ABSTRACT

THERMAL CONDUCTIVITY OF THE CAT (FELIS DOMESTICUS) FOOTPAD EPIDERMIS: CHANGES PRODUCED BY CONTROLLED HYDRATION OF THE STRATUM CORNEUM

By

Kenneth Robert Holmes

Although it has been postulated that the thermal conductivity coefficient (k) of the epidermis is modulated by its hydration state, the relationship of changes in the epidermal k with external (exposure of the skin to a high ambient relative humidity) and internal (sweat gland activation) hydration has not been examined. Stratum corneum hydration was varied in 11 central hind footpads of 6 anesthetized, adult cats (2 to 5 kg body weight) of both sexes. Measurements of the transepidermal, steady state, heat flow (Q; Watts/m^2) and temperature gradient (T/x; ^{o}C/m) allowed 965 calculations of the epidermal thermal conductivity coefficient.

Footpad eccrine sweat gland activation (internal hydration) was elicited by administering supramaximal electrical shocks to the medial plantar nerve. Increased corneum hydration (as reflected by increasing

k) was achieved by delivering the shocks in a sequence of 1, 2, and 3 stimulations per second. Possible peripheral, cutaneous vasoconstriction due to the nerve stimulations was prevented selectively by the intravenous infusion of phenoxybenzamine, an alpha adrenergic receptor blocking agent. Exposure of the footpad epidermis to a high ambient relative humidity produced an external hydration.

For animals exposed to neither hydration effect, k was 0.167 $\pm$ 0.023 Watts/m ^{o}C. Internal hydration produced an average 49.5% increase in animals with pharmacologically blocked vasoconstriction, and an average 17.2% increase in other animals with restricted local (paw) blood flow due to peripheral nerve stimulation. External following internal hydration did not result in higher epidermal k in either group. In phenoxybenzamine treated animals, internal hydration increased k more than did external hydration (49.5% increase to 15.5% increase, respectively) and at a more rapid rate (4.22 x10^{-3} Watts/m ^{o}C min., to 0.63 x10^{-3} Watts/m ^{o}C min., respectively). Generally, for all animals, as k increased, independently of the hydration mechanism, transepidermal temperature gradients decreased. These data are interpreted as indicating that the hydration density of the cat footpad epidermis increases with either exposure to high ambient relative humidity or as a passive consequence of sweat gland activity. This increase in hydration density results in an increase in epidermal thermal conductivity which is speculated to affect patterns of biothermal regulation and the perception of temperature.

THERMAL CONDUCTIVITY OF THE CAT (*FELIS DOMESTICUS*) FOOTPAD EPIDERMIS: CHANGES PRODUCED BY CONTROLLED HYDRATION OF THE STRATUM CORNEUM

By

Kenneth Robert Holmes

A THESIS

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Department of Physiology

1972

ACKNOWLEDGEMENTS

I wish to offer my deepest and most sincere thanks to my friend, counselor, and guide, Professor Thomas Adams. Our many, enjoyable hours of personal and professional conversations will always be remembered and have surely been the keystone of the author's professional development. The support, encouragement, and perpetual enthusiasm which he has freely given have made these past years a most enjoyable experience. I look forward to our continued friendship and associations.

Special thanks are due my graduate guidance committee members, Drs. Lester Wolterink, S. Richard Heisey, James Schwinghamer, and Robert Echt for their friendship, support, and professional expertise in the review of this dissertation. I also wish to express my appreciation to my friend Dr. Lois Calhoun who offered constructive criticisms on portions of this manuscript. The photomicrographs contained herein were taken with a photomicroscope which was gratiously offered by Dr. Al Stinson. Thanks are due Dr. Bruce Walker for allowing this author to use the dark room

facilities in the Department of Anatomy.

Thanks are due Dr. James Beck who, in the early stages of this investigation, introduced the author to the mathematical, and physical principles which are reported herein.

The author wishes to express sincere thanks to his colleagues Drs. Mary Morgan and William Hunter for the years of association in the laboratory and office which have led to many fond memories. An expression of thanks is also due Mr. Frank Kutyna for his friendship throughout the course of this investigation.

Dr. Duane Haines deserves a special word of thanks. His contagious enthusiasm for the joys of research has represented a strong positive force in this author's pursuit of the doctoral degree. I will always value our friendship.

There is inadequate space here to allow an adequate expression of my very sincere thanks to my wife, Linda. She has given of herself completely and unselfishly so that I might fulfill the requirements of the M. S. and Ph.D. degrees; only a small part of those requirements is represented by this dissertation. Throughout the eight years encompasing my graduate training career, she has functioned as a housekeeper, wage earner, student (M. S. degree and doctoral candidate), wife, and above all, as mother to our three children; Denise, Kari, and Kenneth, Jr. This manuscript represents the patient efforts of her role as personal secretary. Her devotion on my behalf are truly monumental. I look forward

to the future, that I may tip the balance of responsibilities to her favor.

The research reported herein has been supported, in part, by funds from a NSF Predoctoral Fellowship in Biometeorology, and from General Research Support Grants from the Colleges of Veterinary and Human Medicine.

TABLE OF CONTENTS

Page

APPENDICES

LIST OF TABLES

LIST OF FIGURES

I. INTRODUCTION

Except for body orifices, man's exposure to the environment occurs at a well defined interface, the integument. The skin performs several important functions: it shields the body interior from the influence of the atmosphere, and mechanically protects the organism by being abrasion resistant; it acts as a barrier to the flow of mass and electrical charge (although the skin appendages, especially the merocrine (eccrine) sweat glands, offer a potential short circuiting of this barrier); it possesses transducers which sense environmental stimuli; and it serves as an organ of heat regulation, not only as a source of information into thermoregulatory centers of the brain, but also as a site for thermal energy exchange.

It is a common experience that one tolerates a cold exposure less well in a humid environment than in a dry one, and that it "seems colder" the higher the relative humidity. These (and other) physiologic reactions of man in a humid environment have been extensively reported, but it was Burton, et al. (1955) who first suggested that the greater cold sensation experienced in a damp cold climate "could be due to the uptake of moisture in skin at high humidities causing an increase in thermal conductivity in the region of the (thermal) receptors." The hypothesis was formed that ambient water vapor somehow interacts with the

integument to change its thermal transfer properties.

In order to define the role of peripheral thermal receptor function in temperature regulation, it is essential to evaluate factors which may modify their response characteristics at any ambient temperature or condition. Those factors which modify skin thermal properties may also affect skin thermal receptor response. Since skin temperature, as transduced by thermal receptors within the lower epidermis, is a critical determinant in body thermoregulatory control, any change in the thermal properties of epidermal tissue is potentially important in this regard.

The present study was designed to test the hypothesis that controlled changes in epidermal hydration as produced by eccrine sweat gland secretion or by a high humidity, warm air environment affects changes in the thermal conductivity properties of the skin.

II. LITERATURE REVIEW

Although there have been numerous reviews discussing the anatomy, histochemistry, physiology, biochemistry, and physical functions of the skin and its appendages (Lobitz and Dobson, 1961; Montagna, 1962; Nicoll and Cortese, 1972; Randall and Kimura, 1955; Rothman, 1954, 1959; Tregear, 1966; Weiner and Hellman, 1960), few report the structural and functional characteristics of the skin of the cat, Felis domesticus. The following review is a description of the biological properties and structure of hairless skin and specifically the merocrine (eccrine) sweat gland, emphasizing these features for the footpad skin of the cat. Literature discussing the role played by epidermal hydration in changing the physical properties of the skin will also be examined. Although data presented in this dissertation report physiologic changes in epidermal tissue as a function of sweat gland activity, this information is interpreted in relation to the structure of the skin, and an examination of epidermal and dermal anatomy is judged appropriate.

2.1 The Integument.

Textbooks of mammalian histology (Andrew, 1959; Dellmann, 1971; Trautmann and Fiebiger, 1957) describe the integument as

consisting of the "skin proper" (composed of two principal layers: an outer epidermis and an inner supporting connective tissue, the dermis) and the associated skin appendages (the hair follicles, the holocrine (sebaceous) glands, the apocrine glands, and the merocrine (eccrine) sweat glands). A subcutaneous layer of fat and connective tissue (called the panniculus adiposus, or simply the subcutaneous fat pad) attaches the skin to the subjacent organs and is sometimes classified as the third basic tissue division of the skin (Rushmer, et al., 1966).

Creed (1958) found merocrine (eccrine) glands in "most parts of the skin (of the cat), but in certain areas they are very sparsely distributed and difficult to trace". Strickland (1958), Strickland and Calhoun (1963), and Conroy (1964) disagree, and report that the merocrine sweat glands are present only in the footpads, whereas Dellmann (1971) stated that the eccrine sweat glands are mainly in skin areas with little or no hair. Trautmann and Fiebiger (1957) specify that in the cat, the eccrine gland may be identified in the oral region, circumanally, in the lower jaw, and in the footpads.

Sebaceous and apocrine glands, which are generally associated with the hair follicle, are not found in the footpads of the cat. Only the eccrine sweat gland occurs as a skin appendage in the hairless region of the footpad (Conroy, 1964; Creed, 1958; Strickland, 1958; Strickland and Calhoun, 1963). This is also true for the human palmar and plantar skin (Copenhaver, 1971; Bligh, 1967).

Associated with the skin and its appendages are muscles, blood

vessels, lymphatic vessels, nerves, and specialized nerve endings. When one considers the hairless skin of the footpad, the erector pili muscle which is associated with the hair follicle need not be of concern.

2.1.1 Epidermis.

The epidermis of the metacarpal pad of the cat's foot is classified as a stratified squamous keratinized epithelium. The epidermis is of ectodermal origin and gives rise to the merocrine (eccrine) sweat gland, the only skin appendage in the footpad. Epithelial tissue of the pad can be divided into two main layers (Trautmann and Fiebiger, 1957); the "succulent deep layer" (stratum germinativum or stratum Malpighii) and the superficial, keratinized, horny layer. These may be further divided into five strata: 1) the stratum basale (cylindricum), 2) the stratum spinosum, 3) the stratum granulosum, 4) the stratum lucidum, and 5) the stratum corneum. The cat footpad epidermal thickness ranges from 284 microns (Conroy, 1964) to 900 microns (Strickland, 1958) with an average thickness of 450 microns (Conroy, 1964).

The stratum germinativum (stratum Malpighii, or Malpighian layer) has been reported to be comprised of the stratum basale and the stratum spinosum (Andrew, 1959; Conroy, 1964; Creed, 1958; Trautmann and Fiebiger, 1957). Dellmann (1971), however, stated that the stratum germinativum represents the stratum basale. He did not define the Malpighian layer described by other authors. The stratum granulosum, lucidum, and corneum compose the "superficial

horny layer" (Trautmann and Fiebiger, 1957).

Crounse (1965) stated that the "prime and unique function" of mammalian epidermis is to serve as a "barrier" between the internal and external environments. He stressed that the prime biochemical product of the epidermis is the fibrous protein or mixture of proteins called keratin.

The stratum basale rests on the underlying dermis and consists of a single layer of generally tall columnar cells whose long axis is oriented perpendicular to the dermoepidermal junction. Scattered among these cells are melanocytes (of neural crest origin) which produce the pigment melanin and give rise to the color of the central, and digital pads (Conroy, 1964; Strickland, 1958; Strickland and Calhoun, 1963).

The cells of the basal layer are strongly basophilic, staining slightly darker than the cells of the other epidermal layers (Strickland, 1958). Basal cells contain a dark staining, basophilic nucleus, and a "scanty amount" of cytoplasm (Conroy, 1964) which contains an abundance of nucleoprotein (Creed, 1958). Creed (1958) reported that there are "certain sulfhydral groups" also present in the cytoplasm, and noted that with continued differentiation and migration through the Malpighian layer, the cells become progressively less basophilic, whereas the cytoplasmic sulfhydryl content increases. It has been postulated that the increase in sulfhydryl content in the germinal cells is related to the synthesis of keratin (Giroud and Leblond, 1951).

However, in studies with the electron microscope (EM) on human skin, Selby (1957) has shown that there is no net change (from the basal cell layer to the succeeding layers of the skin) of the tonofilaments (generally associated with sulfhydryl groups) which coalesce to form the keratin of the horny layer. He suggested that a fibrous keratin precursor is synthesized in the basal layer, and only after reaching the stratum granulosum does it change into the keratin of the stratum corneum. Electron microscopy reveals the basal cells to be rich in ribosomes (Dellmann, 1971) and mitochondria (Montagna, 1962).

The stratum basale is intimately attached to a basal lamina, or basement membrane. Small, cytoplasmic processes (rootlets) of the cells indent the basal lamina where they are surrounded by the lamina and reticular fibers, and attach the epithelium to the supportive dermis (Dellmann, 1971). Trautmann and Fiebiger (1957) stated that these basal cell cytoplasmic processes "penetrate the basement membrane". The findings of Mercer, et al. (1968) indicated that the basal cells are attached to the basement membrane at hemidesmosomes (see page 8). The saccharide cementing material seen between adjacent cells in other areas of the epidermis is not found between the basal cell and the basement membrane (Mercer, et al., 1968).

The dermoepidermal junction is easily disrupted by isosmotic solutions of high, or low pH (Baumberger, et al., 1941; Felsher, 1947). The extremes of pH bring about a swelling of the collagen fibers in the basement membrane, decreasing their cohesive strength, and weaken

the binding of the epidermis to the dermis (Baumberger, et al., 1941).

Superficial to the stratum basale is the stratum spinosum. In the cat foot pad this layer ranges from approximately 16 cell layers (Conroy, 1964) to as many as 38 cell layers thick (Strickland, 1958), thereby distinguishing it as the thickest of all the strata. The cells of the spinous layer are polygonal (Conroy, 1964), are flatter than the cells of the basal layer, and become progressively more flattened as they migrate toward the skin surface (Andrew, 1959; Conroy, 1964; Dellmann, 1971). These cells contain a moderate amount of eosinophilic cytoplasm, and their round-to-oval nuclei are less basophilic than those of the basal layer (Conroy, 1964).

Within the cells of the stratum spinosum are tonofilaments (epidermal fibrils, tonofibrils) which consist of submicroscopic filaments. These cell organells are loosely distributed throughout the cytoplasm as well as being organized into fibrils (Dellmann, 1971; Selby, 1957). Selby (1957) observed that the tonofilaments are, in general, directed from the nucleus to the cell periphery, terminating at the desmosomes. The tonofilaments ultimately evolve into the α-type keratin protein of the stratum corneum (Selby, 1957).

Adjacent cells of the epidermis are attached to each other by specialized structures called desmosomes. EM studies have shown that there is no cytoplasmic continuity at the desmosome. The plasma membrane, which is approximately 80 angstroms thick in the non-cornified Malpighian cells of the human epiderms (Hashimoto, 1969),

is continuous through the desmosomal structure.

Ham (1969) stated that: in a desmosome the membranes of adjacent cells "neither fuse nor come into direct contact with one another". At the desmosome the membranes are "both separated and connected by some material of low electron density". Ham (1969) stated that this material "probably represents the substance of the cell coats" of the adjoining cells. Although full detail of the intercellular adhesion remains unclear, Mercer, et al. (1968) have shown that "a polysaccharide-containing layer closely associated with the outside surface of the plasma membrane is clearly involved. Other components (Ca^{++} and proteins) are probably also".

To either side of this intercellular, desmosomal "substance" is the cell membrane of the contiguous cells. Hashimoto (1969) measured a 280 angstrom intercellular space at the desmosome. On the intracellular side of the membrane, at the desmosome, there is a condensation of electron-dense material. This was called an "attachment plaque" by Ham (1969), and from it bundled filaments (tonofibrils) extend off into the cytoplasm. In some areas, adjacent membranes are not attached by a desmosomal structure, but fuse to form an "occluding zonule or macule" (Hashimoto, 1969).

In contrast to the constant intercellular spacing measured at the desmosome, the plasma membranes in non-desmosomal areas are separated by varying amounts of space (Conroy, 1964). Wislocki, et al. (1951), working with the light microscope, showed that the epidermal

intercellular space is filled with a carbohydrate ground substance. In attempting to clarify whether the intercellular space of the human and pig epidermis represents "an empty lacunar system", Wolff and Schreiner (1968) employed the resolving power of the EM, together with an electron dense dye, ruthenium red, to visualize the location of acid mucopolysaccharide material. Their work has demonstrated the presence of a saccharide material lining the cell membranes and forming a carbohydrate cell coat (glycokalyx). They concluded that this intercellular carbohydrate material represents an intercellular cement. This is in general agreement with the work of Mercer, et al. (1968) who reported that in human epidermis the polysaccharides are located principally where the cell membranes are closely apposed, as represented by the "familiar parallel membranes (which are) spaced about 150 angstroms apart". The latter investigators also noted that there is an increase in the polysaccharide component of the cell membrane as the cell moves towards the stratum corneum, which they associated with cellular differentiation. This disagrees somewhat with the earlier investigations of Wislocki, et al. (1951) who demonstrated in human and rhesus monkey epidermis the distinct presence of the material in the intercellular spaces of the stratum spinosum and stratum corneum, but it is "distinctly less" abundant in the spaces of the stratum granulosum.

Intracellular membranes, such as those involved in the mitochondrial and nuclear structures, do not have a polysaccharide component associated with them (Mercer, et al., 1968).

The stratum granulosum, or granular layer, lies atop the stratum spinosum and is the most superficial of the epidermal layers whose cells are capable of vital processes. In the metacarpal pad of the cat, this stratum ranges from three (Conroy, 1964) to eight (Strickland, 1958; Strickland and Calhoun, 1964) cell layers in thickness. The cells of this layer are diamond or spindle-shaped (Conroy, 1964) and are finely serrated (Trautmann and Fiebiger, 1957).

In a detailed study of the structure and organization of the stratum corneum of several mammals, including man, Menton and Eisen (1971) have shown that the cells in the stratum granulosum of hairy skin are organized in vertical columns resembling "neat stacks of poker chips". The cells in each stack interdigitate at their edges with the cells in adjacent stacks. In contrast, they found that the granular cells of glabrous skin lack such specific organization.

The presence of large, deeply basophilic granular material within the cells of the stratum granulosum is noted in all reports of the histologic features of this layer. These keratohyalin granules increase in size and number as the cell migrates toward the surface and lends the granular appearance to this layer (Trautmann and Fiebiger, 1957). EM investigations have shown that the keratohyalin granules are an association of small granules and tonofilaments, with filaments extending from the aggregate structure (Dellmann, 1971).

Spearman (1970) demonstrated that the keratohyalin granules contain protein-bound phospholipids.

The cells of the granular layer show the first signs of transformation into the cells typically seen in the stratum lucidum and corneum, a process termed cornification, or keratinization. It is for this reason that the stratum granulosum has been referred to as the "transitional zone" by Jarrett, et al. (1965) and the "keratogenous zone" by Selby (1957), while the cells of this layer have been called "keratinocytes" (Wolff and Schreiner, 1968).

Giroud and Leblond (1951), Jarrett, (1965), Montagna (1962), Nicoll and Cortese (1972), and Selby (1957), among others, have described in detail the keratinization of the epidermis. The salient anatomical and chemical features of this process relevant to the present investigation are summarized below.

Matoltsy and Balsamo (1955) and Selby (1957) pointed out that two chemical processes proceed simultaneously during keratinization of a cell: 1) there is a formation and consolidation of keratin, and 2) there is a disintegration, resorption, and possibly the complete metabolic utilization or alteration of those cellular structures not directly involved in the formation of keratin. Keratinization proceeds at the periphery of the cell (Jarrett, et al., 1965) where there is a pronounced consolidation of tonofilaments into tonofibrils (Selby, 1957). Selby (1957) has suggested that the tonofilaments consist of a fibrous keratin precursor which is synthetized in the stratum

basale. The tonofibril contains sulfhydryl groups associated with cysteine residues. During keratin formation the protein-bound sulfhydryl groups are oxidized to the disulfide bond of cystine (Giroud and Leblond, 1951; Spearman, 1970). That the process progresses from the periphery may be due to a greater oxygen concentration in that region of the cell, since the formation of disulfide linkages proceeds spontaneously in the presence of oxygen and catalysts (Jarrett, et al., 1965).

Selby (1957) suggested that keratinization involves a molecular rearrangement of several alpha helices making up one tonofilament with the result that individual tonofilaments become bound to each other laterally through the newly formed disulfide groups. Thus, the tonofibrils are most likely made up of individual polypeptide chains which are joined to form a closely knit mass whose main direction is parallel to the skin surface (Giroud and Leblond, 1951). Giroud and Leblond (1951) speculated that it is the extensive cross-linking between the polypeptide chains of the tonofibrils which accounts, in part, for the strength and chemical inertness of keratin.

X-ray diffraction studies conducted by Rudall (1947) demonstrated that the structural protein of vertebrate epidermis is of the α-keratin type. Baden and Bonar (1968) confirmed this when they reported the isolation of a α-fibrous protein, or proteins" from the insoluble residue of human stratum corneum, and epidermis. They suggested

that the protein is in "an aggregated state" because of its very large molecular weight. They noted that "about 50% of the ∝-protein is helical in structure".

Coincidently with keratinization of the tonofilaments, the cell nuclei shrink and undergo chromatolysis (Trautmann and Fiebiger, 1957), and there is a lysis of intracellular, non-keratin material. Jarrett, et al. (1965) noted that in human palmar and plantar skin, the degree of autolysis is such that only the nucleus is ultimately removed, while most of the cell cytoplasm becomes involved in the process of keratinization.

According to Jarrett, et al. (1965), hydrolytic enzymes such as acid phosphatase, nonspecific esterase, ribonuclease and deoxyribonuclease are released when cells from the stratum spinosum reach the granular layer. Cytoplasmic materials not bonded by disulfide groups are hydrolyzed, while the disulfide linkages protect the keratin from dissolution (Jarrett, et al., 1965). They theorized that these enzymes disrupt the protein moiety of the structural phospholipoprotein, exposing active phospholipid groups. These authors also stated that the binding of the phospholipid to the protein molecule is via the fatty acid side chains.

The stratum lucidum lies between the stratum granulosum and stratum corneum. Although not present in the general body skin, it is best developed in the skin of the foot pad (Andrew, 1959; Creed, 1958; Strickland, 1958; Strickland and Calhoun, 1963). Strickland

(1958) found the stratum lucidum to measure 28 to 40 microns in thickness in the metacarpal foot pad skin of the cat. Trautmann and Fiebiger (1957) reported that the cell boundaries within this layer are "obscured", whereas Spearman (1970 found no discernible cell outlines or intercellular spaces with the light microscope. The high resolving power of the EM reveals, however, patent cell membranes within this layer (Selby, 1957).

The cells of the stratum lucidum are flat, closely packed (Andrew, 1959; Dellmann, 1971; Trautmann and Fiebiger, 1957), and devoid of organelles (Dellmann, 1971). They are generally described as anuclear (Conroy, 1964; Trautmann and Fiebiger, 1957) or as containing a nucleus which is "often shrunken" Dellmann, (1971).

In contrast to the deeply basophilic, granular appearance of the stratum granulosum cells, those of the stratum lucidum contain no hematoxylin-stainable material (Spearman, 1970), and usually do not stain well in histologic preparations (Andrew, 1959). When viewed with the light microscope, the stained stratum lucidum has been described as a shiny, acidophilic, homogeneous, clear, or transparent layer (Conroy, 1964; Dellmann, 1971; Trautmann and Fiebiger, 1957). Because of its minimal stainability, the stratum lucidum is often referred to as the light, or clear layer. The EM has shown, however, that the cytoplasm is packed with filaments which are embedded in an electron-dense matrix (Dellmann, 1971).

Spearman (1970) has demonstrated that protein-bound sulfhydryl

groups are present within the stratum lucidum. In human and guinea-pig skin, this layer shows a strong, diffuse reaction for bound phospholipids (Spearman, 1970), which are attached to the keratin protein (Jarrett, et al., 1965). Spearman (1970) speculated that the keratin-phospholipid complex may be involved in the barrier to epidermal water penetration which is "known to be located at the base of the stratum corneum".

As the granulosum cells migrate into the stratum lucidum, an abrupt change usually occurs in the desmosomal structure (Selby, 1957) and cellular envelope (Hashimoto, 1969). Selby (1957) found that the intercellular material forms a "denser band" at the desmosome than can be seen at the desmosomal structure of the preceeding layers. Hashimoto (1969) reported the development of an electron-dense band on the cytoplasmic side of the inner layer of the trilaminar plasma membrane. This "marginal band", when fully developed, is approximately 160 angstroms thick (Hashimoto, 1969) and is composed of dense packing of fibrous proteins (Christophers, 1971). Hashimoto (1969) observed that the cell membrane retains its original thickness of 80 angstroms as seen in the deeper epidermal cells.

The most superficial layer of the epidermis is the stratum corneum. The cornified epithelium represents the completed product of the keratinization process. "In the simplest sense," noted Loomans and Hannon (1970), "the stratum corneum is a heterogeneous mixture of intracellular keratins, cell envelopes, and intercellular materials."

In the domestic cat, the stratum corneum is thickest, and best developed, in the pads of the foot. There is considerable difference in the measured thickness of this layer as reported by various investigators. Strickland (1958) stated that the metacarpal foot pad corneum ranged from 15 to 35 microns in thickness, whereas Strickland and Calhoun (1963) reported a range of 15 to 81 microns. A foot pad stratum corneum ranging from 92 to 320 microns, with an average of 200 microns, was measured by Conroy (1964).

The cells of the corneum are usually flat (Andrew, 1959; Dellman, 1971; Trautmann and Fiebiger, 1957), but may occasionally be swollen or vesicular (Trautmann and Fiebiger, 1957). Menton and Eisen (1971) pointed out, however, that the cells of the stratum corneum are "significantly thicker" than corresponding cells from the general body surface. In contrast to the neatly stacked vertical columns of cells seen in the stratum corneum of the general body surface, the cornified cells in the foot pads of various mammals and in the human palmar and plantar skin lack a specific architectural organization and are never seen to "stack" into columns (Christophers, 1971; Menton and Eisen, 1971).

Stratum corneum cells stain lightly in normal histologic preparation (Dellmann, 1971), are eosinophilic (Conroy, 1964) and also anuclear. The EM reveals the tonofibril of the corneum to be a more intimate association of granules and tonofilaments than seen in the stratum lucidum, with this complex being embedded in an electron-

dense matrix (Dellmann, 1971). The tonofibril matrix of the cornified cell is "tightly packed" (Matoltsy and Balsamo, 1955). Cells of the stratum corneum are devoid of organelles (Dellmann, 1971).

In a study of the components of the cornified epithelium of human skin, Matoltsy and Balsamo (1955) reported that approximately 10% of the dry tissue is soluble (in "Sorensen's standard phosphate buffer") epidermal keratin (the protein, α-keratin), 10% are dialyzable substances (peptides, lysine, glutamic acid, tyrosine, phenylalanine, aspartic acid and arginine) some of which are water binding (Bull, 1944), 65% insoluble epidermal keratin, 7-9% lipids and 5% cell membranes (which are resistant to strong alkali and reducing substances). Glycogen is also found in the cells of the stratum corneum (Giroud and Leblond, 1951). Sulfhydryl groups, observed within the granular layer of the epidermis, can no longer be demonstrated in the stratum corneum. However, the sulfur contained within the corneum is present in the disulfide linkage of protein-bound cystine (Spearman, 1970).

The lipids and phospholipids in the corneum persist through the keratinization process. However, there is some decrease in content, especially of the phospholipids, from that seen in the Malpighian layer (Giroud and Leblond, 1951). The pronounced reduction in phospholipid has been attributed to the hydrolytic action of alkaline phosphatase (Jarrett, et al., 1965). Giroud and Leblond (1951) reported that some of the lipid carried into the horny layer

must be protein bound since the lipid solvents used in paraffin embedding techniques leave lipid stainable material in the cells. Whereas Jarrett, et al. (1965) supported this view when reporting keratin-bound phospholipids within the "horny layer" of human palmar and plantar skin, Spearman (1970), after processing human skin in alcohol and xylene, or leaching the skin with petroleum ether, could not demonstrate the presence of protein-bound phospholipids in the stratum corneum. The latter investigator found bound phospholipids in the stratum lucidum, however, and suggested that the loss was due to continued enzymatic autolysis to soluble materials.

The keratinized cell envelope, composed of the fully developed marginal band and the plasma membrane, ranges in thickness from approximately 150 angstroms (Matoltsy and Matoltsy, 1966) to 300 angstroms (Mercer, et al., 1968). Hashimoto (1969), reporting EM studies on human stratum corneum, observed that the original plasma membrane, while maintaining its 80 angstrom thickness, generally peels off the marginal band in the upper layers of the corneum. While maintaining its thickness, the marginal band occasionally folds and separates from the filamentous matrix of the cell. The marginal band represents the thickened cellular envelope described by other investigators (Hashimoto, 1969).

In studies on the 300 angstrom thick "cell membrane" of human stratum corneum cells, Mercer, et al. (1968) noted several unusual aspects of this thickened membrane. They reported that the cell

membrane was insoluble in keratinolytic reagents. Also, histologic procedures which normally remove polysaccharides from the tissue failed to do so in the cell membrane. This suggested to them that the cornified "cell membrane" had been "chemically modified" in passing from the stratum granulosum into the keratinized layer. Loomans and Hannon (1970) demonstrated that the cell envelopes are resistant to the proteolytic enzyme, subtilism. In addition, the latter investigators found that once the integrity of the envelope is physically disrupted, the normally insoluble cytoplasmic constituents are subsequently degraded. As previously noted, Matoltsy and Balsamo (1955) found that the "cell membrane" was "highly resistant" to strong alkali and reducing substances.

Matoltsy and Matoltsy (1966) determined the amino acid composition of isolated human plantar stratum corneum cell envelopes. They observed that the protein component of the envelope differed from that of the keratin preparation obtained from the same tissue. "Significantly large" quantities of proline and cystine were found compared to that of the "epidermal keratin". It was concluded that the high proline content indicated that the envelope protein could not be a fibrous protein because the presence of proline in polypeptide chains prevents the formation of alpha-helices. Further, the high cystine content suggested that this protein was probably "more firmly stabilized" by disulfide linkages than the epidermal keratin.

Hashimoto (1969) speculated that the original plasma membrane

serves no useful purpose as a cell membrane in the cornified cells, whereas the developed marginal band "serves as the real cell membrane".

The dense intercellular material seen in the desmosomal structure of the stratum lucidum, is lost in the lower layers of the stratum corneum. As a result, the apposing cell membranes come closer together, and the normal 280 angstrom intercellular, desmosomal space is reduced to 200 angstroms (Selby, 1957). The desmosome of the human stratum corneum is resistant to the proteolytic enzyme, subtilism (Loomans and Hannon, 1970). Although the palmar and plantar stratum corneum cell surface lacks the surface folds and creases seen in corresponding cells of the general body surface, they do have many long, foliated villi distributed evenly over their surface (Menton and Eisen, 1971). Menton and Eisen (1971) speculated that these villi represent the attachment sites of the desmosomes.

There is a condensation of the intercellular material commencing in the mid-stratum corneum (Hashimoto, 1969). Also, the carbohydrate component of this substance which is speculated to represent the intercellular cement (Wolff and Schreiner, 1968) becomes difficult to identify (Mercer, et al., 1968). However, the intercellular material which lies within the limits of the desmosome continues to react strongly to identifying stains (Mercer, et al., 1968).

Mercer, et al. (1968) deduced that the desmosomes were the "main device holding the (stratum corneum) formation together".

2.1.2 Dermis.

The dermis (corium) is the inner, supportive, connective tissue portion of the integument. The bulk of the dermis consists of mesodermally derived tissue which includes collagenic, elastic, and reticular fibers and ground substance (acid mucopolysaccharides hyaluronic acid, and chondroitin sulfate B). It also contains blood vessels, lymphatics, nerves, and specialized nerve endings. Conroy (1964) noted that certain mesodermal cells may also be found in normal feline skin including mast cells, fibroblasts, histiocytes, and melanophores.

The dermis extends from the stratum basale of the epidermis to the underlying fatty, areolar, subcutaneous tissue, the panniculus adiposus. Although its upper border, the basement membrane of the epidermis, is well defined, Andrew (1959) and Dellmann (1971) have reported that the dividing line between the dermis and the subcutaneous tissue is not a sharp one.

Conroy (1964), Strickland (1958), and Strickland and Calhoun (1963) found that the dermis of the cat's footpad is divided into two distinct divisions; the more superficial stratum papillare, and the deeper stratum reticulare. This contrasts with the work of Creed (1958) who reported that the cat footpad dermis is not recognizable as a two-layered structure.

1). The collagenous (and reticular) fibers are fine in texture and densely interwoven in the stratum papillare. Numerous elastic fibers are found, and these form a fine network in this layer (Conroy, 1964). Strickland (1958) observed that these connective tissue fibers are usually oriented parallel to the dermoepidermal junction.

The basement membrane is seen as a condensation of reticular fibers (elastic fibers are probably also present (Dellmann, 1971)) in the form of a flat meshwork lying in a viscous ground substance (Creed, 1958).

2). In the stratum reticulare, the collagen fibers are approximately three times larger than the collagen fibers in the papillary layer (Strickland, 1958). These fibers form prominent bundles which are arranged into a dense, irregular meshwork parallel to the surface of the epidermis. Compared to the papillary layer, there is an increased number of elastic fibers, and these fibers are found to extend in all directions (Strickland, 1958).

The subcutaneous tissue (hypodermis, or panniculus adiposus) is a thick layer in the foot pad of the cat. It is composed of thick bands of collagenous fibers and abundant smaller elastic fibers which interweave and enclose small clusters or large masses of adipose tissue (Trautmann and Fiebiger, 1957).

2.1.3 Innervation and Blood Supply

Blood vessels are numerous and distributed diffusely throughout the dermis (Dellmann, 1971; Rushner, et al., 1966). The blood

vessels of the stratum papillare are predominately in the form of capillary loops (Dellmann, 1971).

Detailed descriptions of the afferent innervation of the foot pads of the domestic cat have previously been reported (Jänig, 1971; Malinovský, 1966). These reports indicate that receptors are located in all three layers of the cat's food pad; the epidermis, corium, and subcutaneous tissue. However, only free nerve endings are found in the epidermis, and these do not penetrate beyond the cells of the stratum granulosum in human skin (Copenhaver, 1971).

Efferent nerves to the blood vessels and sweat glands of the foot pads are postganglionic fibers from the sympathetic division of the autonomic nervous system. They enter the foot pad via brances from, and terminations of, the nerves which supply the skin of the distal extremities; the superficial plantar nerves in the cat (Langley, 1923).

2.2 The Merocrine (Eccrine) Sweat Gland

The merocrine gland is an ectodermally derived exocrine gland. It is classified as a simple, coiled, tubular gland, and secretes its products without cell destruction. Although Munger and Brusilow (1961) noted that this structure in the cat foot pad has been regarded as eccrine in type, Montagna, et al. (1953) stated that the gland in the cat is in no way comparable to the human eccrine sweat gland. However, Munger and Brusilow (1961) found that the cytology of the gland in the cat foot pad, as seen with the light microscope,

is identical with that in the human. Nevertheless, these latter investigators demonstrated with the EM that the structure of the cat sweat duct is "markedly different" from that reported for the human duct. Also, the cat eccrine gland secretion (sampled at the foot pad surface) is a hypertonic solution of sodium and potassium chloride, and differs markedly from human palmar sweat (Munger and Brusilow, 1961).

The eccrine sweat gland is the only skin appendage in the glabrous foot pad of the cat (Conroy, 1964; Creed, 1958; Strickland, 1958; Strickland and Calhoun, 1963). Although the gross anatomy and histology of the cat eccrine gland has been reported (Conroy, 1964; Munger and Brusilow, 1961; Sperling and Koppanyi, 1949), many of the details of the secretory process, innervation, blood supply, and ultrastructural characteristics of the eccrine gland and gland-skin association are found only in reports describing this gland in the human and non-human primate.

The eccrine gland in the cat is described as being divided into two functionally distinct parts: 1) the secretory segment, and 2) the excretory duct, or simply, the duct. In a detailed morphological investigation of the merocrine gland in the cat, Munger and Brusilow (1961) described the duct as extending from the foot pad surface to the base of the epidermis, while the secretory segment extends through the dermis and into the panniculus adiposus. Throughout its length within the dermis and fat pad, the gland forms an undulating tube, and lacks the coiling seen at the dermosubcutaneous junction in

human skin.

According to Holyoke and Lobitz (1952), that portion of the eccrine gland which is located within the epidermis is the "pore" of the gland. Lobitz, et al. (1954) subsequently defined this portion of the duct the "epidermal sweat duct unit" to include the ductal cells together with the periductal epidermal cells which are concentrically arranged around the cells lining the ductal orifice.

In this review, the eccrine sweat gland in the cat's foot pad will be discussed in four parts: 1) the secretory segment, 2) the dermal, excretory segment, 3) the epidermal sweat duct unit, with emphasis on the ductal morphology within the stratum corneum, and 4) the innervation and blood supply to the gland.

2.2.1 The Secretory Segment

The secretory segment of the cat foot pad sweat gland extends from the dermosubcutaneous junction, through the subcutaneous fat pad, and terminates just above the fascia that forms the base of the pad (Munger and Brusilow, 1961). From the gland lumen outward, the secretory segment is composed of three layers: 1) the glandular cells, 2) the myoepithelial cells, and 3) the tunica propria, or basement membrane (Fujisawa, 1959).

Conroy (1964) reported that the secretory cells are arranged in a single layer around the lumen of the gland. However, other authors (Kamamura, 1957; Sperling and Koppanyi, 1949) report that the lining of the lumen is composed of pseudostratified epithelium in which a

"superficial" cell adjoins the glandular cavity while a "basal" glandular cell does not extend to the lumen. Working with human tissue, Montagna, et al. (1953) and Hibbs (1958) found that both the superficial cell and the basally located cell contact the basement membrane of the secretory segment, and concluded that there is only "one real layer" of glandular cells. Fujisawa (1959) noted that the arrangement was "complicated and irregular" in the cat eccrine secretory segment. The glandular cells are variously described as ranging from cuboidal to columnar in shape (Conroy, 1964; Sperling and Koppanyi, 1949).

The lumen in the secretory segment of the gland ranges from 11 microns to 24 microns in diameter (Conroy, 1964). This range encompases the measurement reported by Holyoke and Lobitz (1952) for the human secretory segment lumen, whereas Hibbs (1958) noted that the lumen varied from 5 microns to 30 microns in diameter.

The secretory cells possess abundant cytoplasm and round basophilic nuclei. The cells are classified into two categories, dark and clear, according to their staining characteristics. As viewed with the light microscope, the dark cell ("mucoid cell") has a basophilic cytoplasm with secretory vacuoles which stain selectively for acid mucopolysaccharide (Munger and Brusilow, 1961) and shows a strong acid phosphatase activity (Kamamura, 1957). As revealed by the EM studies of Munger and Brusilow (1961), mitochondria are lightly scattered throughout the dark cell cytoplasm, and

the cell contains a prominent Golgi apparatus.

In contrast with the dark cell, the cytoplasm of the clear cell ("chief cell") is not basophilic, does not stain for mucopolysaccharide (Munger and Brusilow, 1961), and shows little acid phosphatase activity (Kamamura, 1957). The clear cell does, however, contain periodic acid Schiff-positive diastase-digestible material which Munger and Brusilow (1961) presumed to be glycogen. The EM reveals the cytoplasm of the clear cell in the cat eccrine gland to be predominately granular, with many of the granules resembling glycogen units (Hashimoto, 1971a; Munger and Brusilow, 1961). Numerous mitochondria are present in the cytoplasm of the clear cell. These cells are associated with intercellular canaliculi, and numerous closely packed microvilli project into the canaliculi (Munger and Brusilow, 1961). Based on staining characteristics and ultrastructural detail, Munger and Brusilow (1961) deduced that the secretory segment of the cat and human eccrine sweat gland are identical.

A layer of myoepithelial cells is found between a hyalin basement membrane and the secretory cells. The myoepithelial elements are elongated fibrillar cells possessing long processes resembling pseudopodia which extend from each end of the cell body (Sperling and Koppanyi, 1949). According to Sperling and Koppanyi (1949) these cells follow approximately the long axis of the secretory tubule. This differs somewhat from the description offered by Hibbs (1958) who reported that the myoepithelial cell spirals around the periphery of the tubule. He also noted that this

cell may be placed between the secretory cells of the gland. Myoepithelial cells are seen throughout the length of the secretory segment of the gland in the cat (Sperling and Koppanyi, 1949). Sperling and Koppanyi (1947) reported that the myoepithelial cells are not contractile, but rather change their size by retracting the pseudopoid processes while reducing their cell volume. These latter investigators subsequently (1949) speculated that this loss of "water" volume constitutes a considerable contribution to the initial outflow of sweat from a stimulated gland.

2.2.2 The Secretory Process.

Hashimoto (1971a) has established the anatomical features and distribution of the intercellular canaliculi associated with the clear cell of the human eccrine secretory segment. His report hypothesizes a route of fluid transport leading to the formation of eccrine sweat under physiological conditions. Dobson and Sato (1972), in a review which includes supportive metabolic data, have utilized Hashimoto's (1971a) findings to postulate the physiological processes involved in sweat formation.

According to Dobson and Sato (1972) the formation of sweat utilizes an energy-dependent sodium pump. They theorized that sodium is pumped across the membrane of the clear cell into the canaliculus producing a hypertonic solution of sodium within the canaliculus. Concomitantly water flows from the extracellular fluid, across the secretory cell, and into the canaliculus to restore osmotic equilibrium. The canaliculus conducts the secretory product to the secretory segment lumen.

2.2.3 The Dermal Segment.

In the cat, the dermal segment of the merocrine sweat gland has been described as a "slightly undulating tube" whose length is estimated to be one tenth of the total length of the gland (Munger and Brusilow, 1961). In the human, this non-secretory segment is one third to one half of the gland length (Montagna, et al., 1953). The duct lumen in the cat has been measured by Conroy (1964) and averages 10 microns in diameter.

The lining of the dermal segment of the gland has two layers: 1) a superficial layer of lumen-bordering cells, and 2) a deep layer of basal (peripheral) cells resting on a basement membrane which Ellis and Montagna (1961) described as being indistinct in the primate Macaca mulatta. Munger and Brusilow (1961) observed that the superficial cell nucleus is large and irregularily shaped, while the cell contains little cytoplasm. Comparing their observations with those of Munger (1961), Munger and Brusilow (1961) found far fewer mitochondria in the superficial cell of the cat eccrine sweat gland than are found in this cell in the human gland.

The luminal edge of the superficial cell appears homogeneous and dense when viewed with the light microscope (Munger and Brusilow, 1961). This cellular feature corresponds to the "cuticular border", or "cuticle" observed by other investigators (Charles, 1960; Hibbs, 1958; Holyoke and Lobitz, 1952; Montagna, et al., 1953; Munger, 1961; O'Brien, 1952) in the human eccrine sweat duct. According to O'Brien (1952) the cuticle in the human eccrine gland extends from the opening of the duct at the skin

surface, to the junction of the duct with the secretory segment. However, the EM investigation by Ellis and Montagna (1961) showed that there is a gradual disintegration of this structure as the duct traverses the stratum corneum in the monkey, Macaca mulatta.

The cuticle has been reported to be a lining structure separate from, but attached to, the surrounding epithelial cells (O'Brien, 1952). However, EM studies of the human (Hashimoto, 1971b; Munger, 1961) and cat (Munger and Brusilow, 1961) eccrine duct reveal this structure to be a layer of condensed intracellular tonofilaments and granules. Ellis and Montagna (1961) concluded that the ultrastructural features of the luminal border of the superficial cell in the macaque are similar to those reported in man. Hashimoto (1971b) described the cuticle as a "periluminal network" of tonofibrils. In the cat, this network is located just beneath the low microvilli which characterizes the luminal edge of the surface cell (Munger and Brusilow, 1961). Ellis and Montagna (1961) observed tonofilaments from the cuticle inserting on the attachment plaques of the desmosomes along the lateral borders of adjoining luminal cells. Compared to the human, the cuticular structure in the cat is thin, and no mitochondria are embedded in its substance (Munger and Brusilow, 1961).

The cuticle gives an intense staining reaction for disulfide groups. Lobitz, et al. (1954) noted that this structure has a disulfide concentration which is similar to that found in the cells of the stratum corneum. Ellis and Montagna (1961) speculated that the function of the cuticular tonofibrils is to form a rigid ring which prevents the collapse and occulsion of

the duct lumen.

Ellis and Montagna (1961) showed that the plasma membranes of adjoining surface cells in the macaque are extensively and elaborately interdigitated. Numerous desmosomes are also present. These authors found no special junction structure at the luminal interface between adjacent cells. However, close to the luminal border, the membranes of adjacent cells are connected by an elaborate system of desmosomes, some of which are characterized as being large. Ellis and Montagna (1961) postulated that these large desmosomes serve as a buttressing and tonofibril insertion point that strengthens the luminal border architecturally. These authors stressed that this did not rule out possible physiologic functions of the cuticle or the large desmosome.

Using lanthanum as an electron-dense tracer of the intercellular spaces (ics's), Hashimoto (1971b) presented evidence that the luminal end of the ics between the superficial ductal cells is closed by a tight junction. The technique did not allow the confirmation of a similar junction at the basal junction between adjacent peripheral cells.

Ellis and Montagna (1961) observed that the basal cell cytoplasm consists of membranous and granular components embedded in a predominately amorphous matrix. A Golgi apparatus was not observed in the cytoplasm. However, glycogen granules and numerous mitochondria can be seen in the basal cells of the macaque eccrine sweat gland. Whereas numerous mitochondria are likewise reported (Munger, 1961) to be present in the basal cells of the human duct, only very occasional

mitochondria were found by Munger and Brusilow (1961) in this cell in the cat. In Macaca mulatta, the basal cell cytoplasm near the plasma membrane has a fibrous appearance, being considerable denser than the cytoplasm near the center of the cell (Ellis and Montagna, 1961).

Ellis and Montagna (1961) demonstrated that the plasma membranes between adjacent basal cells are highly convoluted. In contrast, the basal border of the cell is usually smooth. Adjacent cells are connected by small desmosomes, and the desmosomes are not nearly as numerous as on the luminal cells.

Human eccrine sweat is hypotonic to blood plasma, although the final composition of the sweat is dependent upon the activity of the gland (Lobitz and Dobson, 1961). Schwartz and Thaysen (1956) first postulated that the hypotonicity of human sweat was the result of reabsorption of sodium in the sweat duct. In contrast, the sweat secretion from the eccrine gland in the footpad of the cat is a hypertonic solution of sodium and potassium chloride (Brusilow and Munger, 1962). Brusilow and Munger (1962) attributed this difference to the rudimentary nature of the duct in the cat; that is, to its shorter duct segment, and to the fewer mitochondria in the duct cell. The mitochondria supply the necessary energy for the ductal reabsorption of sodium ion in the human eccrine sweat gland (Liisberg, 1969). This process which has recently been reevaluated by Hashimoto (1971b) using the supportive enzyme data reported in the studies of Sato and Dobson (1970), and Sato, et al. (1971).

2.2.4 The Epidermal Sweat Duct Unit.

Literature describing the merocrine epidermal sweat duct in the cat is sparse. Sperling and Koppanyi (1949) observed that the duct follows a spiral course through the epidermis. As viewed from the surface, the duct spirals into the stratum corneum of the human palm predominantly in a right-handed, or clockwise direction (Takagi and Tagawa, 1955), while in the M. mulatta, it is consistently so directed (Wolf, 1968b). Sperling and Koppanyi (1949) found that the duct configuration, within the stratum corneum of the cat footpad, changes to that of a loosely convoluted tube following an episode of sweating. Wolf (1968b), in commenting on the screw-like ascent of the sweat duct in the stratum corneum of the macaque palm, reported that the number of threads on the sweat duct screw vary depending on the thickness of the horny layer. Takagi and Tagawa (1955) measured the overall spiral diameter and thread pitch for the duct in the human palmar and plantar stratum corneum to be 40 microns to 80 microns, and 30 microns to 50 microns, respectively.

Sperling and Koppanyi (1949) reported that the diameter of any of the epidermal ducts remains fairly constant throughout its course in the epidermis, although the diameter varies among ducts in the pad. These authors measured lumen diameters ranging from 3.5 microns to 10 microns. Conroy (1964) calculated the average intraepidermal duct lumen in the cat footpad to be 12.5 microns in diameter. As the duct approaches the footpad surface, it assumes a funnel shape, whose base is at the surface. Sperling and Koppanyi (1949) found the duct lumen to vary from 14 microns

to 16 microns in diameter at the footpad surface.

Some authors (Andrew, 1959; Bloom and Fawcett, 1968; Trautmann and Fiebiger, 1957) contend that the lumen of the intraepidermal portion of the sweat gland is devoid of a wall of its own, being simply a channel through, and surrounded by, the epidermal cells. In contrast however, and supported by histochemical staining, chemical corrosion, and mechanical abrasion techniques, many authors conclude that the intraepidermal lumen of the eccrine gland is surrounded by at least one (Zelickson, 1961) or more (Hashimoto, 1971b; Pinkus, 1939; Takagi, 1952; Wolf, 1968a; Zelickson, 1961) layers of cells which are clearly delineated from the cells of the surrounding epidermis. Blair (1968) was able to demonstrate that the human eccrine sweat lumen is wrapped tightly with approximately 16 layers of cells which differ from the general cells of the stratum corneum. According to Conroy (1964) the intraepidermal portion of the merocrine sweat duct in the cat footpad is composed of two to three flattened epithelial cells. Supported by the findings of Pinkus (1939) and Holyoke and Lobitz (1952), as well as by their own histochemical studies, Lobitz, et al. (1954) proposed the phrase "epidermal sweat duct unit" to describe the morphological and biological entity within the epidermis consisting of the different periductal cells, the single layer of epithelial cells (luminal, or superficial cells), and the eccrine sweat duct opening (pore) at the skin surface.

Keratohyalin granules are present in the epithelial cells of the epidermal duct in the cat (Conroy, 1964) and human (Charles, 1960) skin.

Keratinization of the ductal cells begins at a much lower level than the neighboring epidermal cells (Charles, 1960; Hashimoto, 1971b; Takagi, 1952). Whereas Hashimoto (1971b) stated that the outer ductal (periductal) cells are the first to keratinize, Takagi (1952) reported that it is the luminal cells which keratinize first. This latter finding is supported by the work of Lobitz, et al. (1954) in which it was found that the disulfide concentration in the luminal cell is greater than that in the Malpighian cells, which in turn is greater than the concentration in the periductal cells. Zelickson (1961) noted that the human eccrine ductal cells keratinize as do normal epidermal cells. The cells of the "unit" desquamate more quickly than the surrounding cells of the stratum corneum, forming a sunken feature at the surface opening (Wolf, 1970).

As in the dermal segment of the duct, Conroy (1964) found that the luminal cells in the cat eccrine epidermal duct possess a cuticle. In the human gland, the cuticle keratinizes within the stratum germinativum (Charles, 1960). There is a gradual disintegration of the cuticle in the eccrine gland of the M. mulatta as the duct traverses the stratum corneum (Ellis and Montagna, 1961).

Viewed under the light microscope, the inner most layer of ductal cells are so closely packed that they leave no observable interstices between them, as is the case for the adjacent epidermis (Takagi, 1952). Under the EM, Hashimoto (1971b) found that the luminal end of the ics in the lower layers of the epidermis is always tightly closed to lanthanum. One of several desmosomes or tight junctions is responsible for this

closure. In the upper layers of the epidermis, where the ductal cells are keratinized, Hashimoto (1971b) was unable to establish the presence or absence of a luminal tight junction in this portion of the duct, although the luminal ics was tightly approximated by closely set desmosomes.

2.2.5 Innervation and Blood Supply.

Ellis, et al. (1958) have investigated the blood supply to the human eccrine sweat gland. They reported that all of the capillaries which surround the subcutaneous portion of the gland generally arise from the same vessel. In very long glands however, the capillaries supplying this portion of the gland may arise from several arterioles. The capillaries follow the tortuosities of the gland, and give off branches and shunts connecting the vessels around adjacent loops of the gland.

According to Ellis, et al. (1958) the dermal portion of the duct in the human skin is accompanied by one or more capillaries or arterioles that wind loosely about it as it courses toward the epidermis. These vessels are all connected by cross-shunts that form a loose plexus or lattice along the duct. The vessels following the axis of the gland branch at the level of the subepidermal plexus and send capillary loops underneath the epidermis. Near the superficial surface of the dermis, the eccrine duct may also be supplied with capillary branches from the arcades of vessels that lie under the epidermis. There are no blood vessels within the epidermis, and therefore none supplying the epidermal eccrine sweat duct unit.

In periods of profuse sweating from the human forearm, Randall,

et al. (1948) have shown that arterial occlusion does not effect a change in sweating pattern (amount of sweat and number of active glands) for 6 to 7 minutes. After this period, the number of functional glands progressively declines. After 10 minutes of depressed sweating, these investigators were able to reestablish the control level of sweating by the application of radiant heat to the ischemic area. Randall, et al. (1948) concluded that arterial occlusion does not eliminate the possibility of sweating due to direct stimulation. They did not report, however, a time of occlusion required to eliminate the response of the gland to this direct stimulation. Patton (1948) reported that occlusion of the circulation to the hind foot of the cat slowly abolished the sweat gland response to electrical stimulation of the nerves supplying the glands, although he noted that sweating may persist for some 15 to 20 minutes after cessation of the heart beat.

Langley (1891) was first to describe the course and connections of the postganglionic nerve fibers supplying the sweat glands in the feet of the cat. Patton (1948) expanded this work, describing the preganglionic contributions to the cat sweat gland innervation. Electrical stimulation of preganglionic fibers in the 12th thoracic to the 4th lumbar ventral roots, or postganglionic fibers from the 6th lumbar to the 2nd sacral sympathetic ganglia, evokes sweat outflow from the glands in the footpads of the hind limb. Post-ganglionic fibers reach the eccrine glands in the cat hind foot via the sciatic and plantar nerves.

In reporting the characteristics of the eccrine sweat gland activity in the central hind footpad of the cat, Adams (1966) presented evidence

which suggested that approximately 20% of the glands in this pad are doubly innervated. Figures from Adams' work showed that approximately 80% of the sweat glands in the central pad are supplied by the medial plantar n., while approximately 40% of the glands are supplied by the lateral plantar nerve.

The eccrine sweat gland is richly innervated by a network of unmyelinated nerves which surround the gland (Ellis and Montagna, 1961). As viewed under the EM, no nerves can be seen within, or on the glandular side of the basement membrane (Munger, 1961).

Dale and Feldberg (1934) first demonstrated that acetylcholine is released at the eccrine sweat glands in the footpad of the cat following electrical stimulation of the sympathetic nerve supply to the glands. Specific (true, acetyl-, or aceto-) cholinesterase is found in large amounts in the nerve fibers surrounding the secretory segment of the human eccrine sweat gland (Hurley, et al., 1953). Hellman (1952) demonstrated histochemically that all of the cholinesterase activity associated with the eccrine gland in the cat footpad is of the "pseudo" or "non-specific" group. Hurley, et al. (1953) however, criticized the method of assay employed by Hellman (1952), and suggested that the enzyme in the footpad be reinvestigated.

It is recognized that intravenous (iv) injection of atropine, an anticholinergic agent, consistently, and rapidly, abolishes eccrine sweating in cats (Langley, 1923; Patton, 1948) and man (Chalmers and Keele, 1951, 1952; Foster and Weiner, 1970).

The eccrine glands in man (Chalmers and Keele, 1951, 1952; Foster, et al., 1970; Haimovici, 1948, 1950; Sonnenschein, et al., 1951) and cat (Langley and Uyeno, 1922) can be caused to secrete by intradermal or iv injection of adrenergic substances. Langley and Uyeno (1922) showed that the intradermal injection of any aqueous, noninjurious solution can produce some secretory activity in the cat footpad. Other workers (Foster and Weiner, 1970; Haimovici, 1948, 1950; Lloyd, 1963, 1968; Sonnenschein, et al., 1951) have reported that the iv administration of adrenergic blocking agents, including dibenamine, phenoxybenzamine, bretylium, guanethidine, tolazoline and phentolamine, interferes with, or inhibits thermally, emotionally, or pharmacologically elicited sweating in man and cat, as well as sweating associated with the electrical stimulation of the sudomotor nerves in the cat.

Foster and Weiner (1970), studied the effects of cholinergic and adrenergic blocking agents on the activity of the eccrine sweat gland in the human forearm and central hind footpad of the cat, and concluded that any inhibitory action by anti-adrenaline substances is due to interaction with cholinergic receptors in the sweat glands. Chalmers and Keele (1951, 1952), Foster and Weiner (1970) and Foster, et al. (1970) concluded that only cholinergic fibers innervate the human and cat eccrine sweat gland, and adrenergic nerves do not control sweating.

2.3 Hydration of the Stratum Corneum.

Much evidence supports the view that the stratum corneum absorbs water, either by diffusion from the under lying tissues, from the duct of

the eccrine sweat gland, or from the external environment. Blank (1952) was possibly the first to describe and quantify the conditions for epidermal hydration. He found that the stratum corneum easily and quickly takes up water. Later, Mali (1956) reported that the normal human epidermis is, in fact, "hygroscopic".

Blank (1952, 1953) showed that in the human, water can be brought to the base of the epidermis at least 50 to 100 times as fast as it is lost from the skin surface. He found that the barrier against diffusion water loss is not the entire cornified epithelium itself, but is instead a very thin tissue layer near the base of the stratum corneum. Mali (1956) removed successive layers of the epidermis, measured the evaporative water loss (EWL) from the skin surface after each "stripping" and concluded that the diffusion barrier is the stratum lucidum. Blank (1953) concluded that the existence of such a barrier separated the stratum corneum from the easily available water of the underlying tissues. He concluded that the corneum is dependent upon the external environment and sweat gland secretion for moisture which, as he demonstrated, it needs to remain flexible.

Changes in environmental water vapor pressure effect changes in the water content of the stratum corneum. In a mathematical analysis of skin EWL, Mole (1948) showed that, at constant ambient temperature, the water content of the skin varies directly with ambient water vapor pressure. Blank (1952) noted that the stratum corneum does not dry out unless it is in completely dry air. According to Middleton (1968),

there is a near linear relation between the water content of the stratum corneum and ambient relative humidity (r.h.) up to about 70% r.h. at which it contains approximately 13 mg water per 100 mg of dry tissue (Middleton, 1968). At higher r.h.'s, the water content increases sharply. Blank (1952) reported that a ratio of 45 mg water per 100 mg dry corneum at 90% r.h. had increased to 70 mg water at 95% r.h. Baden (1970) reported that the stratum corneum is capable of absorbing up to 200% of its dry weight in water. Working with human palmar skin, Craig (1956) concluded that water moves into the skin whenever it is subjected to either air approximately saturated with water vapor, or distilled water, and that this movement is relatively independent of the air, or water temperature.

Scheuplein and Morgan (1967) showed that human stratum corneum can contain as much as 5 times its weight in water after several days of immersion in distilled water. They also reported a 400% to 500% expansion of tissue volume accompanying this hydration. Peiss, et al. (1953) found that the rate and amount of water uptake is directly related to the thickness of the stratum corneum.

Peiss, et al. (1953) reported that the evaporation of water subsequent to hydration of the skin follows a time course which is very nearly a replica of the process of hydration. However, Mali (1956) demonstrated that the water content of the stratum corneum is a hysteresis function of ambient r.h.; at one r.h., the water content of the skin will be higher if water vapor pressure is decreasing to that

point than if it is increasing to it. That is, between 0% and 100% r.h. the water content of the corneum is not uniquely defined at any one value of r.h. Mali (1956) also noted that this hysteresis is typical of all organic polymers, and emphasized that the past history of the corneum plays an important role in establishing the equilibrium between a value of the environmental r.h. and the water content of the stratum corneum.

Bettley and Grice (1967), Spruit and Malten (1969), and Grice, et al. (1972) demonstrated that the water vapor diffusion coefficient of the stratum corneum is a function of its water content. Grice, et al. (1972) found that, at constant skin temperature, there is a 2 to 3 fold increase in EWL from the forearm skin when ambient r.h. is raised from approximately 0% to 50%. Spruit and Malten (1969) concluded that the corneum does not behave as an "ideal membrane" obeying Fick's law of diffusion, wherein the diffusion coefficient remains constant with changes in the vapor pressure gradient. Increases above a r.h. of 50% lead to a decrease in the water vapor loss which these investigators attributed to the decrease in the skin vapor pressure gradient.

Bull (1944) and Sponsler, et al. (1944) investigated the water vapor absorption characteristics of proteins. This work was reviewed and extended by Pauling (1945). Generally, it is believed that protein hydration centers are associated with the polar side chains at the ends of certain amino acid residues in the protein, as well as with the peptide bonds in the backbone of the polypeptide chain. Bull (1944) noted that the amount of water held by a protein should be primarily determined by the number

and availability of these two types of hydration centers. The amino acids with polar side chains include serine, threonine, proline and hydroxyproline, tyrosine, tryptophan, histidine, lysine, arginine, aspartic acid, glutamic acid and hydroxyglutamic acid. Pauling (1945) observed that the different polar groups can be expected to attract water molecules with different avidity, and that the amount of absorbed water will be related to that initially absorbed as well as to the r. h. of the environment to which the protein is subjected. The water molecule is probably bound to the protein chain through hydrogen bridges (Sponsler, et al., 1944).

Water in the stratum corneum exists as "free water" and "bound water" (Scheuplein and Morgan, 1967). Researchers investigating the nature of the hygroscopic, water-binding material(s) in the corneum generally agree that the "bound water" is largely associated with the protein, or lipid-protein structures in this tissue (Scheuplein and Morgan, 1967; Middleton, 1968; Park and Baddiel, 1972b). Supportive evidence comes from lipid, or lipid/water extraction experiments on mammalian stratum corneum. Specifically, if the lipids are extracted from the corneum with organic solvents (Blank, 1953; Middleton, 1968; Park and Baddiel, 1972b) or detergent solution (Park and Baddiel, 1972b), there is no reduction in the water-binding capacity of this tissue. However, if a lipid extraction is followed by a water (lipid/water) extraction, the stratum corneum loses its water-holding capacity (Blank, 1953; Middleton, 1968; Park and Baddiel, 1972b). The water retaining

characteristics of the lipid/water extracted corneum has been said to resemble wet filter paper (Scheuplein and Morgan, 1967).

Such extraction experiments led Blank (1953) to conclude that the major hydrophilic component of the stratum corneum might be an intercellular mucoprotein which Wislocki, et al. (1951) demonstrated to be present in the epidermis. Blank (1953) further speculated that the cornification process was the mechanism responsible for holding this material within the stratum corneum. Middleton (1968) theorized that the hygroscopic, water-soluble material is surrounded by a lipid-containing membrane system which allows passage of water but not the substances themselves. He also showed that the major extractable lipids are cholesterol, and two different phospholipids which he was unable to identify. The presence of these lipids, he concluded, suggests that the cell membrane of the stratum corneum cells is involved in holding the water-soluble material within the corneum. In support of this postulate, he demonstrated that water extraction per se was capable of removing the water-binding capacity of the corneum if the cell walls are first broken by powdering the tissue. Middleton (1968) also found that the water soluble amino acids in the stratum corneum are bound by its lipids.

In addition to the effect on water-binding, Park and Baddiel (1972b) found that lipid/water extraction also reduces the amount of water which the stratum corneum is able to hold. They suggested that these effects could be due to increased protein-protein interactions in

the absence of hygroscopic substances by creating a more compact epidermal protein structure. In defense of this supposition they reasoned that due to their ionic or dipolar nature, the water soluble hygroscopic substances will be bound to the proteinaceous components of the corneum. The location of these "bulky" molecules between protein chain segments will create a more open structure than would exist if the molecule were absent, leading to enhanced protein hydration. Upon removal of the hygroscopic molecules the protein matrix collapses, resulting in the formation of more protein-protein bonds (mainly hydrogen bonds and ionic interactions). The configuration becomes more rigid, resulting in a reduced swelling capability and consequently, a reduction in the water uptake. They concluded that direct protein hydration, both in the presence and absence of hygroscopic substances, is the essential feature of stratum corneum hydration.

2.3.1 Effects of Hydration on the Mechanical Properties of the Stratum Corneum.

According to Montagna (1962) eccrine sweat glands have been found in the footpads of most mammals. He concluded that the main function of these glands appears to be their ability to change the mechanical properties of the skin by moistening friction surfaces.

The soft and pliable nature of the skin is dependent upon the moisture content of the cornified epithelium (Blank, 1952). Since water is an effective "plasticizer" of the stratum corneum, changes in the

rheological properties of the corneum should be indicative of changes in water content (Park and Baddiel, 1972a).

Wildnaurer, et al. (1971) examined the mechanical parameters, work of fracture, ultimate breaking strength and elongation at fracture, for normal human stratum corneum exposed to an increasing range of 0% to 100% r.h. over which the breaking strength decreased by 85%, while the work of fracture increased 600%. Elongation at fracture increased from 20% at 0% r.h. to 190% at 100% r.h. Park and Baddiel (1972a) found that over the range of 30% to 100% r.h., increasing r.h. decreases the elastic modulus of porcine stratum corneum by a factor of approximately 1000.

Naylor (1955) examined the frictional force characteristics of human skin overlying the anterior surface of the tibia. He noted that 35 minutes after the subject was heated and made to sweat, there was an approximate doubling in the coefficient of friction between the skin and polythene. After removal of the heat load, blowing "air" across the skin surface reduced the friction coefficient to a value below the control level. Naylor (1955) reported that dry or very wet skin-surface conditions reduced the friction coefficient.

Comaish and Bottoms (1971) also investigated the relationship between skin friction and skin hydration. Using polythene, they found that the coefficient of static friction for the dorsum of the hand is lower than for the palm, although the coefficient variability was larger for the palm. They speculated that these features of palmar skin

friction might be due to a relatively larger amount of water in palmar skin. They found that a 30 minute immersion of the hand in water ($37^{o}C$) produces an increase in the coefficient of static skin friction. Twenty minutes after removing the hand from the water, the coefficient had returned to the control value.

Using the skin of the central hind footpad of the cat, Adams and Hunter (1969) were able to control the hydration of the stratum corneum by electrically stimulating the sudomotor nerve fibers in the medial plantar nerve. By measuring the force required to move a weighted, burnished Plexiglas plate across the surface of the footpad, these investigators were able to examine the relationship between controlled changes in corneum hydration and an index of the kinetic friction. At low values of sudomotor activity (stratum corneum hydration) they found that the index of friction increased rapidly to a maximum (a 70% increase over a dry skin measurement) with an increased frequency of nerve stimulation. There is only a slight increase in the surface EWL above resting levels at the frequency which produces the maximum index of friction. Further increases in nerve stimulation frequency increases the EWL whereas the friction force decreases. As water appeared on the skin surface, the index of friction fell below the measured resting level. Adams and Hunter (1969) interpreted these results to indicate that the increase in friction without a substantial increase in the EWL indicated that sweat was penetrating the outer layers of the skin from the subsurface, distal (stratum corneum) end of the sweat

gland duct, i. e., sweat was produced but did not reach the surface for evaporation, although it did penetrate into, and alter the water content of the stratum corneum. As the friction force decreases, the limit of corneal water storage is approached and more water penetrates to the more superficial skin, with a further increase in the measured EWL.

Cellular and macromolecular-protein mechanisms responsible for the epidermal hydration effects on the mechanical properties of the stratum corneum have been offered by Wildnaurer, et al. (1971) and Park and Baddiel (1972a, b). The former investigators speculated that the biomechanical functions and macroscopic properties of the corneum are directly related to its structural organization (the desmosomal attachment plaques and intercellular mucopolysaccharides) as well as the presence of oriented and amorphous keratin fibers enclosed by a tough cellular membrane. Wildnaurer, et al. (1971) attributed the elastic properties of the corneum to the viscoelasticity of the intracellular fibrous macromolecular component, concluding that the r.h. deformation behavior of the corneum is a manifestation of the interaction of absorbed water with these macromolecules. Park and Baddiel (1972a) felt that the simplest model which adequately explains the hydration effects on the elastic properties is provided by the transition of a polymer from a "glassy to a rubbery state". That is, at low r.h., the corneum shows the characteristics of a polymeric glass in which large chain movements are restricted and extension takes place by the

stretching of bonds. With increased r.h., the hydrogen bonds and polar side groups become hydrated, but the disulfide bonds remain intact and the corneum protein chains form a "lightly cross-linked entanglement network similar to rubber".

2.3.2 Effects of Stratum Corneum Hydration on the Electrical Conductance Properties of the Epidermis.

Techniques required for the measurement of small electric currents have been available for nearly 60 years (Tregear, 1966), and over this period many observers have measured the conduction of direct and alternating current through the skin. It is well established that the electrical skin conductance level (SCL) increases as the stratum corneum is hydrated either by an increase in eccrine sweat gland activity, as evidenced in the cat's footpad (Lloyd, 1959a,b; Stombaugh and Adams, 1971) and human palmar skin (Adams and Vaughan, 1965; Thomas and Kawahata, 1962; Thomas and Korr, 1957), or by exposing the human stratum corneum to an increasing water vapor pressure (Edelberg, 1961, 1968; Bettley and Grice, 1967). It has also been shown that the SCL increases as the corneum is hydrated by the water-containing electrode pastes which are commonly employed in its measurement (Blank and Finesinger, 1946; Tregear, 1965). Tregear (1965) found that the application of dry, metal plate electrodes also leads to an increase in the SCL and that this rise is directly related to the area of the electrode.

It is not necessary for the sweat glands to be visibly active to

effect changes in the SCL (Adams and Vaughan, 1965; Perry and Mount, 1954; Thomas and Kawahata, 1962; Thomas and Korr, 1957). Regional variations in the SCL of apparently non-sweating skin have been attributed to the variation in tonic activity of the sudomotor neurons supplying these regions (Thomas and Kawahata, 1962). There is an approximately linear relationship between the number of active sweat glands and the increasing or decreasing value of the SCL (Thomas and Korr, 1957), but this relation shows hysteresis (Adams and Vaughan, 1965; Thomas and Korr, 1957). That is, following a period of increased sweating a persistent increased SCL is measured during the phase of decreasing sweat gland activity, as evidenced by a decrease in the number of visible sweat glands and surface EWL.

2.3.3 Heat Conduction in the Skin.

Tregear (1966) has reviewed the literature reporting the thermal conductivity coefficient (k) of excised and *in vivo* skin, fat, and muscle. Table 1. is taken, in part, from that review. Tregear (1966) noted that excised dermis appears to be 1.5 to 1.8 times as conductive as fat, while both dermis and fat are less conductive than muscle. He speculated that heat conduction through dermis and muscle is via the water molecules, while conduction through fat is via the fat molecules which are larger and of lower conductivity. He concluded that the heat conduction properties of a tissue *in vivo* should vary quite widely with its water content.

Henshaw, *et al.* (1972) have recently investigated the peripheral

TABLE 1. Thermal conductivity coefficient of *in vivo* and excised tissue. All data refer to human tissue, without blood flow (b.f.), except as noted otherwise.

Material	k (Watts/m °C)	Reference
Liquids		
Water (at 27° C)	0.609	Weast (1967)
(at 37° C)	0.623	
Glycerol	0.285	Washburn (1929)
Olive oil	0.167	
Tissue *in vivo*		
Skin (10mm thick)	0.314	Reader (1952)
	0.377	Lipkin and Hardy (1954)
	0.285-0.586	Burton and Edholm (1955)
(canine, with b.f.; 12mm thick)	0.205-0.480	Henshaw, *et al.* (1972)
Muscle	0.531	Reader (1952)

TABLE 1. (continued)

Material	k (Watts/m °C)	Reference
Excised tissue		
Epidermis	0.209	Henriques and Moritz (1947)
Dermis	0.377	Henriques and Moritz (1947)
	0.322	Lipkin and Hardy (1954)
Fat	0.167	Henriques and Moritz (1947)
	0.204	Hatfield and Pugh (1951)
(bovine)	0.205	Hatfield and Pugh (1951)
Muscle	0.460	Henriques and Moritz (1947)
	0.385	Hatfield and Pugh (1951)
	0.406	Lipkin and Hardy (1954)
(bovine)	0.280	Hatfield and Pugh (1951)

thermoregulation in the footpads of two arctic canines. Their data allows the calculation of the k of several tissue compartments within the footpad under conditions where the pad is exposed to a room air environment, and after the footpad has been immersed in water. For the superficial 2 mm of footpad tissue, k was calculated to be 0.040 Watts per meter per ^{o}C and 0.255 Watts per meter per ^{o}C for the "dry" and "wet" conditions, respectively. The value of k, calculated for a 12 mm thickness of footpad tissue (as measured from footpad surface), was found to be 0.205 Watts per meter per ^{o}C and 0.480 Watts per meter per ^{o}C for the "dry" and "wet" conditions, respectively.

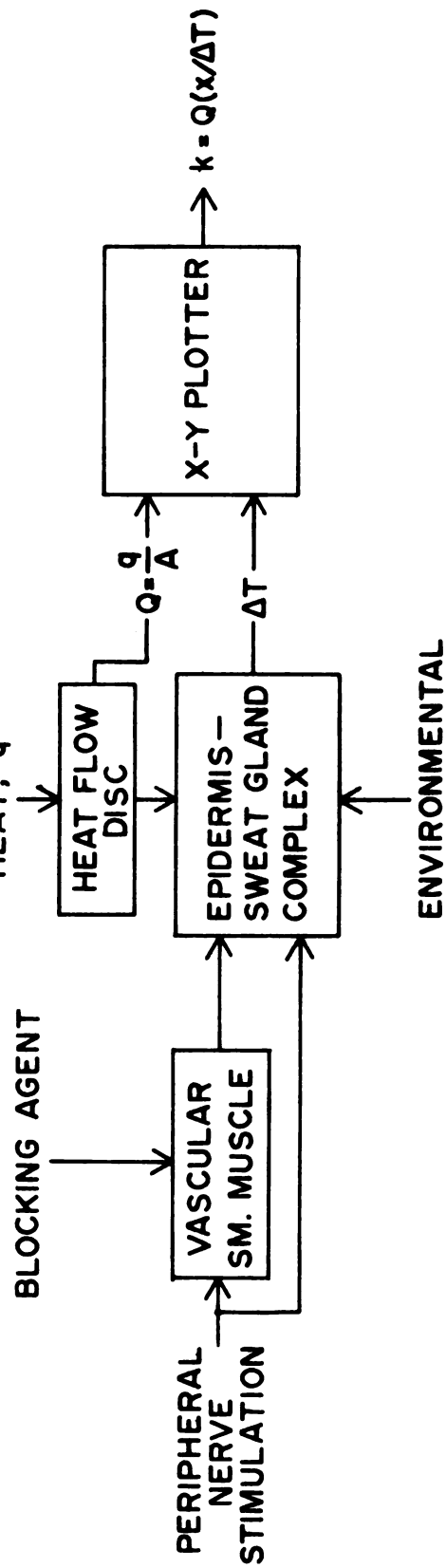
III. MATERIALS AND METHODS

3.1 Objectives.

The present study was designed to measure the changes in the thermal conductivity coefficient of the cat footpad epidermis produced by changes in epidermal hydration. The mathematical formulation required to calculate the epidermal thermal conductivity coefficient and the assumptions for which this formulation hold are stated below (3.2).

Figure 1 is a diagram of the physical and biological factors which allow the calculation, and alteration of the epidermal thermal conductivity coefficient, respectively. The thermal conductivity coefficient k, was calculated by employing the one dimensional steady state case of the Fourier heat conduction equation, where Q represents the heat flux per unit area through the epidermis, ΔT equals the temperature difference between the surface of the footpad the dermoepidermal junction, and x is the distance between two thermocouple junctions used to measure these temperatures. The ratio $\Delta T/x$ represents the temperature gradient within the epidermis. Q and ΔT were simultaneously recorded on an X-Y recorder, and the dimension x was determined at the termination of the experiment. The bio-physical arrangement of the component parts used in the evaluation of the

FIGURE 1. A schematic representation of the biophysical components producing the epidermal hydration and evaluation of the epidermal thermal conductivity coefficient in the central hind footpad of the cat.



EXPERIMENTAL MODEL

conductivity coefficient is illustrated in Figures 2 and 3.

As shown in Figure 1, the hydration of the epidermis was controlled in either of two ways. 1) The distal segment of the severed medial plantar nerve in the anesthetized cat was electrically stimulated to produce sweat gland activation and affect "internal hydration". In some animals (see Table 7), possible indirect effects on the sweat gland apparatus associated with the concurrent stimulation of the vasomotor nerves were eliminated with the intravascular infusion of the alpha-adrenergic blocking agent, phenoxybenzamine. 2) The footpad was exposed to a high humidity, warm air environment to produce the effect of an "external hydration". In either procedure, the tibial nerve was severed at the tarsal joint prior to experimentation to isolate the epidermal-sweat gland complex from the central nervous system.

3.2 Basic Quantitation of Epidermal Heat Transfer.

In 1822, the French scientist J.B.J. Fourier proposed the basic relation for conductive heat transfer (Kreith, 1969). This relation states that the rate of heat flow by conduction (Q) in a material is equal to the product of the following three quantities:

a) k: The thermal conductivity (coefficient) of the material,

b) A: The area of the section through which heat flows by conduction: measured perpendicularly to the direction of heat flow,

c) dT/dx: The temperature gradient at the section: the rate

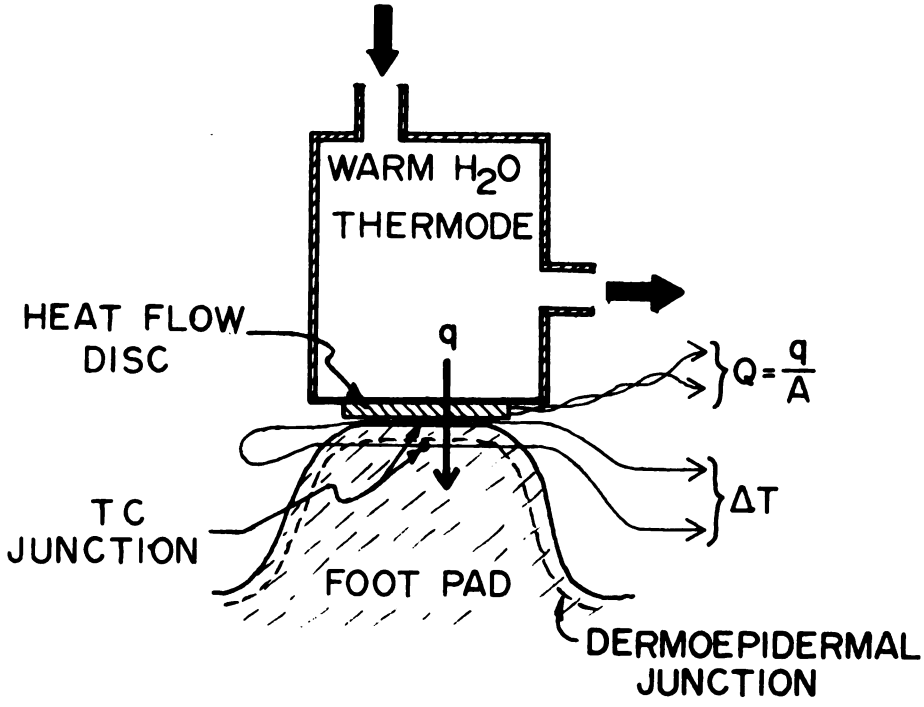


FIGURE 2. A diagramatic representation showing the relationship between the constant temperature, warm water thermode, heat flow measurement device, and transepidermal temperature sensing thermocouples.

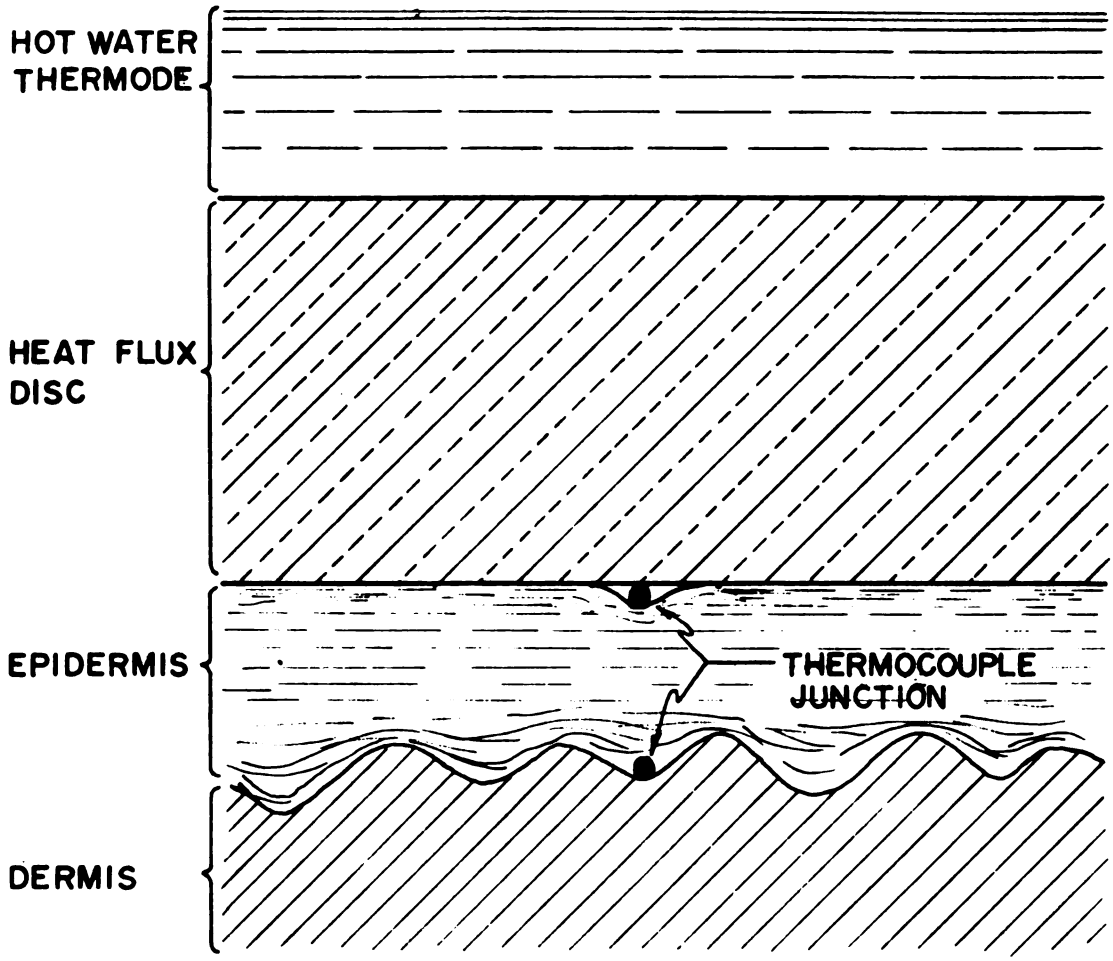


FIGURE 3. An enlarged illustration of the structures shown in Figure 2., emphasizing the thermocouple-heat flux disc-epidermis relationship.

of change of temperature (T) with respect to distance (x) in the direction of heat flow.

Assuming a one-dimensional heat conduction in the steady-state condition, and the constancy of k throughout the thickness of the material, the Fourier conductive heat flow equation can be written:

$$Q = -kA(dT/dx) \qquad (1)$$

By definition, the direction of increasing distance is the direction of positive heat flow. However, heat flows from points of higher temperature to points of lower temperature, resulting in a positive heat flow when the temperature gradient is negative, hence the sign convention of Eq. 1. The parameters in Eq. 1 are expressed in the following units: Q in Watts, area(A) in square meters, and dT/dx in degrees centigrade per meter. The thermal conductivity is a property of the material and is dimensionalized as Watts per meter per degree centigrade.

In general, the thermal conductivity of a material varies with its temperature. However, if the internal body temperature of the cat is maintained relatively constant during the course of experimentation, as well as from animal to animal, then it is assumed that k is independent of temperature in the following derivation. It is also assumed k is independent of depth through the thickness of the epidermis.

It is assumed that the thermode-heat disc complex, in place on the footpad, produces a physical situation wherein the pad surface,

in particular the epidermis, is constrained to form a flat plane. Analytically, this permits the treatment of the footpad epidermis to proceed as though it were a plane wall. Uniform cross-sectional area along the heat flow path is assumed to exist. For the case of steady-state heat flow through a plane wall, the variables in Eq. 1 can be separated as:

$$Q(dx) = -kA(dT) \tag{2}$$

Integration of Eq. 2 proceeds as:

$$Q \int_{0}^{X} dx = -kA \int_{T_{hot}}^{T_{cold}} dT$$

where: 0 = footpad surface

X = dermoepidermal (D-E) junction

T_{hot} = footpad surface temperature

T_{cold} = D-E junction temperature

Then:

$$Q(0-X) = -kA(T_{hot} - T_{cold}) \tag{3}$$

Eq. 3 can be rewritten:

$$Q = (kA/X)\ (\Delta T)$$

where: X = epidermal thickness

ΔT = temperature potential across the thickness of the epidermis (transepidermal temperature difference)

The equivalent of the thermal resistance is given by X/kA. The mathematical reciprocal of the thermal resistance, the thermal conductance, is given by the following relation:

$$K = A(k/X) = AK'$$

where K' represents the unit thermal conductance for conduction heat flow, and has units of Watt-hours per square meter per degree centigrade.

3.3 Animal Selection/Pre-Test Preparation.

Adult cats of either sex weighing between 2 kg and 5 kg were obtained from the Michigan State University Center for Laboratory Animal Resources. Cats were anesthetized with sodium pentobarbitol solution (36 mg per kg, Halatol Solution, Jen Sal Laboratories, Kansas City, Mo.) injected intraperitoneally. Except as noted, 3.52 mg per kg of phenoxybenzamine hydrochloride (POB) (Smith, Kline and French Laboratories, Philadelphia, Pa.), an alpha adrenergic receptor blocking agent, was infused intravenously over a time of 5-10 minutes per mg POB. A minimum time of one hour was allowed to elapse between the end of the POB administration and the commencement of experimentation.

Rectal temperature was maintained between 38.0°C to 39.5°C by placing the animal on an electric heating pad. The temperature was monitored via a YSI Tele-Thermometer (Yellow Springs Instrument Co., Inc., Yellow Springs, Ohio) by means of a thermistor probe inserted into the lower bowel, 10 cm beyond the external anal sphincter.

Except as noted, the central footpad was washed lightly with soapy water, rinsed, and towel dried. In some instances the pad was gently cleaned with a mild debriding agent (Pretty Feet, Chemway

Corp., Wayne, N.J.), carefully rinsed with soapy water, followed by a brief rinsing with 100% ethyl alcohol, and towel dried. In all cases, the pad was allowed to dry at ambient conditions for a minimum of 2 hours prior to experimentation.

3.4 Warm Water Thermode/Water Reservoir Apparatus.

A perfused, warm water thermode was designed to maintain a constant temperature at the skin surface. The thermode was constructed from 7/8 inch, outside diameter (O.D.) copper pipe, cut to a length of 7/8 inches, the ends of which were closed with brass shim stock. A hole drilled in one end of the thermode, and fitted with a 1/4 inch length of 1/4 inch O.D. copper tubing, served as the water inlet. Water was voided from the thermode through a similarily fitted hole in the side of the unit.

The features of the water reservoir-thermode perfusion apparatus are illustrated in Figure 4. A piece of Tygon flexible plastic tubing (Matheson Scientific, Inc., Chicago, Ill.) of 3/8 inch O.D. and 1/16 inch wall thickness was connected to each thermode fitting. The inlet tubing was attached to a water pump (model LGV-275 Pump; Little Giant Pump Co., Oklahoma City, Oklahoma) situated in a 5 gallon, warm water reservoir. The tubing from the thermode outlet directed the voided water back into the reservoir, completing the closed, thermode perfusion system. The perfusate was warmed with a Tecam Tempunit (Lapine Scientific Co., Chicago, Ill.) to a temperature of approximately 39^{o}C,

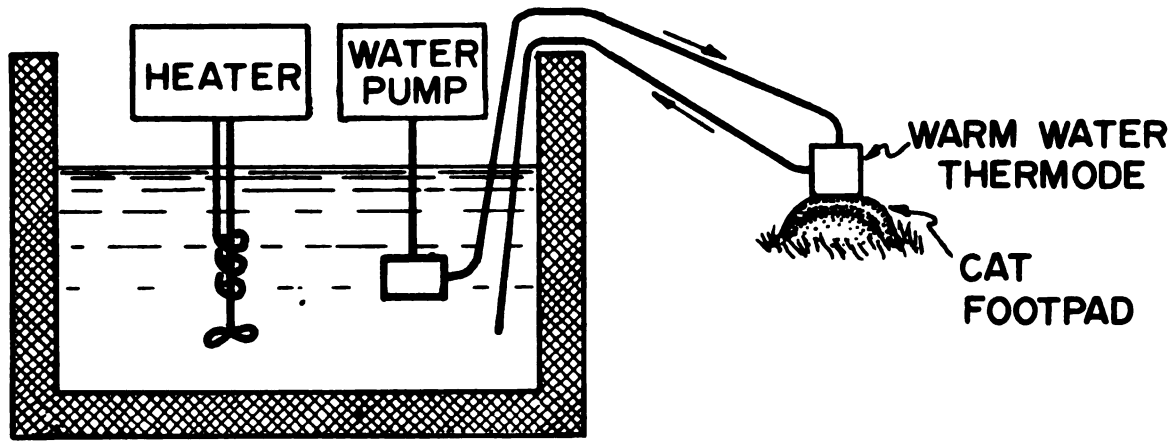


FIGURE 4. The warm water reservoir and thermode (not shown to scale). This diagram indicates the relationship between the reservoir, pump, thermode, and cat footpad.

producing a transepidermal temperature difference of 1^{o} C to 3^{o} C (pad surface temperature higher than the D-E junction temperature), with the thermode in place on the footpad.

The thermode was attached to one end of a counterbalanced, pivoted arm. The pivoting mechanism was in turn attached to a platform which secured and stabilized the cat's foot. This arrangement allowed the investigator to raise and lower the thermode, yet permitted the re-establishment of the desired initial placement of the thermode on the pad.

The counterbalancing weight on the pivoted arm was adjusted to produce a minimal deformation of the footpad surface while giving a heat flow disc-to-footpad surface contact of approximately one square centimeter. These conditions were satisfied when the water perfused thermode rested on the footpad with a force ranging from 25 grams to 29 grams.

3.5 Measurement of Transcutaneous Heat Flow.

The warm water perfused thermode provided a source of heat, whose flow, Q, into the footpad was measured with a JLC-Hatfield Meter Disc (Joyce, Loeble, and Co., Ltd., Vine Lane, Newcastle-on-Tyne, England) (Hatfield, 1950). To facilitate its attachment to the thermode, the heat flow disc was collared with a 7/8 inch O.D., pressure fitting, Plexiglas ring. Prior to attachment, a thin layer of thermoconductive silicone-base paste (DC-Z9, G.C. Electronics, Rockford, Ill.) was applied to the thermode-contacting

surface of the disc, insuring an intimate disc-to-thermode contact. The collar-disc assembly was then pressed into place, and secured to the thermode with tape. The electrical output of the heat flow disc (microvolts per Watt per square meter) was recorded on the "X" axis of a Hewlett-Packard/Moseley X-Y Recorder (Model 7000AM, Hewlett-Packard Corp., Pasadena, Calif.).

3.6 Measurement of the Transepidermal Temperature Difference and the Inter-thermocouple Junction Distance.

The transepidermal temperature difference (ΔT) was measured with two butt welded, 0.003 inch diameter (40 gauge) copper-constantan (Cu-Co) thermocouple (TC) junctions. A typical Cu-Co junction is shown in Figure 5. All TC's were welded in a nitrogen environment. Measurement of ΔT necessitated the placement of one of the TC junctions at the dermoepidermal junction within the central footpad. Placement of this TC junction was made with the aid of a 27 gauge needle-trocar. The trocar was inserted through the epidermis at the periphery of the pad to the D-E junction, then advanced parallel to the surface across the center of the pad, finally exiting at a point on the opposite side of the pad. One TC lead wire was then advanced through the needle lumen. The trocar was removed, leaving the wire within the footpad. The TC junction was subsequently pulled into the footpad tissue and placed at the center (bulbous crest) of the central hind footpad. A second TC junction was placed on the surface of the pad, directly superior to the intrapad TC junction.

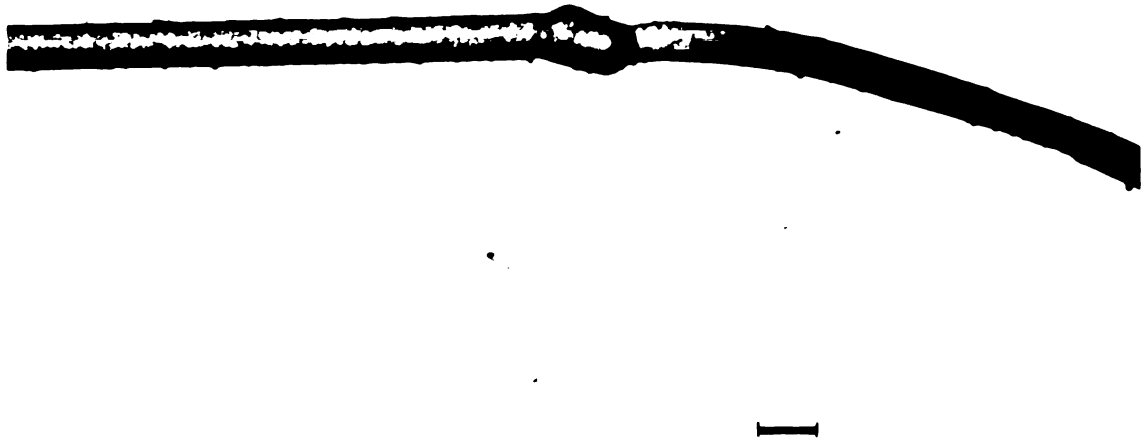


FIGURE 5. Typical copper-constantan (Cu-Co) thermocouple junction: constructed by the butt-welding of 0.003 inch diameter Cu and Co wires. Reference dimension: 0.1mm.

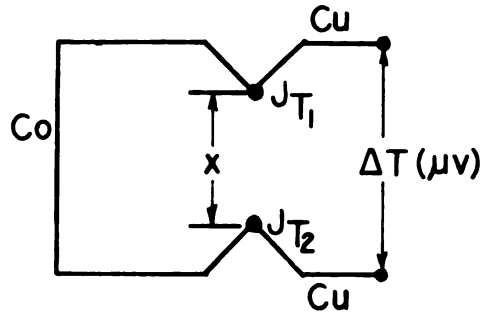
Once properly positioned, the TC's were secured by fastening the wire leads to the footpad periphery with rubber cement. Figure 6 shows diagramatically the wiring of the TC leads for the measurement of ΔT. The microvolt output generated by the difference in TC junction temperatures (40 microvolts per degree centigrade) was amplified and recorded on the "Y" axis of the X-Y recorder.

At the conclusion of experimentation on any one cat, the animal was killed, the footpad dissected from the hind foot, transected perpendicular to its surface at the location of the TC junctions, and the interTC dimension measured under a binocular dissecting microscope. As described in section 3.2, this dimension is required in the calculation of the epidermal thermal conductivity coefficient.

3.7 Preparation of Tissue for Histologic Examination.

Following the measurement of the interTC junction dimension, the footpad was promptly placed in Lavdowski's mixture (Guyer, 1949) for fixing, cleared in Cedar Wood Oil (Fisher Scientific, Chicago, Ill.), and embedded in paraffin (Paraplast Plus, 56-57°C melting point, Aloe Scientific, St. Louis, Mo.) prior to cutting, mounting, and staining. Photomicrographs were made with a Zeiss Photomicroscope (Carl Zeiss, Oberkochen, Wuerttemberg, Germany) provided with an automatic exposure setting device.

3.8 Epidermal Hydration: Sweat Gland Activation (Internal Hydration).



THERMOCOUPLE WIRING DIAGRAM

FIGURE 6. The copper-constantan (Cu-Co) thermocouple junctions (J) are shown, where the junctions are at different temperatures (T_1, T_2). the microvolt (uv) output is proportional to the difference in junction temperatures (T). Knowledge of the inter-junction dimension (x) allows for the calculation of a temperature gradient.

The tibial nerve was exposed and severed distal to its emergence from beneath the gastrocnemius muscle in the distal portion of the lower hind leg. Access to the medial and lateral nerves was attained through an incision of approximately 2 cm in length, made on the plantar surface of the hind foot, proximal to the central footpad. The lateral plantar nerve was dissected free and transected, whereas the medial plantar nerve was freed from the surrounding fascia, and placed on two platinum stimulating electrodes. The nerve-electrode complex was immersed in a mineral oil moat, whose structure was formed by the raised edges of the incised skin. The technique for immobilizing and stabilizing the hind limb has previously been reported by Adams (1966).

The eccrine sweat glands in the cat's footpad were activated with the application of supramaximal, square wave shocks (8 volts, 2 msec duration), delivered as a train of 3 impulses (2 msec separation) to the medial plantar nerve by a Grass S-8 Stimulator (Grass Instruments, Quincy, Mass.).

Control of the epidermal hydration produced by the sweat gland activation was achieved by delivering the pulse trains at one, two, or three trains per second, and designated (1), (2), and (3), respectively, over a fixed period of time. A series of preliminary experiments indicated that a graded hydration of the epidermis could be attained with a succession of stimulation periods, each 30 seconds in duration.

3.9 Epidermal Hydration: Exposure to a Humid Environment (External Hydration).

Epidermal hydration produced by exposing the footpad to a humid environment was affected with the system shown schematically in Figure 7. Room air was pumped (Dyna-Vac Pump, Cole-Palmer Instrument Co., Chicago, Ill.) through a humidifier/heater unit (H/H), and the humidified warm air effluent was directed to the footpad capsule. The H/H consisted of a "fish tank aerator" which was placed at the bottom, open end of a Laboratory Gas Drying Unit (W. A. Hammond Drierite Co., Xenia, Ohio) partially immersed in a warm water reservoir. This reservoir simultaneously served the warm water thermode. Room air was pumped out of the aerator, bubbled through the warm water, and evacuated from the top of the gas "drying" unit.

The relationship of the footpad capsule to the central hind footpad is illustrated in Figure 8. With the capsule in place over the footpad, the warm, H/H effluent air produced a thermal environment within the capsule such that under steady state conditions, ΔT ranged from 0° C to 0.5°C, with the surface temperature equal to, or greater than the D-E junction temperature.

Control of the environmentally affected epidermal hydration was realized with the exposure of the footpad to the generated warm, humid air atmosphere for varying periods of time. Except as noted, these periods were composed of sequential 30 second exposures.

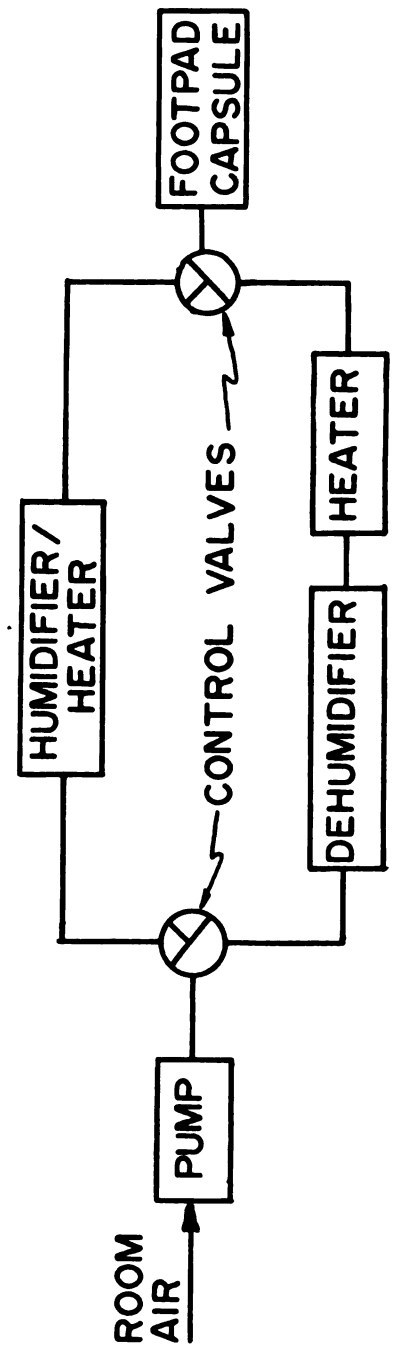


FIGURE 7. Schematic diagram of the room air humidification/dehumidification system.

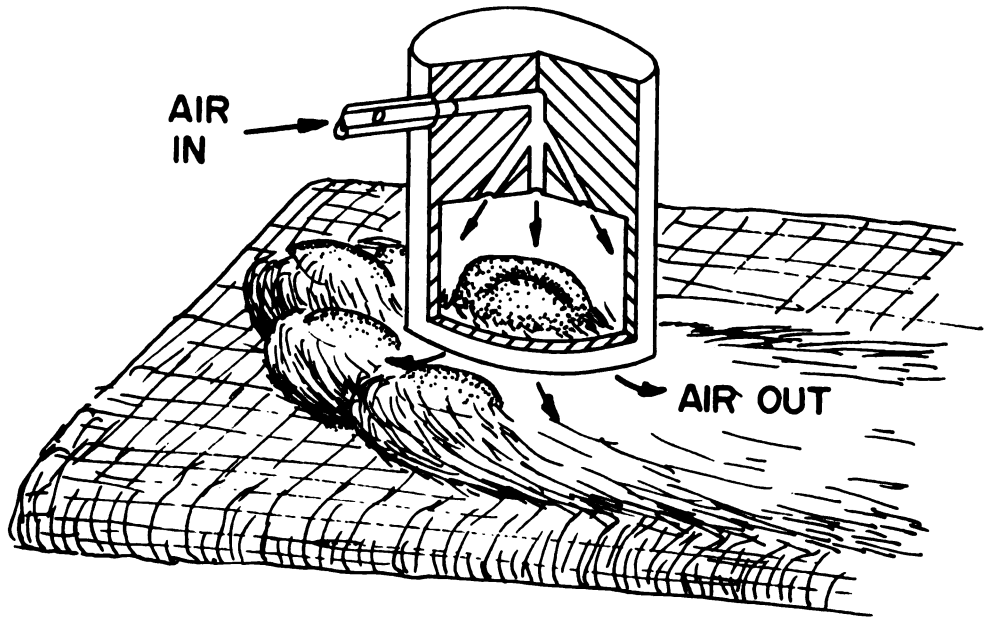


FIGURE 8. Cutaway view of the air circulation capsule in relation to the central hind footpad. The capsule is loosely positioned over the pad, and stabilized by the "air in" tubing. The "air in" tubing is connected with the humidification system. (Adapted from Adams, 1966).

3.10 Epidermal Dehydration.

Unless noted otherwise, the central hind footpad epidermis was exposed to a period of controlled dehydration prior to the initiation of controlled dehydration prior to the initiation of controlled hydration. The dehumidification system is shown schematically in Figure 7. Room air was dehumidified with passage through a Laboratory Gas Drying Unit (W.A. Hammond Drierite Co., Xenia, Ohio) containing anhydrous calcium sulphate (W.A. Hammond Drierite Co., Xenia, Ohio). The dry air was warmed while moving through Tygon tubing immersed in the filled, warm water reservoir. The relationship between the pump, footpad capsule, and footpad (Figure 8) have previously been described (3.9).

With the capsule in place over the footpad, the flow of warm, dry air produced a thermal environment such that under steady state conditions, ΔT ranged from $0.0 - 0.5^{o}$ C, with the surface temperature equal to, or greater than the D-E junction temperature.

3.11 The Sequence of Hydration/Dehydration and Parameter Measurement.

Buettner (1951) mathematically analyzed the effects of heat on skin temperature changes caused by heat flowing to the skin in contact with a hot body of constant temperature. His analysis predicted that there will be relatively little change in ΔT after 30 seconds of skin surface contact with the warm body. Assuming ΔT is constant with time after 30 seconds, it follows that there is no change in the

amount of heat flowing (Q) to the skin (3.2). It must also be assumed that the conductivity coefficient, k, is constant after this time. Under these conditions, the amount of heat leaving the skin site is balanced by the amount of heat entering the site, and Henriques and Moritz (1947) stated that the skin could then be considered to be "heat saturated". Once "saturated", the amount of heat flowing through the skin will depend only upon the thermal conductivity and the constant temperature of the skin surface (Henriques and Moritz, 1947). The surface temperature was held constant at a value determined by the temperature of the warm water thermode in the present investigation.

Preliminary investigations by the author, supported the analysis of Buettner (1951) and the report by Henriques and Moritz (1947), by demonstrating that the calculated thermal conductivity coefficient (see section 3.2) attained a steady state value 30 seconds after the thermode contacted the skin. This suggested the need to standardize the length of time that the heat source (warm water thermode) would be in contact with the skin surface, as well as the establishment of the time(s), after thermode-to-skin contact, when Q and ΔT would be measured.

The average value of three measurements of Q and ΔT, recorded 30, 45, and 60 seconds after thermode/skin contact were employed to calculate k (3.2) at any one of the established epidermal hydration conditions. Following the 60-second measurement of Q and ΔT, the thermode was raised from the footpad surface and another experimentally

produced hydration condition was established. Except as noted, this involved either 30 seconds of sweat gland activation, 30 seconds of exposure to a humid environment, or 30 seconds of exposure to a dry environment. In general, the timed sequence of 60 seconds of "thermode-on for measurement of Q and ΔT", followed by 30 seconds of "thermode-off for epidermal hydration/dehydration" continued uninterrupted through a series of epidermal hydration conditions.

Except as noted, the thermal conductivity coefficient was first determined for the epidermis at a "room dry", or control-dehydrated condition, establishing a "reference" level of hydration for a given footpad. This "reference" condition was followed by a series of controlled hydrations involving sweat gland activation (3.8) and exposure to a humid environment (3.9), providing a timed sequence of graded epidermal hydration in each cat footpad.

3.12 Data Analysis.

The Null Hypothesis was stated as follows:

H_o: The cat footpad epidermal thermal conductivity coefficient, k, is unrelated to the hydration of the stratum corneum affected by either sweat gland activation (internal hydration) or exposure of the footpad to a humid, warm air environment (external hydration).

A least squares linear regression analysis was performed on the

calculated value of k (see section 3.2) determined at each epidermal hydration condition in each footpad, as a function of the accumulated time of the hydration effect, on the CDC 3600 Digital Computer. The computer program for these calculations is presented in Appendix G. The generated regression lines were constrained such that each hydration condition-related line segment intersected adjoining segments at the time of change in the hydrating effector, i.e., in changing from a peripheral nerve stimulation of (1) to (2), etc. The slope of the regression line segment was tested for statistical significance, by the computer, using the standard F-statistic. The relationship between k and stratum corneum hydration (dehydration), as described by the slope of the regression line, was termed "significant" if H_o was rejected at the 0.01 significance level. If the rejection of the hypothesis that k and epidermal hydration are unrelated could not be made with at least 99.0 percent confidence, then the relationship was termed "not significant".

IV. RESULTS

Cat footpad skin consists of a superficial epidermis overlying a supportive dermis (Figure 9). The footpad epidermis has five distinct layers (as shown in Figure 9): the stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, and stratum basale. The dermis is composed of the stratum papillare and the stratum reticulare. Below the dermis is the panniculus adiposus, a tissue composed of large masses of adipose tissue which are enclosed by an interwoven network of elastic and collagenous fibers.

Figure 9 shows the location of the thermocouple (TC) junction used to measure the temperature at the dermoepidermal junction. The TC was removed prior to tissue fixation. Its position within the footpad was identified by injecting India ink into the puncture wound which facilitated its initial placement (see section III 3.6). The inter-thermocouple distance (x), as measured in each footpad (reported in Table 2) averaged $5.0 \pm 1.4 \times 10^{-4}$ meters.

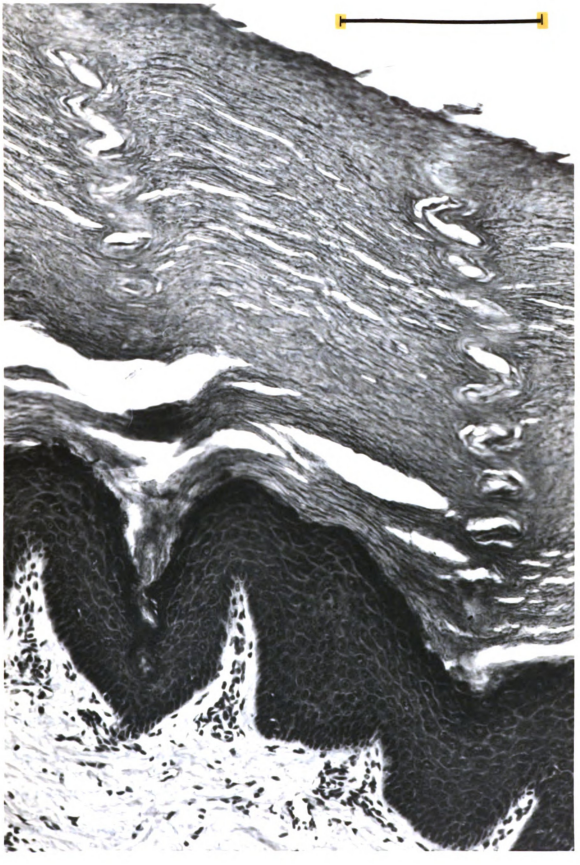
Figure 10 is a photograph of a histologic section through the footpad epidermis which shows the characteristic spiralling of the distal portion of the eccrine sweat duct as it lies within the stratum corneum. This feature of the eccrine duct is first seen within the lower strata of the epidermis.

FIGURE 9. Section through the central hind (metacarpal) footpad of the cat. H. and E. stain. Reference dimension: 200 microns.

1. Stratum corneum.
2. Stratum lucidum.
3. Stratum granulosum.
4. Stratum spinosum.
5. Stratum basale.
6. Stratum papillare.
7. Stratum reticulare.
8. Location of intrapad thermocouple junction.
9. Merocrine (eccrine) sweat ducts.
10. Blood vessels.
11. Panniculus adiposus.


1
2
3
4
5
6
7
8
9
10
11

FIGURE 10. Section through the epidermis of the cat footpad showing the spiralling nature of the eccrine duct as it passes through the stratum corneum. H. and E. stain. Reference dimension: 200 microns.



The pattern for data presentation will be to report representative data for each major section of the total experiment in both tabular (Appendix A-F) and graphic (Figures 11-16) display, and to present a summary of all observations at the end of this section of the report (Table 2; Figure 17). The logical inference is tacitly assumed that an increase in skin thermal conductivity reflects an increase in the stratum corneum hydration (Adams and Hunter, 1970; Adams and Vaughan, 1965; Comaish and Bottoms, 1971; Edelberg, 1961, 1968; Henshaw, et al. 1972; Lloyd, 1959 a,b; Mole, 1948; Park and Baddiel, 1972a; Stombaugh and Adams, 1971; Thomas and Kawahata, 1962; Thomas and Korr, 1957; Tregear, 1966; Winslow, et al. 1937).

In Figures 11-16, individual datum points represent the average of 3 separate steady state determinations of the epidermal thermal conductivity coefficient (k) which were measured after 30 seconds of skin exposure to each hydration effect. Both statistically and non-statistically significant slopes for each regression line correspond to data grouping defined for computer analysis (see section III 3.12). Similarly, in Appendices A-F are reported mean values for each thermal conductivity coefficient reported in the appropriately referenced figure, mean transepidermal temperature difference (ΔT), and heat fluxes (Q) used to calculate k in each test, as well as the matching interthermocouple distance (x).

During the episodes of internal hydration of the stratum corneum

elicited by the electrical stimulation of the medial plantar nerve with 1, 2, or 3 pulse trains per second (see section III 3.8), the skin surface of the footpads was visually examined for signs of sweating, as evidenced by sweat exuding from the eccrine duct orifice. Although sweating from the toe pads was observed in 6 (Cat #5-6-L, 5-6-R, 6-7-L, 6-7-R, 5-13-L, 5-21-R) of the 11 animals subjected to sweat gland activation by peripheral nerve stimulation (Table 2), only 3 of these animals (Cat #6-7-L, 5-13-L, 5-21-R) showed evidence of sweating from the central hind footpad. The relationship of calculated k to hydration effects for these 3 footpads are shown in Figures 12, 14, and 15.

In Figure 11 are presented data which are selected to be representative of experiments on 8 separate footpads. These data reflect the changes in skin thermal conductivity as functions of passive hydration (exposure to room air), internal hydration (produced by peripheral nerve stimulation), and external hydration (produced by exposure to water saturated air). Although there was no change in k either during passive hydration following 35 minutes of exposure to dry air (see section III 3.10) or low frequency of stimulation of the peripheral nerve (1 pulse train per second), increased sweat gland activity (2 pulse trains per second) elevated ($P < 0.0005$) stratum corneum hydration, as did exposure to high ambient humidity ($P < 0.005$). At no time during the sweat gland activation did sweat appear at the central hind footpad skin surface.

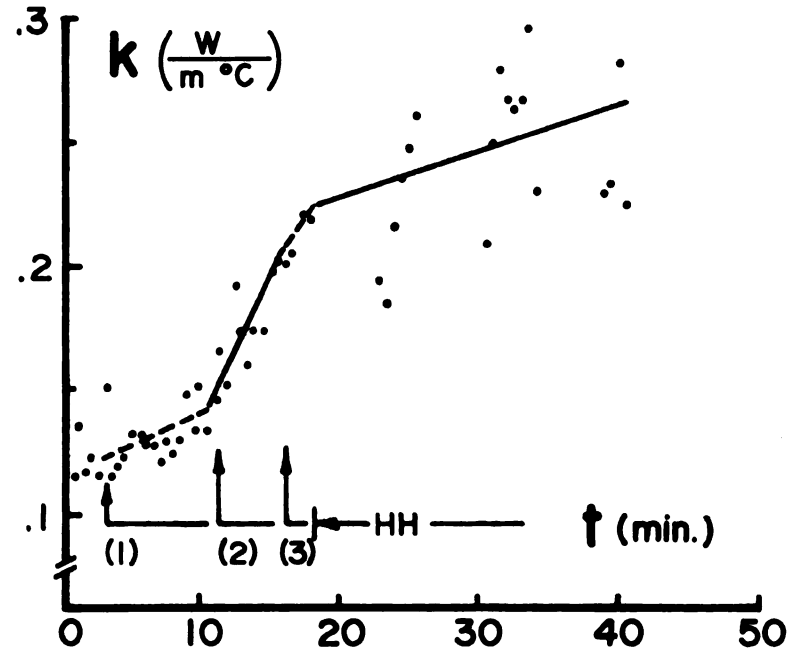


FIGURE 11. Skin thermal conductivity during hydration. Thermal conductivity (k) of the cat footpad (Cat #5-6-L) is shown as a function of time (t) during 3 levels of nerve stimulation (pulse trains/second) and during exposure to high ambient relative humidity (HH). Solid lines represent a slope which is statistically different from zero, dashed lines represent a slope which is not significantly different from zero.

Data indicating a similar change in skin thermal conductivity with an analogous sequence of hydration are reported in Figure 12. Although there was no change in skin thermal conductivity during passive hydration, k increased significantly ($P < 0.001$) during stimulation of the peripheral nerve (internal hydration) at a frequency of 1 pulse train per second. There was no further increase in k (reflecting skin hydration) with increased sweat gland activity. Sweat was seen exuding from the sweat duct orifices on the central hind footpad after 1.5 minutes of stimulation at 2 pulse trains per second. There was a resumption in the increase in k ($P < 0.0005$) during external hydration. Supportive data for figures 11 and 12 are reported in Appendices A and B, respectively.

In a second series of experiments, the phases of internal and external hydration were reversed compared to the experiment summarized in figures 11 and 12 (and Appendices A and B). As reported in Figures 13 and 14 (selected to be representative of data from experiments on 3 separate footpads), exposure to high ambient humidity (external hydration) preceeded peripheral nerve stimulations involving 3 levels of sweat gland activity. As shown in Figure 13, beginning from a level of passive hydration, k (reflecting the footpad water density) progressively increased ($P < 0.0005$) during 56 minutes of external hydration but did not increase further with peripheral nerve stimulation. Data reported in Figure 14 in a corresponding hydration series, show that skin thermal conductivity increased

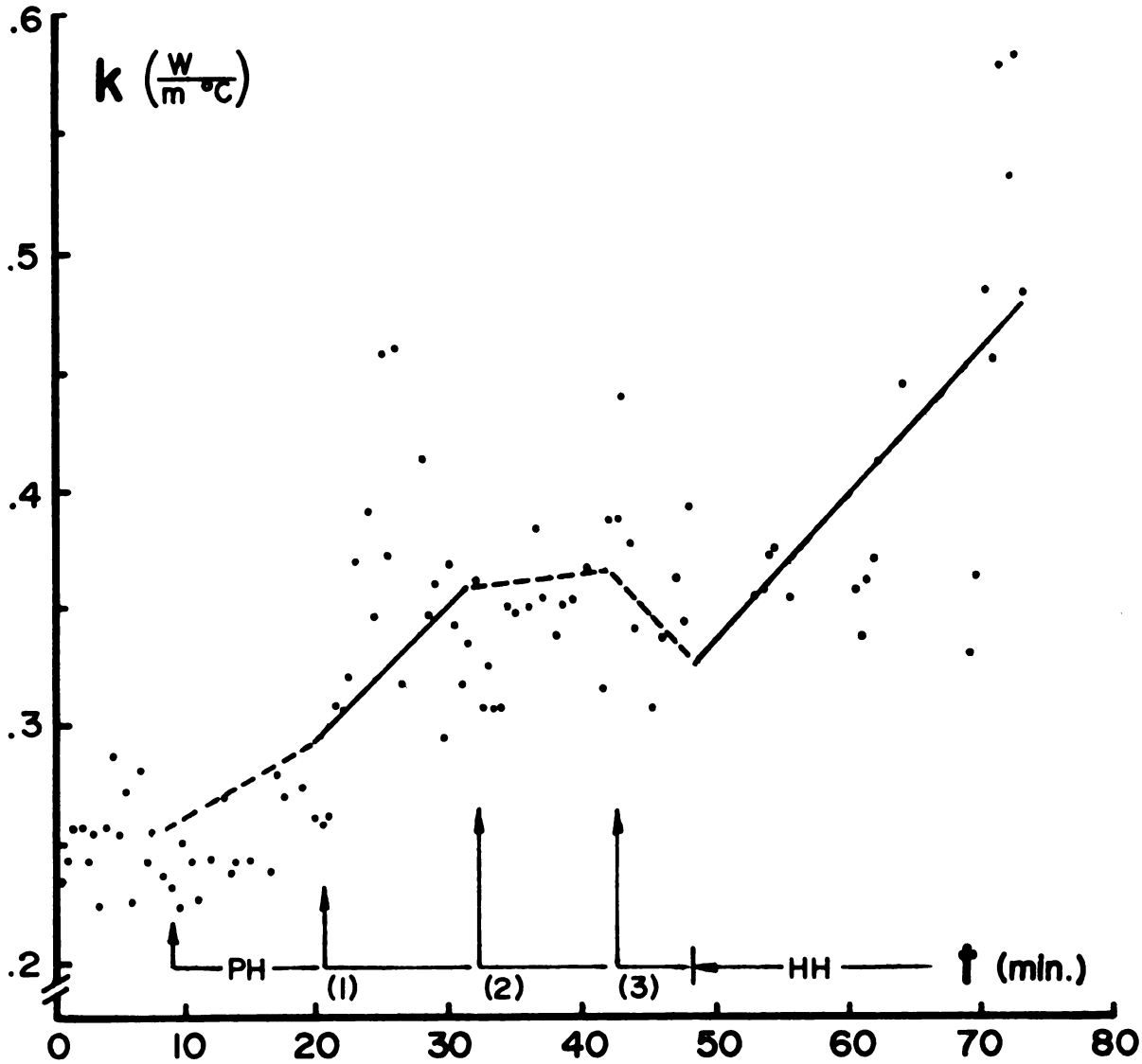


FIGURE 12. Skin thermal conductivity during hydration. Thermal conductivity (k) of the cat footpad (Cat #6-7-L) is shown as a function of time (t) during a period of passive hydration (PH) (exposure of the footpad to room air), followed by 3 levels of nerve stimulation (pulse trains/second) and during exposure to high ambient relative humidity (HH). Solid lines represent a slope which is statistically different from zero, dashed lines represent a slope which is not significantly different from zero.

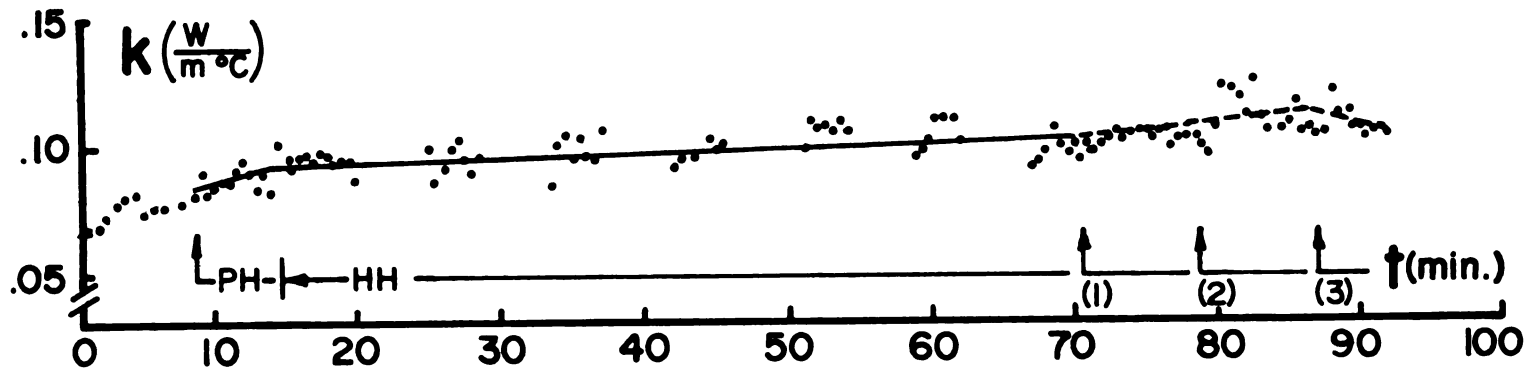


FIGURE 13. Skin thermal conductivity during hydration. Thermal conductivity (k) of the cat footpad (Cat #5-21-L) is shown as a function of time (t) during a period of passive hydration (PH) (exposure of the footpad to room air), followed by a period of exposure to high ambient relative humidity (HH), and during 3 levels of nerve stimulation (pulse trains/second). Solid lines represent a slope which is statistically different from zero, dashed lines represent a slope which is not significantly different from zero.

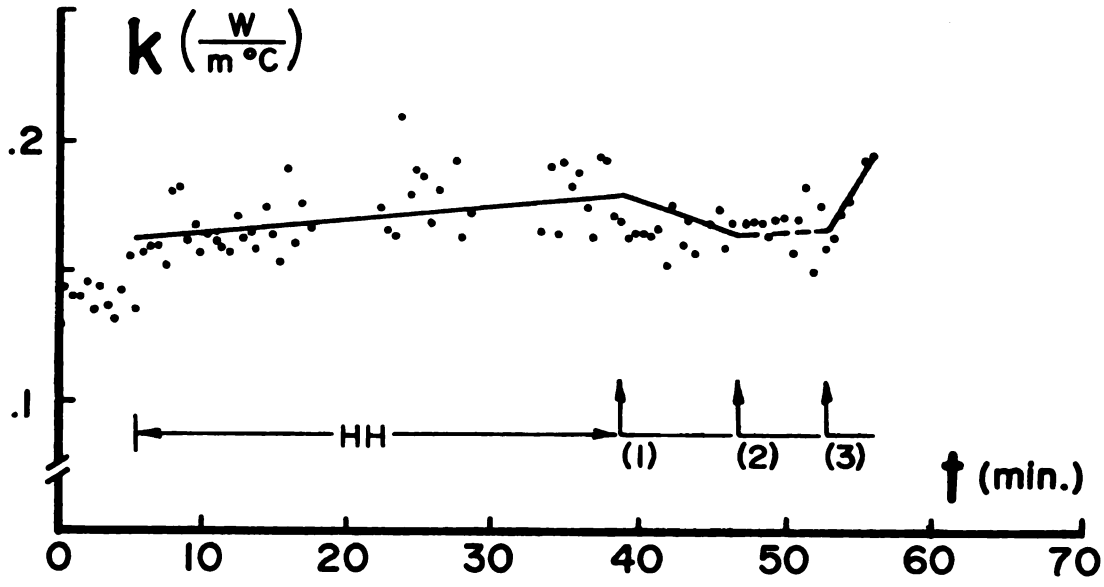


FIGURE 14. Skin thermal conductivity during hydration. Thermal conductivity (k) of the cat footpad (Cat #5-21-R) is shown as a function of time (t) during a period of exposure to high ambient relative humidity (HH) preceeding a sequence of 3 levels of nerve stimulation (pulse trains/second). Solid lines represent a slope which is statistically different from zero, dashed lines represent a slope which is not significantly different from zero.

($P < 0.0005$) during external hydration (33.5 minutes) but subsequently decreased significantly ($P < 0.005$) during the following phase of low sweat gland activity (1 pulse train per second). However, the corneum regained water, as indicated by a significant increase ($P < 0.0005$) in k, at a higher level of sweat secretion (3 pulse trains per second). Only after 2 minutes of sweat gland activation at the higher level of nerve stimulation (3 pulse trains per second) did sweat appear at the skin surface. Supportive data for Figures 13 and 14 are reported in Appendices C and D, respectively.

In a separate test series, external hydration of the footpad skin was followed by exposure to dry air (see section III 3.10) prior to sweat gland stimulation. As reported in Figure 15, corneal water density increased ($P < 0.001$) progressively during exposure to high ambient humidity. After 34.5 minutes of drying, skin hydration ($k = 0.117$ W/m ^{o}C) had not returned to the level preceeding 34.0 minutes of external hydration ($k = 0.103$ W/m ^{o}C). It did, however, increase significantly ($P < 0.0005$) with subsequently induced sweat gland activity. The footpad began to sweat, as indicated by sweat appearing at the skin surface in a liquid phase, only after 0.5 minutes of high level (3 pulse trains per second) nerve stimulation. Supportive data are reported in Appendix E.

A similar hysteresis in the rates of skin absorption and desorption of water is implied by data reported in Figure 16. In this test series, peripheral nerve stimulation preceeded external

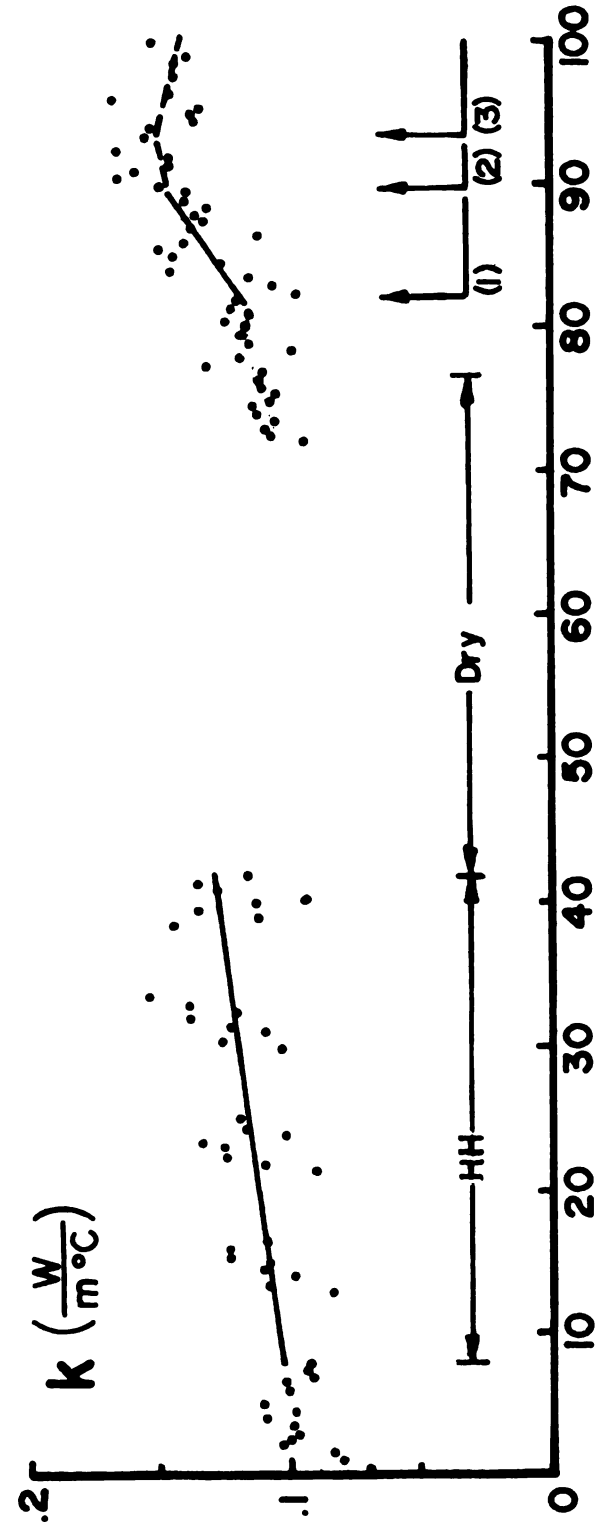


FIGURE 15. Skin thermal conductivity during hydration. Thermal conductivity (k) of the cat footpad (Cat #5-13-L) is shown as a function of time (t) during a period of exposure to high ambient relative humidity (HH) and during 3 levels of nerve stimulation (pulse trains/second), with an intervening period of dehydration (Dry). Solid lines represent a slope which is statistically different from zero, dashed lines represent a slope which is not significantly different from zero.

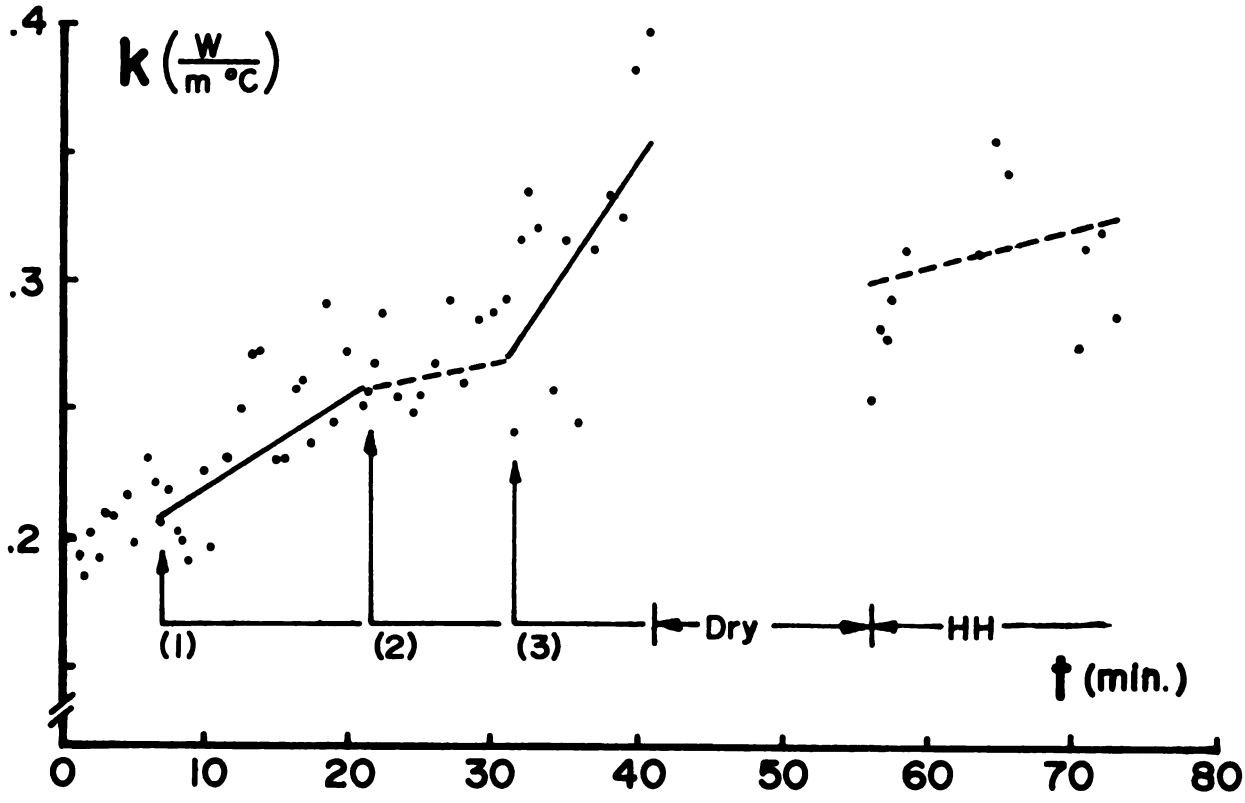


FIGURE 16. Skin thermal conductivity during hydration. Thermal conductivity (k) of the cat footpad (Cat #6-7-R) is shown as a function of time (t) during 3 levels of nerve stimulation (pulse trains/second) and during a period of exposure to high ambient relative humidity (HH), with an intervening period of dehydration (Dry). Solid lines represent a slope which is statistically different from zero, dashed lines represent a slope which is not significantly different from zero.

hydration with an intervening drying period. Skin thermal conductivity after 15 minutes of drying was not the same as that preceeding 34 minutes of nerve stimulation following a matching drying phase. Supportive data are reported in Appendix F.

A summary of data for all test phases is reported in Table 2 and Figure 17. Data reported in Table 2 reflect thermal conductivity coefficient (k) values at the beginning and end of each experiment testing separate hydration effects, as well as changes and percent changes in calculated k. Also reported in Table 2 is the measured inter-thermocouple dimension (x) and total time (minutes) of the respective hydration effect.

Ten of eleven footpads were subjected to both a period of sweat gland activity ( ), producing an internal hydration effect, and to a period of exposure to high ambient relative humidity (HH) to give an external hydration effect. As shown in Table 2, the stratum corneum in 8 separate experiments was subjected to an initial effect, followed, in 7 of these experiments, by a period of HH. The animals possessing 5 of these 8 footpads had been given an i.v. infusion (see section III 3.3) of phenoxybenzamine (w/POB), an alpha adrenergic receptor blocking agent, whereas the other 3 footpads in this hydration sequence were from animals without such treatment (w/o POB).

In contrast to the hydration sequence of nerve followed by HH, the central hind footpads of 3 animals, treated w/POB, were

TABLE 2. Skin thermal conductivity coefficient, k (Watts/m ^{o}C), *vs* skin hydration: A summary of the data analysis. The mean "pre-hydration" value of k for all (n=11) footpads investigated is 0.167 $\pm$ 0.023 Watts/m ^{o}C.

For each footpad (Cat #), the inter-thermocouple dimension (x) and footpad preparation is shown. The values of "k-Begin" and "k-End" were determined by computer analysis (see section III 3.12) of calculated k versus the hydration effect. Similarily, the significance of the change in k (Δk), over its respective period of hydration, was established by computer analysis.

WITH iv POB			SWEAT GLD. ACTIVATION (pre-"HUMIDITY HYD.")					HUMIDITY HYDRATION (post-"SW. GLD. ACT.")				
CAT #	x ($x10^{-4}m$)	FOOT PAD PREPARATION*	k Begin	k End	Time (min.)	Δk	% Δk	k Begin	k End	Time (min.)	Δk	% Δk
5-6-L	6.6	2-1	0.122	0.224	15.5	0.102	+83.6 •	0.224	0.266	22.5	0.042	+19.1 •
5-6-R	5.6	2-1	0.095	0.125	9.5	0.030	+31.6 •	0.125	0.123	46.0	-0.002	- 1.6 ■
6-7-L	7.6	1-2	0.292	0.366	28.0	0.074	+25.3 •	0.366	0.480	25.0	0.114	+31.1 •
6-7-R	4.1	1-2	0.207	0.355	34.5	0.148	+71.3 •	0.300	0.326	9.5	0.026	+ 8.7 ■
7-14-R	4.1	1-2	0.157	0.213	10.5	0.056	+35.7 •	0.213	0.196	27.5	-0.017	- 8.0 ■
				$\bar{X}$	19.6		+49.5			26.1		+ 9.9
				±SEM	±5.0		±11.7			±3.1		± 7.0

WITHOUT iv POB			SWEAT GLD. ACTIVATION (pre-"HUMIDITY HYD.")					HUMIDITY HYDRATION (post-"SW. GLD. ACT.")				
CAT #	x ($x10^{-4}m$)	FOOT PAD PREPARATION*	k Begin	k End	Time (min.)	Δk	% Δk	k Begin	k End	Time (min.)	Δk	% Δk
7-13-L	4.6	1-2	0.126	0.157	29.5	0.031	+24.8 •					
7-27-L	6.1	2-3	0.315	0.350	24.0	0.035	+11.1 ■	0.398	0.495	6.0	0.097	+24.4 •
7-28-R	4.6	2-3	0.159	0.184	25.5	0.025	+15.7 •	0.184	0.197	25.0	0.013	+ 7.1 ■
				$\bar{X}$	26.3		+17.2			15.5		+15.8
				±SEM	±1.6		± 4.0			±9.5		±8.7

WITH iv POB			HUMIDITY HYDRATION (pre-"SW. GLD. ACT.")					SWEAT GLD. ACTIVATION (post-"HUMIDITY HYD.")				
CAT #	x ($x10^{-4}m$)	FOOT PAD PREPARATION*	k Begin	k End	Time (min.)	Δk	% Δk	k Begin	k End	Time (min.)	Δk	% Δk
5-13-L	3.0	2-1	0.103	0.129	34.0	0.026	+25.2 •	0.117	0.142	18.5	0.025	+21.4 •
5-21-L	3.3	2-1	0.093	0.103	56.0	0.010	+10.8 •	0.103	0.104	22.0	0.001	+ 1.0 ■
5-21-R	5.3	1-1	0.164	0.181	33.0	0.017	+10.4 •	0.181	0.196	17.0	0.015	+ 8.3 ■
				$\bar{X}$	41.0		+15.5			19.2		+10.2
				±SEM	±7.5		± 4.9			±1.5		± 6.0

TABLE 2 (continued)

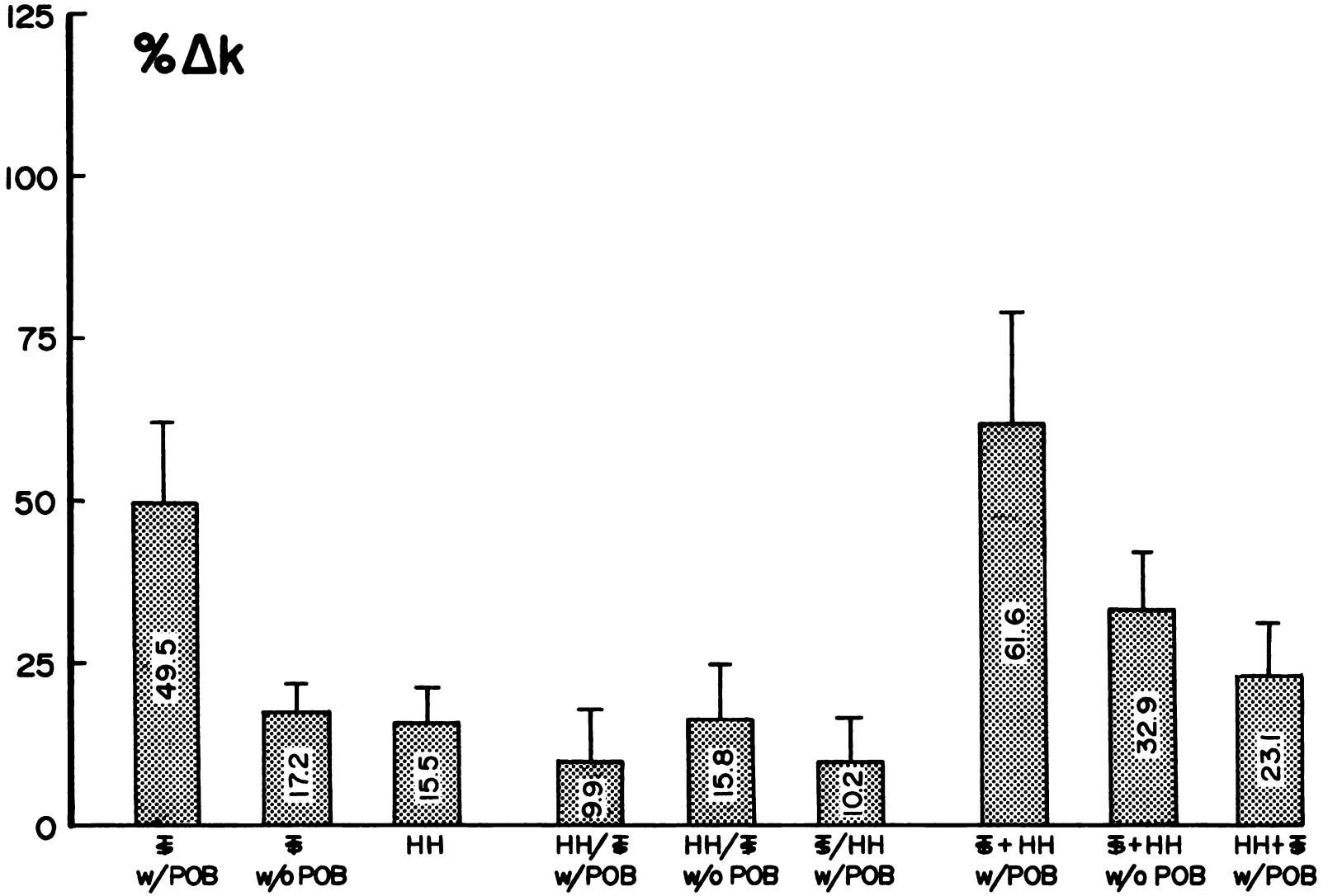
WITH iv POB			SWEAT GLD. ACTIVATION + HUMIDITY HYD.				
CAT #	x ($\times 10^{-4}$m)	FOOT PAD PREPARATION*	k Begin	k End	Time (min.)	Δk	% Δk
5-6-L	6.6	2-1	0.122	0.266	38.0	0.144	+118.0
5-6-R	5.6	2-1	0.095	0.123	55.5	0.028	+ 29.5
6-7-L	7.6	1-2	0.292	0.480	53.0	0.188	+ 64.4
6-7-R	4.1	1-2	0.207	0.355	34.5	0.148	+ 71.3
7-14-R	4.1	1-2	0.157	0.196	37.5	0.039	+ 24.8
				$\bar{X}$	43.7		+ 61.6
				±SEM	±4.4		± 16.8
WITHOUT iv POB			SWEAT GLD. ACTIVATION + HUMIDITY HYD.				
CAT #	x ($\times 10^{-4}$m)	FOOT PAD PREPARATION*	k Begin	k End	Time (min.)	Δk	% Δk
7-27-L	6.1	2-3	0.315		30.0	0.132	+41.9
7-28-R	4.6	2-3	0.159	0.197	50.5	0.038	+23.9
				$\bar{X}$	40.3		+32.9
				±SEM	±10.3		± 9.0
WITH iv POB			HUMIDITY HYD. + SWEAT GLD. ACTIVATION				
CAT #	x ($\times 10^{-4}$m)	FOOT PAD PREPARATION*	k Begin	k End	Time (min.)	Δk	% Δk
5-13-L	3.0	2-1	0.103	0.142	48.5	0.039	+37.9
5-21-L	3.3	2-1	0.093	0.104	78.0	0.011	+11.8
5-21-R	5.3	1-1	0.164	0.196	50.0	0.032	+19.5
				$\bar{X}$	58.8		+23.1
				±SEM	±9.6		± 7.7

POB: phenoxybenzamine
x: inter-thermocouple dimension

* First numeral: 1 = foot pad debrided prior to experimentation
2 = foot pad not debrided
Second numeral: 1 = foot pad washed with water prior to experimentation
2 = foot pad washed with 100% alcohol, but not water, prior to experimentation
3 = foot pad not washed with alcohol or water

• Significant ($P \leq 0.01$)
■ Not significant

FIGURE 17. A summary of data: the mean ±S.E.M. of the percent change in the epidermal thermal conductivity coefficient (k) is shown as it is affected by peripheral nerve stimulation (Ⓕ; internal hydration), by exposure of the epidermis to a high ambient relative humidity (HH; external hydration), and by combinations (HH following Ⓕ (HH/Ⓕ), or Ⓕ following HH (Ⓕ/HH)) and sums (Ⓕ + HH, or HH + Ⓕ) of the hydration effects.


%Δk
125
100
75
50
25
0
49.5
17.2
15.5
9.9
15.8
10.2
61.6
32.9
23.1
HH
HH/ w/POB
HH/ w/o POB
HH+ w/POB
HH+ w/o POB
HH+ w/POB

subjected to an initial external hydration effect, followed by a sequence of peripheral nerve stimulations (HH followed by $\overline{E}$) (Table 2).

In footpads subjected to an initial $\overline{E}$ effect, the 49.5% increase in the calculated epidermal thermal conductivity coefficient in animals treated w/POB was significantly greater ($P \leqslant 0.025$) than the 17.2% increase in k produced in the epidermis of animals w/o POB. This difference in k (reflecting an increased stratum corneum hydration in the w/POB-animals compared to w/o POB-animals) was evidenced without a significant difference ($P \leqslant 0.05$) in the time of the $\overline{E}$ effect (Table 2).

Data summarized in Table 2 report that exposure of the footpad to a high ambient relative humidity (HH) prior to sweat gland activation produced a 15.5% increase in the thermal conductivity coefficient which was significantly ($P \leqslant 0.025$) less than the 49.5% increase in k produced by an initial hydration with sweat gland activation ($\overline{E}$). Each response was elicited in animals treated with POB. This lesser k-HH related effect was observed despite a greater ($P \leqslant 0.025$) time of HH exposure.

As shown in Table 2, a "total" hydration sequence consisting of an initial $\overline{E}$ effect followed by a HH effect ($\overline{E}$ + HH; representing 7 separate experiments) produced no significant ($P \leqslant 0.05$) difference in the accumulated increase of k between the w/ and w/o POB animals. However, in 8 separate experiments on animals treated w/POB, the

61.6% increase in k attained after a "total" hydration effect produced by the TF + HH sequence was significantly ($P \leqslant 0.05$) greater than the 23.1% increase in k produced by a HH + TF effect. Although this difference in k for the accumulated effects of internal and external hydration was a function of the sequence of hydration, it was not ($P < 0.05$) a function of a difference in respective test time.

V. DISCUSSION

In the following discussion, the logical inference is tacitly assumed that an increase in skin thermal conductivity coefficient reflects an increase in stratum corneum hydration (Adams and Hunter, 1970; Adams and Vaughan, 1965; Comaish and Bottoms, 1971; Edelberg, 1961, 1968; Henshaw, et al. 1972; Lloyd, 1959 a,b; Mole, 1948; Park and Baddiel, 1972a; Stombaugh and Adams, 1971; Thomas and Kawahata, 1962; Thomas and Korr, 1957; Tregear, 1966; Winslow, et al. 1937).

5.1 The Dermis, Epidermis, and Eccrine Sweat Duct.

Histologic features of the central hind footpad skin of the cat (Figures 9 and 10) support earlier evidence (Conroy, 1964; Creed, 1958; Strickland and Calhoun, 1963) that the epidermis is composed of 5 strata: the stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, and stratum basale. The avascular epidermis is supported by the dermis which contains numerous blood vessels and eccrine sweat gland ducts. The meandering course which the eccrine sweat duct follows through the dermis (Munger and Brusilow, 1961) is evident from the many cross-sections of the ducts seen in Figure 9.

The eccrine duct follows a spiral course through the stratum

corneum (Figure 10) of the cat footpad epidermis, as has been reported previously by Sperling and Koppanyi (1949). Although the duct configuration is reported to change to a loosely convoluted structure during a bout of sweating (Sperling and Koppanyi, 1949), the screw-like configuration of the duct illustrated in Figure 10 was consistently seen in the corneum of footpads subjected to peripheral nerve stimulation in the present investigation. The patterns of duct configuration were unchanged in this study, regardless of the hydration level of the stratum corneum at the time of tissue sampling.

A sampling of ducts within the corneum showed that the number of "threads" in the screw-like ascent of the duct through the stratum corneum toward the skin surface depends on corneal thickness, supporting similar findings by Wolf (1968b) for the eccrine duct in the corneum of the macaque palm. This spiral feature offers, of course, a much greater duct-to-stratum corneum interface for transductal water exchange during and after a sweating episode than would be available with a straight duct traversing a similar thickness of the corneum. This larger surface area of the duct lumen would facilitate water movement across the duct wall, that is between the sweat gland duct and the peripherally adjacent stratum corneum. For example, Takagi and Tagawa (1955) reported that the eccrine sweat duct forms a "fairly regular" cylindrical spiral in traversing the human palmar and plantar epidermis.

They measured the girth (diameter) and pitch of the spiral to be approximately 50 microns and 40 microns, respectively. A modelling of this structure in conjunction with the present study showed that the length of duct under these conditions is approximately 4.5 times the length of a straight duct spanning an equal dimension. Assuming the eccrine sweat duct configuration to be approximated by a right cylinder, then the curved surface area of the spiralling sweat duct will be approximately 4.5 times larger than a straight duct, of the same diameter, spanning an equal stratum corneum thickness.

The anatomical location of the cutaneous thermal receptors is unresolved (Zotterman, 1959), and histologic techniques employed in the present investigation do not permit a speculation in this regard. However, Zotterman (1959) has reported that cold receptors (identified on the basis of physiological testing) lie adjacent to the dermoepidermal junction in the skin.

5.2 Stratum Corneum Water Exchange.

Many investigators (Baden, 1970; Blank, 1952, 1953; Craig, 1956; Mali, 1956; Mole, 1948; Peiss, et al., 1953; Scheuplein and Morgan, 1967) have demonstrated that the stratum corneum is "hygroscopic" and is capable of accepting water either by diffusion from the underlying tissues or from the external environment. Others have suggested that the reported changes in the mechanical (Adams and Hunter, 1969; Comaish and Bottoms, 1971; Naylor, 1955) and electrical (Adams and Vaughan, 1965; Lloyd, 1959 a,b, 1960;

Stombaugh and Adams, 1971; Thomas and Kawahata, 1962; Thomas and Korr, 1957) properties of the skin following sweat gland activation are the result of water leaving the eccrine sweat duct to diffuse into the stratum corneum away from the axis of the duct. Their data imply that water movement transiently, or water storage in a steady state may be a three dimensional phenomenon for superficial skin layers.

The location and movement of water in the stratum corneum may depend, in part, upon the distribution of water-binding, hydrophilic protein. Matoltsy and Balsamo (1955) have shown that 75% of the dry stratum corneum is composed of the epidermal protein, keratin. The physical-chemical basis for the hydration of proteins has been described by Bull (1944), Pauling (1945), and Sponsler, et al. (1944). In general, the hydration potential of a protein depends upon its molecular size, the number of peptide bonds, the relative number of constituent polar amino acid residues, and the initial number of water molecules bound to the molecule. The keratin molecule is believed to consist of closely packed polypeptide chains (Montagna, 1962). However, the amino acid constituency of keratin has not been reported. The physical-chemical evidence imply that the keratin molecule is the major water binding molecule in the stratum corneum. Recent investigations (Jelenko and Ginsburg, 1971; Middleton, 1968; Park and Baddiel, 1972b; Scheuplein and Morgan, 1967) report that the lipid component of the corneum is

responsible for the regulation of water exchange between the corneum (involving the keratin molecule) and its environment.

In the present investigation, as shown by data reported in Figures 11-16 and Appendices A-F, the water content of the stratum corneum was inferentially increased by 1) electrical stimulation of the sudomotor nerves affecting controlled levels of "internal hydration", and by 2) exposing the epidermis to a high ambient relative humidity producing an "external hydration". Data summarized in Table 2 and Figure 17 support the earlier data of Mole (1948), Tregear (1966), and Winslow, et al. (1937) and show that highly significant ($P < 0.001$) increases in the thermal conductivity coefficient of the epidermis are produced by increasing the water content of the corneum. The hypothesis is supported that the increased thermal conductivity of the skin in the present experiments was directly related to its increased hydration. Such variations in skin hydration most likely occur in the avascular, stratum corneum, as suggested earlier (Blank, 1952, 1953; Mole, 1948) and strengthens the concept of a cutaneous "hydraulic capacitance" phenomenon (Adams, 1966). The physical-chemical properties of the skin which allow it to vary its water density are discussed in the following section of this report.

5.3 Stratum Corneum Water Exchange: Hydration/Dehydration.

Analyzes of the water exchange properties of the stratum corneum show that water contained in the corneum can be classified

as "free water" and "bound water" (Scheuplein and Morgan, 1967). The "bound water" is largely associated with the protein or lipid-protein molecules in the corneum (Middleton, 1968; Park and Baddiel, 1972b; Scheuplein and Morgan, 1967) which chemically accept and hold water molecules. It is suggested that the "free water" resides in the intercellular spaces of the stratum corneum as well as within the cornified cells, but remains dissociated from the hygroscopic keratin protein structures in these cells. Scheuplein and Morgan (1967) have shown that the corneum exchanges its "free water" with relative ease compared to the difficulty with which the "bound water" is removed.

The relationship between the rates of stratum corneum hydration and dehydration for the skin of the cat central hind footpad are illustrated in Figures 15 and 16. From data presented in Figure 15 and Appendix E, the rate of increase in k (reflecting an increasing stratum corneum water content) with exposure of the footpad to a high ambient relative humidity (external hydration) was calculated to be 0.76×10^{-3} Watts/m ^{o}C minute. The calculated rate of decreasing k with stratum corneum dehydration (Figure 15) was 0.36×10^{-3} Watts/m ^{o}C minute. These data are inconsistent with those of Peiss, et al. (1953) who reported that the rate at which ambient water vapor enters the stratum corneum is very nearly the same as the rate at which it leaves the corneum. The present data (Figure 15 and Appendix E) lend support to the suggestions of Mali

(1965) who showed that the hydration-dehydration relationship for water vapor exchange in the excised stratum corneum shows hysteresis. Mali (1956) found that the water content of the corneum is not uniquely defined by the ambient relative humidity, but rather, depends on its past history of hydration. The corneum would be predicted to have a higher water content if ambient water vapor pressure were decreasing toward a hydration reference level than if it were increasing toward it, as suggested by data reported in Figure 15 and Appendix E. Mali (1956) noted that this hydration hysteresis is typical of the water transfer properties of organic polymers; presumably, the closely-packed polypeptide chains constituting the keratin protein (Montagna, 1962) are representative of such a structure and demonstrate its hydraulic characteristics. Data illustrated in Figure 15 and Appendix E suggest further that water molecules removed from a humid environment are "bound" to the protein moiety of the corneum, as evidenced by the difficulty of their subsequent removal, in contrast to the rates of movement of so called "free" (unbound) water.

Calculations using data presented in Figure 16 and Appendix F show that k decreases with epidermal dehydration at a rate of 3.7×10^{-3} Watts/m ^{o}C min. following a period of internal hydration as affected by sweat gland activation. Assuming that the processes for water loss are comparable, this rate of decrease in k (reflecting a decreasing epidermal water content) is approximately 10 times

greater than the rate evaluated for analogous dehydration conditions following exposure of the epidermis to a humid environment (Figure 15; Appendix E). Epidermal hydration by sweat gland activation is postulated as being due to the transductal passive diffusion of water in a liquid phase from the duct lumen into the periductal stratum corneum along a hydration gradient. As a possible explanation for the increased rate of water loss following an internal hydration (as evidenced by decreasing k), it is suggested further that a large percentage of the water enters, and exists as "free water" within the corneum, at least during the time course of hydration experienced in the present investigation. The data presented in Figure 16 and Appendix F are consistent with the postulate that the large rate of decrease in epidermal k following sweat gland activation is due to the relative ease with which epidermal "free water" is lost.

Based on data presented here (Figures 15 and 16 and Appendices E and F) and that reported earlier (Scheuplein and Morgan, 1967), water may be held in the stratum corneum differently, depending upon the manner in which it is presented to the skin. Exposure to water in a vapor phase (high ambient relative humidity) penetrates skin layers to be bound chemically to hydrophilic keratin molecules normally in skin. The dehydration rate of skin so hydrated is slow due to the energetics required to uncouple water molecules from their cutaneous binding sites. Water in a liquid phase penetrates the skin at different rates, however, depending upon the orientation

of its diffusion paths in reference to the flattened, anuclear cells which are densely layered to form the stratum corneum (see Figure 10). Liquid water at the skin surface readily diffuses into the stratum corneum (Blank, 1952, 1953). Similarly, liquid water is exposed to the cell margins in the stratum corneum as sweat rises in the ducts toward the skin surface from its site of secretion deep in the dermis. Data presented in Figures 11-16 and Appendices A-F, suggest (as reflected in k with sweat gland activation) that this secretion water readily diffuses into the epidermis along a gradient which is spatially related to the sweat duct. It is proposed that water in a liquid phase penetrating the cellular mass of the stratum corneum (as it does during sweat gland activity) not only resides in the skin bound to hydrophilic molecules, but also is represented interstitially as "free" water which is the more rapidly exchanged cutaneous resident. Data presented in Figures 11, 14-16 and in Appendices A, D-F, are consistent with this hypothesis.

After hydration, the stratum corneum can lose its stored water until a new equilibrium is reached between the rates of water entering and leaving the corneum, as shown by data reported in Figure 14 and Appendix D. Following a significant increase in stratum corneum water content (as reflected by an increased k) produced by a humidity hydration, electrical stimulation of the sudomotor nerves at a frequency of 1 pulse train per second does not furnish sufficient water to the corneum to prevent its significant

loss of water. At a frequency of 2 pulse trains per second, the amount of water leaving the sweat duct and entering the stratum corneum balances the water leaving the corneum. Increasing sweat gland activity (3 pulse trains per second) affords the stratum corneum a net inflow (gain) of water, and k again increases (Figure 14).

Data reported in Figure 13 and Appendix C show the changes in k produced by a hydration series similar to that used to obtain data reported in Figure 14 and Appendix D. Stratum corneum hydration increased (as indicated by increasing k) during 56 minutes of exposure of the skin to a humid environment. Subsequently, k did not decrease with sweat gland activity as shown by data reported in Figure 14 and Appendix D. Possibly, the low frequency of stimulation (1 pulse train per second) induced sufficient gland secretion to balance the efflux of water from the stratum corneum. Data reported in Figure 12 and Appendix B, support this postulation and show that the low frequency of nerve stimulation is capable of producing a significant increase in corneum water content. Under these conditions, the corneum is apparently as hydrated as possible with sweat gland activation since further increases in nerve stimulation frequency do not produce increases in the thermal conductivity coefficient. An alternative hypothesis is that sweat glands in this footpad were not functioning, but some unusual water binding, and/or skin surface features prevented a reflux of water into the

environment. The simpler explanation is that the hydraulic capacitance of the stratum corneum was as saturated as possible by sweat gland activation during the period when the nerve was stimulated.

Animals treated w/POB showed a significantly greater increase in epidermal k with sweat gland activation (ST) than did similarly treated animals subjected to the humidity hydration (HH) effect. This increased stratum corneum hydration with ST was observed even though the time of footpad exposure to the external hydration conditions was significantly longer. Data reported in Figures 11-14 and Appendices A-D illustrate the lower rates of increase in epidermal k (and increasing stratum corneum water content) with the HH exposure, compared to those with nerve stimulation. It is hypothesized that this reduced rate of increase in k with HH may, in part, be due to a lesser amount of water (water vapor) which is available to the corneum for absorption from the humid environment as compared to the amount presented to the corneum by transductal diffusion during eccrine sweat gland activity.

Although in vivo skin exposed to a high ambient relative humidity (external hydration; see section III 3.9) transiently increases its water content presumably through water storage in the stratum corneum (5.3), the source of this stored water may not be from the air. It more likely originates from within the body with

"transepidermal water loss" (Grice, et al., 1972) or "evaporative water loss" (Huheey and Adams, 1967) as its source. Exposure of the skin to high humidity reduces the rate at which such diffused water is evaporated into the environment and facilitates its availability for corneum storage.

The potential for water evaporation from the skin surface is importantly dependent upon the difference between the ambient and skin surface water vapor pressure. The non-sweating footpad skin of the cat looses 0.3 mg of water per cm^2 per min. to a dry ambient environment (Huheey and Adams, 1967). With increasing ambient water vapor pressure (humidity hydration), the stratum corneum looses a smaller quantity of its water through diffusion, resulting in a water storage and an increased thermal conductivity coefficient (Figures 11-15; Appendices A-E). Earlier data (Blank, 1952, 1953; Middleton, 1968) leave little doubt that the stratum corneum can extract water from the ambient environment. It may be conjectured that the increase in k with humidity hydration (Figures 11-15) is a complex relationship between the storage of diffusion water and the absorption of water from the humid environment. A resolution of the efficacy of these two causative effects on changes in k awaits further investigation.

5.4 Changes in the Thermal Conductivity Coefficient of Apparently Non-Sweating Skin.

Evidence presented in Figures 12 and 15 and in Appendices B and E suggests that the stratum corneum can be completely hydrated following a relatively short (approximately 10 minutes) episode of sweat gland activation at a stimulation frequency of 1 pulse train per second, since further increases in stimulus frequency failed to increase the epidermal thermal conductivity coefficient. In each of these experiments (Figures 12 and 15) sweat did not appear at the skin surface until k had reached its maximum stimulation induced value, suggesting that visible sweating (liquid water at the skin surface) is not a reliable indicator of active stratum corneum hydration by the eccrine sweat glands. Similar conclusions appear in reports noting the changes in the mechanical (Adams and Hunter, 1969; Comaish and Bottoms, 1971) and electrical (Adams and Vaughan, 1965; Lloyd, 1959b, 1960; Perry and Mount, 1954; Thomas and Kawahata, 1962; Thomas and Korr, 1957) properties of skin, as affected by sweat gland activation. Adams (1966) arrived at a similar conclusion through the evaluation of skin surface evaporative water loss and by the direct observation of sweat in a liquid phase on the skin surface.

5.5 Phenoxybenzamine and Sweat Gland Activity.

Sweat gland activity in the cat footpad is not an adrenergically mediated phenomenon (Foster and Weiner, 1970). Several authors (Foster and Weiner, 1970; Lloyd, 1963, 1968) have reported, however, that systemic or local injection of phenoxybenzamine (POB) interferes

with, or inhibits sweating associated with the electrical stimulation of the sudomotor nerves to the eccrine gland in the cat footpad. Randall, et al. (1948) and Patton (1948) have shown that the number and functional capacity of the eccrine sweat glands in the human forearm and cat hind footpad decrease with increasing time of arterial occlusion. Therefore, in 8 of 11 footpads investigated in the present report (Table 2) POB was administered iv to produce an alpha adrenergic receptor blockade, preventing the vasomotor responses in the footpad skin, and at the sweat gland secretory unit, which would be normally expected with electrical stimulation of the medial plantar nerve.

Analysis of the data summarized in Table 2 and Figure 17 show that a significantly greater increase in the epidermal thermal conductivity coefficient is achieved with sweat gland activation ($\mathfrak{T}$) in animals treated w/POB compared to that in animals without such treatment. This difference in the increase in k (reflecting an increased stratum corneum hydration in the w/POB-animals compared to the w/o POB-animals) was observed without a significant difference in the time of the $\mathfrak{T}$ effect.

It is presumed that the small increase in k with $\mathfrak{T}$ in animals not treated with POB is in large part due to effects produced by a reduced blood supply to the sweat glands coincident with induced secretory activity. This does not, of course, eliminate the possibility that each animal in this group (w/o POB) possessed fewer potentially

functional sweat glands. No visible sweating was seen on any footpad of animals in this group, but the lack of overt sweating does not eliminate the possibility of active sweat gland secretion (Adams and Hunter, 1969; Adams and Vaughan, 1965; Comaish and Bottoms, 1971; Lloyd, 1959b, 1960; Perry and Mount, 1954; Thomas and Kawahata, 1962; Thomas and Korr, 1957).

POB did not inhibit sweat gland activity as reflected by the significant increase in k in animals so treated. If POB affected a reduction in the secretory potential of sweat glands, then this effect is minimal relative to the reduction in sweat gland secretory output due to vaso-constriction induced in animals not treated with POB.

5.6 Thermal Conductivity of In Vivo and In Vitro Skin.

Henriques and Moritz (1947) indirectly determined the thermal conductivity of excised pig skin. They first evaluated k for the entire sample of skin and then subtracted from this measure k calculated following the removal of the epidermis. The difference between these two values of k was reported to be 0.209 Watts/m ^{o}C. As reported herein (Table 2), the average value for the "dry", in vivo, epidermal k, as calculated from measurements made on 11 cat footpads, was 0.167 Watts/m ^{o}C and is in reasonable agreement with data reported by Henriques and Moritz (1947). The calculated epidermal k for "dry" and "totally" hydrated skin, as shown in Tabe 2, ranged from 0.093 Watts/m ^{o}C to 0.480 Watts/m ^{o}C, respectively. This range of values agrees with similar, calculated

values of k made from measurements on the dog footpad skin by Henshaw, et al. (1972) (for the superficial 12 mm of skin, k ranged from 0.205 Watts/m ^{o}C to 0.480 Watts/m ^{o}C for "dry" and water soaked skin, respectively).

5.7 Skin Hydration and Its Effect on Body Temperature Regulating Control Systems.

It is commonly expressed that a cold, damp environment is less comfortable than one which is cold and dry. Renbourn (1959) reported that the French physician Senac commented as early as 1752 that air "both humid and cold ... produces a more intense impression than when dry". Senac, and others in the 18th and 19th centuries (Renbourn, 1959) attributed this phenomenon to the erroneous assumption that "wet" air has a higher density than dry air and therefore is able to "absorb" more heat from the body. More recently the heat transfer properties of dry and humid air have been evaluated in relation to the relative effectiveness of each on the convective heat transfer at the skin surface. Such studies have attempted to establish a physical basis for the characteristic feeling of discomfort in cold-damp environments.

Burton, et al. (1955) noted that the heat capacity (c_p) of water vapor is similar to that of any other gas, although the specific heat capacity (c_p/gm of air) of water saturated air is slightly greater than that of dry air. However, the density of moist air is less than

that of dry air. The net effect is that the thermal capacity per volume of humid air is less than that of dry air (Burton, et al., 1955). Guillemin (1954) commented that the thermal conductivity is "nearly the same" for dry air and for that saturated with water vapor. In examining the relative chilling effects of a moist-cold vs a dry-cold environment, Guillemin (1954) tested the heat exchange properties of a "clothed" and a bare hollow steel cylinder placed in various environmental humidities. He concluded that "for an inanimate test object simulating the thermal properties of a nude or clothed sedentary man in windy and calm air, there is no significant difference in the chilling effect of dry cold and moist cold environments".

Man, placed in an environment where ambient temperature is less than that of the skin is subjected to a continuous, obligatory, insensible evaporative heat loss involving a change in the phase of water from a liquid to a vapor state within the epidermis. The driving force for this evaporative water loss from the skin surface is linearly proportional to the difference between skin and ambient water vapor pressures. With an increasing ambient water vapor pressure there will be a decrease, not an increase, in the evaporative heat loss at the same temperature.

Physical theory as well as data from direct experimentation show that there is no difference in non-evaporative heat loss from a warm body whether the environmental humidity is high or low. To the contrary, evaporative heat loss may be expected to decrease

with increasing relative humidity. Based on this evidence, one should have the feeling of comparable warmth and comfort when placed in a damp environment, compared to an analogous exposure in a dry one at the same ambient temperature. Personal experience appears to present a paradox to these physical phenomena.

A mathematical model describing the relative humidity of the skin (stratum corneum) has been formulated by Mole (1948). He showed that theoretically the relative humidity of the skin, together with skin thermal conductivity will increase with increasing ambient vapor pressure. The present investigation provides direct experimental data (Figure 17; Table 2) which support the suggestions of Mole (1948), and shows moreover that even for limited exposures (approximately 40 minutes) to a high ambient relative humidity, the thermal conductivity coefficient of the cat footpad epidermis increased by approximately 15%. Burton, et al. (1955) speculated that it is the increase in skin thermal conductivity which affects the temperature in the vicinity of the thermal receptors, and offered this causal relationship as a possible explanation for the sensation of greater cold which is associated with high humidities.

In a recent literature review related to the regulation of internal body temperature, Hammel (1968) argued that skin temperature is clearly an input to the central controller for homeothermy, affecting the thermoregulatory "set point" for panting, thermally induced peripheral vasoconstriction and shivering in animals, as

well as sweating and shivering in man. In cats exposed to mild cold exposure, Adams, et al. (1970) concluded that regional or average skin temperature may be a more important thermal input than deep body temperature as a thermal drive in regulated thermoregulatory function.

Concepts presented in Figure 18 illustrate that changes in the epidermal thermal conductivity coefficient will alter the temperature profile within the epidermis. Ambient (T_a) and internal body (T_b) temperatures are assumed to remain unaltered with changes in k (reflecting different states of stratum corneum hydration) in the following discussion. Although the anatomic location of all types of thermal receptors is unclear (Zotterman, 1959), cold receptors have been localized to the region of the dermoepidermal junction. For this analysis however, cold receptors, at a temperature $T_{s'}$, will be considered to lie at the dermoepidermal junction, a justifiable generalization required to simplify the discussion pertinent to data reported here. Similarily, changes in the skin surface temperature (T_s) and $T_{s'}$ with low and high k are extreme for descriptive purposes.

Total body heat exchange should be no greater in a damp environment than in a dry one (Guillemin, 1954), and an exposure to a high relative humidity may actually impose a reduction in the heat loss from the body (Burton, et al., 1955). If this loss remains constant with increasing k, then from the equation describing the

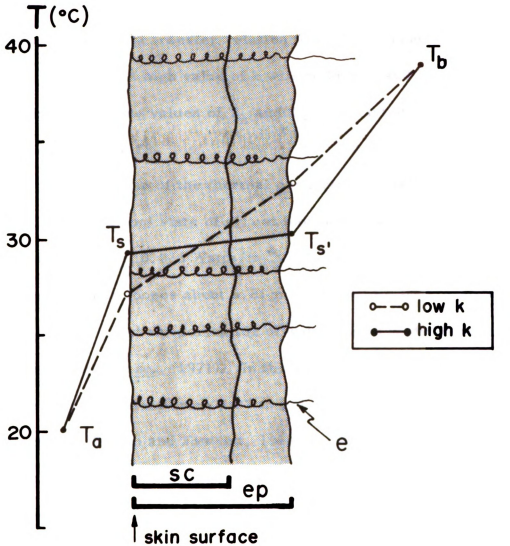


FIGURE 18. A representation of the temperature profile within the epidermis (ep) under conditions of changing stratum corneum (sc) hydration. High and low values of the thermal conductivity coefficient (k) result in the skin surface (T_s) and dermoepidermal junction ($T_{s'}$) temperatures, independently of changes in the ambient (T_a) and internal body (T_b) temperatures. The distal ends of the eccrine sweat ducts (e) are shown spiralling through the epidermis.

steady state conductive heat transfer ($Q = k \Delta T/x$; see section III 3.2), the transepidermal temperature difference (ΔT) must decrease for the heat transfer relation to cold. Therefore, T_s and $T_{s'}$ defined by a high value of k will be higher and lower, respectively, than those values of T_s and $T_{s'}$ associated with a low k, as shown in Figure 18.

The mean value of the thermal conductivity coefficient for the control (prehydration) state of all cat footpads examined for this report was 0.167 ± 0.023 Watts/m ^{o}C (Table 2). The average non-sweating man looses about 5.81 milliWatts per square meter of body surface by the vaporization of water which is diffused through the skin (Hardy, et al., 1971). In the adult human, the thickness of the epidermis varies from 0.07 to 0.12 mm over the general body surface (Bloom and Fawcett, 1968). For purposes of calculation, an average epidermal thickness of 0.10 mm will be assumed. These values of k (Watts/m ^{o}C), Q (Watts/m^2), and x (m) can be substituted into the heat conduction equation (see section III 3.2) in order to examine the consequences of increasing k on the transepidermal temperature difference (ΔT).

Figure 19 reports data which indicate the relationship between increasing k (from 0.167 Watts/m ^{o}C) and the transepidermal temperature difference, ΔT (^{o}C). For a 25% increase in k, there is a 0.7^{o} C fall in ΔT. If skin surface temperature remains unchanged with increasing k, then $T_{s'}$, the receptor temperature,

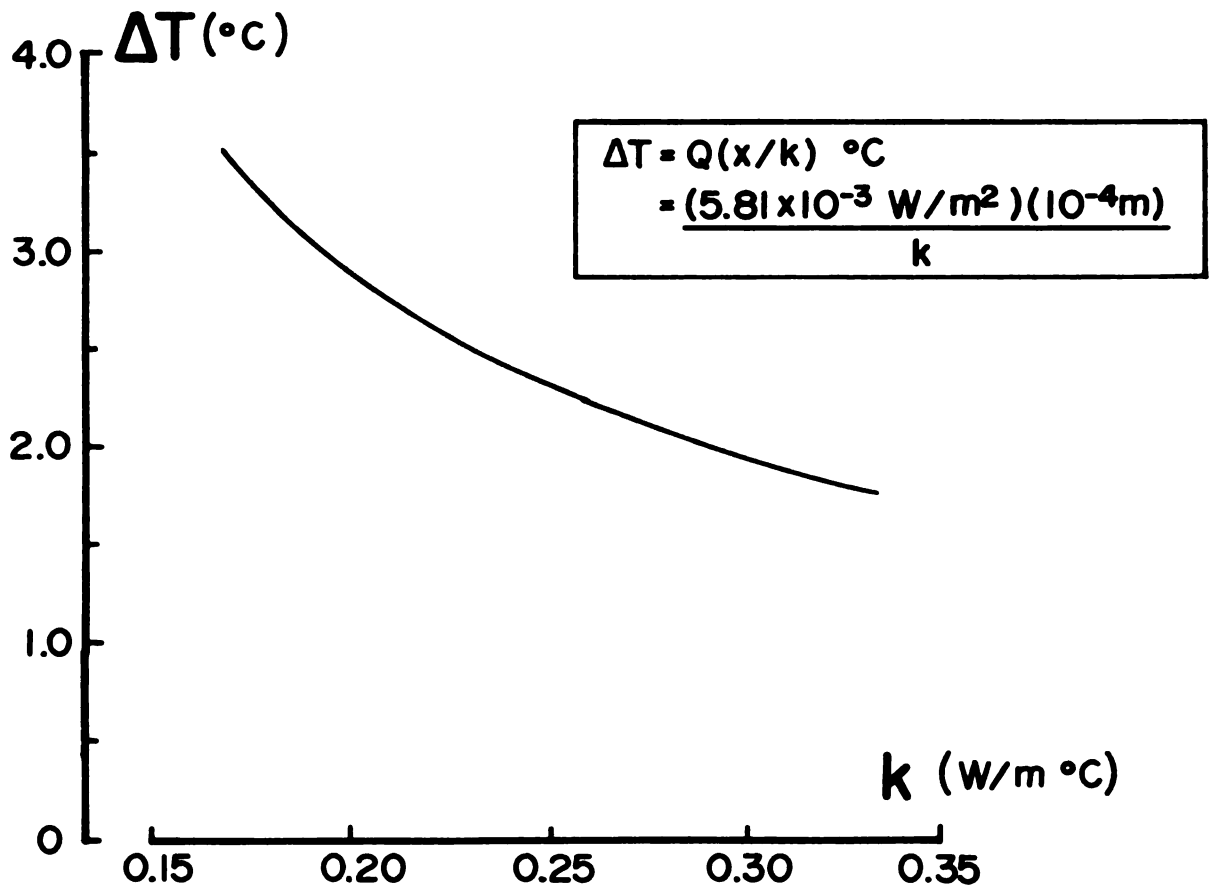


FIGURE 19. The calculated relationship between the transepidermal temperature difference (ΔT) and an increasing epidermal thermal conductivity coefficient (k). The abscissa encompasses a 100% increase in k from the mean, prehydrated value of 0.167 W/m °C reported in this investigation (Table 2). The choice of values for Q and x is explained in section V 5.6.

decreases by 0.7°C. Also, the greatest change in ΔT with increasing k is seen at the lower values of k. In the cat, it has been shown (Hensel, et al., 1960) that a change in skin temperature of 0.2° C is sufficient to excite the most sensitive cold fibers. Under conditions of constant T_s, a 6% increase in the thermal conductivity coefficient (from 0.167 to 0.177 Watts/m °C) decreases $T_{s'}$ by at least this critical amount. It may be concluded therefore, that small (6%) changes in k are sufficient to provide transduced temperature inputs to higher centers within the central nervous system (the cerebral cortex and the hypothalamus, for example) which reflect changes in the temperature, not of the external environment, but of the tissue in juxtaposition to the thermal receptors. That is, if a man were exposed to a cool, constant temperature environment, then increasing ambient relative humidity a certain "critical" (6%) amount should reflect a decrease in the "environmental" temperature which is sufficient to evoke the appropriate thermal defense mechanisms. The literature supports this conclusion (Burton, et al., 1955; Iampietro, et al., 1958; Lemaire and Benceny, 1962; Renbourn, et al., 1959).

Although there was no change in ambient temperature (19° C), Lemaire and Benceny (1962) reported that the average skin temperatures of men placed in increasing r.h.'s (20% to 90%) fell from 31.5° C to 30.6° C, suggesting that the decrease in $T_{s'}$ (Figure 18) associated with increased r.h. was sufficient to elicity thermally induced

peripheral cutaneous vasoconstriction, a well recognized cold defense mechanism (Hammel, 1968).

Burton, et al. (1955) and Iampietro, et al. (1958) found that total body heat loss is independent of ambient relative humidity in men placed in a cool (9 - 16° C) environment. It was reported, however, that heat production (as indicated by the oxygen consumption) is greater in men placed in a humid (80-90% r.h.) environment than it is in men placed in a dry (30% r.h.) environment at the same temperature. This result is seen despite the fact that measured skin temperatures are "remarkably the same" (Burton, et al., 1955) throughout the ambient temperature range of 9 - 16° C. The consequence of an increased epidermal thermal conductivity coefficient may, in part, offer sufficient information to the homeothermic controller to induce a cold defense mechanism, namely, an increase in body heat production (Hammel, 1968).

Average skin temperature (represented as T_s in Figure 18) remains the same (Impietro, et al., 1958; Renbourn, et al., 1959) or decreases (Lemaire and Benceny, 1962) with increasing relative humidity at the same ambient temperature (T_a). Changes in $T_{s'}$ will be more closely related to the changes in epidermal thermal conductivity than is illustrated in Figure 18. In each case, it can be speculated that the thermal receptors at a value $T_{s'}$ will transduce a temperature more closely approximating that of the environment (T_a) as the water content of the epidermis, and k, increases.

Projected to the cerebral cortex, the afferent "temperature" ($T_{s'}$) information offers the potential of giving rise to the subjective impression, as is often reported, that damp cold is less comfortable than dry cold. Projected into the hypothalamus and other central neural sites of biothermal controller function, information arising from peripheral thermal receptors reporting $T_{s'}$ bias thermoregulatory effector responses (increased body heat production (Burton, et al., 1955; Iampietro, et al., 1958)and peripheral vasoconstriction (Lemaire and Benceny, 1962)) as an influence of modified body temperature regulation.

The paradox between a subjective evaluation and a theoretical and experimental analysis of dry or wet cold exposure appears to have a resolution. Although net heat flux is the same for both environments, the perception that a wet-cold exposure is "colder" is based more upon information relayed centrally into the nervous system than it is to transcutaneous heat loss directly. Simply, the shift in cutaneous thermal gradient due to a change in epidermal k reduces the temperature of peripheral thermal receptors. It isn't really any colder in a damp environment (in that no greater loss of stored body heat occurs), it just seems that way.

VI. CONCLUSIONS

1. The thermal conductivity coefficient (k) of the cat footpad epidermis increased with epidermal hydration produced either by sweat gland activation (internal hydration) or by exposure of the footpad to a high ambient relative humidity (external hydration).

2. The internal hydration-induced increase in epidermal thermal conductivity coefficient of animals treated with phenoxybenzamine (POB) (an alpha-adrenergic receptor blocking agent) was significantly greater than that seen in untreated animals.

3. A statistically shorter internal hydration exposure elicited a significantly greater increase in the epidermal thermal conductivity coefficient than did the longer exposure to external hydration in POB treated animals.

4. Rates of epidermal water storage, as reflected by increasing epidermal thermal conductivity, were greater with internal than external hydration, and these rates of storage were in turn greater than the rates of epidermal water loss, as reflected by decreasing k, with subsequent stratum corneum dehydration.

5. The results of this study were interpreted as suggesting that a small "critical" increase in epidermal hydration (reflecting an increase

in k), if associated with a "cool" ambient temperature, is sufficient to provide transduced temperature inputs to higher neural centers (cerebral cortex and hypothalamus, for example) which reflect changes in temperature, not of the external environment, but of the tissue in juxtaposition to the cutaneous thermal receptors. This afferent temperature information is sufficient to elicit cold defense mechanisms as well as producing the perception that a wet-cold exposure is "colder" than a dry one at the same ambient temperature.

BIBLIOGRAPHY

Adams, T. 1966. Characteristics of eccrine sweat gland activity in the foot pad of the cat. J. Appl. Physiol. 21:1004.

Adams, T., and W.S. Hunter. 1969. Modification of skin mechanical properties by eccrine sweat gland activity. J. Appl. Physiol. 26:417.

Adams, T., and J.A. Vaughan. 1965. Human eccrine sweat gland activity and palmar electrical skin resistance. J. Appl. Physiol. 20:980.

Adams, T., M.L. Morgan, W.S. Hunter, and K.R. Holmes. 1970. Temperature regulation of the unanesthetized cat during mild cold and severe heat stress. J. Appl. Physiol. 29:852.

Andrew, W. 1959. Textbook of Comparative Histology. Oxford University Press. New York.

Baden, H.P. 1970. The physical properties of nail. J. Invest. Dermatol. 55:115.

Baden, H.P., and L. Bonar. 1968. The α-fibrous proteins of epidermis. J. Invest. Dermatol. 51:478.

Baumberger, J.P., V. Suntzeff, and E.V. Cowdry. 1941. Methods for the separation of epidermis from dermis and some physiological and chemical properties of isolated epidermis. U.S. Natn. Cancer Inst. J. 2:413.

Bettley, F.R., and K.A. Grice. 1967. The influence of ambient humidity on transepidermal water loss. Brit. J. Dermatol. 78: 575.

Blair, C. 1968. Morphology and thickness of the human stratum corneum. Brit. J. Dermatol. 80:430.

Blank, I.H. 1952. Factors which influence the water content of the stratum corneum. J. Invest. Dermatol. 18:433.

Blank, I.H. 1953. Further observations on factors which influence the water content of the stratum corneum. J. Invest. Dermatol. 21: 259.

Bland, I.H., and J.E. Finesinger. 1946. Electrical resistance of the skin. Effect of size of electrodes, exercise and cutaneous hydration. Arch. Neurol. Psychiat. 56:544.

Bligh, J. 1967. A thesis concerning the processes of secretion and discharge of sweat. Environ. Res. 1:28.

Bloom, W., and D.W. Fawcett. 1968. A Textbook of Histology. W.B. Saunders Co. Philadelphia.

Brusilow, S.W., and B. Munger. 1962. Comparative physiology of sweat. Proc. Soc. Exptl. Biol. Med. 110:317.

Buettner, K. 1951. Effects of extreme heat and cold on human skin. I. Analysis of temperature changes caused by different kinds of heat application. J. Appl. Physiol. 3:691.

Bull, H.B. 1944. Absorption of water vapor by proteins. J. Am. Chem. Soc. 66:1499.

Burton, A.C., and O.G. Edholm. 1955. Man in a Cold Environment. E. Arnold. London.

Burton, A.C., R.A. Snyder, and W.G. Leach. 1955. Damp cold vs dry cold. Specific effects of humidity on heat exchange of unclothed man. J. Appl. Physiol. 8:269.

Chalmers, T.M., and C.A. Keele. 1951. Physiological significance of the sweat response to adrenaline in man. J. Physiol. 114:510.

Chalmers, T.M., and C.A. Keele. 1952. The nervous and chemical control of sweating. Brit. J. Dermatol. 64:43.

Charles, A. 1960. An electron microscopic study of the eccrine sweat gland. J. Invest. Dermatol. 34:81.

Christophers, E. 1971. Cellular architecture of the stratum corneum. J. Invest. Dermatol. 56:165.

Comaish, S., and E. Bottoms. 1971. The skin and friction: Deviations from Amonton's laws, and the effects of hydration and lubrication. Brit. J. Dermatol. 84:37.

Conroy, J.D. 1964. Feline Medicine and Surgery. E.J. Catcott, ed. Am. Vet. Pub., Inc. Wheaton, Ill.

Copenhaver, W.M. 1971. Bailey's Textbook of Histology. Williams & Wilkins, Co. Baltimore.

Craig, F.N. 1956. Uptake or output of water by the skin as influenced by external vapor pressure in liquid or vapor contact and by atropine. J. Appl. Physiol. 8:473.

Creed, R.F.S. 1958. The histology of mammalian skin, with special reference to the dog and cat. Vet. Rec. 70:171.

Crounse, R.G. 1965. Keratin and the barrier. Arch. Environ. Health. 11:522.

Dale, H.H., and W. Feldberg. 1934. The chemical transmission of secretory impulses to the sweat glands of the cat. J. Physiol. 82:121.

Dellmann, H.D. 1971. Veterinary Histology: An Outline Text-Atlas. Lea and Febiger. Philadelphia.

Dobson, R.L., and K. Sato. 1972. The secretion of salt and water by the eccrine sweat gland. Arch. Dermatol. 105:366.

Edelberg, R. 1961. Microelectrode study of the galvanic skin response. Fed. Proc. 20:326.

Edelberg, R. 1968. Biopotentials from the skin surface: The hydration effect. Ann. N.Y. Acad. Sci. 148:252.

Ellis, R.A., and W. Montagna. 1961. Electron microscopy of the duct, and especially the cuticular border of the eccrine sweat glands in Macaca mulatta. J. Biophys. Biochem. Cytol. 9:238.

Ellis, R.A., W. Montagna, and H. Fanger. 1958. Histology and cytochemistry of human skin. XIV. The blood supply of the cutaneous glands. J. Invest. Dermatol. 30:137.

Felsher, Z. 1947. Studies on the adherence of the epidermis to the corneum. J. Invest. Dermatol. 8:35.

Foster, K.G., and J.S. Weiner. 1970. Effects of cholinergic and adrenergic blocking agents on the activity of eccrine sweat glands. J. Physiol. 210:883.

Foster, K.G., J. Ginsburg, and J.S. Weiner. 1970. Role of circulating catecholamines in human eccrine sweat gland control. Clin. Sci. 39:823.

Fujisawa, N. 1959. Cytological and cytochemical reaction of the cat sweat gland to adrenalin injection. Odajimas folia Anat. Japonica. 33:255.

Giroud, A., and C.P. Leblond. 1951. The keratinization of epidermis and its derivatives, especially the hair, as shown by X-ray diffraction and histochemical studies. Ann. N.Y. Acad. Sci. 53: 613.

Grice, K., H. Sattar, and H. Baker. 1972. The effect of ambient humidity on transepidermal water loss. Dermatol. 58:343.

Guillemin, V. 1954. Relative chilling effects of moist cold and dry cold climates. J. Aviation Med. 25:651.

Guyer, M.F. 1949. Animal Micrology. Univ. Chicago Press. Chicago.

Haimovici, H. 1948. Evidence for an adrenergic component in the nervous mechanism of sweating in man. Proc. Soc. Exptl. Biol. Med. 68:40.

Haimovici, H. 1950. Evidence for adrenergic sweating in man. J. Appl. Physiol. 2:512.

Ham, A.W. 1969. Histology. J.B. Lippincott Co. Philadelphia.

Hammel, H.T. 1968. Regulation of internal body temperature. Ann. Rev. Physiol. 30:641.

Hardy, J.D., J.A.J. Stolwijk, and A.P. Gagge. 1971. Man. Chapter 5 in Comparative Physiology of Thermoregulation. Vol. II. Mammals. G.C. Whittow, ed. Academic Press. New York.

Hashimoto, K. 1969. Cellular envelopes of keratinized cells of the human epidermis. Arch. Klin. Exptl. Dermatol. 235:374.

Hashimoto, K. 1971a. Demonstration of the intercellular spaces of the human eccrine sweat gland by lanthanum. I. The secretory coil. J. Ultrastruct. Res. 36:249.

Hashimoto, K. 1971b. Demonstration of the intercellular spaces of the human eccrine sweat gland by lanthanum. II. The duct. J. Ultrastruct. Res. 37:504.

Hatfield, H.S. 1950. A heat-flow meter. J. Physiol. 111:10P.

Hatfield, H.S., and L.G.C. Pugh. 1951. Thermal conductivity of human fat and muscle. Nature. 168:918.

Hellman, K. 1952. The cholinesterase of cholinergic sweat glands. Nature. 169:113.

Henriques, F.C., and A.R. Moritz. 1947. The conduction of heat to and through skin and the temperatures attained therein. A theoretical and an experimental investigation. Am. J. Pathol. 23:531.

Hensel, H., A. Iggo, and I. Witt. 1960. A quantitative study of sensitive cutaneous thermoreceptors with C afferent fibers. J. Physiol. 153:113.

Henshaw, R.E., L.S. Underwood, and T.M. Casey. 1972. Peripheral thermoregulation: Foot temperature in two arctic canines. Sci. 175:988.

Hibbs, R.G. 1958. The fine structure of human eccrine sweat glands. Am. J. Anat. 103:201.

Holyoke, J.B., and W.C. Lobitz, Jr. 1952. Histologic variations in the structure of human eccrine sweat glands. J. Invest. Dermatol. 18:147.

Huheey, M.J., and T. Adams. 1967. Local effect of temperature on skin evaporative water loss. J. Appl. Physiol. 22:939.

Hurley, H.J., W.B. Shelley, and G.B. Koelle. 1953. The distribution of cholinesterases in human skin, with special reference to eccrine and apocrine sweat glands. J. Invest. Dermatol. 21:139.

Iampietro, P.F., D.E. Bass, and E.R. Buskirk. 1958. Heat exchanges of nude men in the cold: Effect of humidity, temperature, and windspeed. J. Appl. Physiol. 12:351.

Jänig, W. 1971. The afferent innervation of the central pad of the cat's hind foot. Brain Res. 28:203.

Jarrett, A., R.I.C. Spearman, P.A. Riley, and A.K. Cane. 1965. The distribution of epidermal phospholipids and their relation to alkaline phosphatase activity of the granular layer. J. Invest. Dermatol. 44:311.

Jelenko, III., C., and J.M. Ginsburg. 1971. Water-holding lipid and water transmission through homeothermic and poikilothermic skins. Proc. Soc. Exptl. Biol. Med. 136:1059.

Kamamura, S. 1957. A cytological study of cat sweat glands. Okajimas folia Anat. Japonica. 30:81.

Kreith, F. 1965. Principles of Heat Transfer. Internatl. Textbook Co. Scranton, Pennsylvania.

Langley, J.N. 1891. On the course and connections of the secretory fibres supplying the sweat glands of the feet of the cat. J. Physiol. 12:347.

Langley, J.N. 1923. The vascular dilation caused by the sympathetic and the course of vasomotor nerves. J. Physiol. 58:70.

Langley, J.N., and K. Uyeno. 1922. The secretion of sweat. Part II. The effect of vasoconstriction and of adrenaline. J. Physiol. 56: 206.

Lemaire, R., and C. Benceny. 1962. Influence de l'humidité de l'ambiance sur la température cutanée moyenne. In Bio-meteorology, S.W. Tromp, ed. Macmillan. New York.

Liisberg, M.F. 1969. A new histophysiological concept of the striated tubules based on a very simple and new method for staining of mitochondria. Acta Anat. 73:496.

Lipkin, M., and J.D. Hardy. 1954. Measurement of some thermal properties of human tissues. J. Appl. Physiol. 7:212.

Lloyd, D.P.C. 1959a. Secretion and reabsorption in sweat glands. Proc. Natl. Acad. Sci. 45:405.

Lloyd, D.P.C. 1959b. Average behavior of sweat glands as indicated by impedance changes. Proc. Natl. Acad. Sci. 45:410.

Lloyd, D.P.C. 1960. Electrical impedance changes of the cat's foot pad in relation to sweat secretion and reabsorption. J. Gen. Physiol. 43:713.

Lloyd, D.P.C. 1963. Action of phenoxybenzamine on neural and humoral activation of sweat glands. J. Physiol. 169:116P.

Lloyd, D.P.C. 1968. Effect of phenoxybenzamine on neural and humoral control of sweat glands. Proc. Natl. Acad. Sci. 59:816.

Lobitz, W.C., and R.L. Dobson. 1961. Dermatology: The eccrine sweat glands. Ann. Rev. Med. 12:289.

Lobitz, W.C., J.B. Holyoke, and W. Montagna. 1954. Epidermal eccrine sweat duct unit: Morphologic and biologic entity. J. Invest. Dermatol. 22:157.

Loomans, M.E., and D.P. Hannon. 1970. An electron microscopic study of the effect of subtilism and detergents on human stratum corneum. J. Invest. Dermatol. 55:101.

Mali, J.W.H. 1956. The transport of water through the human epidermis. J. Invest. Dermatol. 27:451.

Malinovský, L. 1966. Variability of sensory nerve endings in foot pads of a domestic cat (Felis ocreata l., F. domestica). Acta Anat. 64:82.

Matoltsy, A.G., and C.A. Balsamo. 1955. A study of the components of the cornified epithelium of human skin. J. Biophys. Biochem. Cytol. 1:339.

Matoltsy, A.G., and M.N. Matoltsy. 1966. The membrane protein of horny cells. J. Invest. Dermatol. 46:127.

Menton, D.N., and A.Z. Eisen. 1971. Structure and organization of mammalian stratum corneum. J. Ultrastruct. Res. 35:247.

Mercer, E.H., R.A. Jahn, and H.I. Maibach. 1968. Surface coats containing polysaccharides on human epidermal cells. J. Invest. Dermatol. 51:204.

Middleton, J.D. 1968. The mechanism of water binding in stratum corneum. Brit. J. Dermatol. 80:437.

Mole, R.H. 1948. The relative humidity of the skin. J. Physiol. 107:399.

Montagna, W. 1962. The Structure and Function of Skin. Academic Press. New York.

Montagna, W., H.B. Chase, and W.C. Lobitz, Jr. 1953. Histology and cytochemistry of human skin. II. The eccrine sweat glands. J. Invest. Dermatol. 20:415.

Munger, B.L. 1961. The ultrastructure and histophysiology of human eccrine sweat glands. J. Biophys. Biochem. Cytol. 11:385.

Munger, B.L., and S.W. Brusilow. 1961. An electron microscopic study of eccrine sweat glands of the cat foot and toe pads - Evidence for ductal reabsorption in the human. J. Biophys. Biochem. Cytol. 11:403.

Naylor, P.F.D. 1955. The skin surface and friction. Brit. J. Dermatol. 67:239.

Nicoll, P.A., and T.A. Cortese, Jr. 1972. The physiology of skin. Ann. Rev. Physiol. 34:177.

O'Brien, J.P. 1952. Some observations of the sweat ducts as observed in disease. I. The cuticle. J. Invest. Dermatol. 18:473.

Park, A.C., and C.B. Baddiel. 1972a. Rheology of stratum corneum. I. A molecular interpretation of the stress-strain curve. J. Soc. Cos. Chem. 23:3.

Park, A.C., and C.B. Baddiel. 1972b. Rheology of stratum corneum. II. A physico-chemical investigation of factors influencing the water content of the corneum. J. Soc. Cos. Chem. 23:13.

Patton, H.D. 1948. Secretory innervation of the cat's footpad. J. Neurophysiol. 11:217.

Pauling, L. 1945. The absorption of water by proteins. J. Am. Chem. Soc. 67:555.

Peiss, C.N., W.C. Randall, and A.B. Hertzman. 1953. Relations of hydration of the skin to repenetration of water, sweating and evaporation. Fed. Proc. 12:108.

Perry, D.J., and G.E. Mount. 1954. A comparison of the effect of atropine and placebo on the galvanic skin resistance. J. Invest. Dermatol. 22:497.

Pinkus, H. 1939. Notes on the anatomy and pathology of the skin appendages. I. The wall of the intraepidermal part of the sweat duct. J. Invest. Dermatol. 2:175.

Randall, W.C., and K.K. Kimura. 1955. The pharmacology of sweating. Pharmacol. Rev. 7:365.

Randall, W.C., R. Deering, and I. Daugherty. 1948. Reflex sweating and the inhibition of sweating by prolonged arterial occlusion. J. Appl. Physiol. 1:53.

Reader, S.R. 1952. The effective thermal conductivity of normal and rheumatic tissues in response to cooling. Clin. Sci. 11:1.

Renbourn, E.T. 1959a. A contribution to the physiology of damp cold, an aspect of temperate climate. Part I. The chills of a damp cold climate. An historical survey. Int. J. Bioclim. Biometeorol. 3:IV-A-4, 1.

Renbourn, E.T., A.M. Reid, and D.R. Gilling. 1959b. A contribution to the physiology of damp cold, an aspect of temperate climate. Part II. An investigation on clothed men under indoor conditions. Int. J. Bioclim. Biometeorol. 3:IV-A-4, 9.

Rothman, S. 1954. Physiology and Biochemistry of the Skin. Univ. of Chicago Press. Chicago.

Rudall, K.M. 1947. X-ray studies of the distribution of protein chain types in the vertebrate epidermis. Biochem. Biophys. Acta. 1: 549.

Rushmer, R.E., K.J.K. Buettner, J.M. Short, and G.F. Odland. 1966. The skin. Sci. 154:343.

Sato, K., and R.L. Dobson. 1970. Enzymatic basis for the active transport of sodium in the duct and secretory portion of the eccrine sweat gland. J. Invest. Dermatol. 55:53.

Sato, K., R.L. Dobson, and J.W.H. Mali. 1971. Enzymatic basis for the active transport of sodium in the eccrine sweat gland. Localization and characterization of Na-K-adenosine triphosphatase. J. Invest. Dermatol. 57:10.

Scheuplein, R.J., and L.J. Morgan. 1967. 'Bound water' in keratin membranes measured by a microbalance technique. Nature 214: 456.

Selby, C. C. 1957. An electron microscopic study of thin sections of human skin. II. Superficial cell layers of foot-pad epidermis. J. Invest. Dermatol. 29:131.

Sonnenschein, R. R., H. Kobrin, H. D. Janowitz, and M. I. Grossman. 1951. Stimulation and inhibition of human sweat glands by intradermal sympathomimetic agents. J. Appl. Physiol. 3:573.

Spearman, R. I. C. 1970. Some light microscopical observations on the stratum corneum of the guinea-pig, man and common seal. Brit. J. Dermatol. 83:582.

Sperling, F., and T. Koppanyi. 1949. Histophysiologic studies on sweating. Am. J. Anat. 84:335.

Sponsler, O. L., J. D. Bath, and J. W. Ellis. 1944. Water bound to gelatin as shown by molecular structure analysis. J. Phys. Chem. 44:996.

Spruit, D., and K. E. Malten. 1969. Humidity of the air and water vapour loss of the skin. The changing permeability. Dermatologica. 138:418.

Stombaugh, D. P., and T. Adams. 1971. Skin electrical phenomena, sweat gland activity, and epidermal hydration of the cat footpad. Am. J. Physiol. 221:1014.

Strickland, J. H. 1958. The Microscopic Anatomy of the Skin and External Ear of Felis Domesticus. M. S. Thesis, Dept. of Anatomy, Michigan State University, E. Lansing.

Strickland, J. H., and M. L. Calhoun. 1963. The integumentary system of the cat. Am. J. Vet. Res. 24:1018.

Takagi, S. 1952. A study on the structure of the sudoriferous duct transversing the epidermis in man with fresh material by phase contrast microscopy. Jap. J. Physiol. 3:65.

Takagi, S., and M. Tagawa. 1955. Predominance of right-handed spirals in human eccrine sweat ducts. Jap. J. Physiol. 5:122.

Thomas, P. E., and A. Kawahata. 1962. Neural factors underlying variations in electrical resistance of apparently nonsweating skin. J. Appl. Physiol. 17:999.

Thomas, P.E., and I.M. Korr. 1957. Relationship between sweat gland activity and electrical resistance of the skin. J. Appl. Physiol. 10:505.

Trautmann, A., and J. Fiebiger. 1957. Fundamentals of the Histology of Domestic Animals. Comstock Publ. Assoc. Ithica, New York.

Tregear, R.T. 1965. Interpretation of skin impedance measurements. Nature. 205:600.

Tregear, R.T. 1966. Physical Functions of Skin. Academic Press. New York.

Washburn, E.W. 1929. International Critical Tables. McGraw-Hill. New York.

Weiner, J.S., and J. Hellman. 1960. The sweat glands. Biol. Rev. 35:141.

Weast, R.C., ed. in chief. 1967. Handbook of Chemistry and Physics. Chemical Rubber Co. Cleveland, Ohio.

Wildnaurer, R.H., J.W. Gothwell, and A.B. Douglass. 1971. Stratum corneum biomechanical properties: I. Influence of relative humidity on normal and extracted human stratum corneum. J. Invest. Dermatol. 56:72.

Winslow. C.E.A., L.P. Herrington, and A.P. Gagge. 1937. Physiological reactions of the human body to various atmospheric humidities. Am. J. Physiol. 120:288.

Wislocki, G.B., D.W. Fawcett, and E.W. Dempsey. 1951. Staining of stratified squamous epithelium of mucous membranes and skin of man and monkey by the periodic acid-Schiff method. Anat. Rec. 110:359.

Wolf, J. 1968a. The screwlike ascent of the sweat ducts as an indicator of the analogous screwlike ascent of germinative material in the epidermis. Folia Morphol. 16:131.

Wolf, J. 1968b. Uniformity of dextrogyrate screw-like ascent of sweat ducts in the epidermis. Folia Morphol. 16:139.

Wolf, J. 1970. Configuration of orifices of the sweat ducts on the surface of the horny layer of the skin in man. Folia Morphol. 18:14.

Wolff, K., and E. Schreiner. 1968. An electron microscopic study on the extraneous coat of keratinocytes and the intercellular space of the epidermis. J. Invest. Dermatol. 51:418.

Zelickson, A.S. 1961. Electron microscopic study of epidermal sweat duct. Arch. Dermatol. 83:106.

Zotterman, Y. 1959. Thermal sensations. Chapter 17 in Handbook of Physiology. Vol. 1. Am. Physiol. Soc. Williams & Wilkins Co. Baltimore.

APPENDICES

APPENDIX A

Data from Cat #5-6-L

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)	CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
dry	0.0	86.3	306	0.127	(2)	13.5	86.0	385	0.160
↓	0.5	95.7	309	0.115	↓	14.0	79.0	384	0.174
↓	1.0	84.3	318	0.135	↓	14.5	79.7	387	0.174
↓	1.5	98.0	321	0.117	↓	15.0	72.0	395	0.197
↓	2.0	92.0	318	0.123	↓	15.5	70.3	396	0.202
↓	2.5	100.0	323	0.115	(3)	16.0	75.0	423	0.201
stimulation					↓	16.5	75.0	433	0.206
(1)	3.0	107.3	343	0.151	↓	17.5	72.0	443	0.220
↓	3.5	109.7	358	0.116	↓	18.0	72.0	438	0.217
↓	4.0	106.7	356	0.119	humidity hydration				
↓	4.5	105.0	362	0.123	↓	23.0	88.0	479	0.194
↓	5.0	96.3	358	0.132	↓	23.5	84.3	435	0.184
↓	5.5	101,0	370	0.131	↓	24.0	68.3	414	0.216
↓	6.0	103.3	371	0.128	↓	24.5	62.0	409	0.236
↓	6.5	105.0	372	0.127	↓	25.0	58.3	401	0.247
↓	7.0	106.7	367	0.122	↓	25.5	53.3	388	0.261
↓	7.5	102.3	372	0.130	↓	30.5	76.7	447	0.209
↓	8.0	103.3	361	0.124	↓	31.0	60.3	420	0.249
↓	8.5	100.7	367	0.130	↓	31.5	52.0	404	0.278
↓	9.0	88.3	368	0.148	↓	32.0	53.3	397	0.267
↓	9.5	97.7	366	0.134	↓	32.5	53.7	394	0.263
↓	10.0	87.0	371	0.152	↓	33.0	53.7	398	0.267
↓	10.5	96.0	358	0.133	↓	33.5	51.3	422	0.296
(2)	11.0	92.0	375	0.145	↓	34.0	62.0	398	0.231
↓	11.5	84.0	385	0.164	↓	39.0	71.7	465	0.230
↓	12.0	88.3	378	0.152	↓	39.5	64.3	421	0.234
↓	12.5	72.3	385	0.191	↓	40.0	54.7	423	0.281
↓	13.0	78.0	378	0.173	↓	40.5	63.7	401	0.225

Calculation of k: $k(\text{Watts/m } ^{o}\text{C}) = (\text{c.f.})(Q)(x/\Delta T)$,

where:

c.f. = conversion factor, 53.9 (Watts/m^2 ^{o}C)

$x = 6.6 \times 10^{-4}$ meters for Cat #5-6-L

Q and ΔT have units of microvolts, each being the average of three steady state measurements for each observation.

APPENDIX B

Data from Cat #6-7-L

CONDITION	TIME	ΔT(uv)	Q (uv)	k (W/m °C)
dry	0.0	83.3	478	0.235
	1.0	79.7	474	0.244
	1.5	74.3	467	0.257
	2.0	67.0	421	0.257
	2.5	78.0	466	0.244
	3.0	76.3	472	0.254
	3.5	88.0	484	0.225
	4.0	75.3	474	0.258
	4.5	70.0	491	0.288
	5.0	78.0	486	0.255
	5.5	74.7	497	0.273
	6.0	88.7	492	0.227
	6.5	71.7	492	0.281
	7.0	83.0	491	0.242
	7.5	80.0	499	0.256
↓	8.5	84.3	491	0.238
passive hydration				
	9.0	88.7	502	0.232
	9.5	89.0	487	0.224
	10.0	78.7	482	0.251
	10.5	81.0	482	0.244
	11.0	87.7	491	0.229
	12.0	82.7	492	0.244
	13.0	75.3	497	0.270
	13.5	83.3	487	0.239
	14.0	83.0	492	0.243
	15.0	83.7	498	0.244
	16.5	85.3	500	0.240
	17.0	71.0	486	0.280
	17.5	74.5	490	0.270
↓	18.0	80.0	493	0.252

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
passive hydration				
	19.0	74.3	499	0.275
↓	20.0	76.3	488	0.262
(1)	20.5	80.7	505	0.259
	21.0	79.3	509	0.263
	21.5	68.0	513	0.309
	22.0	67.0	503	0.307
	22.5	69.0	541	0.321
	23.0	59.0	532	0.370
	24.0	56.0	535	0.391
	24.5	62.7	530	0.346
	25.0	49.3	553	0.459
	25.5	59.7	542	0.372
	26.0	47.0	529	0.461
	26.5	70.0	543	0.318
	27.0	63.0	549	0.357
	28.0	57.3	564	0.403
	28.5	64.3	547	0.348
	29.0	61.3	540	0.361
	29.5	76.0	550	0.296
	30.0	61.7	558	0.370
	30.5	64.7	541	0.343
	31.0	71.0	553	0.319
↓	31.5	67.0	548	0.335
(2)	32.0	63.3	558	0.361
	32.5	75.0	566	0.309
	33.0	70.7	560	0.325
	33.5	77.0	579	0.308
	34.0	75.0	566	0.309
	34.5	65.7	562	0.351
↓	35.0	65.3	557	0.349

APPENDIX B (continued)

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
(2)	36.0	67.5	579	0.351
↓	36.5	60.7	571	0.385
	37.0	65.3	566	0.355
	38.0	72.0	593	0.338
	38.5	69.3	595	0.351
	39.0	66.7	593	0.364
	39.5	68.0	587	0.354
	40.5	63.0	566	0.368
	41.5	80.3	621	0.317
↓	42.0	62.0	587	0.388
(3)	42.5	61.7	585	0.388
↓	43.0	54.3	583	0.440
	43.5	63.3	584	0.378
	44.0	71.3	593	0.341
	45.0	77.0	581	0.309
	46.0	69.3	571	0.338
	47.0	64.3	569	0.362
	47.5	69.3	584	0.345
↓	48.0	59.7	574	0.394

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
5 minute period of humidity hydration				
humidity hydration				
↓	53.0	75.0	650	0.355
	53.5	69.0	603	0.358
	54.0	60.7	551	0.372
	54.5	59.7	547	0.375
	55.5	61.7	533	0.354
	60.5	65.7	576	0.359
	61.0	66.7	550	0.338
	61.5	60.0	531	0.362
	62.0	58.7	530	0.370
	62.5	52.3	527	0.413
	64.0	51.7	562	0.445
	69.0	69.7	563	0.331
	69.5	60.3	532	0.364
	70.5	44.0	522	0.486
	71.0	45.3	505	0.457
	71.5	36.0	509	0.579
	72.0	38.3	500	0.535
	72.5	35.7	507	0.582
↓	73.0	43.0	509	0.485

Calculation of k: $k(\text{Watts/m }^{\circ}\text{C}) = (\text{c.f.})(Q)(x/\Delta T)$,

where: c.f. = conversion factor, 53.9 (Watts/m^2 °C)

$x = 7.6 \times 10^{-4}$ meters for Cat #6-7-L

Q and ΔT have units of microvolts, each being the average of three steady state measurements for each observation.

APPENDIX C Data from Cat #5-21-L

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
dry	0.0	125.7	420	0.060
	0.5	107.3	419	0.069
	1.5	98.3	412	0.069
	2.0	95.7	398	0.073
	3.0	92.7	404	0.078
	3.5	90.0	402	0.080
	4.5	88.0	413	0.083
	5.0	94.7	403	0.075
	5.5	96.0	417	0.077
	6.5	95.0	417	0.077
	7.0	90.7	419	0.082
↓	7.5	93.7	415	0.079
passive hydration				
	8.5	90.3	417	0.082
	9.0	81.3	417	0.091
	9.5	85.7	398	0.083
	10.0	85.0	408	0.085
	10.5	84.7	413	0.087
	11.0	83.7	407	0.087
	11.5	80.3	415	0.092
	12.0	76.0	406	0.095
	12.5	78.7	403	0.091
	13.0	82.7	397	0.085
	13.5	82.3	415	0.090
↓	14.0	85.0	399	0.083
humidity hydration				
	14.5	77.3	442	0.101
	15.0	80.7	435	0.096
	15.5	83.3	432	0.092
	16.0	77.3	420	0.097
	16.5	78.3	427	0.097
	17.0	80.3	431	0.095
↓	17.5	77.0	424	0.098

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
humidity hydration				
	18.0	76.0	414	0.097
	18.5	80.0	422	0.094
	19.0	78.7	420	0.095
	19.5	82.3	440	0.095
	20.0	85.7	429	0.089
	25.0	84.3	468	0.099
	25.5	89.3	432	0.086
	26.0	76.7	402	0.093
	26.5	72.0	401	0.099
	27.0	70.0	415	0.104
	27.5	77.5	413	0.095
	28.0	79.7	404	0.090
	28.5	77.0	422	0.097
	33.5	89.5	438	0.086
	34.0	74.3	423	0.101
	34.5	69.3	412	0.104
	35.0	78.3	419	0.095
	35.5	74.3	440	0.105
	36.0	79.0	430	0.097
	36.5	77.0	417	0.096
	37.0	84.7	424	0.108
	42.0	90.7	472	0.092
	42.5	83.0	449	0.096
	43.5	78.0	427	0.097
	44.5	76.0	440	0.103
	45.0	81.3	452	0.098
	45.5	79.7	461	0.102
	51.0	91.7	514	0.100
	51.5	79.3	490	0.110
	52.0	79.3	488	0.109
	52.5	76.3	472	0.109
↓	53.0	79.3	476	0.107

APPENDIX C (continued)

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)	CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
humidity hydration					(1)	77.0	83.7	476	0.101
↓	53.5	75.0	469	0.111	↓	77.5	82.3	477	0.104
	54.0	81.0	486	0.106	↓	78.0	79.7	474	0.105
	59.0	97.0	531	0.097	(2)	78.5	87.3	506	0.103
	59.5	89.7	503	0.099	↓	79.0	89.0	502	0.101
	60.0	86.0	497	0.104	↓	79.5	87.7	480	0.097
	60.5	76.7	481	0.111	↓	80.0	80.0	491	0.109
	61.0	77.0	484	0.111	↓	80.5	72.0	503	0.124
	61.5	74.3	468	0.112	↓	81.0	72.7	504	0.123
	62.0	82.3	481	0.104	↓	81.5	73.7	496	0.120
	67.0	103.3	540	0.093	↓	82.0	77.3	497	0.114
	67.5	92.0	489	0.095	↓	82.5	68.7	500	0.128
	68.0	88.3	494	0.099	↓	83.0	79.0	496	0.112
	68.5	78.0	477	0.109	↓	83.5	74.7	449	0.107
	69.0	82.3	473	0.102	↓	84.5	84.3	508	0.107
	69.5	83.7	467	0.099	↓	85.0	83.0	519	0.111
↓	70.0	80.7	466	0.103	↓	85.5	75.7	504	0.118
(1)	70.5	99.7	531	0.095	↓	86.0	85.7	514	0.107
↓	71.0	89.0	517	0.103	↓	86.5	85.7	520	0.108
	71.5	91.7	508	0.099	(3)	87.0	88.3	529	0.106
	72.0	88.0	489	0.102	↓	87.5	86.0	511	0.106
	72.5	86.0	504	0.104	↓	88.0	73.7	508	0.122
	73.0	81.0	492	0.107	↓	88.5	80.7	512	0.113
	73.5	85.3	497	0.104	↓	89.0	79.0	512	0.115
	74.0	81.0	487	0.106	↓	89.5	85.7	522	0.108
	74.5	82.0	497	0.107	↓	90.0	84.3	518	0.109
	75.0	84.3	513	0.107	↓	90.5	88.3	521	0.105
	75.5	81.7	484	0.105	↓	91.0	88.3	525	0.106
	76.0	80.7	482	0.107	↓	91.5	89.7	540	0.107
↓	76.5	79.3	486	0.108	↓	92.0	89.0	526	0.105

Calculation of k: $k(\text{Watts/m } ^\circ\text{C}) = (\text{c.f.})(Q)(x/\Delta T)$,

where: c.f. = conversion factor, $53.9(\text{Watts/m}^2\ ^\circ\text{C})$; $x = 3.3 \times 10^{-4}$ meters for Cat #5-21-L;
Q and ΔT have units of microvolts, each being the average of three steady state measurements for each observation.

APPENDIX D

Data from Cat #5-21-R

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
dry	0.0	110.0	506	0.131
↓	0.5	97.6	500	0.146
	1.0	98.3	493	0.143
	1.5	98.0	492	0.143
	2.0	93.0	483	0.148
	2.5	100.0	484	0.138
	3.0	93.0	473	0.147
	3.5	94.7	459	0.139
	4.0	100.3	478	0.134
	4.5	96.0	487	0.145
	5.0	85.7	469	0.158
↓	5.5	95.3	461	0.138
humidity hydration				
↓	6.0	89.7	498	0.159
	6.5	84.3	477	0.162
	7.0	85.0	485	0.162
	7.5	89.0	478	0.155
	8.0	74.3	476	0.183
	8.5	73.7	473	0.184
	9.0	87.0	498	0.164
	9.5	83.7	493	0.170
	10.0	87.0	490	0.160
	10.5	84.0	494	0.167
	11.0	86.7	495	0.164
	11.5	87.0	484	0.161
	12.0	97.0	548	0.160
	12.5	87.3	531	0.174
	13.0	92.0	525	0.165
	13.5	76.0	504	0.168
	14.0	90.0	508	0.160
↓	14.5	82.0	506	0.177

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
humidity hydration				
↓	15.0	86.0	499	0.166
	15.5	91.7	501	0.156
	16.0	71.3	489	0.193
	16.5	85.0	492	0.164
	17.0	78.3	491	0.179
	17.5	82.7	491	0.170
	22.5	85.3	529	0.177
	23.0	84.3	495	0.168
	23.5	83.0	482	0.166
	24.0	66.7	490	0.212
	24.5	75.0	479	0.182
	25.0	71.0	478	0.192
	25.5	73.3	481	0.189
	26.0	81.7	469	0.171
	26.5	75.7	485	0.183
	27.5	68.0	463	0.195
	28.0	82.3	477	0.165
	28.5	79.0	484	0.175
	33.5	91.3	537	0.167
	34.0	73.0	496	0.193
	34.5	84.0	489	0.166
	35.0	70.0	478	0.195
	35.5	69.0	480	0.184
	36.0	73.3	484	0.190
	36.5	80.7	496	0.177
	37.0	83.3	482	0.166
	37.5	70.3	483	0.196
	38.0	72.3	491	0.195
	38.5	80.7	487	0.173
↓	39.0	80.7	484	0.172

APPENDIX D (continued)

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)	CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
stimulation					(2)	47.5	97.7	583	0.169
(1)	39.5	100.0	581	0.165	↓	48.0	97.0	587	0.171
↓	40.0	96.3	565	0.167		48.5	97.0	582	0.171
	40.5	96.7	567	0.167		49.0	98.0	572	0.166
	41.0	96.7	566	0.166		49.5	95.7	581	0.172
	41.5	95.7	566	0.169		50.0	97.7	589	0.172
	42.0	104.7	566	0.155		50.5	104.7	579	0.159
	42.5	87.3	545	0.177		51.0	96.3	580	0.172
	43.0	98.0	557	0.162		51.5	89.7	577	0.183
	43.5	93.0	560	0.172		52.0	109.3	578	0.151
	44.0	102.3	569	0.159		52.5	94.3	584	0.177
	45.0	96.0	573	0.170	↓	53.0	103.7	579	0.160
	45.5	91.7	565	0.175	(3)	53.5	101.0	584	0.165
	46.0	101.0	571	0.161	↓	54.0	96.3	588	0.174
	46.5	94.5	564	0.170		54.5	93.7	585	0.178
↓	47.0	97.0	564	0.167		55.5	87.3	588	0.194
					↓	56.0	84.3	584	0.197

Calculation of k: $k(\text{Watts/m }^{\circ}\text{C}) = (\text{c.f.})(Q)(x/\Delta T)$,

where:

c.f. = conversion factor, 53.9(Watts/m^2 °C)

$x = 5.3 \times 10^{-4}$ meters for Cat #5-21-R

Q and ΔT have units of microvolts, each being the average of three steady state measurements for each observation.

APPENDIX E

Data from Cat #5-13-L

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
dry	0.0	92.3	503	0.088
↓	0.5	93.0	403	0.070
	1.0	79.3	394	0.080
	1.5	76.7	393	0.083
	2.0	70.3	449	0.103
	2.5	66.0	406	0.100
	3.0	68.3	408	0.097
	3.5	67.7	415	0.099
	4.0	61.7	421	0.110
	4.5	67.7	410	0.098
	5.0	62.0	419	0.110
	6.0	67.7	420	0.101
	6.5	68.0	427	0.102
	7.0	74.7	426	0.092
↓	8.0	72.3	415	0.093
humidity hydration				
↓	13.0	91.3	474	0.084
	13.5	63.3	420	0.108
	14.0	66.0	392	0.098
	14.5	59.0	395	0.110
	15.0	62.7	412	0.108
	15.5	56.0	420	0.123
	16.0	57.3	426	0.123
	16.5	64.3	433	0.109
	21.5	88.0	489	0.090
	22.0	68.3	460	0.109
	22.5	57.7	442	0.125
	23.0	57.0	442	0.125
	23.5	53.7	438	0.134
	24.0	68.7	429	0.102
↓	24.5	60.3	432	0.117

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
humidity hydration				
↓	25.0	57.3	418	0.119
	30.0	78.3	495	0.103
	30.5	60.7	472	0.126
	31.0	74.0	501	0.110
	31.5	63.3	473	0.122
	32.0	54.7	459	0.138
	32.5	62.0	456	0.121
	33.0	57.0	486	0.139
	33.5	52.7	495	0.154
	38.5	60.3	539	0.144
	39.0	74.3	511	0.112
	39.5	56.7	469	0.135
	40.0	64.3	447	0.113
	40.5	78.0	452	0.094
	41.0	58.0	456	0.128
	41.5	54.7	453	0.135
↓	42.0	62.0	444	0.117
dry for 30 minutes				
dry	72.0	87.7	504	0.094
↓	72.5	68.7	453	0.107
	73.0	66.0	445	0.109
	73.5	69.0	444	0.105
	74.0	64.7	439	0.112
	74.5	62.7	435	0.113
	75.0	68.7	454	0.107
	75.5	68.7	445	0.105
	76.0	65.3	448	0.111
↓	76.5	65.3	446	0.111
passive hydration				
↓	77.0	71.3	484	0.110

APPENDIX E (continued)

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)	CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
passive hydration					stimulation				
↓	77.5	52.3	422	0.131	(1)	88.0	58.7	491	0.136
	78.0	54.7	397	0.119	↓	88.5	60.3	489	0.131
	78.5	64.7	391	0.099		89.0	60.7	523	0.140
	79.0	53.7	375	0.115		89.5	60.6	522	0.139
	79.5	52.3	377	0.118	(2)	90.0	59.7	546	0.149
	80.0	54.3	383	0.116	↓	90.5	55.3	566	0.165
	80.5	52.0	398	0.125		91.0	58.0	570	0.159
	81.0	57.0	399	0.115		91.5	67.3	604	0.146
	81.5	54.3	403	0.122		92.0	63.7	571	0.146
↓	82.0	55.7	407	0.120		92.5	54.3	558	0.166
stimulation					↓	93.5	61.3	586	0.155
(1)	82.5	85.3	526	0.097	(3)	94.0	62.3	589	0.153
↓	83.0	81.0	533	0.106	↓	94.5	69.7	586	0.136
	83.5	71.3	503	0.115		95.0	69.7	588	0.137
	84.0	58.3	528	0.146		95.5	72.3	597	0.133
	84.5	62.7	487	0.126		96.0	59.7	614	0.167
	85.0	58.7	520	0.144		96.5	66.7	597	0.145
	85.5	55.7	514	0.150		97.5	67.3	600	0.144
	86.0	56.7	488	0.140		98.5	64.7	574	0.144
	86.5	70.3	487	0.112		99.0	68.0	582	0.139
	87.0	60.0	508	0.137		100.0	62.0	587	0.152
↓	87.5	60.3	491	0.132	↓	100.5	67.7	596	0.143

Calculation of k: $k(\text{Watts/m }^{\circ}\text{C}) = (\text{c.f.})(Q)(x/\Delta T)$,

where:

c.f. = conversion factor, 53.9(Watts/m^2 °C)

$x = 3.0 \times 10^{-4}$ meters for Cat #5-13-L

Q and ΔT have units of microvolts, each being the average of three steady state measurements for each observation.

APPENDIX F

Data from Cat #6-7-R

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)	CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
dry	0.0	67.7	433	0.141	(1)	21.0	40.3	457	0.251
↓	0.5	68.3	434	0.140	(2)	21.5	41.0	478	0.257
↓	1.0	46.6	406	0.192	↓	22.0	39.7	479	0.267
↓	1.5	49.7	415	0.184	↓	22.5	36.3	470	0.286
↓	2.0	44.3	406	0.202	↓	23.5	39.7	457	0.254
↓	2.5	48.3	420	0.192	↓	24.5	41.3	464	0.248
↓	3.0	44.3	418	0.209	↓	25.0	40.3	465	0.255
↓	3.5	44.7	419	0.207	↓	26.0	38.7	465	0.267
↓	4.5	43.7	426	0.216	↓	27.0	35.7	470	0.291
↓	5.0	49.3	443	0.198	↓	28.0	38.7	455	0.260
↓	6.0	41.0	427	0.230	↓	29.0	36.3	465	0.283
↓	6.5	43.0	430	0.221	↓	30.0	35.0	454	0.287
(1)	7.0	49.7	464	0.206	↓	31.0	33.3	441	0.292
↓	7.5	46.3	457	0.218	(3)	31.5	43.0	468	0.240
↓	8.0	47.0	429	0.202	↓	32.0	34.0	484	0.315
↓	8.5	51.7	466	0.199	↓	32.5	30.7	463	0.333
↓	9.0	52.7	457	0.191	↓	33.0	32.0	464	0.320
↓	10.0	45.3	461	0.225	↓	34.0	40.0	464	0.257
↓	10.5	53.7	475	0.195	↓	35.0	33.0	470	0.315
↓	11.5	45.0	469	0.230	↓	36.0	44.7	493	0.244
↓	12.5	41.0	462	0.249	↓	37.0	33.7	476	0.312
↓	13.5	37.7	463	0.271	↓	38.0	31.7	476	0.332
↓	14.0	38.0	468	0.272	↓	39.0	32.3	475	0.325
↓	15.0	44.3	461	0.230	↓	40.0	27.3	472	0.382
↓	15.5	44.7	466	0.230	↓	41.0	26.0	467	0.397
↓	16.5	39.0	454	0.257	15 minute period of drying				
↓	17.0	38.7	457	0.261	dry	56.0	40.3	459	0.252
↓	17.5	42.0	451	0.237	↓	56.5	33.3	422	0.280
↓	18.5	34.7	455	0.290	↓	57.0	32.3	406	0.277
↓	19.0	41.0	453	0.244	↓	57.5	30.7	405	0.291
↓	20.0	36.7	452	0.272	↓	58.5	28.7	403	0.310

APPENDIX F (continued)

CONDITION	TIME	ΔT (uv)	Q (uv)	k (W/m °C)
humidity hydration				
↓	63.5	37.0	518	0.309
	64.0	23.3	473	0.448
	64.5	28.0	448	0.354
	65.5	31.7	489	0.341
	70.5	39.3	484	0.272
	71.0	33.0	465	0.312
	72.0	32.0	460	0.318
	73.0	36.7	474	0.285

Calculation of k: $k(\text{Watts/m } ^\circ\text{C}) = (\text{c.f.})(Q)(x/\Delta T)$,

where:

c.f. = conversion factor, 53.9(Watts/m^2 °C)

$x = 4.1 \times 10^{-4}$ meters for Cat #6-7-R

Q and ΔT have units of microvolts, each being the average of three steady state measurements for each observation.

APPENDIX G

```
$DEMAND,MT
$EQUIP,20=MT(STAT)
$FOR,L,X
      SUBROUTINE TRANS (X)
      COMMON/A/NR,NT,IS,IDR,JP $ DIMENSION X(200),TJ(100),T(100),E(100)
      DOUBLE PRECISION X,T,TJ,E
      IF (NR.GT.1) GO TO 3
      READ 1, K
    1 FORMAT (I3)
      READ 2, (TJ(I), I=1,K)
    2 FORMAT (13F6.1,1X)
      KM=K-1
    3 DO 10 I=2, K
      T(I)=0.0DO
      IF (X(2).LE.TJ(I).AND.X(2).GT.TJ(I-1)) T(I)=X(2)-TJ(I-1)
   10 CONTINUE
      T(1)=0.0DO
      IF (X(2).LE.TJ(1)) T(1)=X(2)
      DO 20 I=1, KM
      E(I)=0.0DO
      IF (X(2).GT.TJ(I))E(I)=1.0DO
   20 CONTINUE
      KP=K+1
      DO 30 I=4, KP
   30 X(I)=T(I-2)+(TJ(I-2)-TJ(I-3))*E(I-2)
      X(3)=T(1)+TJ(1)*E(1)
      X(K+2)=T(K)
      RETURN
      END
```