it is fatigued, then it does not work either. Obviously, there are limits. On the whole, we have operated within those limits.

It is also clear that if one uses these models to study deposition of energy at very high levels such as the NCI people are interested in, then an area where knowledge of thermoregulation is very poor is being approached. Our formal knowledge of how thermoregulation works when the body temperature is at 42 °C is very poor indeed. Many radiologists and surgeons are now exposing people to very high amounts of microwave and ultrasound energy and to other ways of heating human tissues. They have put them in hot wax. They do almost anything to get temperature up very high. What I am concerned with is that thermal physiologists should be associated with them so that we may learn as much as we can from these heroic experiments. I do not know how effective it will be but this is clearly something that ought not be lost.

DR. HORVATH: We treated syphilis this way about 25 years ago and had the same response. One of the major troubles is that nobody looked at the original data collected over the last 4 years nor bothered to make any definitive attempt to reevaluate that data. Many of the problems of local thermal heating have been worked on by physiatrists for many years. When I first entered this field we did all this infrared radiation, electromagnetic stimulation and microwave radiation of all kinds of areas. I do not see where anybody has improved on the data available in the late 1940's.

DR. STOLWIJK: I think in the late 1940's there was a considerably greater body of experience around than there is now.

DR. HORVATH: I think it is quite true that people were not only more interested but this happened to be an area of effective treatment for many diseases. However, it turned out to be ineffective. But we did use it. I can remember easily taking people up to 42 and 44 °C, and not worrying too much about it. In fact, I have had a more recent experience in reporting a temperature of 42 °C in a marathon runner. He maintained the temperature for a period of 50 minutes and continued to run. This would indicate under ordinary circumstances according to the models which have developed, that he should have been dead from the moment he started and should have finished the race dead. However, he finished in the first three.

DR. JUSTESEN: There is a lot of data emerging on tolerance, both cellular and whole-body level.

DR. HORVATH: I think all that data has been around a long, long time.

DR. JUSTESEN: I don't know how many average human beings could sustain a sudden, incrementing, whole-body temperature of 42 °C for 50 minutes.

DR. HORVATH: Quite true, fatalities do happen. In the South African marathon runs we have them rather routinely. But that is considered evidence of your manhood - whether you survive or not.

DR. JUSTESEN: Incidentally, what was the kill ratio on those human beings you took down to -60 °C?

DR. HORVATH: Not a single one, because we took them out before anything like that happened.

(Afternoon Session)

DR. ATHEY: Dr. Francis Dukes-Dobos, from the NIOSH laboratory in Cincinnati will speak to us about the philosophies of standards-setting for thermal environments. He has worked on NIOSH criteria documents and recommendations to OSHA on regulations for hot environments in the workplace.

DR. FRANCIS DUKES-DOBOS

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Our responsibility was to use data from basic research and try to apply it for the purpose of practical application for prevention of heat illnesses in industry. What kind of conditions do we want to prevent when we are talking about development of a heat standard?

Figure 1 (no figures available) is from a publication of the late Dr. Harwood Belding who wanted to document and demonstrate how humans respond when they are exposed simultaneously to heat and exercise as may occur in industry. This figure shows both the experimental conditions to which the human subject was exposed over a period of 2 hours and the responses. In particular, those responses were measured which are most important from the point of view of thermoregulation.

In the first one-half hour the subject was exposed to the resting condition, which means that his heat generation by metabolism was about 70 kcal. In the next one-half hour he was walking on a treadmill and his internal heat generation was about 270 kcal. Then, again after one-half hour he was observed in a condition of rest, so his heat generation returned to 70 kcal. At the same time, he was exposed to heat in the resting condition, 36 °C with 13 mercury mm pressure. At the resting condition after the exposure, it decreased to 30 °C and again 12 mercury mm vapor pressure.

The reactions measured and demonstrated here are heart rate, sweat rate, rectal temperature, skin temperature and subjective feeling of comfort or discomfort. In spite of the high temperature, the subject's heart rate remained quite constant in this first one-half hour. The subject was dressed only in shorts, so he did not suffer too much heat stress, and was able to maintain a constant heart rate.

Then, until the end of the second one-half hour, there was a constant rise in the heart rate up to 160 beats per minute, which is about 80 percent of this subject's maximal heart rate. It is uncertain whether this condition would have continued, or whether it would have come into a steady state. Under these conditions, the person may not be able to eliminate completely the heat which was gained due to metabolism as well as from the environment.

In the third phase, the heart rate recovered, at first very fast, and then very slowly until the end of the hour, at which time it was still not recovered completely.

I would like to emphasize that this adaptive mechanism of increasing the heart rate is due to the effect of heat and of oxygen consumption on the regulatory centers in the brain which can then stimulate the cardiovascular system to adapt to the requirements. In the exercise and heat exposure situation, there is a double load on the circulation. First, for purposes of exercise, the blood has to transport oxygen to the muscles in order to generate energy. From the point of view of heat adaptation, an increased circulatory volume has to be moved around in the body and toward the skin surface in order to enable the body to eliminate, at the skin surface, the heat generated by metabolism and also the heat taken up from the environment.

We know that the energy from exposure to radiofrequency microwaves is absorbed in the deep tissue layers. Dr. Belding has performed an experiment, and his results have been confirmed which show that as far as cardiovascular load is concerned, the heat generated by metabolism causes twice as much cardiovascular load as the heat which is absorbed from the environment. This is due not only to the fact that heat is generated in the deep tissues

and has to be transported to the surface, but there also is another load on the cardiovascular system to transport oxygen to the tissues. Nevertheless, from the point of view of microwaves and radiofrequency, the heat is absorbed in the deep tissues. This would cause a higher cardiovascular load per calorie heat gain than if the heat were absorbed from outside. This is pure speculation, but I want to draw your attention to this possibility.

The next response is evaporation of sweat. You can see that the subject exposed to the resting condition did not sweat particularly. However, immediately after the heat exposure of his exercise started, the sweat rate was high, 1 l/h, which is considered to be the maximum level a person can maintain throughout the 8-hour work day. After the exposure, the evaporation rate decreased, but not completely. And even at the end of the resting period there was still some sweating.

The significance of this is that by evaporation man is able to eliminate from the body a great deal of heat, particularly if the humidity is not very high and permits evaporation of sweat. In a very dry climate such as the desert, men may be exposed to quite high heat without even noticing it because sweat is immediately evaporated. Thus, there is not a great deal of discomfort.

The deep body temperature, or rectal temperature, is in the resting state about 37.3 °C in this particular subject. It constantly increases and even continues to increase a little bit at the beginning of the resting period, indicating the rectal temperature is lagging behind the period when the actual heat generation in the muscles occurs, and also from the point of view of the ability to dissipate the heat gained from the environment. However, in the resting period the rectal temperature is constantly decreasing, not suddenly just slowly. At the end of the hour the temperature still did not reach the resting level.

The skin temperature shows a phenomenon similar to the evaporation rate. Unlike the rectal temperature which shows a gradual increase, the skin temperature shows an immediate increase and an immediate fall. This is due to the fact that when a person has sweated all over, he is wet and he is getting out in a cool environment. The evaporation very effectively cools the skin and this is immediately shown in a drop in skin temperature.

After the point when rectal temperature starts to fall, the subject is still in discomfort - in a great deal of discomfort. Then his comfort 'vote' starts to recover to the resting period in the beginning. As a matter of fact, it indicates a feeling of coolness because the skin is still covered with sweat making him actually feel a little bit cool. The environment, because the sweat is evaporating from his skin, effectively cools the skin.

The feeling of comfort is very much influenced by various physiological functions. One may feel discomfort due to either heart rate, hot skin temperature or general feeling of heat in the body. It is known that the only sensors of temperature which directly make people aware of heat are in the skin. There are heat sensors in different organs but the firing of these neurons are brought to the consciousness of the person only in an indirect way. If a person starts to sweat, he feels the sweat, or only after the person has a vasodilation. The skin sensation then reacts to this vasodilation because that gives a feeling of heat. The deep body temperature may be quite low, but if there is vasodilation, one feels hot. If one is exposed to very cold temperatures and drinks alcohol, a vasodilation effect is achieved and there is a feeling of warming. This is, in fact, a dangerous effect, a false feeling, and one may be exposed to greater heat loss and a further disadvantageous situation if in a very cold environment.

Under this situation, which was in a laboratory, the experiment was stopped before any heat disorder or heat illness may have developed. But these heat disorders and heat illnesses which occur in industry are related to these responses: the circulatory capacity, the sweating capacity, and the ability of men to tolerate increases in body temperature without harmful effect to the body organs, particularly, to the brain tissue. But all other organs may be affected as a consequence of increasing temperature.

If we come to the area of heating due to microwaves where specific organs may be heated up, we have to ask the question what is the limit for heating up specific organs? We are not very knowledgeable on this question. Heat stroke occurs when the brain tissues are damaged because they are the most sensitive to heat. What happens if the liver or the intestines are heated excessively.

Following is a short review of the heat-related illnesses which may develop when one is exposed to conditions beyond his tolerance. When one is exposed to heat stress, his deep body and skin temperature rises. This leads to an increased heart rate and an increased cardiac output which enables heat to be transferred from the deep tissues to the surface of the skin faster and then eliminate it from the skin by convection and radiation. However, sweat is necessary for elimination of heat by evaporation. Sweating is a beneficial reaction if the water loss and the salt loss is satisfactorily replaced. If there is not satisfactory replacement of salt, then heat cramps develop which are muscle cramps, usually in the legs or the abdominal muscles. If the person is removed from the hot environment and given salt replacement, the cramps are eliminated and the worker can shortly actually go back to his occupation. If he is not given enough water to replace what he lost by sweating, then the condition of dehydration develops and we know that if the dehydration exceeds 1.5 percent of total body weight, then loss of physical fitness is observable which can be measured in terms of increased heart rate and increased body temperature. In the condition of dehydration, there is a reduced sweating rate which is harmful because the ability to get rid of heat is further inhibited. If this happens, then the question arises whether some of the heat which is gained from the environment and developed due to metabolic heat generation in the body will or will not exceed the amount of heat which can be dissipated from the body by convection, radiation and evaporation. If the amount of heat gained or generated is higher than what can be dissipated, the body temperature constantly rises. Under these conditions, at a certain point, certain cellular structures in certain organs of the body will be damaged from this excessive heat. The most sensitive tissues are in the brain. If these tissues are damaged the first observable sign is that the thermoregulative coordination will suffer and the individual will cease to sweat. This starts a vicious circle because if sweating does not take place heat accumulates much faster and there is further brain tissue damage. The subject will lose consciousness, collapse and show convulsions. If he is not immediately removed from his hot environment and quickly cooled in some way, such as being placed in an ice bath, further damage will occur in other organs, particularly the kidneys. The myocardium may be damaged and death will eventually occur although he may survive in a coma for days.

There is a person now in the hospital in a coma for several months whom doctors have failed to bring back. This is why removal and immediate cooling is so important to prevent irreversible damage.

Another heat illness is called prickly heat. This occurs when a person is exposed for long periods to hot and humid conditions. The sweat ducts are obliterated by creatine and carotene. Sweat cannot be eliminated through the sweat ducts at the surface, and heat cannot be eliminated from the body. Such hot environmental conditions cannot be tolerated for too long because the body temperatures will rise. If he is not removed from the hot conditions he will also suffer heat stroke.

On the other side of this heat illness schematic presentation is heat exhaustion. Heat exhaustion is first manifested in a feeling of fatigue and headache. The person may also show an insecure gait, feel weak, and eventually collapse. When this happens the person cannot cope with the circulation requirements; the blood cannot be moved to the brain. When the brain does not receive enough blood, it does not receive the correct amount of oxygen thus affecting the function of the entire body and causing the person to collapse. This is a self-limiting condition because when a person is flat down, blood circulation to the brain is being improved due to the hydrostatic conditions, and consciousness will be regained, especially if the person is removed from the hot environment.

This circulatory inefficiency may be accentuated when a person suffers from dehydration because not enough body fluid was replaced during loss. Poor physical fitness renders an individual more sensitive to heat exhaustion. However, heat exhaustion is not as dangerous as heat stroke unless the person collapses near a furnace where he may suffer burns. Basically, heat exhaustion is not very dangerous from a health point of view since after a recovery and rest, an individual may be sent back to work. Going back to a job is not a very good idea for a person who has just recovered from heat collapse, but in industry when an individual collapses and is taken to the first aid section and allowed a short rest, he is sent back to work. In some cases persons have suffered further and more serious damage during a subsequent collapse shortly after.

To illustrate how heat stroke has been treated historically, when no bathtub was nearby a victim was placed on a stand and covered with a sheet and sprinkled with cold water. This may not have been very effective. The second best thing to do if there is no bathtub at hand is to make sure to blow an airstream over the wet sheet to speed evaporation if it is completely wetted down.

The first thing which can be done is to hire so that people who are high risk potential heat stroke candidates are not assigned to hot jobs. Some conditions which make one susceptible to heat stroke follow. A person who is not acclimatized is a higher risk and more prone to suffer heat stroke than normal; also, poor physical fitness, fatigue, lack of sleep, dehydration, febrile illness, acute and convalescent infections, reactions to immunizations, conditions affecting sweating, skin diseases, alcohol and certain drugs such as barbiturates and atropine; past history of heat injury; past history of living in climatic areas with more atmospheric cooling power (this is practically the same as non-acclimatization); chronic diseases, diabetes, cardiovascular disease; lesions of the hypothalamus, brain stem, and parts of the spinal cord following certain surgical operations; recent heavy intake of food (large amounts); sustained output of muscular metabolic heat; and increased susceptibility due to biological variability. There are more, but these are probably the main factors.

SPEAKER: Would emotional stress be a factor?

DR. DUKES-DOBOS: On the basis of logic and speculation, if a person who suffers from emotional stress is in a state of agitation, it would increase work metabolism. It would limit his ability for proper reaction under working situations. I think definitely emotional stress could be considered as a risk factor.

We were talking about heat acclimatization in terms of improving the person's ability to tolerate heat. An acclimatized person is sweating at a higher rate or starts sweating earlier than another; therefore, he is at an advantage as compared to the unacclimatized person and his heart rate and body temperature will not be as high.

This graph taken from Lithead and Lind shows the time required for achieving acclimatization. In about 7 days, the flattening of the acclimatization curves occur. Even after 5 days, the largest part of acclimatization in terms of sweat increase and rectal temperature and heart rate decrease occurred.

MR. JANES: Does the introduction of weekends change that picture at all?

DR. DUKES-DUBOS: No, these were continuous days. After a weekend there is a loss of acclimatization. Therefore, it has been noted that the Mondays are particularly dangerous days from the point of view of heat injury.

NIOSH, in its standard, recommends the application of heat acclimatization measures so every worker who is exposed to hot environmental conditions is acclimatized. To accomplish this acclimatization procedure the worker should be slowly introduced into the hot exposure conditions over a period of 5 days. We know that this is certainly not a 100 percent solution, but it greatly decreases the heat illness risk and this is what we want to achieve.

The problem is to find a middle road between feasibility and optimal situation. We have to compromise since after 5 days a person is not completely acclimatized but perhaps enough that risk of heat illness is diminished.

Heat tolerance and physical fitness of an individual decreases greatly in the state of dehydration. What this figure shows is a 4-hour experiment which was conducted in the Natick Army Environmental Research Center. The subjects were either acclimatized or unacclimatized, and either received water or did not. If an unacclimatized person received water in the experiment, his heart rate went up to 165. However if an acclimatized subject did not receive any water his heart rate at the end of 4 hours was almost as bad. This is just to demonstrate the importance of hydration.

In our field studies we have observed workers in different industries, among them heavy equipment operators in the California desert area, foundry men, aluminum reduction workers, and workers in a chemical plant. We recorded how much they sweated in an 8-hour work day and the extent of dehydration. The spread is from 1 liter up to 10 liters per day. Most people got less water than they were sweating and so they dehydrated. A few got a little more water.

This figure is the 1.5 percent critical level at which we found a deterioration of physical fitness. Many of the observed workers dehydrated more than 1.5 percent, but the main emphasis of these results is that the heavy equipment workers got no salt replacement but the aluminum reduction workers did get salt in water and the foundry men got it in tablets. The workers receiving salt replacement in water, in spite of the fact that they were the heaviest sweaters (9 and 10 liters a day), did not dehydrate much above the 1.5 percent. However, those who did not get salt replacement or only salt in tablet form dehydrated much more. From the accident frequency data, these heavy equipment operators had a much higher rate of accidents than workers not exposed to very hot desert conditions but doing the same work.

The heavy equipment operators did not know they were dehydrating because they were in the desert where it is dry and the sweat immediately evaporated from their skin. The greatest danger is that people dehydrate without really being conscious of it. They lose their fitness as well as the capacity to respond as well to dangerous situations. Their reaction times also increase although there is no clear evidence whether this is related to dehydration. It is known, however, that in high heat response time is longer. There is no doubt this contributed to the increased frequency of accidents.

In exposure to radiofrequency or microwaves, one can assume that in a dry climate, if the deep body tissue temperature increases, humans do not even feel they are hot. They can compensate for the increase in body temperature by behavioral or autonomic regulations such as sweating more. However, they are not aware of sweating because it is immediately evaporated. Even though the average body temperature remains within tolerable limits, the dehydration may reach excessive levels.

The next question we asked was what levels of permissible exposure limits should we consider acceptable and safe from the point of view of prevention of heat illness? We turned to the experimental results of Lind which are shown in this figure. Lind exposed a few subjects to increasingly hot conditions and higher work rates including the low, the moderate, and the high work rate. He measured the equilibration point of rectal temperature after about a 90-minute exposure. He found that even though the environmental temperature was increased, the rectal temperature remained constant while the workload remained constant. Only if the workload increased did the rectal temperature increase. This was true up to a certain point, an environmental heat limit.

If the environmental temperature increased beyond the heat limit, the the deep-body temperature suddenly started to increase after the end of the exposure.

From these experiments Lind drew the conclusion that depending on the work intensity, there is a level at which the human organism can not continue to maintain thermal equilibrium. Above that level the deep-body temperature will steeply increase with relatively minor changes in environmental temperature. The inflection point where this condition occurs is at lower work rates. Lind called these conditions at this inflection point the upper limit of the prescriptive zone suggesting that people should not be permitted to work under environmental conditions exceeding the levels at which they are not able to maintain an equilibrium temperature, which is just under the influence of the work intensity.

A panel of the World Health Organization recommended that industry conditions should be such that the worker's deep-body temperature should not exceed 38 °C. This is quite liberal because this work rate is 6.6 kcal/kg/h, about 420 kcal/h which is a quite high work rate, very seldom exceeded in industry. This level, 38 °C, is beyond the thermal equilibrium level which occurs at 420 kcal/h.

This limit of 38 °C should also be the permissible limit for industry in the United States. However, the question arose whether we can recommend measurement of physiological responses such as rectal or oral temperature of workers exposed to hot conditions. We came to the conclusion that measurement of physiological responses on industrial workers is not acceptable under present conditions, particularly in hot industries. Therefore, instead of recommending a physiological limit, we were trying to recommend environmental conditions which would lead to 38 °C deep-body temperature in different combinations with different work intensities.

For radiofrequency and microwave exposure it is quite a different situation. In very hot environments everyone is aware of the heat, however, very often people are not aware of radiowave exposure, radiofrequency exposure and microwave exposure, at least at the beginning of their exposure. If their sweat evaporates freely, they may maintain relatively lower temperature for a while. If people are exposed to humid conditions where evaporation is not possible, their deep-body temperature may increase. There may be a risk that persons can unknowingly go into areas where there is a high intensity of microwave radiation, and thus suffer some adverse health effects.

In industry people usually know they are being exposed to microwaves and may suspect they feel something abnormal and think they are being overexposed. The only diagnostic measure for this is to measure body temperature. Suppose you measure a body temperature and find it is 38 °C. What does it tell you if you did not know the deep-body temperature before the individual started to work under the exposed conditions? However, even if one knew what the body temperature was before, there is in the body temperature a circadian rhythm over a period of 24 hours. In the morning it is usually low; in the afternoon, it is usually high. How does one know whether the increased body temperature was due to circadian rhythm or to the fact that the worker is a variant who has generally high body temperatures? Or did he come in with a virus and have a high temperature because of that? Or perhaps he was exposed to just the regular environmental heat or engaged in heavy physical exercise.

All these problems could be answered if a worker who is potentially exposed to high levels of microwave radiation would have his temperature measured in the beginning of the day. It takes only a minute with the electronic thermometer.

There is also the possibility of establishing the circadian rhythm of an individual on a particular day that he is not exposed to microwave radiation. If one has all this information on an individual in the medical department, then at any time the person suffers complaints or suspected overexposure, he can be diagnosed with elevated body temperature as a symptom.

But there is one question which is still not answered. Suppose the worker was exposed to environmental heat and worked very hard. It would be easy to construct a table, a graph or a series of graphs to show expected increases of body temperature at given work rates and

given environmental temperatures. If the measured temperature exceeded the expected temperature, the person could have been exposed to excessive radiation.

Lofsted's work showed that even resting people show signs of thermoregulative strain if their rectal temperature exceeds 38.2 °C. There is a breaking point in the increase of the rectal temperature and the ability of thermoregulating decreases when body temperature exceeds 38 °C.

As far as environmental heat in industry is concerned, we have recommended that these breaking point temperatures should be adopted as permissible exposure limits; but not only these levels were presented as limits, but also certain combinations of work and rest regimen. If workers are given the opportunity to rest 25 percent of the working time, higher temperatures are permissible. If 50 percent rest and 50 percent work is allowed, then even higher temperatures are permissible. This shows the permissible limits versus work intensity in terms of kilocalories or BTU's and the environmental temperature in terms of the WBGT or Wet Bulb Globe Temperature Index. This is not recommended as a NIOSH standard. The results of these experiments and recommendations have been adopted as threshold limit values by the American Conference of Government Industrial Hygienists. They are not mandatory guidelines for industry, although in many foreign countries they have already been adopted as mandatory.

For assessing the WBGT Index you have to measure the globe temperature of the environment, for measuring radiation effects, and radiation and temperature combined values. The natural wet bulb must be used which is a thermometer covered with a wick and emersed into distilled water. The combination of these readings then results in the WBGT Index.

Because NIOSH recommended the use of the WBGT Index for industry use, and because it is also used in the Navy and Army as a heat stress index, industry has developed improved instrumentation. Among improved instruments are the Reuter Stokes instrument, which has a smaller globe and responds faster; and with electronic compensation, the difference in the globe size is minimized so that with the smaller globe one gets the same reading as with the 6-inch diameter globe as well as faster equilibration time. With a 4-inch globe, one receives a response, an equilibration in about 5 minutes. Dr. Dassler tells me that there is a newer model now with a smaller globe, and its equilibration time is 2.5 minutes. This greatly improves the applicability of this index for practical purposes.

Some people have not been working properly with the WBGT Index. It is misleading if one gives a temperature level in WBGT values because the WBGT values are usually much lower than the dry-bulb temperatures. If the limit is 90 WBGT, this may correspond to an environmental dry-bulb temperature of 125 or 130 degrees depending, of course, on what the globe temperature and humidity was.

We went out to actually take measurements of workers in industry, the deep-body temperature, through measurement of oral temperature and metabolic rate by oxygen consumption measurements, using the Michaelis's gasometer, and the environmental temperature using environmental instruments. We found that the oral temperature of different workers shows a great variability at different environmental conditions in terms of WBGT.

This figure shows the level corresponding to the upper permissible limit which was shown on the graphs. These levels are plus or minus WBGT degrees beyond or below the recommended limit. In terms of oral temperature, 37.55 °C oral temperature corresponds to a 38 °C rectal temperature, at the permissible limit. If the environmental conditions were below the recommended TLD, then very few people exceeded the 37.5 °C limit. However, when the environmental conditions went beyond the recommended level, more and more people started to show increased oral temperatures. We considered this as proof that the recommended limits are protecting at least 95 percent of a mixed worker population, of different races, different ages, etc.

A similar relationship has been observed between exposure and 1-minute recovery heart rates which is considered by Brouha as an indicator of excessive heat stress.

We got all these results on male workers. At the University of Alabama, a series of experiments was performed by Kuhlmeir and Miller in which female subjects from hot industries and from not-hot industries were tested. The subjects were exposed to the exact same conditions as the subjects in the Lind experiments. The study showed that the females' upper limit of prescriptive zone was similar to the males, except that at the inflection point the women have higher heart rates, although this was not significantly different. This is comparable with recent findings of Drinkwater in Dr. Horvath's laboratory which showed that women can adapt just as well to heat as men if they are properly acclimatized to heat and if their physical fitness is equivalent.

When it came to the point that we have to recommend a mandatory standard, it was generally assumed that the measurements which are required for complying with a permissible upper limit to heat stress are not currently available to the industry because they require measurement of work metabolism and constant monitoring of the environmental conditions. Therefore, instead of recommending upper limits, we recommended an action level at which certain preventive measures have to be operating to prevent heat illnesses. In setting the action level, we said that in industry we do not expect workers to work harder than 400 kcal/h. This corresponds to a level of about 79 degrees WBGT. Therefore, if conditions exceed 79 degrees in industry, then certain preventive measures should be introduced.

These preventive measures include adequate water supply, acclimatization, first aid training, training of workers for health and safety procedures and work practices. While acclimatization would not be very justified in a situation where workers are exposed to radiofrequency or microwave radiations, first aid training and training of workers in health and safety procedures would be justified, because if they are accidentally exposed to high levels and the proper knowledge of first aid is not available the danger of irreversible damage or death is very great.

Recently, there were several heat death cases in industry partially due to the fact that first aid was not available. Even in the hospital, residents did not make the correct diagnosis. When the person started to have convulsions the police were called in to restrain him.

Engineering controls, work/rest regimens, adaptive work scheduling - already in effect in Arizona where heat is the greatest in the middle of the day - are also preventive measures. In Arizona work is scheduled in the morning, starting at 4 a.m. Then work is stopped during the hottest part of the day. Protective clothing is also preventive although it may not be of any significance in terms of radiofrequency. Freedom to interrupt work during extreme discomfort may also be an important consideration. In very extreme heat conditions, the judgment of experienced workers is important and should be taken into consideration as well as preplacement and periodic medical examinations.

SPEAKER: What do you look for during those medical examinations?

DR. DUKES-DOBOS: Physical fitness and the conditions listed under risk factors. This is an interesting consideration. If a worker is exposed to very high heat and we set this level up to 86 degrees WBGT because we found from military data that the number of heat deaths from heat stroke starts just above 86 degrees WBGT, then we recommend if exposure was above this the worker should not be permitted to be alone in such an area but should be observed by another worker. This is relevant to microwave radiation in that an individual at high risk of being exposed inadvertently should not be alone in the area.

In this figure the frequency of accidents, according to some data by McMahon and Belding, seems to follow the environmental temperature conditions over a period of 4 years. The reason for this, as shown, may be that the reaction time increases above certain environmental exposure conditions. The number of errors may also increase as environmental

temperature increases. According to Poulson's studies, the higher mental acuity required for a certain task the larger the decrement will be if the rectal temperature increases.

MR. JANES: Is the reaction time correlated with core temperature or with environmental temperature?

DR. DUKES-DUBOS: It is probably coordinated with rectal temperature. However, it was done in a large population exposed to environmental conditions and it showed that when the environmental conditions exceeded certain average daily temperatures, the reaction times decreased.

DR. STOLWIJK: If the measurements have been made on the basis of environmental temperature, the implication is that the problem is -

MR. JANES: Right.

DR. HORVATH: But the slide before this was related to rectal temperature.

DR. DUKE-DUBOS: Yes, that is right. But, this was not reaction time, this was percent errors in rectal temperature. This is not necessarily identical with response time.

DR. HORVATH: Who did this?

DR. DUKES-DOBOS: Poulson. In the NIOSH recommendation, a certain time limitation was recommended for upper limits of exposure for unimpaired mental performance based on these studies.

This figure shows that in animal experiments, the animals showed increased susceptibility to toxic substances depending on their deep-body temperature, indicating perhaps that threshold limits for toxic substances should be taken into consideration when workers are exposed to heat. That may also be relevant to microwave radiation exposure.

DR. HORVATH: The same things happen with cold or any extreme environment; one gets a U-shaped curve.

DR. GLASER: This may be significant to note that susceptibility to toxic substances is increased. Especially in situations such as workers using radiofrequency sealers in which vinyl polymers are melted, the vinyl material released in gaseous form may be an added hazard above the RF energy.

DR. DASSLER: Our findings so far indicate that contact with toxic substances does affect exposure limits considerably. The major impact found even with fuel combustion gas and vapors of distillate fuels is that these substances shorten the exposure time by approximately one-third. The major effect is on the cardiovascular system and not on thermal stress.

DR. POSTOW: You indicated that the kidneys may be one of the first organs to show the effect of thermal stress. Exactly what part of the kidneys shows thermal stress and what is the mechanism?

DR. DUKE-DUBOS: If the body temperature goes beyond the tissue tolerances, the first and most sensitive organ is the brain, second the kidneys. In military heat accidents it was recorded and published that a high degree of kidney damage was found in both the glomerulus and in the tubules.

DR. POSTOW: Not the loop of Henle?

DR. HORVATH: The damage is actually due to the accumulation of myoglobin in the tubules, and the kidneys go into renal failure due to this excessive quantity of myoglobin. This shows up in anyone who has temperatures above 105 °F.

DR. DASSLER: That is really a coexistent problem of myoglobinuria plus the heat element. How do you feel about the liver as second?

DR. HORVATH: I would put it as second.

SPEAKER: For what reason?

DR. HORVATH: One recovers from liver damage but not from renal damage which more often results in death and so receives more attention.

DR. DASSLER: Also in part because the liver is where a great deal of the body's enzyme reactions are temperature-dependent.

DR. HORVATH: However, those are transitory. The advantage of a transitory phenomenon is that one can recover from it.

DR. ADAIR: I would like to draw your attention back to the first slide we saw. That figure showed the thermal environment to which man can be exposed and in which he has the technology to survive. There were several zones within that range of environmental temperatures. In the middle, there was an extremely narrow zone of thermal comfort. There was a wider zone over which the physiological capabilities of the organism would allow it to survive unaided for a reasonable period of time. There was also a very wide zone both above and below this zone of physiological regulation over which the organism's behavior, plus his technology, would allow survival for an unlimited period of time.

Thermal comfort and discomfort are very strong motivating conditions for humans particularly, and for all animals. When any form of thermal discomfort is produced either by the environment or deep in the body core, the organism immediately initiates behavioral action to remedy the situation without waiting for built-in involuntary responses. We all utilize our behavior and do not sit around and shiver and sweat, unless we do this voluntarily through exercise or unless it is imposed upon us through our work or by febrile disease. So thermoregulation may stretch beyond behavioral control. However, about 90 percent of the time our behavioral responses are relied on to provide relief.

Although a source of thermal energy may not trigger the receptors in the skin so that it is directly sensed, there is a good deal of experimental evidence that shows that behavioral and physiological actions can be initiated through thermal stimulation of specific sites inside the body in the absence of a specific sensory cue. It is unknown how many of these specific sites would be involved, for example, in a whole-body exposure to microwave radiation. However, the sites are there and a great many of them are sensitive and have implications of thermoregulatory behavior as well as physiological responses.

DR. HORVATH: In considering the problems related to the use of thermal energy a basic problem for man is that this energy only reaches certain depths in man. Older observations indicated that the magnitude of the effect, depending on the size of the body that was being irradiated, was dependent on the distance from the surface to some deeper portion. Whether any other systems can be activated by microwave irradiation at the levels we are discussing is doubtful. How deep do you think these things go?

MR. SWICORD: All the way to the center or through.

DR. ATHEY: It is frequency-dependent. At frequencies of around 30 MHz that the Committee is currently considering one gets pretty deep penetration.

MR. SWICORD: Penetration depends on the total geometry involved. At a given frequency, the peak field strength could appear in the middle of the head rather than at the surface due to the standing wave that is established.

We purposely did not provide information to you on penetration because we want your views on the opposite question: Suppose that this energy can reach this level, what will be the result?

DR. HORVATH: We can probably tell you a little more about regional distribution, the movement of heat - heat flux - if we had this information. If we know that "x" amount of energy is in place "y" at this distance, and we can relate this to the known volumes of flow which have to redistribute this heat, and, secondly, the effects upon some special tissues (like the receptors in the brain or just general tissue in the brain, general neurons, the general response of other receptors in the spinal cord and other places) I think we would have given you much better information.

MR. JANES: The question is whether a 1-degree core temperature rise would be an acceptable way to proceed to look at radiofrequency stresses? This is related to whether the generation of heat at depth is tied to metabolic sources or to external sources and must be considered to arrive at figures.

For certain frequencies, the rates of energy absorption are highly dependent on geometry. The question of what size volumes should be released to certain delta-t's over the normal level must also be addressed. A more interesting question is what is needed externally to maintain a 1-degree temperature differential between locations? We are not dealing in the areas we are principally interested in - we are not in the cancer therapy area so we are not dealing with very high levels. One needs to get a feeling for the limits that traditionally have been set and which are now open to some discussion concerning the impacts on the physiological system.

DR. STOLWIJK: If we had been asked specific questions, we could have been much more specific. The brain is one of the most metabolically active organs and functions at about 10 W/kg. Its temperature rise over the supplying blood temperature is .4 °C created by the metabolic rate. If you should put in again as much, another .4 °C rise would result. That is a highly dense flux. The muscles routinely run at a temperature above that of the supplying blood, and there is a relationship between the oxygen-supplying and the heat-carrying capacity of the blood which creates a constant differential in the steady state regardless of the muscle activity. The muscle is always .9 °C above the supplying blood temperature.

DR. HORVATH: The most important part is that it shifts to the association curve too, which makes a big difference. One degree Celsius would make no difference, unless it was in the brain.

DR. STOLWIJK: However, in the brain it is difficult to create a 1-degree differential.

MR. JANES: Will you generalize from the working population to the entire population where spectrums of abilities to handle heat exist? Would you modify that statement?

DR. HORVATH: We are talking about the young, healthy 20- to 25-year old, and not about the very young, the aged or the infirm.

MR. JANES: Our interests here extend from the occupational setting on OSHA's end to the rest of the population. So there is a wide spectrum of interest.

DR. STOLWIJK: Well, if you are concerned with the brain alone, the area that would exhibit the biggest effects if heated, then the degree of perfusion in the brain over the entire population is not very different because, basically, there is heavy deterioration if the circulation in the brain is deficient. This results in strokes and other unpleasant things. Thus, circulation remains at a high level of about 50 ml/100g of brain.

DR. HORVATH: There is another thing I want to caution about. We are now able to measure circulation in the local areas of the brain while previously we referred to total mass. We now are able to measure and find that certain areas of the brain get more,

certain areas get less. Thus, absolute total circulation, and absolute heat flux going into the total area is meaningless. What we need to discuss is the blood and heat circulation to the hypothalamus or other specific areas of the brain. We now have methods by which we have been able to differentiate, which we did not have 3 or 4 years ago.

DR. STOLWIJK: There is a factor of 2 difference between gray matter and white matter.

DR. HORVATH: That is a crude measure.

MR. SWICORD: We were hesitant to present a scenario of energy deposition, and that is simply because you pick the scenario and it is a possible one. Any scenario is possible and for standard-setting we must consider the infinite set before one can say what is safe and what is not safe. We are posing the question the other way around. If any portion of the body were raised 1 degree or more, or received a certain amount of energy, what would be the situation?

DR. HORVATH: Many years ago we did some studies where we irradiated the spine and had animals go into convulsions. Their rectal temperature had only gone up a tenth of a degree but was not due to generalized overall heat, but was rather an effect on a specific origin area of the body. I think the real question is where one is getting the heat and how much is getting at that one place. One also has to think in terms of susceptibility. Certainly the greatest susceptibility will be the central nervous system.

MR. SWICORD: How much energy was pumped into the spine in that study?

DR. HORVATH: I have forgotten.

DR. GLASER: Would a core temperature rise of 1 degree make a difference if it were due to exposure of the entire body to radiofrequency energy or just a portion of the body? The total temperature rise still would be 1 °C, but it would result from a different fraction of the total body.

DR. HORVATH: There would be a complete gradient. To produce a temperature gradient which amounts to a 1 °C rise in a 70 kilogram man - let's say there is a kilogram someplace that is getting a huge amount. One would have to raise the temperature to levels which would destroy the proteins.

MR. CURTIS: 5 °C?

DR. HORVATH: No, more than that - like 10 °C. One would be destroying the proteins if the increase were concentrated in 1 kilogram. Mathematically it is easily figured out.

MR. JANES: There is some data from the diathermy literature.

DR. HORVATH: Yes, but that was all local, just superficial.

DR. GLASER: Would you say then that if just a portion of the body is going to be exposed, then one would not tolerate a 1 °C temperature rise and that you might lower the measurable or the observable rise allowed.

DR. HORVATH: I recall some old studies in which, basically, if certain body parts, especially the spinal cord, were heated, effects were seen without any great change in the overall temperature in large animals such as a dog and a pig. The same thing would probably happen to man. I think we are very close, especially if you use a larger animal such as a 200-pound pig.

DR. STOLWIJK: The tissue that is most able and most resistant to large changes in temperature is the muscle mass. Muscle mass is a very large proportion of the total weight

and a large part of it would be heated up because muscles are fairly superficial and would be catching most of the heat. That part of the tissue is not a tissue that we would be worried about.

DR. HORVATH: Well, 41 °C in the muscle is a very common observation. We can record those temperatures after people have been exercising, which is very common. This is something that I think is perfectly acceptable to that particular tissue. Muscle tissue needs that elevation in temperature to stimulate its metabolic processes to produce the extra energy that is required for adneural crosses. This is a very definitive, facilitative response for that tissue. The real question goes to other tissues.

DR. STOLWIJK: The kidney, the liver, the heart, the brain -

DR. HORVATH: The liver, kidney, and heart will do. The heart is all right I think.

DR. STOLWIJK: It is well-perfused.

DR. HORVATH: It does raise the question in individuals who have insufficient circulation whether this condition is induced by such environmental factors as carbon monoxide exposure, or whether the individual has one-vessel, two-vessel, or three-vessel disease. But I think you are asking questions about things we have never really given a lot of thought to. Basically, I think what you really want to know is not temperature regulation, but circulatory physiology.

DR. STOLWIJK: And you need to know the thermobiology of certain tissues.

DR. HORVATH: All of this heat has to be moved someplace and that is basically a circulatory problem.

DR. STOLWIJK: When the artificial heart program had the problem of what to do with 100 watts from a nuclear generator, they raised the question of how do you dissipate this and what effect does it have? It turned out that if the proper spot was selected, 100 watts was not a difficult thing to dispose of.

DR. HORVATH: But, you cannot put it in the wrong place.

DR. GLASER: That is another area of questioning. Faced with the concern for the worker who may be exposed to some exogenous heat load, how would one best monitor this other than asking for permission to insert a needle probe into a muscle, or a rectal probe, or a tympanic membrane temperature? What are other things to look for?

DR. HORVATH: I have had marathon runners run with rectal probes for 2-1/2 hours. I have had people wear those rectal probes for 2 and 3 weeks at a time removing them only occasionally to replace them. I do not think this is a real problem.

I do not think the real problem is the muscle or the rectum, but a matter of identifying that special tissue. And, if you tell me that microwave radiation will go all the way through you and that the center of energy is in the middle then you have a lot to worry about. If you are going to tell me you can get it past the skull and into the center over here, well --

MR. JANES: The possibilities for doing this have been experimentally demonstrated.

DR. STOLWIJK: One thing to keep in mind, however, is that there are certain things that can be said if one has the total flux densities and the range of absorption rates. There are certain limits that can be placed on potential temperature rises. Temperature rises in the kidney are not very likely unless one is exposed to a huge amount of heat because of the high blood flow. The same is true for the liver. This might not be true for muscle that is resting because that does not have very much blood flow. I think the best way to monitor is to worry about field strength.

DR. HORVATH: But I am still quite worried about the kidney because I have measured enough renal blood flow to know that when you are in your 20's your renal blood flow is 1.2 liters, but when you are 65 it decreases to approximately 700 ml, a fairly good decrease. If people are exposed to this sort of stuff at different ages, one must be careful. We cannot take the data we get on young people and apply it to older or very young individuals since their kidneys take a couple of years to mature.

DR. STOLWIJK: There is a difference between something that does 1 ml per 100 ml per minute and something that does 50 or 100. That is a great difference.

DR. HORVATH: What we would like to see is some information on energy loads that you are putting in. We have to know something about circulatory rates, volumes of flow, amounts of energy put into these various places. With these things we can give you the approximate values.

DR. STOLWIJK: If anybody is interested in the blood flows and metabolic rates in various tissues in various locations, this article gives you diverse quantitative information that might be useful. It also includes the model on body temperature regulation that can interact and tell you what happens if something changes.

MR. BASSEN: Is there any evidence that chronic heat stress causes damage to organs causing irreversible damage to a particular body part or organ but not necessarily death? A health detriment.

DR. STOLWIJK: Basically, information does not exist concerning the situation where a particular organ is chronically kept at an unusual temperature. This is a condition that does not occur. There are people who are exposed to lots of infrared and claim that they have trouble with their eyes as a result. There are cases of that nature.

MR. BASSEN: The classic in the microwave area is the cataract which may or may not be induced by microwave exposure except at very high levels. Still this is localized permanent damage to an organ due to repeated exposure.

DR. STOLWIJK: One would then specifically examine those organs that do not have a very great blood supply and as a result are in poor thermal contact.

MR. BASSEN: Not necessarily. We would be looking at the consequences of local thermal elevation that shows up, not in death or immediate acute illness, but in a delayed effect, a health impairment not as severe as heat stroke.

DR. STOLWIJK: Most tissues go up and down during the day as a result of a diurnal rhythm so there is a range of temperatures that the tissues and the body can deal with.

MR. JANES: That brings up an interesting point. If you talk about diurnals then the noise around that is the noise around the time course of that rhythm. What are the effects, or what would the effects be of changing the naturally established rhythms either in the workplace or in some other way? Does the body regulate around that rhythm or does external heat shift it?

DR. STOLWIJK: The body regulates around that rhythm. If you go to work on a night shift or take a trip to Europe the rhythm will reestablish itself on a new diurnal rhythm. If you exercise at 4 a.m. you will regulate to a different temperature than if you started work at 4 p.m. The difference will be as great as .9 °C, at least a half a degree. Thus, absolute temperature is difficult to establish.

If one works at 50 percent of one's maximum aerobic capacity for 10 or 20 minutes, the body temperature will increase by 1 °C in response to the voluntary activity. Even if the body or a portion were chronically increased by .2 °C to determine whether that resulted in

a risk the effect would disappear into a thermal noise. So even if there were such a thing, it would be extremely difficult to establish.

MR. CURTIS: Have there been any epidemiology studies of populations exposed routinely to extremely hot environments resulting in adverse effects?

DR. DUKES-DOBOS: A mortality study was recently completed in the steel industry. Results showed that there is an excess of deaths from nonmalignant gastrointestinal diseases. There is also an excess of mortality from cardiovascular causes in workers who worked less than 6 months in heat.

The interpretation which we suggest is that workers who worked less than 6 months left the job because they had a low level of cardiovascular fitness. This probably was a self-selective process. Subsequently, they died primarily from cardiovascular disease causes. However, we do not think there was a cause relationship between cardiovascular mortality and heat exposure. But it reflected a situation where there was self-selection.

The gastrointestinal morbidity is a different question. There is no certain explanation for this but there are several possibilities. If people are exposed to metabolic and external heat, they tend to shift their circulatory blood to the skin as an adaptive mechanism to dispose of the heat more efficiently. However, as a consequence, there is less blood circulating in other tissues. In an extreme case, in heat exhaustion, not enough blood reaches the brain. If there is enough blood for the brain, it is a known fact that there is a definite decrease of circulatory blood in the abdominal organs. The abdominal organs constrict and if this situation is repeated daily over a period of 8 hours, sooner or later these organs will weaken and perhaps in some places with ischemia may become damaged to such a point that the tissues may be necrotizing without causing a major problem because they are heating very fast, but, scar tissue remains which may be less resistant to pressures and may lead to conditions such as diverticulitis and the involved intestines may weaken to the point where they easily rupture and can cause death. This is a speculation based on several facts.

As far as microwave irradiation is concerned, circulatory shifts may develop even at levels which do not damage the organ. The circulatory shift occurs in the organ which is heated, but other organs may receive insufficient amounts of blood and suffer chronically more damage than the irradiated organ.

MR. CURTIS: The same question goes to a developing fetus. Could the circulatory shift result in adverse effects to the developing fetus?

DR. DUKES-DUBOS: There is a high probability of this although in our laboratory we found that pregnant animals' bodies shift circulation as much as possible to the developing fetus if other organs may suffer damage.

DR. STOLWIJK: Another thing is anytime there is a heat wave in July in New York City, the normal mortality of about 300 per day will increase to 600 or 1,000 per day. These deaths are not being borrowed from the next few days, they never come back. They are obviously heat-related. We do not know whether these people are particularly vulnerable (we suspect that they are) and we also do not know whether they have the combination of being vulnerable and being highly exposed. This combination information has never been sought out. We need to make the connections and go back to places where these individuals died to find out which of them had air conditioning and which did not. This information is important to know because things could be done to improve conditions where necessary, and, in the case of well air conditioned environments there is no specific reason to worry about the statistics.

SPEAKER: What was the age distribution in the heat wave death statistics?

DR. STOLWIJK: The age distribution was the same as it is normally. We have a proposal that is about ready at the moment to actually take a look at that for a couple of days. It is

a difficult and expensive thing because you have to send interviewers fairly shortly after the deaths to find out what the conditions were. Then we can reconstruct from information on the weather, the kind of building, what sort of thermal conditions existed. There we will have a better case.

Of course, there must be controls which are occurring on a normal day to see whether there is a systematic difference between the populations that died. The figures for the number of people involved is not negligible, and it is difficult when you consider the entire population and all the possible causes that might have contributed to them. In this particular case, we are not sure that it is the hot weather that directly killed these people.

MR. CURTIS: We have the regulatory authority to require medical monitoring and this is routinely done for certain chemical exposures. Is there an appropriate battery of tests which would be useful for people exposed to extremely high microwaves, radio waves, and lower frequency waves, or an extremely high acute dosage, or at extremely high levels for long terms?

DR. STOLWIJK: I think in microwaves and in workplace exposure this is not a likely event because there is already 10 mW/cm^2 as a guideline. Is that heavily violated?

MR. CURTIS: That is heavily violated, particularly in these frequencies we are currently discussing.

DR. STOLWIJK: The lower frequencies?

MR. CURTIS: Yes.

DR. STOLWIJK: I was in Sofia not too long ago looking at infrared for WHO. At that time, we had the opportunity to find out what the Bulgarians, who are operating at a level closer to 10 microwatts, are doing. I looked around in some of the factories in which I was making the measurements. These were typically case-hardening kinds of things, fairly low frequency, but very heavy fields. They were routinely running into fields that were 1,000 times what their guidelines were.

MR. CURTIS: We are talking about maybe 100 mW/cm^2 for 8 hours a day.

DR. STOLWIJK: They had levels like that. They said they were going to correct them eventually. Meanwhile, people were getting hazard pay.

DR. GLASER: That is an interesting observation about the fact that those fields do exist there.

DR. STOLWIJK: You are now talking about lower frequency because case-hardening is in the kilocycle range.

DR. GLASER: Induction furnace types of devices?

DR. STOLWIJK: Right.

DR. GLASER: Did you have an opportunity to observe any of the other frequencies, a higher frequency, or microwaves?

DR. STOLWIJK: There were not many higher frequencies because it was mostly metallic operations and there was no plywood or anything similar.

MR. CURTIS: Are there any medical tests that might -

DR. STOLWIJK: I think you mean the kind of test used for suspected heat stroke. That is what I would suggest. In other words, a kidney and liver function test after an acute exposure. I would go after the standard liver and kidney function battery.

MR. CURTIS: And how about a chronic exposure, about 100 mW/cm^2 , 8 hours per day?

DR. STOLWIJK: If you have a really heavy acute exposure, I would go after that battery. But for chronic exposure it is not worthwhile because there is no baseline. Without a baseline it is very difficult. To establish a baseline for kidney and liver function for a large population is difficult; moreover, there are too many extraneous influences that can have an effect on the baseline, such as alcohol.

MR. JANES: I am intrigued with the observation of the change in reaction times with loading.

DR. STOLWIJK: You should look at some of the work of David Wyon.

MR. JANES: I was wondering if this is as easily tested in a work situation as a diagnostic?

DR. STOLWIJK: Yes, but it is also one of the worst Hawthorne effects that you could possibly imagine. It is very difficult to do.

David Wyon has been conducting tests in terms of performance and productivity of factory populations as a function of ambient temperature, which ultimately then becomes body temperature. He followed an arousal theory that states there is an optimum arousal level for every task. If you overdo it, you are going to lose performance; if you underdo it, you will lose attention. However, he has been getting some rather interesting results and he basically concludes that if you supply people with an optimum of thermal comfort, they will probably perform at their worst. They will be sleepy, and perform at their worst.

DR. GLASER: Mumford suggested some years back that the 10 mW/cm^2 guideline should be modified in the presence of high environmental ambient temperature or high humidity conditions. Should that factor be considered for building into any recommendation at this point?

DR. STOLWIJK: I would worry about peak levels, especially about the cataractogenic kind at high temperatures. One ought to lower those levels because there has been a proven correlation between the ability of microwaves and infrared to produce cataracts in rabbits' eyes if it is done at a higher temperature. If it is done at a lower temperature, you have a huge amount of protection out of it. There is a direct relationship, and it obviously seems that at least the thermal factor is very closely identified with it. I would be concerned about peak levels.

For normal low levels, operating levels, I find it hard to believe that at 10 mW/cm^2 there is going to be more effect than that gained by raising the ambient temperature 2°C .

There is a similar problem in infrared, we have a recommended level for infrared at 10 mW/cm^2 . I think the Russians use 50 and relate it to the sun.

MR. JANES: The field is in such a position that for at least some frequencies one could give reasonable rates of absorption in watts per kilogram, then with that distribution as the question, what would you as a thermophysiolgologist expect to happen?

DR. STOLWIJK: I think that if one looks at this model and all the values in it, one may find that it can be used quite effectively. People at NASA and other places have used it effectively. I would be happy to try a particular set of conditions for which you would like an answer, and give you my expectation of temperature rises.

MR. JANES: Have you seen any of the modeling work that Emery and Guy have been doing out at the University of Washington, along with Lehman, in predicting temperature rise?

DR. STOLWIJK: Yes. I think I mentioned that Swann and Kritikos are doing something similar in Philadelphia. Guy is not using physiological changes as much. They are not built into the models. Also, I do not think he has the ability to deal with convective heat transfer by blood flow through the tissues.

MR. JANES: Emery's model has been used to predict temperature elevations for their diathermy applications. Lehman has some experimental verification, from actual sampling at depth, that the model is predictive.

DR. STOLWIJK: I think Swann and Kritikos have 1 or 2 students who are integrating models of deposition and models of temperature regulation, but I do not know how far along they are.

MR. JANES: However, the question still returns to what does .1 °C or 1 °C elevation in brain tissue mean physiologically? Could it explain some of these strange phenomena that have been reported as nonthermal effects in Eastern literature?

DR. STOLWIJK: Ellie Adair's monkeys are able to respond to levels of 2450 MHz that you would not think raise the temperature, yet they still make thermal adjustments to it.

MR. SWICORD: What complementary studies on a physiological basis could you perform to establish that fact? She is looking at a behavior endpoint.

DR. STOLWIJK: She is looking at a behavior endpoint that has consequences in changing the monkey's own temperature. It is done in a set of conditions where the monkey knows if there is something wrong with his temperature, he pulls the chain.

DR. ELDER: But in that experiment you do not actually measure any temperature change in the monkey. What can you physiologically monitor in animal studies that might give an index of thermal stress?

DR. STOLWIJK: I think we are going to have to turn to tissue temperatures. Ultimately, everything must be related to tissue temperatures if there is a thermal effect.

DR. ELDER: Are there biochemical changes that one might be able to find even before you get a temperature change?

DR. DASSLER: Definitive ones? No.

DR. GLASER: Is it possible that something could be occurring which is not accompanied by a measurable temperature change, such as stimulation of the nervous system?

DR. STOLWIJK: This is the Russian view. The difficulty is that the methodologies they use are very poor and there are no controls. You cannot get any kind of a handle on what they are doing and they are not willing to tell you. There are all sorts of problems you have to deal with. They are still doing studies in chickenwire kinds of cages and with everything bouncing around.

MR. JANES: But there are some more subtle things one can ask. If an animal is placed in a heat deficit situation where he has to control his body temperature by metabolic heat, and if you supply some of the heat exogenously, then are there subtle changes that might accompany dietary shifts or oxygen-balance shifts that you might pick up from the heat substitution? One would certainly see a temperature increase if there was substitution of heat sources.

DR. STOLWIJK: No.

MR. JANES: I don't know whether there is any physiology that goes along with that or not.

DR. STOLWIJK: No. One might see whether the monkey would prefer infrared over microwaves if placed in a deficit situation.

MR. JANES: This is a potential for expressing an effect that is not accompanied by a temperature increase.

DR. STOLWIJK: That is right. The monkey might prefer the heat one way over another. There are ways to get at this.

DR. DUKES-DOBOS: Reading the first draft of the criteria document, I find much of the controversial data contradicting. One of the greatest problems is that when the animals were exposed to radiofrequency or microwave radiation, there were no control groups exposed to heating by other means. If there had been controls one would be able to determine whether there was an additional effect and if the heat was brought about by radiofrequency or just heat by other means.

Any future experiments on radiofrequency effect should be accompanied by a control group where the same organ is heated by other means. Only through this will it be known whether there is a special radiofrequency effect, whether it is biochemical, nervous, etc.

MR. JANES: Certainly such experiments would help. The problem is that unless one is looking at steady state, uniform temperature distributions, it is not at all clear that one can deliver equal thermal loads to animal systems in a variety of ways. The distribution may be quite different, and it is that difference in distribution which uniquely leads to the results seen with whatever exposure modality one is using.

DR. STOLWIJK: If one wants to compare the monkey's attraction to microwaves or infrared, there are some dose estimation problems. In infrared, the fur affects the infrared dosage in strange ways that would have to be established. One knows where the infrared is deposited but not precisely where the microwaves are deposited. Even if one delivered what were thought to be equal doses, they might still not be equal.

MR. SWICORD: One would expect different responses from heating the surface than heating deeper in.

MR. JANES: Exactly.

DR. STOLWIJK: As a matter of fact, experiments have been conducted by Vendrick and Von Eych in Holland--Hendler had done some here, I think--in the days when people were still liberally exposing themselves to microwaves. The studies attempted to see why the perception of warmth from microwaves was so different than it was from infrared, because it takes a lot more microwaves to feel warm than it does infrared. Obviously, the reason is that it goes deeper and distributes itself. It deposits in a much larger mass and, as a result, the temperature increase is smaller.

MR. JANES: There is a difference in the sensory inputs too, isn't there?

DR. STOLWIJK: Yes. You are reporting what the sensory input is.

DR. GLASER: You might not ever even feel the sensation of warmth.

DR. STOLWIJK: The sensation of warmth is felt if enough is given.

DR. GLASER: How about down to 10 to 40 MHz diathermy frequency.

DR. STOLWIJK: No, you wouldn't feel it there.

DR. GLASER: Some years back, Belding published a paper in a heating and air conditioning journal.

DR. DASSLER: As I recall, about 4 or 5 years ago the question arose about Mumford's work and how Belding's would fit relative to it. The problem Belding had with the 1955 or 1956 paper was that coefficients were changed some years later and not published in the place one would expect to find them. These new coefficients were the reason I questioned reviewing the work. When I went over Mumford's paper and used even what we knew about 5 years ago, I had some reservations about whether there were enough effects from microwaves in contrast to what was seen in industrial conditions. In other words, microwaves did not seem to be that much of a contributing factor. I would like to recheck that. Using our computers with today's knowledge, we could take another look at the paper and perhaps at least remove any doubts that currently exist in my mind. As I recall, the paper was insignificant compared to what we would gain from the industrial study.

I am concerned with Dr. Stolwijk's observations in Sofia. Have the Russians any medical evidence of harm at these levels that they are working at currently? I am talking about subjective responses that people have. I would not call them medical problems but they do complain about headaches and vision. However, headaches and vision problems are found in 10 percent of any population, so it is difficult to judge these complaints.

MR. CURTIS: Would you feel right telling an industry that it would be illegal to expose people to more than 10 mW/cm^2 because of the thermal load on the worker? Are we, as a regulatory agency, proper in enforcing that 10 mW/cm^2 standard based on a thermal load?

DR. STOLWIJK: I feel that a 10 mW/cm^2 thermal load leaves a margin of safety for something that I do not know about. However, based on my knowledge, I would say it is a very conservative standard.

MR. CURTIS: Is there some level you would not consider conservative? I say this because, in the regulatory situation we need to know a definitely dangerous level, as opposed to a safe level. I cannot force a company to do something unless I can tell them, "Well, here is what I am protecting against." Is there some upper level that you would consider definitely too great of a thermal load?

DR. DASSLER: Probably for weakened tissue.

DR. STOLWIJK: I think you are probably thinking about eyes mostly.

MR. CURTIS: Are you talking about eyes and reproductive system problems, or just eyes?

DR. STOLWIJK: Eyes are the most sensitive. They have no circulation and very poor heat dissipation mechanism.

MR. JANES: That is a partial body exposure, though. There are some animal systems which will expire at cataractogenic doses before they produce cataracts. Thus, it is partial body exposure.

DR. STOLWIJK: Based on the thermal problem, I consider 10 mW/cm^2 a conservative standard. That provides you a lot of protection against things that might arise in unfortunate ways.

MR. JANES: But those ratios can exceed 1. We need to talk in terms of watts per kilograms or kilocalories and get away from this 10 mW/cm^2 . There is a model study with some experimental verification that shows that thigh temperatures in humans will exceed 44°C after 3 hours exposure at 10 mW/cm^2 to 70 MHz irradiation. That is a body resonance and that is where the body is absorbing factors of 10 greater than it does at higher or lower frequencies.

DR. STOLWIJK: Seventy MHz, 10 mW/cm^2 , and you go to 44°C .

MR. JANES: After 3 hours.

DR. GLASER: Thigh?

MR. JANES: Thigh.

DR. STOLWIJK: You are looking at a tissue which is very poorly perfused. The flow rate through there is about 1 or 2 ml per 100 per min. Thus, its ability to dissipate is not very good. The normal protective mechanism that you have in vasoactive tissue, that the circulation increases substantially before you get to 44°C , does not work very well either because the metabolic rate is still very low at that time. I have a little difficulty accepting a value that high, however.

MR. CURTIS: What kind of effect would you be worried about?

DR. STOLWIJK: At 44°C one is getting too close to protein denaturation.

MR. JANES: Vigorous diathermy treatment.

DR. STOLWIJK: Yes. Diathermy treatment is very short, isn't it?

MR. JANES: Twenty or 30 minutes.

DR. ATHEY: What kind of heat deposition do you think one should worry about? What rate?

DR. STOLWIJK: One should not have to worry about a heat deposition rate which approaches the basal metabolic rate of the body which is basically 1 W/kg . One watt per kilogram should be disposable with whatever circulation there is so that one does not get any accumulation.

MR. JANES: All tissues.

DR. STOLWIJK: Yes.

DR. ATHEY: Where should one start to worry?

DR. STOLWIJK: That depends on where you are.

DR. ATHEY: And conditions.

SPEAKER: What would be a worst case?

DR. STOLWIJK: The worst case would be, when you started going above 44°C with the possibility of very poorly perfused tissues going to denaturation, slipping away and going over 45°C . I would not be worried about the well-perfused tissues. Things like joints, eyes, and things that basically have no real perfusion would heat up under a very slow, persistent dissipation that was totally unexpected. I cannot think of what particular tissues I would be worried about but that would be the category.

MR. JANES: How would one factor dynamics into that in terms of some of the things we have heard concerning redistribution of blood supplies? If someone is exposed, whole-body, to something that begins to elevate the brain temperature, do the viscera get shut down?

DR. STOLWIJK: In general, there is a system in the body that deals with the distribution of blood, and there are certain reservoirs that are utilized when the blood is in short supply. When a big vascular bed is opened, some blood is going to stay and not return. It takes a

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