Chemical Protective Clothing and the Skin:

Practical Considerations

by Mark Boeniger

National Institute for Occupational Safety and Health/CDC
Cincinnati, Ohio

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Preface

The history of protective clothing and improvements in the material technology and construction methods over time are well documented. In 2000, the AIHA Chemical Protective Clothing Committee responded to an inquiry about the emerging issues in protective clothing. Although world events in the past year quickly changed the perception, significance, selection, and use of protective clothing, many of these changes were initiated by events of the past decade. The rapid introduction of terrorism, and chemical and biological threats into standard business risks have, in many ways, elevated the significance of the identified issues. Advances in the chemical, pharmaceutical, and other high-tech industries increased the number of workers who rely on protective clothing to reduce exposures because their ever-changing work environment prevents the effective implementation of engineering controls. In jobs where personal protective clothing and equipment are the only available control options, the purpose of the clothing and equipment is to shield or isolate individuals from the chemical, physical, and biological hazards. Protective clothing must be designed and sized to properly fit and protect the growing numbers of female and minority workers; it must not only be effective, but also practical for use in the workplace.

Standards, Test Methods, and Performance Data

An increasing number of standards and practices emphasize the need for protective clothing to be part of an overall safety and health plan. The OSHA requirements to complete and revise PPE assessments for all workplace hazards remain a significant challenge for many companies and workplaces. Even after the completion of the hazard assessments, all of the new materials and models have made the selection of the appropriate protective clothing more challenging. Performance data for protective clothing have become widely available over the past several years, but guidelines for the use and interpretation of the data continue to be developed. Test methods were developed to provide a basis for evaluating clothing and material effectiveness for protection against a specific hazard. Although

methods are designed to allow comparisons among the relative performances of various products, the influence of other factors, such as size and fit, must be incorporated into the selection process. Without adequate interpretation guidelines, the selection process can remain confusing for many safety and health professionals, particularly when the test method does not simulate the conditions of the actual exposure.

Product Development and the End User

The development of new clothing materials and the sophisticated advances in polymer technology and laminate methods broadened the capabilities of available products, and at the same time provided additional variables to consider, making selections more difficult. In addition to the development of new materials, the focus has shifted to the factors that affect the end user. Improvements in manufacturing have increased the selection of garment sizes and models. More attention is focused on understanding ergonomic issues, heat stress implications, and the relationship between the task and the clothing. As new materials, garments, and standards and test methods are developed, the focus will need to be on the willingness of the end user to wear the protective clothing as intended. Easy methods of identification, such as color-coding, will need to be incorporated to simplify the selection process. The development of field-based end-of-service indicators will help improve the usefulness and protection afforded by the clothing, and will minimize risks associated with the reuse of previously exposed clothing materials. Improved fit and comfort will be necessary to help ensure proper and consistent use at all times.

Risk Analysis

The combination of suits and other clothing components form ensembles for true full-body protective clothing. The increased reliance on protective clothing in emergency and disaster situations increases the need to determine effectively the protection offered by the collective ensemble. As information about combinations of protective clothing components are developed, questions about "overprotection" of workers will emerge. The realization of chemical and biological threats has shifted the emphasis onto preplanning, so that quick and timely

selection decisions can be made. Risk-based decisions about the appropriate level of protection may result in accepting some level of exposure.

As future considerations are made regarding protective clothing, the issue of dermal exposures will need to be addressed further. Development of quantitative evaluation techniques that are more sophisticated, but more field-adaptable than those that currently exist, will be necessary. In addition, simple indicators of acceptable dermal exposures will need to be developed. Overall, this will mean an increased emphasis on examining multiple exposure routes, including sources of dermal exposures from surface contamination as well as from direct contact. Eventually, this may necessitate developing dermal occupational exposure limits and broadening the available biological exposure indices.

The Future

Information about the selection, use, and evaluation of protective clothing and equipment continues to evolve. Development of a comprehensive program covering these aspects of protective clothing can enhance the level of protection afforded to the workers. An understanding of the performance data in conjunction with the integration of risk assessment into the selection process can lead to better selections and therefore better protection for workers who rely on protective clothing to minimize or prevent exposures.

Conclusion

The Chemical Protective Clothing and Equipment Committee currently is editing and preparing the full second edition of *Chemical Protective Clothing,* from the AIHA Press. New information also is being published as a series of individual booklets. The first two custom publications in the series: "Chemical Protective Clothing: Managing Heat Stress," and "Chemical Protective Clothing and the Skin: Practical Considerations" are now available from the AIHA Press. The next topics in the series, covering test methods and standards, and evaluation of full-body protection are expected early this summer. The fully revised, updated, and expanded second edition of *Chemical Protective Clothing* is scheduled for publication in late 2002.

Chemical Protective Clothing and the Skin:

Practical Considerations

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Introduction

Many occupational safety and health professionals consider chemical protective clothing (CPC) as the "last line of defense" for protecting the skin from chemical and physical hazards. CPC is in several respects justly regarded this way. First, it physically is very close to the skin. Because of its intimate contact with the skin, its purpose is to form a physical barrier that separates the skin from the outside environment.

Aside from this rather obvious physical description of its proximity to the skin, CPC as a last line of defense can also be considered from a pragmatic viewpoint. There exists in industrial hygiene practice a hierarchy of controls that has evolved from the effectiveness, reliability, user comfort, and operating costs of each of the interventions. Generally, personal protective equipment (PPE) is considered a last resort for protecting workers, to be issued only when all other options for control are considered inadequate. This is clearly accepted to be true for inhalation hazards where use of respirators is acknowledged to have practical limitations. However with regard to protecting the skin, CPC is often considered first without giving much consideration to possible alternative approaches. Use of CPC should not be preferred over other options because there may be adverse consequences and costs associated with this choice. This chapter will provide some basic information about the skin, and focuses on the direct consequences of wearing CPC upon the skin and on the effectiveness of exposure reduction.

Skin Anatomy and Physiology

The skin is the largest organ of the body, constituting 10–15% of the normal body weight, with a surface area of approximately 1.8 m^2. After over a century of scientific study, much is now known about the seemingly amazingly effective function of the skin as a barrier to the outside environment and of helping to maintain homeostasis within. However, research is still intensely attempting to understand all the physicochemical aspects of the skin, especially among the cosmetic and pharmaceutical industries who venture to profit from improving the condition of the skin, and by delivery of drugs through the skin, respectively.

There are several excellent comprehensive books that are presently available that should be referred to if more information is needed on skin anatomy and function.[1-6] The purpose of this chapter is to provide only a basic broad background about the skin as it relates to occupational exposures. More specifically, this overview will provide the reader who is involved with the use of CPC with information that is relevant to the impact of wearing CPC on the skin. The close proximity of CPC to the skin, especially for gloves, and its potential health importance make this discussion essential.

For review, the skin constitutes three structurally and functionally distinct important regions: the stratum corneum, viable epidermis, and dermis. The stratum corneum is the uppermost and thinnest layer exposed to the outside world (see Figure 1). It is composed of flattened denucleated cells called corneocytes, which contain mainly highly cross-linked fibrous keratin proteins. Keratin has a high affinity for water, which is necessary for it to remain flexible. If dried, the stratum corneum will become brittle and crack.[7] The corneocytes are nonrespiring cells that are tightly connected forming a surprisingly rugged membrane. Each corneocyte is typically 25–40 μm (micrometers) in diameter and only 0.2 to 0.5 μm thick. These are randomly stacked some 15 to 25 layers thick over most human skin surfaces, which have an approximate total thickness of about 15 μm.[8] This varies somewhat by anatomical location, being thickest on the palmar skin and soles of the feet with a thickness of 400–600 μm. Figure

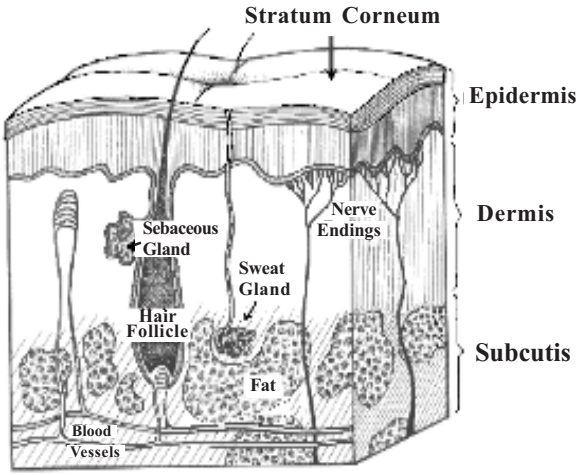

Figure 1: Simplified diagram of the skin including the upper stratum corneum consisting of flattened corneocytes, and the viable epidermin, dermis, and underlying subcutis tissue. The skin can be an important route for absorption of chemicals into the body, can be adversely affected resulting in serious medical conditions, and is an important immunologic organ of the body.

2 shows a scanning electron photomicrograph of the surface of the skin.

The intercellular space between the corneocytes has a diameter of between 0.01–0.1 μm and has been estimated to occupy approximately 20% of the total stratum corneum volume.[9-11] Within this space are well-organized lipophilic and hydrophilic domains that represent parallel channels (lamallar bilayers) of least resistance to diffusion of either nonpolar (lipophilic) or polar (hydrophilic) compounds, respectively.[12-14] These structured layers in turn occupy a space of only 0.5–1.0 μm.[15] These domains constitute an important, tortuous pathway for molecular transport through the stratum corneum. Normally the intercellular fluid is predominantly lipid, consisting mainly of lipid classes called ceramides (~45%), cholesterol (~25%), and free fatty acids (~15%), which spontane-

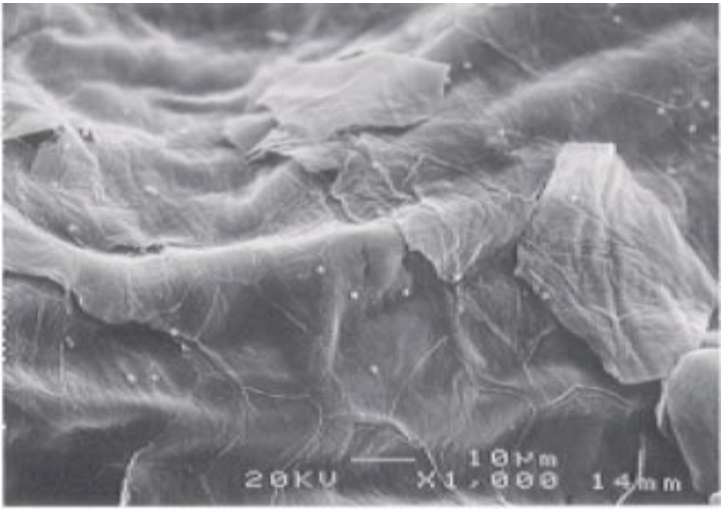

Figure 2: Scanning electron photomicrograph of the surface of the skin showing varied topography and plate-like corneocytes. Small particles of 1 µm are shown for comparison (courtesy of Dr. Sally Tinkle, NIOSH, Morgantown, WV).

ously form multilayer bilayers.[16] Lipids comprise approximately 8% of the total stratum corneum dry weight.[17] It has been found that long chain ceramides covalently bind to the surface proteins on the corneocytes, acting as anchors to which the other lipids adhere and also participate in intercellular adhesion.[18] Because the normal intercellular space consists predominantly of lipids, chemical solubility and diffusion of lipophilic (fat soluble) compounds through the skin occur more readily than for hydrophilic (water soluble) compounds. This will be discussed in more detail below. A simplified schematic of the stratum corneum construction with its dense corneocytes and intercellular fluid was first referred to as a brick and mortar model by Michaels et al. in 1975 and is depicted in Figure 3.[19] We know at present that the skin barrier is probably far more complicated than was previously understood due to the organization of the intercellular lipids.[20]

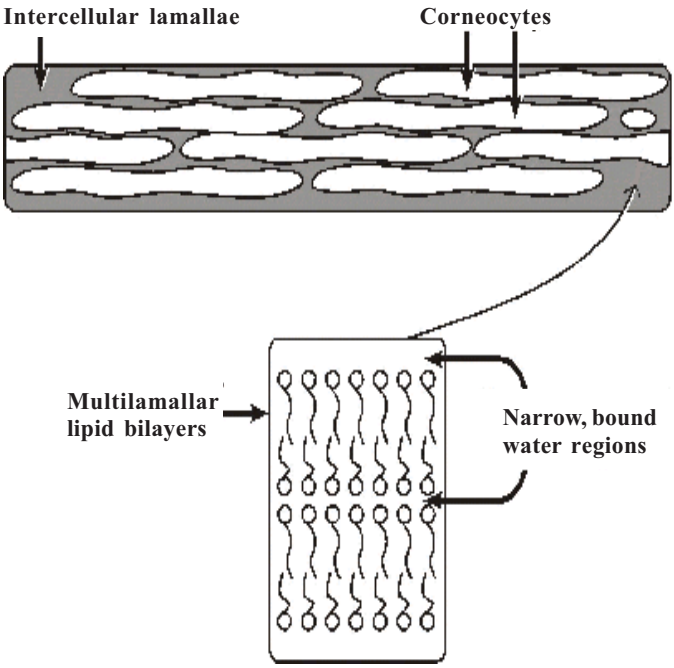

Figure 3: Organization of the stratum corneum and intercellular lipids.

The thickness of the stratum corneum varies by anatomical location on the human body. Table 1 shows the average skin thickness for several locations.[21] Overall, the stratum corneum is surprisingly thin. The stratum corneum on most of the body surface is only 10 to 16 μm thick, with limited areas of increased thickening related to the need for abrasion resistance, such as on the palms of the hands and soles of the feet where it is 400–600 μm thick. To appreciate how thin the majority of the stratum corneum is in respect to other familiar objects, the average human hair is about 50–70 μm in diameter. Polyester adhesive tape (3M Scotch Tape®) is about 25 μm thick. The thinnest synthetic glove is about 7 μm.

It is clear that the stratum corneum provides an important physical and chemical barrier. Because chemicals permeating the skin are not likely to pass directly through the corneocytes but must instead traverse the long distances of the intercellular spaces

Table 1: Human Skin Thickness by Anatomical Site*

Skin Area	Stratum Corneum Thickness, µm
Abdomen	15
Volar Forearm	16
Back	10.5
Forehead	13
Scrotum	5
Back of Hand	49
Palm	400
Sole	600

*Adapted from reference 21.

surrounding the flattened corneocytes, permeability is reduced by about 1000 times relative to a pure lipid phase.[19] As such, the apparent effective thickness of the stratum corneum has been calculated to be between 500 to 750 mm.[22,23] Another way to look at this is that it would require a homogeneous film at least 500 mm thick, impregnated with the same lipids as present in the skin, to provide equivalent protection from chemical permeation.

Beneath the stratum corneum is the viable epidermis. Within this layer is the location of the germinal stratum granulosum where new corneocytes are formed from keratinocytes. The viable epidermis is about 50 to 100 mm in thickness, depending on location. A complete replacement of the skin corneocytes that make up the stratum corneum occurs every 14 to 28 days in humans.[24] However, it has been shown that continuous occlusion increases this duration by about two-fold.[25]

The viable epidermis provides an important and rather unique immune capability by providing both specific and non-specific protection against pathogenic microorganisms and environmental antigens. The epidermis is unique in having enhanced capability over the respiratory or oral routes in recognizing foreign materials and mounting a immune re-

sponse.[26,27] Respiratory sensitization may be effectively induced solely by cutaneous exposure to both low molecular weight compounds (i.e., haptens),[28,29] and high molecular weight organic substances, (i.e., allergens) such as natural rubber latex proteins.[30-33] The major immunologically active cellular constituents are keratinocytes, Langerhan's cells, skin-infiltrating T-lymphocytes, and postcapillary venule endothelial cells. Langerhans cells are mobile, can seek out foreign agents, and play an important role in immune processes, especially allergic contact dermatitis. It is important to recognize that this immune capability is just below the thin stratum corneum. Regional lymph nodes link the skin with the systemic immune system, which together are referred to as the skin-associated lymphoid tissue.[34,35]

The thickest layer of the skin is the dermis, which is about 500 mm to 3 μm thick, depending on anatomical region. This highly vascular layer contains the appendegeal structures like the hair follicles, eccrine, and sebaceous glands that originate in this layer. Within a cubic centimeter of human skin are 11–100 philosebacious glands with hair follicles and 100–400 eccrine glands. The total cross-sectional area of the appendages is probably 0.1–1% of the surface area of the skin, and the total volume available for percutaneous absorption (excluding hair diameter) is only about one-tenth of that.[36] Although these appendegeal structures represent less than 1/100th of the skin surface area, they may represent an important shunt through the stratum corneum for large hydrophobic compounds and small particles.[37]

Significance of Occupational Skin Exposure

Chemicals that contact the skin can cause adverse health effects in two ways. First and most obvious is when the skin itself is affected, and there are pathological changes. The most likely effects include allergic and irritant contact dermatitis, which comprise the bulk of occupational contact dermatitis (OCD). Another way skin contact can affect the

worker, but is often much more obscure, is when potentially toxic chemicals are absorbed through the skin, adding to the systemic body burden and toxicity in internal organs.

The Bureau of Labor Statistics (BLS) estimates that skin disease currently accounts for 13% of all reported occupational disease.[38] According to the BLS the rate of occupational skin diseases was 81 cases per 100,000 workers in 1997. The estimated annual cost may be upward of $1 billion.[39] According to the latest available data, dermatitis is the third most common cause of compensable temporary total and partial disability and the sixth most common cause of permanent partial disability in the United States.[40] Although both major causes of OCD are highly preventable through avoidance of exposure, the prognosis of untreated OCD is generally poor.[41,42]

The extent skin absorption contributes to other possible causes of disability such as systemic poisoning, neurotoxic effects, and ill-defined conditions, is presently poorly documented. A full understanding of the health significance of skin exposure leading to systemic toxicity is far less clear because of the difficulty in objectively determining the role of skin absorption to an adverse health outcome, especially if the illness were the result of chronic exposures. If skin absorption contributed to a fraction of the estimated total annual 60,000 deaths and 860,000 occupational illnesses attributed to workplace exposures, it could be a substantial number.[43]

Occupational Dermatitis

Occupational skin disease includes any abnormality of the skin induced or aggravated by the work environment. The term dermatitis relates only to skin conditions having an inflammatory component involved with its pathogenesis, while dermatosis relates to skin disease from any cause and with any pathologic outcome.[44]

Causes of occupational dermatoses include (1) mechanical, caused by friction, pressure, and mechanical disruption, (2) chemical, (3) physical, caused by extremes in temperature and

radiation (principally ultraviolet), and (4) biological, caused by microbiological and parasitic organisms.[44,45] One estimate is that about 75% of occupationally related skin disease seen in the infirmaries of industrial plants was attributed to mechanical trauma. It was noted that while this type of injury is usually relatively minor, it can predispose the skin to more serious dermatoses due to the skin's compromised mechanical barrier.[44] About 90–95% of all work-related dermatoses, not including those that are caused by mechanical trauma, are considered OCD or eczema.[46] Occupational contact dermatitis is typically characterized by inflammation and erythema (reddening), itching, or the formation of scales as a result of contact with external chemicals or substances. The occurrence of pustules (small pus-containing superficial lesions) is rare and usually is a sign of secondary infection. Contact dermatitis can be further divided into two etiological classes—allergic and irritant.

Allergic contact dermatitis is a delayed-type immunological reaction in response to contact with an allergen in sensitized individuals. This reaction is also referred to as Type 4, or T-cell-mediated immune reaction, since there is a procession of cellular events within the body leading up to the inflammatory response. In predisposed individuals, initially in the induction period allergenic chemicals penetrate the intact skin as small molecules (usually <400 MW), and they are incompletely allergenic (haptens) until they bind to protein and form a complete allergen.[47] Langerhans cells are specialized cutaneous immune effector cells that bind with the allergen and direct the allergen to a regional lymph node. Within the lymph node, interaction with T lymphocytes is followed by replication of sensitized T lymphocytes and completion of the induction phase. Sensitization can occur after just one single exposure, but requires a lag period of a few days to a couple of weeks for induction to be complete. Once sensitized, and upon re-exposure to the allergen (the elicitation phase), normally it takes from 12 to 96 hours for a reaction to occur, but more usually 48 to 72 hours after exposure.[48] Table 2 lists some common chemicals known to cause allergic contact dermatitis in industry. Allergic contact dermatitis accounts for about 30 to 50% of the cases of contact dermatitis in the workplace.[49]

Table 2: Some Chemicals Causing Allergic Dermatitis Among Workers

Chemical	Occurrence
acrylates	paint plasticizer, plastics
bacampicillin	pharmaceutical
benzocaine	pharmaceutical
chloracetamide	water-base preservative in paints, glues,cosmetics
colophony	electronic solder flux, adhesives
cobalt metal, fume, and dust	metal smelting
diglycidyl ether of bisphenol A	epoxy, product fabrication with resin
ethylenediamine	solvent and chemical intermediate
formalin	textiles, embalming
hydrazine	soft solder flux, chemical intermediate, metal cleaning
d-limonene	cleansers, degreasers
mercaptobenzothiazole	rubber, PPC, antimicrobial agent
methacrylate compounds	dental laboratory denture technicians
methylene diisocyanate	rigid polyurethane
neomycin sulfate	pharmaceutical antibacterial
nickel	stainless steel, metal products
p-phenylenediamine	oxidative hair dyes, cosmetology
parabens mixture	preservative in skin medication, cosmetics,cleansers
phenyl glycidyl ether	epoxy resin
picric acid	battery manufacture, colored glass, explosives
poison ivy	outdoor work
potassium dichromate	histology, leather, matches, spackle cpd., photography
substilisins	detergent manufacture
thiram	rubber manufacture, PPC, food disinfectant, lub oils
toluene 2,4-diisocyanate	polyurethane foam manufacture

Induction of allergic contact dermatitis is known to depend on the concentration of the allergen on the skin surface. If a sensitizing dose of the allergen is spread over a larger surface area, the likelihood of sensitization appreciably declines. It is believed that sensitization is dependent on the number of allergen molecules per Langerhans cell—a small number of cells bearing many molecules being more effective than having many cells bearing a few molecules.[50] There appears to be a threshold surface concentration for induction of all sensitizers, and the range of induction concentrations is quite large. Caution is warranted in strictly interpreting experimental laboratory data since influences in the workplace might alter percutaneous absorption of chemicals. Also, repeating the exposure over a period of time seems more effective in inducing sensitization than is a single dose. Genetic disposition plays a prominent role in determining individual susceptibility.[51] Although there appears to be a fairly linear dose-response to sensitizing compounds among humans, once sensitized there is wide individual variability in the provocation (elicitation) threshold concentration. The concentration necessary for eliciting an individual response in sensitized individuals can span at least a 100-fold range.[52]

It has been reported that 90% of all occupational allergic contact dermatitis was found on the back of the hands and the

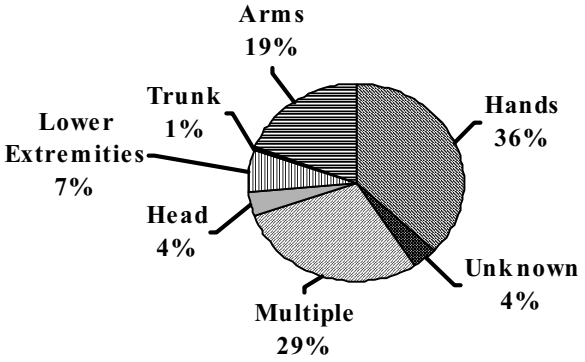

Figure 4: Locations on the body affected by occupational contact dermatitis resulting in worker's compensation in Oregon, 1988–1992. Data from reference 56.

forearms.[53] However, contact dermatitis among homemakers occurred in almost 50% of the cases on the palms, whereas 15% of the time it affected the back of the hands and fingers.[54] In a different study of dental laboratory technicians, the fingertips were primarily involved in allergic contact dermatitis (93%), whereas in irritant contact dermatitis, the dorsum of the fingers were affected in 80% of the cases. [55] Figure 4 depicts the locations on the body for occupational contact dermatitis based on 879 recent Oregon workers' compensation cases for the period 1988–1992.[56]

Contact urticaria (Type I immune reaction) is an immediate immunological response in the skin resulting from circulating chemical-specific antibodies coming into contact, most commonly, with exogenous proteinaceous molecules (e.g., animal dander, natural rubber latex proteins, foodstuffs, industrial enzymes). The reaction becomes apparent as a wheal, or hive, which is a firm, rounded or flat-topped elevated lesion that results from edema (swelling) of the dermis. Wheals are often pink in color, priuritic, and the individual lesion persists fewer than 24 hours.

In type I reactions, in addition to the skin, the respiratory and gastrointestinal tracts, as well as the cardiovascular system, may respond after cutaneous exposure to allergens. Much less frequently, contact urticaria can result from exposure to low molecular weight chemicals forming chemical–protein conjugates (e.g., 2-ethylhexyl acrylate) in the epidermis. Response is mediated by allergen-provoked release of histamine from cutaneous mast cells. In Finland, a recent survey of OCD cases from 1990–1994 found that almost 30% of all occupational immunologically mediated dermatoses were due to contact urticaria, while the remainder were allergic contact dermatitis.[57]

Contact dermatitis from irritants constitutes about 50 to 80% of all OCD cases.[58] There are several forms of response common to irritant exposures that are dependent on the chemical substance, concentration, duration, and the individual exposed. The first type is caused by a single application of a strong compound, which results in a toxic, acute reaction primarily associated with reddening (erythema) and possibly a burn-

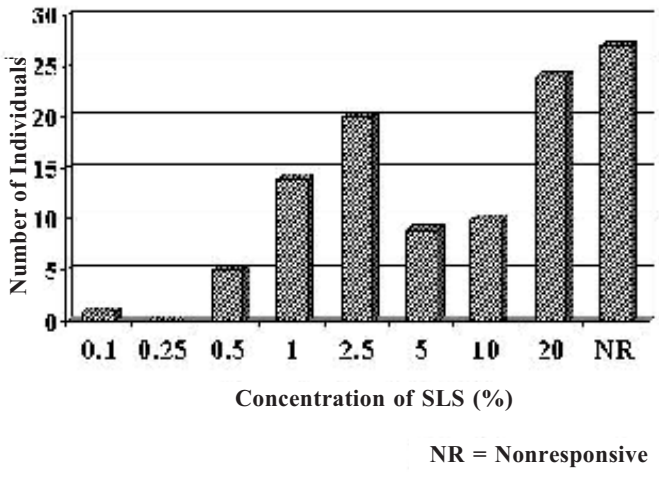

Figure 5: Acute irritant response thresholds among individuals with six skin types. Minimum SLS concentrations inducing irritation from 110 individuals with all skin types showing wide variation in susceptibility. Data from reference 66.

ing or stinging sensation. The second type results from repeated exposure, which results in erythema, chapping, and fissures in the skin. The third type also results from repeated exposures, but develops into a chronic dermatitis that is characterized by erythema and scaling, with frequent fissuring of the stratum corneum.[59] A compensatory process of tolerance for irritants, sometimes called "hardening," can occur that results in lichenified (thickened) skin. A subcategory of irritant dermatitis manifests only after a lag time of 8 to 24 hours or longer, and is thus referred to as being a delayed type.[59] Some industrial chemicals known to cause delayed effects include epichlorohydrin, ethylene oxide, hydrofluoric acid, some acrylates like hexanediol and butanediol diacrylate, and propane sulfone. In agriculture, the pesticide triphenyl tin hydroxide can cause delayed skin effects. Such compounds that cause a delayed irritant reaction characteristically penetrate the stratum corneum slowly and are cytotoxic to the viable epidermis.

Usually acute irritant response is rapid and begins to subside in 24 to 72 hours but as mentioned above some compounds

can take longer, responding similarly to delayed allergic reactions.[60] However, in experimental studies with sodium lauryl sulfate (SLS), complete functional skin recovery after a single 24-hour exposure had not completely occurred 12 days following exposure.[61] The prognosis for complete resolution of both the first and second type of acute irritation is good if exposure is quickly discontinued. The prognosis for chronic irritation of the skin is variable but generally poor.[41,62-64]

Substantial individual range of susceptibility has been found to exist among individuals when exposed in the same way to a model irritant, such as the detergent SLS.[65,66] The range of threshold concentrations necessary to induce an irritant response to SLS is indicated in data depicted in Figure 5 for a 4-hour occluded patch test. One hundred and ten individuals representing all skin types ranging from very fair skin (burns easily, never tans) to deep normal pigmentation were included. There seem to be little relationship between skin pigmentation type, ability to sunburn, or gender as predictors of skin sensitivity to irritants.[67] Using sensitive measures that do not include erythema, black skin may be more sensitive than white skin.[68] Young skin seems more susceptible than older skin in spite of the fact that older skin tends to thin with advancing age.[69] People with respiratory atopy without outward signs of cutaneous atopy are generally no more susceptible to irritants than nonatopics but persons with a history or current atopic dermatitis seem several fold more prone.[70-72] The probability of a given concentration to induce irritation is also dependent on the season. This is because of seasonal differences in ambient humidity and hence skin hydration. In one test group, 45% reacted to 20% SLS in summer, whereas 91% reacted to this concentration in the winter.[73] For other compounds, like alkalies and powders, irritant response seems more likely in the summer.[60]

Chemical Protective Clothing and Occupational Dermatitis

The recent increase in occupational sensitization to natural rubber latex proteins due to use of latex gloves has received much attention. This is a type I allergy involving high molecular

weight allergens resulting in immediate type urticarial responses. Fortunately steps have been taken to reduce the incidence of this problem and latex gloves should not be commonly used in occupations outside of health care industries where bloodbourne pathogen protection is the primary intent.[74] Another type of allergic response due to small molecular weight chemicals, commonly used as accelerators in the polymerization of natural and synthetic rubber, is responsible for type IV, delayed response sensitization (allergic contact dermatitits). Most of the cases of glove-related contact dermatitis involve rubber gloves whereas cases reported from use of synthetic rubber gloves are relative few.[75] These allergen compounds belong to classes of chemicals including thiazoles, thiurams, dithiocarbamates, guanadines, thioureas, and amine aldehydes.[76] Other potential allergen additives are antioxidants, typically derivatives of *p*-phenylenediamine, that are primarily used in rubber products. These compounds may leach out of gloves and into the wearer's skin.[77] Because damaged skin is more likely to absorb chemicals, it should be kept in mind that if a person with dermatitic skin begins using gloves that contain allergens, this could be the cause of more serious problems later.[78,79]

In Finland, 1991, the eight most common types of chemicals responsible for allergic contact dermatitis were rubber chemicals, nickel, epoxy resins, formaldehyde, thiuram sulfides, chromate (hexavalent), isothiazolinones, and colophony. It is likely that the principal contact with rubber chemicals, thiuram sulfides, and isothiazolinones occurred from wearing chemical protective gloves.[80] In a later report, the most common causes of allergic contact dermatitis were rubber chemicals (26%), synthetic resins, plastics, glues, and paints (19%), and metals (16%). While the sources of the rubber chemical allergies were most often attributed to protective gloves, no cases of occupational allergic dermatoses were detected in the rubber industry during 1993.[81] Paradoxically hand cleansers and gloves were among the top causes of occupational dermatitis in most other studies as well. [82]

In the United Kingdom, the most frequent agents for contact dermatitis were rubber chemicals and materials (14.1% of cases reported by dermatologists), soaps and cleaners (12.7%),

nickel (11. 9%), wet work (11.1%), personal protective equipment (6.2%), petroleum products (6.3%), cutting oils and coolants (5.6%), and epoxy and other resins (6.1%).[83]

In addition to allergens, the wearing of gloves may cause or exacerbate skin irritation (also see section on occlusion below). According to Taylor, irritant contact dermatitis is probably the most frequent adverse glove reaction, especially among those that wear latex gloves.[84] Wilkinson recently reported the type of dermatitis among 44 patients with glove intolerance and found that 75% had irritant contact dermatitis, 20% had contact urticaria, and 8% had allergic contact dermatitis.[85] Contributors to skin irritation may include powders that are added to enhance donning and doffing, trapping of irritating hand cleaners or other chemicals underneath an occlusive covering, or just the simple friction of glove to skin contact that occurs when flexing.[86] The degree to which each individual variable or combined causes exacerbates skin irritation has not been well characterized, but there are limited studies relating to this in the literature. For instance, a questionnaire survey of dental surgeons revealed that 29% of the respondents indicated that they experienced skin irritation. This was more evident among those who wore gloves most often.[87] In another study of hospital and dental care workers, 37% reported skin problems associated with frequent glove use.[88]

Cornstarch powder is presently commonly used as a donning agent on most powdered gloves and replaced talc for the most part, although talcum powder may still used on a limited basis as a mold release agent in glove manufacturing.[89] Thus, even powder-free gloves are likely to contain some powder, albeit at considerably lower levels.[90] More common presently is the use of calcium carbonate as a mold release agent. Also in use are silicone oils and chlorination, which enhance the slipperiness or smoothness of the inside surface. Brehler et al. found the glove irritation effect variable depending upon the glove and powder used.[91] They also found some gloves with alkaline surface pH conditions (up to 10.2) that reportedly could alter the skin surface pH for hours afterward. Although in their experimental studies unpowdered gloves seemed less irritating than powdered gloves, other user acceptance surveys indicated little consistency with this.[87] It is likely that several factors acting in combination may contribute to glove irritancy.

Permeation and Penetration of Substances Through the Skin

Certain chemicals will be absorbed through the skin much more readily than others. In intact skin, the main means of absorption is through permeation. Permeation is the molecular diffusion of chemicals within a matrix like the skin. The solubility of chemicals in the stratum corneum plays a big part in determining the concentration gradient achieved between the outside and inside. If one knows the skin absorption rate, and it is combined with the toxicity of the chemical once absorbed, one can estimate the potential risk of skin exposure.

It has been found from extensive study of the experimental permeation data for humans that the two principal factors that determine a chemical's likelihood to permeate are its solubility and molecular size. Solubility is typically expressed as water solubility or preferentially as the octanol–water partition coefficient, the latter being a representation of the chemical's solubility in a nonpolar phase versus a polar phase. Because of the wide numerical range of octanol–water coefficient values, or K_{ow}, the log of the K_{ow} is usually reported. The majority of chemicals have a log K_{ow} of less than -1 to 6, representing indeed a very wide range of solubilities. Because the intercellular channels contain bipolar moieties, chemicals with a log K_{ow} between 1 and 3 most readily permeate the skin. Chemicals that are very lipophilic will not readily diffuse through the hydrophilic epidermis, and therefore may remain in the stratum corneum for a considerable time. Very hydrophilic compounds may also remain in the skin for prolonged periods because of their poor penetration of the stratum corneum, possibly exceeding one week in duration.[92] In addition, some compounds appear to have an affinity for proteins, reversibly interacting with specific chemical sites.[93] Prolonged residence in the stratum corneum is referred to as chemical substantivity. Another term referring to this phenomenon is the skin depot.

In one evaluation of the chemical features of 17 compounds with a wide range of octanol–water solubilities, the strongest

positive correlations were found between partition coefficient (K_{ow}) and protein binding, a marginal correlation was found between protein binding and concentration in the epidermis, while partition coefficient was unable to predict concentration in the epidermis.[94] The second chemical-specific property of importance is the molecular size of the compound. Above a molecular weight of 500 daltons, permeation flux through the intact skin is usually negligible for most chemicals. Within this range, however exist a large number of chemicals of commercial importance.

In addition to permeation that occurs through molecular diffusion, compounds and small particles may penetrate the skin through discontinuities in the stratum corneum or perhaps through physical processes that occur during skin flexing. For instance, contact urticaria can result from cutaneous contact with natural protein allergens. Contact urticaria is a quite common problem among workers exposed to animal products, enzymes, and food proteins.[95] Typically these high molecular weight (HMW) proteins are usually >10,000 MW (>10 kilodalton), but are apparently able to traverse the stratum corneum to first induce sensitization and then result in a subsequent elicitation of response. Mice, for instance, have been sensitized through topical application on intact skin by ovalbumin and other allergens.[96,97] The molecular weight of ovalbumin (OVA) is 45 kilodalton. These experiments resulted in statistically significant elevations in OVA-IgE specific antibody in the dosed group. Also found was that the concentration required to induce sensitization decreased with repeated epicutaneous exposures. Natural rubber latex proteins have also been shown to penetrate intact human skin with much greater penetration if the skin is damaged, and topical dosing has produced respiratory sensitivity in mice.[98,99]

Factors Affecting the Skin Barrier

The following section describes some of the main variants that affect individual skin barrier function and health. Understanding these influences is essential to better protecting workers' skin and determining the prudent use of CPC.

Table 3: Comparative Relative Permeability of Human Skin to Topical ^{14}C Hydrocortisone, Parathion, Malathion, and Water

Regional Variation	Parathion[1]	Malathion[1]	Hydrocortisone[1]	Water[2]
Forearm (ventral)	1	1	1	1
Palm	1.3	0.9	0.8	3.7
Ball of foot	1.6	1	—	12.6
Abdomen	2.1	1.4	—	1.1
Back of hand	2.4	1.8	—	1.8
Scalp	3.7	—	3.5	—
Angle of jaw	3.9	—	13	—
Forehead	4.2	3.4	6	2.7
Axilla	7.4	4.2	3.6	—
Scrotum	11.8	—	42	5.5

[1]Data from reference 100.
[2]Data from reference 21.

Anatomical Differences

All skin over the human body is not exactly the same. In addition to differences in thickness, as shown in Table 1, there are compositional differences in the main pathways of diffusion. Permeation of chemicals through the stratum corneum was stated above to be primarily through the intercellular bipolar lipid channels. It has been found that there are regional variations in skin permeability that correspond to the differing amounts of intercellular lipids therein. Table 3 shows the relative difference in skin permeation of three organic compounds as well as water through various regions of the human body.[21,100] Parathion is the least water soluble while hydrocortisone is the most. The increase in hydrocortisone permeation in some regions of the

body appears to correspond to eccrine sweat production. Note how the palm, even though about 27 times thicker than the forearm (refer to Table 1), is almost equivalent in its barrier function. The planar stratum corneum (palms and soles of the feet), although thicker and able to resist physical abrasion better, has less intercellular lipid and is a poor diffusion barrier to chemicals, especially by those compounds that are more hydrophilic. The percentage weight of lipids in the planar stratum corneum is 1.3%, whereas lipids account for 7.2% by weight in the forehead skin.[101] Comparison of the water loss through each site (planar: 20–40 g/m^2/hr versus forehead: 4-7 g/m^2/hr) also correlates with the difference in intercellular lipid content.[102]

Just as there are regional anatomical differences in skin permeability, there are also differences in regional susceptibility to skin irritants. Permeability and irritant response are probably at least partly related, although biological mediators of response also play a role.[103] Cua et al. found the thigh to be the most sensitive to the irritant sodium lauryl sulfate while the palm and ankle were least responsive.[104] This is fortunate given the increased likelihood of contamination of these sites.

Inter-Individual Differences

Inter-individual differences in persons with apparently healthy skin appear common and can be appreciable. According to Feldman and Maibach, the standard deviation of expected

Table 4: Individual Range in Alveolar Air Concentration Following a 30-Minute Dermal Exposure*

Solvent	Subjects	End of Exposure
carbon tetrachloride	3	0.11–0.83
trichloroethylene	3	0.033–0.76
tetrachloroethylene	5	0.17–0.17
methylene chloride	3	2.3–3.6
1,1,1-trichloroethane	6	0.19–1.02

*Adapted from reference 110.

skin permeabilities should be expected to be one-third to one-half the mean value.[105] Assuming a normal distribution, 1 person in 10 will absorb twice the mean value, while 1 in 20 will absorb three times this amount. Up to tenfold differences in interpersonal skin absorption rate have been seen within small group studies that have been reported in the literature for such compounds as hydrocortisone and parathion.[106-108] The apparent transdermal absorption rate of nitroglycerin in healthy volunteers, using the same site, resulted in variations from 21% to 78% within six subjects.[109] Individual variation in alveolar air concentrations following a 30-minute skin exposure to five different chlorinated solvents is shown in Table 4. A large range in the apparent uptake was seen, assuming minor confounding from differences of *in vivo* metabolism of the absorbed compound.[110] Similar large inter-individual differences were seen by Lauwerys et al. when 11 male volunteers were asked to immerse both hands into pure m-xylene for 20 minutes.[111] The skin of all volunteers was free of lesions. The total amount of m-xylene absorbed ranged from 16 to 110 mg (6.9-fold range). Same person differences tested twice during a one-week period were twofold or less. The range of skin permeability seen in healthy individuals may also account for the large range of susceptibilities of response to irritants.[65]

Gender and race, as these relate to the skin, have only been marginally studied to date. However, significant gender-

Table 5: Effect of Type of Physical Damage on Skin Absorption of Nicotinic Acid in Human Skin*

Condition of Skin	% Absorbed	
	In Vivo	In Vitro
Normal	7	5
Abraded	47	51
Tape stripped		58
UV irradiated[1]		
1.5 minutes	22	7
6 minutes	51	13

[1]Application was made 3 days after irridation.
*Adapted from reference 118.

related differences have not been found after repeated, daily application of an irritant.[112,113] Black skin was found more responsive to irritation than white skin using objective techniques such as transepidermal water loss and increased cutaneous blood flow, but no differences in erythema or in diagnosed cases of dermatitis have been noted.[114-116] Age decreases the thickness of the stratum corneum, the lipid content, and transepidermal water loss, but visual and objective measures of responsiveness to both irritants and allergens appear to decline with age.[69,117]

Physical Damage

The barrier properties of the stratum corneum, given its thinness, make it quite unique. The important practical aspect of this knowledge is the realization that when the stratum corneum is healthy, it can perform an outstanding job, relative to its thickness, of resisting chemical insults. But if this thin barrier is physically damaged, or the intercellular lipids are altered, the stratum corneum becomes much less of a barrier. Table 5 presents some examples of damage by abrasion and ultraviolet light irradiation to the stratum corneum and the effect on absorption that different types of damage might have.[118]

Abrasions and cuts are probably the most common insults to workers' skin. A nonintact stratum corneum offers little protection against permeation. There have been numerous documented cases where exposure to chemicals, not normally absorbed through the skin in sufficient amounts to cause even mild effects, have actually resulted in death when a few scratches were present. In one case, a women pruning orchard trees that had been sprayed earlier with paraquat developed scratches on her unprotected arms and hands during her work. Normally, paraquat is not a dermal exposure hazard due to its poor permeation through healthy skin. In her case, death ensued from respiratory failure a few days later.[119] Experimentally removing the stratum corneum by tape stripping resulted in 2.6- to 8.5-fold increase in absorption of seven different pesticides.[120] Some dangerous radionuclides, like cobalt-chloride, which are poorly absorbed through intact skin (<0.1%) will rapidly penetrate abraded skin (52%) after 60 minutes.[121]

Table 6: Effect of Chemical Irritation on Percutaneous Penetration*

Compound	Log Partition Coefficient	Percent Enhancement
HC	1.6	260
IM	3.1	160
IB	3.5	190
AC	6	140

*Adapted from reference 129.

Dermatoses

Dermatoses constitute a broad range of skin conditions that can result from a variety of chemical and physical traumas to the skin, and as pointed out before, damaged skin presents a less effective barrier. Dermatitis is certainly a form of damage. This is especially true when the dermatitic skin is in the acute stage of response.

For instance, percutaneous absorption of the pesticide lindane in patients with severe scabies was 10- to 40-fold greater than in normal persons.[122] In other studies, measurable differences were seen in metabolite excretion of carbon disulfide exposed workers and in dimethylformamide exposed workers who had skin irritation or skin disease.[123,124] Percutaneous absorption of xylene vapor appeared to be about three times greater in a volunteer with atopic dermatitis.[125] Finally, a higher blood concentration of a pesticide was seen in a formulator as compared to his coworkers, which was attributable to the presence of scleroderma in the worker with the high blood levels.[126] Hyperproliferation of the stratum corneum, as in psoriasis, exfoliative dermatitis, or ichtyosis, also results in increased permeability of the skin.[127,128] Rapidly generated stratum corneum, while thicker, is usually a poorer barrier.

Irritation Effects

Irritation of the skin can also result in increased percutaneous absorption. The data in Table 6 shows an enhancement in percutaneous absorption that is related to the water solubility

of four model compounds.[129] These compounds were applied to the upper back of hairless guinea pigs after 0.5% sodium lauryl sulfate in water was applied in an occlusive chamber for 24 hours. Because the resistance of the stratum corneum to diffusion is greater to polar compounds than to nonpolar compounds, any disruption of the barrier should enhance penetration of hydrophilic compounds to a greater extent than would occur for lipophilic compounds. In this cited experiment, enhancement was 2.6-fold for the most hydrophilic compound but only 1.3-fold for the most lipophilic.

In another study where sodium lauryl sulfate was used to induce skin irritation, response to nickel salts in sensitized persons and animals was appreciably increased with the addition of the irritant.[130] Irritation, as well as several other factors that can influence sensitization, are reviewed elsewhere.[131]

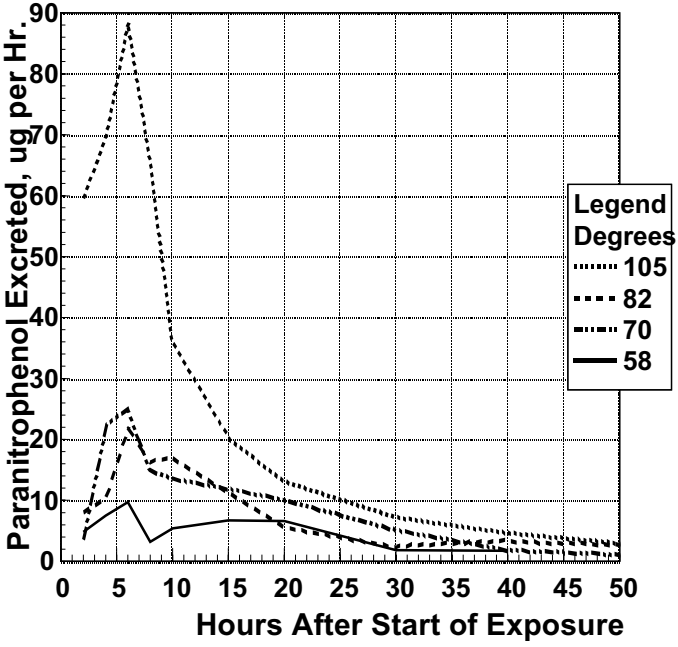

Figure 6: Affect of ambient temperature on percutaneous absorption of parathion dust from the forearm skin. Data from reference 132.

Temperature and Relative Humidity

Molecular diffusion and dissolution will increase within matrices as the temperature increases. It should be no surprise that as temperature increases, the permeation of chemicals through membranes such as the skin will also increase. Normally, the skin surface temperature is between 32–35 °C, but this can increase or decrease with heightened or lowered ambient temperature, or if the temperature of a liquid contacting the skin were different.

Figure 6 shows how the ambient temperature affected the excretion of p-nitrophenol in the urine of human volunteers after 5 grams of 2% parathion dust had been applied topically for 2 hours. Only one hand and forearm were exposed and placed into a temperature-controlled chamber. Following the 2-hour exposure, the skin surface area was decontaminated by scrubbing with soap and water for 5 minutes, followed by two washes with ethyl alcohol. The average excretion rate increased from 4.9 mm/hr at 58 °F (14 °C) to 19.6 mm/hr at 105 °F (40 °C) over a total period of 41 hours.[132] Chemical vapor penetration also has been experimentally determined to increase with ambient temperature. Percutaneous absorption of aniline vapor, for example, increases about 20% for each 5 °C increase in air temperature.[133] Percuta-

Table 7: Percutaneous Absorption of M-Xylene and Mixed Solvent Effects in *In Vivo* Human Skin*

Solvent	Symptoms	Methylhippuric Acid Excretion
Pure Xylene	Erythema No "tightness"	1.0
1:1 Xylene + Isobutanol	Erythema No "tightness"	0.4
10:10:1.5	Mild wrinkling; skin dry and oily	1.1

*Adapted from reference 125.

neous uptake was also significantly increased for 2-butoxyethanol vapor when the air temperature (but also humidity) was increased from 23 °C to 33 °C.[134]

Increasing relative humidity has been shown to increase percutaneous absorption. Chang and Reviere found under constant temperature the percutaneous absorption of parathion increased by two- to fourfold when the humidity was increased from 20% to 90%.[135]

Vehicle

A vehicle in this context is commonly a liquid in which another contaminant, which may be more toxic, is contained. Vehicles are important to percutaneous absorption because they may enhance the absorption rate by either disrupting the stratum corneum barrier function, or encouraging partitioning toward the skin, or a combination of these processes. As will be shown in the next examples, vehicles, or the co-components of a mixture, can have significant effects on how much of a toxic chemical enters the skin.

Another example of vehicle effects on percutaneous absorption, particularly where the vehicle is a mixture of solvents, is demonstrated in the data in Table 7. In this experiment, xylene absorption as measured by methylhippuric acid excretion, was compared to exposures of pure xylene, 1:1 mixture of xylene plus isobutanol, or 10:10:1.5 mixture of xylene, isobutanol, and water to saturation.[125] In each case volunteers immersed both hands up to the wrists in the solvents for 15 minutes at room temperature. Interestingly, the addition of a small amount of water to the mix dramatically increased xylene permeation rate so that it was almost three times greater than the xylene–isobutanol mix, and slightly more than pure xylene alone. With only xylene and isobutanol, there appeared to be a conspicuous dehydration of the skin by isobutanol and a delay in the absorption of xylene evident in the methylhippuric acid excretion (data not shown). The result seen by adding a small amount of water might be due to the increased hydration of the stratum corneum provided by the addition of water, or increasing the partitioning of xylene out of the saturated aqueous mixture towards the skin. This example

may have relevance to wearing CPC as perspiration buildup is commonly associated with this.

More typically, the effect of the vehicle is compared among different pure solvents. The rule of thumb that "likes dissolve likes" applies to permeation in that hydrophilic solutes will tend not to partition to the skin if in a hydrophilic solvent, and lipophilic solutes will tend not to partition as well into the skin if present in a lipophilic solvent. This principle is exemplified by the 10-fold difference in the skin flux rate of benzocaine when in a water (lipophobic) vehicle or in polyethylene glycol (PEG) 400 (lipophilic) vehicle. The solubility of benzocaine in water is 1.26 g/L whereas the solubility in PEG 400 is 435 g/L. The skin flux rates were 0.1 mg/cm^2/hr and 0.01 mg/cm^2/hr, respectively.[136]

Occlusion

Occlusion is one of the most effective means of increasing chemical absorption through the skin and the adverse effects on the skin of occlusion are probably the most important outcomes of wearing CPC. It should be realized

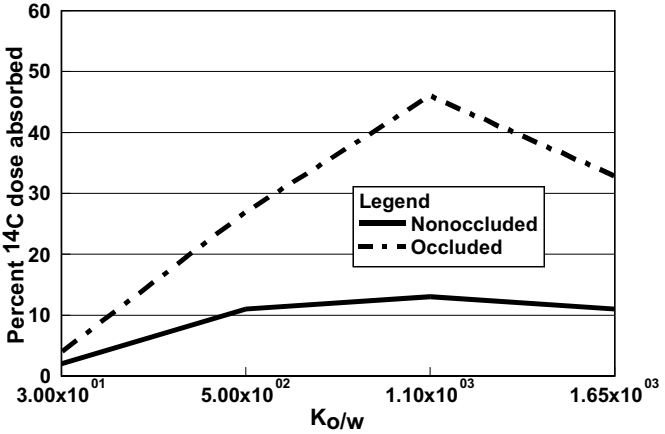

Figure 7: Percutaneous absorption of 4 steroidal compounds with and without occlusion. A single application of 4 μm/cm^2 was applied to the ventral forearm. Occlusion was continuous for 24 hours, after which the site was washed. Mean and SD shown. Data from reference 135.

that in referring to the skin permeation effects of occlusion, the workplace scenario most similar to this is when the contaminant gets underneath CPC. Polymer gloves provide excellent occlusive coverings. Because of the enhanced permeation attributed to occlusion, situations have been reported where increased absorption occurred because the personal protective clothing became contaminated on the inside (see Performance of CPC below).

Covering the skin with a moisture impenetrable barrier not only prohibits evaporative loss of any chemical that may have contaminated the surface of the skin, but increased skin hydration and increased temperature enhances the absorption rate of the contaminant. This effect has long been known, as demonstrated by Burckhardt in 1939, who successfully used occlusion to experimentally promote sensitization to turpentine.[137] With occlusion, nearly all animals were sensitized; without it none were sensitized. In this experiment, the site of exposure was occluded for 8 to 12 hours.

The stratum corneum normally contains between 5–15% water, but this can be increased to as much as 50% by external factors.[138] Occlusion is an effective way to hyperhydrate the skin. The mechanisms by which hydration can influence percutaneous absorption include altering the partitioning between the surface chemical and the skin due to the increasing presence of water, swelling the corneocytes and possibly altering the intercellular lipid phase organization, increasing the skin surface temperature, and increasing the subcutaneous blood flow. It has been postulated that with hyperhydration of the normally lipophilic stratum corneum, the effective partition coefficient of the penetrant between the stratum corneum and viable hydrophilic epidermis is reduced since the two tissue phases now appear more similar.[139] Thus occlusion has been shown to enhance absorption from several percent to several fold in experimental studies.

Occlusion does not appear to influence equally the percutaneous absorption of all compounds. Rather, the impact of occlusion is influenced by the polarity of the chemical. It most increases the absorption of moderately lipophilic molecules but

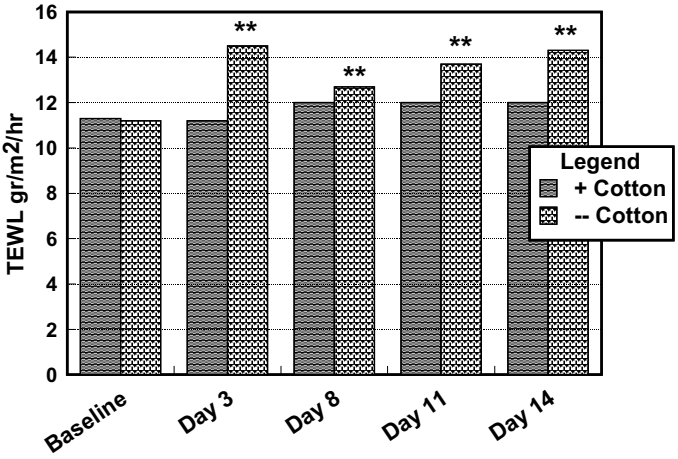

Figure 8: Effect of long-term experimental occlusion on skin integrity. A significant detrimental effect of wearing a glove for 6 hours per day for 14 days was detected by measuring transepidermal water loss, which is indicative of barrier integrity. It was concluded that gloves may be a substantial factor in the pathogenesis of cumulative irritant contact dermatitis, but that with proper use the risk might be minimized. Adapted from reference 144.

is less effective on the absorption rate of highly lipophilic or highly hydrophilic compounds. Figure 7 illustrates this process for four steroids with and without occlusion.[140] There may be some chemical-specific factor that also affects occlusive penetration, since the same degree of enhancement per the K_{ow} is not always seen with all compounds.[141-142] Nevertheless, occlusion appears to enhance percutaneous absorption to some extent for all compounds tested.

Just as the permeability of human skin was shown to vary from location to location, it seems that there are anatomical differences in the extent of enhancement of percutaneous absorption due to occlusion. In an experiment by Qiao et al. using weanling pigs, occlusion greatly increases parathion absorption in most sites tested but to a lesser degree in the skin of the shoulder region.[143] In terms of human relevance, the pig abdominal skin absorption value matches the absorption value for

human forearm skin in nonoccluded tests with parathion. These data also underscore the importance of skin site selection when conducting animal experimentation and comparing results among laboratories.

The above studies demonstrate the increase in permeation due to a one-time occlusion of contaminants on normal skin. In addition, prolonged occlusion has been found to produce chronic impairment of the barrier function of the skin. Figure 8 shows the results of an experiment to determine the long-term effect on barrier function by prolonged wearing of an occlusive glove.[144] The protocol involved having 18 volunteers wear a nonlatex hypoallergenic glove for a minimum of 6 hours per day for 14 days while sleeping at night. It was noted that during sleep skin temperature and friction are reduced (a best-case situation). Half of the volunteers wore a cotton glove underneath the occlusive glove. The results indicated increased transepidermal water loss at each of the measurement days up to day 14 for the skin with the occlusive glove only. However, wearing of the cotton glove prevented this damage. The authors concluded that prolonged occlusion can damage the barrier function of the skin and might enhance susceptibility to irritants and sensitizing agents. Minimizing the wearing of gloves and wearing of a cotton glove underneath are two ways to reduce the occlusive effects on the skin.

Lasting susceptibility to irritants has been demonstrated by Graves et al. after the skin was occluded.[145] In their experiment, the skin was occluded for 4 hours or 8 hours. After the covering was removed, skin permeability was evaluated by measuring the time to onset of hyperthermia due to topical application of the irritant hexyl nicotinate. After 4 hours of occlusion, the time to onset was reduced to 59% of its preocclusion value. After 8 hours of occlusion, this was further reduced to 38% of the preocclusion value. After occlusion, transepidermal water loss was also significantly reduced.

Direct physiological damage to the skin due to skin occlusion is evident. Within two days of occlusion marked cytotoxic damage to Langerhans cells, melanocytes, and keratinocytes occurs.[146] Intercellular edema and marked swelling of

corneocytes are also prominent. Occlusion inhibits production of all key intercellular lipids after barrier disruption, prolonging the normal barrier restoration process.[147-149] The damaging effects of prolonged occlusion can quickly lead to dermatitis.

Interesting questions asked by Graves et al. include the following: (1) at what duration of wearing a glove continuously would there be a significant impairment of the stratum corneum barrier function?; (2) how frequent and how long should nonoccluded periods be to prevent a cumulative effect?; (3) is the impairment of barrier function seen in these experiments sufficient to increase the incidence of irritant contact dermatitis?; and (4) does this impairment correspond to an increased susceptibility to mechanical trauma?[145] These are all relevant and practical questions, and further research will be needed to provide the answers.

Decontamination of CPC and Reuse

Decontamination of used CPC remains a perplexing problem due to great variability of success depending on the CPC material and the chemical of interest. Furthermore, reliable test methods to validate decontamination effectiveness are needed in order to make an informed judgment. If internal contamination of CPC occurs due to incomplete decontamination, wearing of this CPC due to the factors of occlusion described above could lead to substantial absorption of the contaminant. This is the primary health-based reason why reuse of CPC should be avoided, unless confirmation of decontamination effectiveness can be assured.

Performance of CPC In-Use

Several studies have attempted to document the benefit of CPC by measuring the chemical absorbed dose using biological monitoring to reflect internally absorbed dose.[150-154] These studies have found little or no benefit of using CPC compared to working with unprotected skin. Since CPC is expensive to pur-

chase and uncomfortable for the user to wear, this is an unepected and undesired outcome. Assuming that the CPC should provide some barrier protection, there are two possible explanations for this outcome.

One possibility for failing to demonstrate benefit of wearing CPC is that because of poor work practices chemical contamination is allowed inside the user's CPC. Seldom is the contamination that might occur inside CPC checked, which can occur by repeated doffing and donning of the same CPC. Workers' unprotected skin may contact contaminated surfaces when the CPC is not worn, even if for a brief time, or when removing contaminated CPC incorrectly.[155-158] The effect of occlusion, as described above, can significantly enhance percutaneous absorption. The second possibility is that previous chemical contamination residing within the skin depot from previous days may be mobilized by the occlusion caused by CPC. This skin depot mobilization could significantly confound the significance of exposure reduction intervention, especially if the pre-inter-

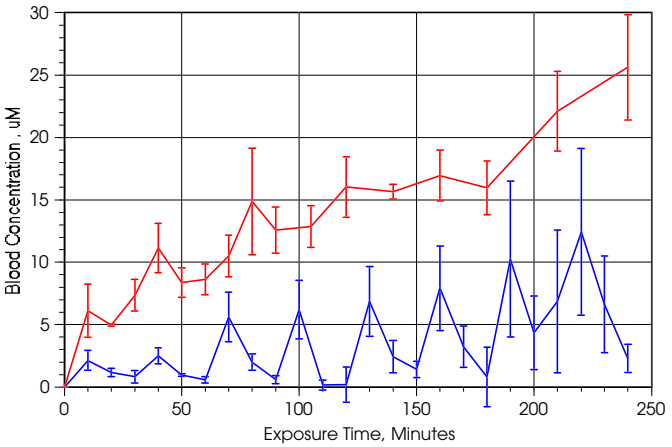

Figure 9: Concentration of n-butanol in blood of guinea pigs during continuous (**---**) and intermittent (-■-) skin exposure. Evaporative loss of volatile chemicals from uncovered skin will prevent large amounts of absorption from occurring, but continuous exposure may occur if solvents penetrate holes in CPC. Adapted from reference 163.

vention consisted of unprotected exposure and the intervention being evaluated consisted of wearing CPC. All of the cited CPC intervention effectiveness studies performed biological monitoring soon after introduction of the CPC. Both scenarios, consisting of enhancing absorption of albeit lesser amounts of exposure, or mobilizing residing skin depot, are both effects of occlusion that can come from wearing CPC. To reiterate, the outcome was among these CPC intervention effectiveness studies was that no difference or an increase in absorbed dose occurred after the introduction of CPC.

On the other hand, workers who have been regularly wearing gloves for a period of time, compared to workers who typically do not wear gloves, appear to benefit.[159,160] For instance, in one study of greenhouse workers who wore new thin nitrile gloves each day there was a statistically significant difference of serum cholinesterase activity compared to workers who worked bare-handed.[161] Only in future studies, where good work practices are ensured and where the worker is allowed an adjustment period that will factor out this second scenario, will the real benefit of using CPC be known.

In the workplace contact with chemicals may be intermittent and sporadic. A key characteristic of the chemical that will determine the residence time of a single contact is the volatility of the chemical. For uncovered skin, highly volatile chemicals will evaporate before appreciable percutaneous absorption occurs.[162] Volatility inversely correlates with the persistence of a chemical on the skin surface and the amount of chemical ultimately absorbed systemically. Figure 9 presents the results of continuous dermal exposure to n-butanol (vapor pressure = 6 mm Hg) and 1-minute exposure every 30 minutes. The periodic exposure results in a blood concentration that is lower than for continuous exposure. For more volatile compounds, such as toluene (v.p. = 21 mm Hg) and 1,1,1-trichloroethane (v.p. 100 mm Hg), no such cumulative effect occurs.[163] The absorbed dose of highly volatile compounds from repeated short exposures is appreciably less when compared to continuous immersion.[110] Presumably, the systemic absorption of less volatile compounds than n-butanol would eventually approach continuous contact conditions as evaporative loss decreases.

The relevance of this is that liquid chemicals entering pinholes or cuts in gloves will likely remain in contact with the skin for much longer periods of time if not allowed to evaporate. Liquid chemicals are typically low molecular weight compounds and are readily absorbed through the skin. Pinholes in certain new gloves have been reported in a substantial proportion of the time and in used gloves the chance of cuts increases with duration of use.[164-165] Double gloving has been shown to be effective in reducing the probability of skin contact due to the occurrence of tears or chemical permeation. Furthermore, it is important to monitor the condition of gloves periodically and not to use them for extended durations.[166-170]

Summary

Human skin is a marvelous creation that should be treated with care. The skin evolved long before the existence of chemicals that are encountered in the 21st century. It also evolved to be exposed to the open air. Therefore, chemical exposures and the use of CPC are to the skin unnatural conditions. There must be balance and judicious use of CPC in order for it to be most effective. Having a good understanding of the skin and its limits by interaction with the environment and to chemical exposures is important to optimizing the benefits of CPC and for reducing absorption of toxic chemicals or deleterious effects on the skin itself. The goal of this chapter was to highlight those factors that the occupational health and safety person responsible for a CPC program should be aware of in order to meet those aims.

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