Dermal Exposure to Environmental Contaminants in the Great Lakes

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This paper reviews the literature to determine the importance of the dermal route of exposure for swimmers and bathers using Great Lakes waters and summarizes the chemical water contaminants of concern in the Great Lakes along with relevant dermal absorption data. We detail in vivo and in vitro methods of quantifying the degree of dermal absorption and discuss a preference for infinite dose data as opposed to finite dose data. The basic mechanisms of the dermal absorption process, routes of chemical entry, and the environmental and physiological factors affecting this process are also reviewed, and we discuss the concepts of surface slick exposure to lipophilic compounds and the adsorption of contaminants to water sediment. After presenting mathematical constructs for calculating the degree of exposure, we present in vitro data concerning skin absorption of polyaromatic hydrocarbons adsorbed to Great Lakes water sediment to show that in a worst-case scenario exposure via the dermal route can be equally important to the oral route. We have concluded that prolonged exposure of the skin, especially under conditions that may enhance dermal absorption (e.g., sunburn) may result in toxicologically significant amounts of certain water contaminants being absorbed. It is recommended that swimming should be confined to public beaches, people should refrain from swimming if they are sunburned, and skin should be washed with soap as soon as possible following exposure. Future studies should be conducted to investigate the importance of the dermal exposure route to swimmers and bathers. — Environ Health Perspect 103(Suppl 9):103–114 (1995)

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Introduction

The potential for dermal exposure to water contaminants in the Great Lakes is high since it is likely that people using these lakes for occupational or recreational purposes will expose their skin to lake water and hence to the wide variety of chemical contaminants known to pollute these waters. In a worst-case scenario, a marathon swimmer would be expected to be dermally exposed over the entire body surface area for an extended duration of time. Conversely, short-term exposure to local inhabitants bathing in the water and even indirect exposure resulting from skin contact to wet clothing must be considered.

Skin contamination may also occur via exposure to sands and soils at the lakeshores. Shu et al. (1) have reported a low degree of bioavailability (about 1% of the applied dose) of tetrachlorodibenzo-p-dioxin (TCDD) via the dermal route in rats exposed to soil bound TCDD. Yang et al. (2) observed skin absorption of benzo[a]pyrene (B[a]P) from soil spiked with petroleum crude oil. Wester et al. (3) reported dermal absorption of B[a]P and 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane (DDT) from soil in rats, and Skowronska (4) has related the effect of soil composition (sand versus clay) to the dermal absorption of toluene in rats. In vitro studies conducted with skin specimens removed from animals have also indicated that dermal absorption of contaminants from soils may occur; these studies include those of Wester et al. (5) (cadmium into human cadaver skin) and Wester et al. (6) (chlordan into human cadaver skin). Bucks et al. (7) recently reviewed the dermal absorption of environmental contaminants from soils and should be consulted for a more quantitative assessment.

Percutaneous absorption of water contaminants has only very recently been considered by the scientific community to be a significant exposure route. Previously the inhalatory (breathing) and oral (ingestion) routes were considered to be the most significant routes of exposure to environmental contaminants. Wester et al. (8), however, have reported that chemicals can be absorbed through the skin in quantities sufficient to be considered toxicologically significant and have detailed a mathematical construct for calculating the bioavailability of water contaminants during bathing and swimming. More recently we have reported that dermal absorption of low levels of cyanuric acid, a swimming pool stabilizer, can be observed employing an in vitro flow-through procedure with human skin to mimic swimming pool exposure scenarios (9). This in vitro study followed early in vivo observations that cyanuric acid exposure could be quantified by high-performance liquid chromatography (HPLC) analysis of the urine of long-distance swimmers in a controlled swimming pool study (10). Unfortunately, as discussed in our report (9), the in vitro data could not be related to the in vivo data of Allen et al. (10) because their study did not permit an accurate estimation of the degree of dermal absorption due to a wide variation in the reported data.

Before considering a number of studies pertinent to percutaneous absorption including in vitro and in vivo methods of quantifying absorption, routes of exposure (dermal, oral, inhalatory), as well as the concept that absorption may result from exposure to water contaminants either bound to water sediment (silt, phytoplankton, etc.) or unassociated (free) contaminants dissolved
in lake water, it is necessary to consider the types of chemicals known to contaminate the Great Lakes waters and to review the literature concerning the dermal absorption of these compounds. A list of these chemicals of concern is shown below.

**Organochlorines**

- Polychlorinated biphenyls
- Mirex
- Dioxins and furans
- DDT and metabolites
- Dieldrin
- Hexachlorobenzene
- Hexachlorobenzene
- Chlorodane and metabolites
- Heptachlor and heptachlor epoxide
- Toxaphene
- Octachlorostyrene

**Metals**

- Mercury
- Lead
- Tin
- Cadmium

**Others**

- Volatile organic compounds (tetra-chloroethylene, trihalomethanes, etc.)
- Polyaromatic hydrocarbons (BaP, etc.)
- Phthalates (DEHP, etc.)

After briefly outlining the basic mechanisms thought to govern the ability of chemicals to be absorbed through the skin, this review will consider factors (both environmental and physiologic) that have been reported to affect the degree of skin absorption. Some data recently acquired in our laboratory will be presented concerning the dermal absorption of polychlorinated hydrocarbons (PAHs) from sludge samples taken from the Great Lakes. The dermal uptake for swimming or bathing exposure scenarios will be calculated and conclusions and recommendations will be made.

**Organochlorines**

Organochlorine (OC) water contaminants of concern in the Great Lakes basin include a wide variety of compounds [e.g., polychlorinated biphenyls (PCBs), mirex, dioxins, and furans, 1,1,1-trichloro-2,2-bis (p-chlorophenyl)ethane (DDT) and metabolites, dieldrin, pentachlorophenol (PCP), hexachlorobenzene (HCB), hexachlorocyclohexanes (HCHs), chlordane and metabolites, heptachlor and heptachlor epoxide, toxaphene, and octachlorostyrene]. Exposure to low molecular weight OCs such as chloroform will be discussed later in a separate section concerning exposure of bathers to tap water.

PCBs are ubiquitous in the environment. They are extremely fat-soluble (lipophilic) compounds [log $K_{ow} > 6$; log $K_{ow}$ (log octanol/water partition coefficient) and hence may bioconcentrate in the body fats of aquatic organisms including the aquatic microflora (phytoplankton) and microfauna that comprise much of the waterborne sediment present in the Great Lakes. Hence, although the water solubility of PCBs is very low (µg/l; ppb range), these and other lipophilic compounds may be carried in relatively high concentrations on suspended sediment in lake water; these sediments may act as a carrier for transdermal delivery of lipophilic compounds. Dermal absorption of PCBs has been reported both in vivo and in vitro (11,12); however, there are no literature reports concerning PCB dermal absorption in bathing, showering, or swimming situations. Lees et al. (13) has provided evidence that dermal absorption following occupational exposure is the major route of exposure to PCBs by hydro transformer repair and maintenance personnel.

Mirex is a lipophilic OC Insecticide that was commonly used in the 1960s and 1970s in the United States to control imported fire ants and as a flame retardant. Although mirex is no longer registered for use in Canada or in the United States, it is persistent in the environment and may reach the Great Lakes basin via surface runoff from contaminated soils or by leaching from hazardous waste sites. Recently Sergeant et al. (14) reported that mirex was detected in several water and fish samples taken from the Great Lakes basin and expressed concern that the occurrence of mirex in the Great Lakes was widespread. Dermal penetration data for mirex, however, were not located in the literature. Residues of mirex and its photodecomposition product, photomirex, have been observed in herring gulls from Lake Ontario (15). The acute toxicity, mutagenicity, and biodistribution of photomirex in rats treated orally was addressed by Hallet et al. (16). Residues of mirex, PCBs, and dichlorodiphenyldichloroethylene (DDE), a metabolite of DDT, were reported in waterfowl by Kim et al. (17), and it is interesting to question whether dermal absorption of water contaminants plays a significant role in waterfowl exposure. The oral route via ingestion of contaminated fish is commonly considered to be the major route of exposure to fish-eating birds since biomagnification of lipophilic water contaminants in fish has been frequently addressed (18-23).

Dioxins and furans are extremely lipophilic compounds with log $K_{ow}$ values ranging up to 7. Organochlorine residues including dioxins have been quantified by Williams et al. (24) in human adipose samples collected in Ontario. Skin exposure to environmental contaminants including dioxin has been reviewed by Shah et al. (25). In vitro dermal absorption of TCDD has been investigated by Weber et al. (26). The in vivo dermal absorption of TCDD in rats was reported by Brewster et al. (27), who also investigated the dermal absorption of three PCB dibenzofurans. Brewster et al. (27) demonstrated a lower percentage of dermal absorption of TCDD when the dose concentration was increased. They also observed that up to 48% of the applied TCDD was absorbed dermally. Banks and Birnbaum (28) reported 41% dermal absorption with TCDD applied in low dose applications.

The insecticide DDT, another lipophilic compound (log $K_{ow} < 6$) has been observed to be dermally absorbed in humans, although only 10% absorption was obtained from a dose of 4 μg/cm² of the pesticide when applied to the skin using ace tone as the vehicle (29). Grissom et al. (30) reported approximately 25 to 30% absorption of DDT in mice; however, mouse skin is considered to be more permeable than human skin, and problems concerning the use of animal models to predict human dermal absorption have been discussed by Bronaugh and Maibach (31). Bronaugh et al. (32) related the effect of skin viability to the dermal metabolism of compounds applied topically, including DDT. Biotransformation of the OC insecticide aldrin to its dieldrin metabolite has been reported to occur in rat skin (33).

Of the remaining OC compounds listed above, there is a paucity of reports relevant to dermal absorption. Biodistribution, fat storage, and metabolism of the wood preservative PCP has been observed for rats dosed orally (34). The effect of water pH and the log $K_{ow}$ of PCP has been established (35) and is relevant here to the affect of lake water pH on dermal absorption. The in vivo dermal absorption of PCP and tetrachlorophenol has been reported in human skin (36). Skin absorption of PCP was greater from diesel oil than from water. Dermal toxicity and adipose persistence of HCH have been reported in rabbits (37). The toxicity of toxaphene in rats and beagle dogs has been described by Chu et al. (38).

**Metals**

Water contamination by mercury, lead, tin, and cadmium is of particular concern in the
Great Lakes basin. Dermal absorption of mercury vapor in humans has been observed in a study by Hursh et al. (39), and only 2.6% of that absorbed via inhalation was found to be absorbed through the skin of the forearm. Dermal absorption of mercury vapor following exposure of the tails of rats was reported by Wansher et al. (40). Analysis of human sweat has been used to monitor the absorption of lead through the skin (41). In vitro skin absorption of organolead, inorganic lead, and lead salt with human skin and in vivo absorption with guinea pigs has also been discussed (42). Wester et al. (5) recently reported that cadmium applied as the chloride salt was dermally absorbed from both water and soil following in vitro tests with human cadaver skin. Wester et al. (5) calculated that, assuming a value of 0.5% dermal absorption following whole-body immersion, a total of 10.4 μg of cadmium would be absorbed daily by a human subject continuously exposed to water containing 116 ppb of cadmium. This calculation will be discussed in detail when we consider mathematical models of dermal absorption.

Others

Other chemical contaminants of concern in the Great Lakes basin waters include volatile organic compounds (VOCs) (tetrachloroethylene, trihalomethanes etc.), PAHs (B[a]P, etc.) and phthalates (di-2-ethylhexyl phthalate [DEHP], etc.). The dermal absorption of tetrachloroethylene and other organic solvents (e.g., benzene and toluene) in a vapor (gaseous) state has been reported by Tsuruta et al. (43) using nude mice tested in vivo. Tsuruta et al. (43) obtained a linear correlation between dermal absorption and the Kww for the compounds tested. Bogen et al. (44) reported dermal absorption of tetrachloroethylene, trichloroethylene, and chloroform when hairless guinea pigs were bathed in water containing low concentrations of these compounds. Morgan et al. (45) observed the blood levels of several VOCs (chloroform, benzene, toluene, xylene, tetrachloroethylene, etc.) in Fischer rats exposed dermally to aqueous VOC concentrations ranging from one-third of water saturation to full saturation. Dermal absorption of B[a]P from a soil matrix has been discussed previously. Kao et al. (46) reported in vitro dermal absorption and skin metabolism data for B[a]P applied topically to six mammalian species including humans. Bickers et al. (47,48) observed that B[a]P could be metabolized in the skin of mice and rats and that it was metabolized by cutaneous aryl hydrocarbon hydroxylase (AHH) enzymes in humans. The more recent study by Alexandroff et al. (49) suggests that B[a]P cutaneous metabolism may be localized predominantly within the region of the epidermal hair follicles. In vitro data is available to show that α-phthalate diesters can be absorbed through human and rat skin (50) and Elsea et al. (51) reported in vivo skin absorption data for phthalate diesters with rats. The in vitro and in vivo dermal absorption of DEHP, pyrene, and B[a]P in hairless guinea pigs was described by Ng et al. (52). In the Ng study (52) it was necessary to include the residues of the test compounds persisting in the dosed skin region to obtain good agreement between the in vitro and in vivo dermal absorption data. This concept of a bioavailable skin depot of persistent residues will be discussed in detail when we consider the mechanism of the dermal absorption process.

Johnsen et al. (53) discussed the possibility of a health risk resulting from the formation of chlorinated PAHs in drinking water. A health risk could exist for bathers using chlorinated tap water derived from the Great Lakes basin if PAH levels are permitted to exceed safe levels and are not filtered out by the water treatment facility.

Mixtures

Most of the literature concerning percutaneous absorption deals with skin exposure to only one chemical at a time. This is due to the fact that the main interest in dermal absorption in the past has been focused either upon the efficacy of transdermal delivery of pharmaceuticals or the occupational exposure of field workers to individual pesticides. Dermal contact with lake water, however, involves exposure to a complex mixture of water contaminants. Given frequent reports of synergistic and antagonistic effects of chemicals in the toxicology literature, it seems likely that such mixture effects may play a part in determining the degree of dermal absorption of water contaminants. Mixture effects of PAH compounds on the dermal absorption of B[a]P have been investigated in mouse skin (54). Dankovic et al. (54) reported that greater skin persistence of B[a]P was observed when it was present on the skin with PAH; this was explained on the basis that PAH inhibited the cutaneous metabolism of B[a]P. As well as inhibition, it is likely that exposure to PAH compounds can induce cutaneous AHH activity, although whether this would occur at the low levels of PAH present in the Great Lakes basin waters remains to be determined. Boman (55) observed enhanced dermal penetration by organic solvents in a ternary mixture applied to the skin of guinea pigs.

Percutaneous Absorption via Environmental Media

Dermal exposure to environmental water contaminants in the Great Lakes basin may follow skin contact with contaminants dissolved in the lakewater, with contaminants either adsorbed or absorbed to water sediment floating in the lakewater, or by contact with sands and soils situated at the lake shores. Dermal exposure to airborne particulates and gaseous state pollutants or to those present in rainfall in the Great Lakes basin are thought to be insignificant in comparison to water pollutants and will not be considered further here.

Most of the compounds of concern in the Great Lakes basin discussed so far are not very water soluble. For example, DDT is only soluble up to about 1.2 ppb in water, and many of the other compounds discussed are less hydrophilic than DDT (e.g., TCDD, PCBs). Hence, dermal exposure to lipophilic compounds has previously tended to be ignored since water concentrations of these contaminants are usually very low. This rationale, however, does not take into account the fact that high levels of these contaminants can bind or partition into the organic component of lake-water sediment suspended in the water column. Furthermore a thin layer of oil known as a surface slick is present over all natural bodies of water and lipophilic compounds would tend to concentrate in this layer (56,57). Hence, it is likely that swimmers and other people contacting the lake-water surface would encounter this surface slick and the concentrated source of water contaminants therein. Dermal exposure to environmental contaminants in lake-water sediment and surface slicks will be considered in greater detail after the discussion of the mechanisms of dermal absorption.

Factors Affecting Exposure via the Dermal Route

Mechanisms of Absorption

Passive diffusion, as governed by Fick's First Law, is held to be the main process whereby chemicals enter and permeate through the skin. The human skin is the largest organ of the body. It consists of a thin (approximately 100 μm) epidermal layer superimposed on a thick dermal layer.
The stratum corneum (SC) consists of four layers, the outermost layer being the stratum corneum (SC) (approximately 10–40 μm), which overlays the strata lucidum, granulosum, and germinativum (Figure 1). The SC layer is composed of flat highly keratinized squamous cells that are nonviable and are thought to maintain the barrier properties of the skin. If the SC layer is removed by tape stripping, for example, the permeability of the skin to chemicals increases dramatically.

Perhaps the simplest analogy of the dermal absorption process has been put forward by Tojo (58), who used a random brick and mortar concept to illustrate the dermal permeation of chemical molecules. The bricks are the SC cells, or keratinocytes, and the mortar between the bricks comprises the network of intercellular channels. Hence, dermal absorption can be viewed as both an intercellular and intracellular immigration of water contaminant molecules through the cell layers of the SC. Since the intracellular route is constituted mainly by a lipid milieu of cell membranes, it is commonly held to be the diffusion pathway for lipophilic peramets. The intracellular route with its component of aqueous cytoplasmic materials is thought to be the route for the more water-soluble hydrophilic compounds. A lipidic transcellular absorption route has also been described that involves intracellular diffusion through lipid microfibrils present within the cell cytoplasm. The hair follicle shafts are thought to provide a further route of entry known as the transappendageal shunt pathway. The shunt pathway is considered to be most important during the early stages of the absorption process, especially for lipophilic compounds. The eccrine sweat glands and the apocrine glands are also thought to confer permeation routes. After entering the epidermis, the permeant molecules diffuse to the dermis where a microcapillary bed of blood vessels serves to carry the contaminant molecules away from the dermis. Once the permeating molecules have entered the blood, they are considered to be bioavailable.

**Hydration.** Several reviews have discussed the basic mechanisms that are thought to explain the ability of a chemical molecule to migrate through the skin (31, 59, 60). These reviews, however, have been mainly concerned with absorption of chemicals contacting skin exposed to the air, not to an aqueous medium as encountered by swimmers, bathers, and others exposed to Great Lakes basin water. This difference is critical since even the fact that the skin is exposed for an extended duration to water may dramatically enhance the permeability of the skin to water contaminants. It is well documented in the medical literature that skin hydration may increase skin permeability to certain compounds by factors ranging up to 1000-fold (for review see Roberts and Walker (61)). In fact, to promote penetration of a topically applied medicament, physicians will often resort to occlusion of the treatment region to enhance drug permeation and thereby provide maximal efficacy for a topical pharmaceutical formulation. It is thought that occlusion of the skin with a bandage, for example, will keep a fully humid atmosphere above the skin dose region and the resulting uptake of water by the skin will cause a swelling of the skin tissue that in some way increases its permeability to water soluble compounds. One theory of how skin hydration increases skin permeability is simply that the resultant swelling of the SC tissue layer produces a more diffuse integument to the immigrating chemical peramets. Another explanation concerns the cracking of the intercellular lipid mortar by the swelling of the keratinocyte bricks (61). Of course hydration of the skin following sweat exudation from the eccrine glands may also enhance skin permeability. In fact, once the swimmer has left the water, sweat may interact with the water sediment adhering to the skin in ways that could decrease exposure via runoff or increase exposure by liberating the environmental contaminants adsorbed to the sediment deposit. The stratum corneum milieu of a typical beach person is a changing and complex environment where sweat, sun tan oils, mosquito repellents, etc., may interact to influence the persistence and bioavailability of contaminant deposits.

**Thickness of the SC and Anatomic Site.** The SC varies in thickness with anatomic region and is thickest on the palms and the soles of the feet and thinnest about the genital region and in the axilla. SC thickness has been cited in the past to explain the wide variation in anatomic site-related skin permeabilities that have been reported for humans, rhesus monkeys, and other animal species (62–64). For example, Maibach et al. (62) found 100% absorption of parathion applied to the testicular

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**Figure 1.** The microanatomy of human skin.
region in humans. Since a swimmer or bather would be fully immersed in water, one must consider the potential for a high rate of entry of chemicals through regions unprotected by thick SC layers.  

**The Effect of $K_{ow}$.** The SC layer tends to be a lipid-rich milieu and hence provides a barrier to hydrophilic compounds but permits the entry of lipophilic compounds. Some preliminary studies have examined the correlation of the permeation rate ($K_p$) of a compound with its lipophilicity as quantified by the octanol/water partition coefficient ($K_{ow}$). The permeation rate is usually expressed as a $K_p$ value with units of centimeter per hour. Several reports have suggested linear correlations between $K_{ow}$ and $K_p$ for chemicals belonging to homologous series (e.g., benzene, naphthalene, phenanthrene, etc.); however, more recent studies have indicated that these correlations fail at extremes of hydrolipophilicity, and even parabolic correlations have been described (65, 66). It is interesting that a similar parabolic correlation has recently been reported between the logarithm of $K_{ow}$ and the logarithm of the bioconcentration factor (BCF) of 154 chemicals found in naturally exposed freshwater fish (67). Similar to that observed in dermal absorption studies, the positive correlation between log $K_{ow}$ and log BCF fails for very lipophilic compounds.

An important difference here from the usual percutaneous paradigm is that lipophilic water contaminants will tend to be strongly sequestered within the water sediment component of the aquatic habitat. In fact, if the water contaminant were irreversibly bound to the water sediment, skin absorption would be unlikely. If, however, the water contaminant was loosely associated with the sediment particle, for example, via partitioning of the chemical within a lipid component of the particle (e.g., within the lipid membranes of unicellular phytoplankton [algae]), then the chemical could depauperate to the stratum corneum and thereby enter the skin. The rate of sediment/skin transfer would be dependent on the “darmaphilicity” of the compound. It should be apparent that this is not necessarily an abiotic chemico-physical process. A large proportion of aquatic sediments borne in the water column are living microorganisms such as algae and other microbria that are known to bioconcentrate water contaminants. Bioconcentration of the lipophilic ($\log K_{ow} = 3.2$) pesticide, fenitrothion, was observed in suspended water sediment taken from a stream following a spruce budworm spray program near Winnipeg; it was suggested that this bioconcentration of the pesticide was due in part to microalgae (68). Subsequent field studies demonstrated bioconcentration of fenitrothion into three common species of microalgae in a controlled field study (69) and laboratory studies (RP Moody, unpublished data) indicated that this bioconcentration of the insecticide was highly regulated by solar irradiation. Hence, the risk of dermal exposure to water contaminants by swimmers may be controlled partially by environmental conditions such as solar illumination. The situation becomes more complex when one considers the fact that microbria can metabolize water contaminants (69). As well as dermal exposure via depauperation of water contaminants from suspended sediment particles, direct exposure may occur by adherence of the sediment particles to the skin. Transfer of chemical contaminants from soil particles to the skin has been discussed previously. One would expect a slower rate of transdermal delivery of the soil-associated contaminants than if the compound was applied alone to the skin. Washing the skin with soap immediately following exposure would be advisable to remove this sediment depot before transdermal delivery could occur. The process of sediment/skin transfer of water contaminants is shown in Figure 2.

**The Dermal Microdepot.** Recent in vitro studies have suggested that a dermal reservoir or depot may form and persist following topical applications of environmental contaminants (52, 70, 71). Considering the relatively long exposure period expected for swimmers, it is quite possible that a similar skin depot could form during exposure. Given the low concentrations of water contaminants in the Great Lakes basin waters, however, it is unlikely that this depot would amount to anything comparable with that following direct topical exposure to a chemical; we will refer to this persistent residue as a microdepot. Although this microdepot may persist in the skin for some time following exposure, our studies suggest that a washing in of this microdepot may occur following soapy water washing of the skin and that these residues could then become bioavailable (71). The early pioneering work of Maibach (62) suggests that the length of time that elapses between exposure and washing will affect the washability of skin residues; the shortest elapsed time intervals will provide the best success with skin decontamination. Hence, it may be advisable to shower as soon as possible following swimming.

**The Effect of Surface Slicks.** It is well documented in the literature that surface slicks comprised of fatty substances (e.g., lipids from decomposed organisms and oil from petroleum contamination) cover the surface of all natural bodies of water. A swimmer submerging or emerging from the lake water would be expected to contact this oil film over large areas of body surface. Due to wind action, this oil slick is often concentrated near shore regions where swimming is most prevalent. It would be expected that lipophilic compounds (such as PCBs, DDT, dioxin, etc.) would tend to concentrate within this oily surface slick; in fact, a relatively high level

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**Figure 2.** Schematic diagram of the transfer of water contaminants from lake water sediment particles to the skin surface.
of the lipophilic insecticide fenitrothion has been reported in the surface slick of river-water samples collected following the aerial spray program mentioned previously (68). Platford et al. (56) have observed the preferential partitioning of DDT and HCB residues in a surface film set up in the laboratory to model aquatic surface slicks. To our knowledge this concept has not been examined previously in reference to dermal exposure of swimmers. We suggest that a research study be undertaken to examine the importance of surface slicks may have on increasing dermal exposure to water contaminants.

Other Factors Influencing the Degree of Absorption
As well as factors already discussed (such as skin hydration, lipophilicity, SC thickness, degree of sediment binding, the presence of surface slicks, and anatomic site-related differences in skin permeability), many factors, both environmental and physiologic, are known to affect the degree of dermal absorption. Environmental factors include water temperature, pH, turbidity, flow rate (current), and degree of solar illumination. Physiologic factors include genetic-related sensitivity (e.g., tendency to sunburn) and individual differences (e.g., age, the presence of skin disease, skin abrasions).

Solar Irradiance. The sunburn factor may be critical since peeling off of the SC layer following a severe sunburn could in theory increase the skin permeability by several orders of magnitude. This follows from the observation that tape stripping of the SC is known to increase skin permeability severalfold. Skin exposure to ultraviolet (UV) radiation may improve barrier function due to a UV-B (290–320 nm) induced thickening of the SC according to one study (72); however, increased skin permeability to primary alcohols (e.g., ethanol) was reported by McAuliffe and Blank (73) following exposure of human skin to UV-A (320–400 nm) irradiance. No significant effect of shortwave UV (200–400 nm) light was observed for the permeability of human skin to the insect repellent DEET (74).

Temperature. According to literature reports with in vitro tests conducted over a range of temperatures, the effect of water temperature could be predicted to roughly double the rate of dermal absorption for each increase of 10°C in the lake water (60). The effect of temperature should be investigated in controlled in vitro studies with tests being conducted through the range of 4°C to 45°C to include exposure to cold lake water in the early spring and hot bath and shower water.

Water Flow Rate. The effect of the flow rate of water over the skin surface, whether resulting from local currents in the lake or the swimming motion itself, is a further confounding factor. In theory a faster flow rate should increase the rate of transfer of sediment-associated contaminants by increasing the frequency of sediment/skin hits. Also in theory, a stagnant interfacial layer of water would exist between the skin and the flowing lake water, and unassociated contaminant molecules dissolved in the flowing water would have to traverse this layer via the slow process of diffusion. At faster water flow rates, the thickness of this stagnant water layer would diminish with the result that decreased time would be required for diffusional transfer and hence dermal exposure would increase. The in situ effects of such factors on the rate of dermal absorption of water contaminants will have to await research studies to examine their combined effect.

Physiologic Factors. The effect of age on skin permeability is most relevant when considering the risk of exposure of children and the elderly. Dick and Scott (75) have reported in vitro Kp values for tritiated water permeation of 1.16 and 1.41 × 10−3 cm/hr for epidermal skin sections taken from Alderley Park and Sprague-Dawley rats, respectively. As well as demonstrating similar Kp values for the two rat species tested, Dick and Scott (75) observed no significant effect of rat age on skin permeability except in Sprague-Dawley rats older than 80 days, which exhibited somewhat lower Kp values than the skin from younger rats. Roskos and Maibach (76) have recently reviewed studies concerning the effect of age on skin permeability, and Wester and Maibach (77) can be consulted for review of skin conditions (e.g., abrasions, disease) that may alter the permeability of the skin to environmental contaminants.

Animal Models of Dermal Absorption
Both in vitro models with isolated skin specimens and in vivo models with living animals are in common use for estimating dermal absorption. These methods have been extensively reviewed (31,59,60). The excreta of animals including human subjects has been analyzed following swimming exposures to estimate dermal exposure; however, it is difficult to control for the water that might be ingested during such experiments as well as for inhalation of volatiles, although face masks with air tanks have been used. In vitro tests with isolated skin specimens have been used in place of in vivo tests with living animals although the in vitro/in vivo concordance of the dermal absorption data obtained is not yet validated. For example, in the Wester et al. (5) in vitro chlordane study, in vivo tests with rhesus monkeys were also conducted. Although the rhesus monkey is commonly considered to be an accurate model for predicting human dermal absorption, the Wester (5) in vivo monkey tests predicted a much higher degree of skin absorption than that observed in vitro with human skin. The reliability of in vitro studies for predicting in vivo dermal absorption is a concern of ongoing validation tests.

In vitro methods do have several advantages to in vivo procedures. For example, ethical concerns rule out the testing of animals at the extremes of environmental conditions such as water temperature and pH. Also, in vitro methods are usually preferable for precise control of environmental conditions. Wester et al. (5) have described the use of Franz in vitro skin permeation cells for investigating dermal uptake of cadmium dissolved in water; however, a finite dose procedure was used in these studies since water volumes of only 2.5 and 5 μl/cm² of skin surface area were employed. A more relevant dose procedure employs an infinite dose to mimic the exposure scenario encountered by a swimmer. We have recently reported a modified flow-through cell design for monitoring dermal exposure of cyanuric acid in a swimming pool type of situation (9). The design of this skin permeation cell permits an interface with both infinite flowing receiver and donor solutions, and the chemico-physical conditions of the donor (lake) solution (e.g., flow rate, temperature, pH) can be varied and monitored during each study (Figure 3). Currently, we are establishing an automated HPLC analysis
Method of Calculating Dermal Absorption

The method of calculating dermal absorption has been described in previous reports for both in vivo and in vitro dose studies (71,78). These studies commonly rely upon radiotracer methodology with liquid scintillation counting analysis. Basically the in vivo procedure involves treating a known area of skin (usually about 1 to 5 cm²) with a ¹⁴C-radiolabeled test compound and then collecting the excreta (urine and feces) until ¹⁴C activity in the excreta are no longer detectable (usually 5–7 days). The total percentage of recovery of the ¹⁴C-radiolabel in the excreta is reported as the percent dermal absorption.

The preferred in vitro procedure involves obtaining a viable skin specimen either by removal following necropsy of animals or from a donation of a specimen following human surgery. Human-derived tissue cultured skin models are also available (71). With the exception of the thin tissue-cultured specimens that are used as is, the outer skin layer (approximately 0.3–0.5 mm) is removed with a dermatome, the section including the epidermis, and some of the dermis (79). The skin specimen is then clamped into an in vitro permeation cell. Several types of permeation cells are in use, the most commonly used being the glass Franz cell and the Teflon Bronaugh cell. Although Ault et al. (80) have reported the use of a modified Franz cell in a microdialysis procedure that permitted them to conduct a flow-through type assay, the standard Franz cell uses a stagnant (non-flow-through) receiver solution for collecting the permeative residues from the untreated skin surface. The Bronaugh cell uses a flow-through receiver solution that mimics the flowing nature of the dermal vasculature. In more recent in vitro studies, serum albumin and other factors (e.g., glucose and other nutrients) are added to the receiver solution to maintain skin viability during the permeation assay. Neither permeation cell type, however, permits the use of a flow-through donor solution over the skin epidermal surface; we have reported the design of an aluminum cell that permits multireplicate analysis of skin permeation from a flowing stream [Figure 3; (9)]. After dissolving the ¹⁴C-labeled test compound in the donor solution, the receiver solution is collected for analysis until permeation equilibrium has been established. Once the permeation rate of the test compound has reached steady state, the $K_p$ of the compound (centimeter per hour) can be calculated simply by dividing the flux (J) of the compound (microgram per square centimeter per hour) by the concentration ($C_w$) of the test compound (microgram per cubic centimeter) in the donor solution as follows:

$$K_p = J / C_w \quad [1]$$

It should be clear that the $K_p$ cannot always be derived from finite-type dosing situations since steady state permeation kinetics are not necessarily attained unless infinite (nonlimiting) dose volumes are employed. However, as described in a recent interim draft on dermal exposure assessment by the U.S. Environmental Protection Agency (U.S. EPA) (60), Wester et al. (8) have described a method for calculating the absorbed dose from percent dermal absorption data by calculating the flux (J) from the product of the applied dose (applied volume times applied dose) and the absorbed dose (percent absorbed times applied dose). The flux (J) is then divided by the applied dose (C) as in Equation 1 to give $K_p$. For an example calculation, see U.S. EPA (60).

Dermal Absorption of PAHs from Great Lakes Basin Sludge

We take the opportunity to report here previously unpublished data concerning the dermal absorption of PAH contaminants present in Great Lakes basin water sediment samples. Great Lakes basin sludge sediment was obtained from the St. Mary’s River region near Sault Ste. Marie, Ontario and was spiked with ¹⁴C-radiolabeled B[a]P, naphthalene, and phenanthrene. This ¹⁴C-spiked sediment was applied as a thin film to the dermatomed (0.3 mm) skin obtained from hairless guinea pigs and human subjects. During application of the sediment, the skin was held clamped in a Bronaugh flow-through Teflon permeation cell (0.64 cm²). Hank’s HEPES buffered saline solution, pH 7.4, was used as a receiver solution at a flow rate of 1.5 ml/hr. The receiver solution was collected at 2-hr intervals for 24 hr in a fraction collector. The percentage of radiolabel permeating the skin and detected in the receiver solution was added to that found persisting in the skin at 24 hr so that any dermal depot of PAH would be included in the estimate of dermal absorption. The total percent dermal absorption expressed in this fashion is reported for the three compounds and two
Table 1. Total percent dermal absorption (mean ± SD) of three PAH compounds in hairless guinea pig (n = 5) and human skin (n = 14) in vitro.

| Species      | Naphthalene | Phenanthrene | B[a]P |
|--------------|-------------|--------------|------|
| Guinea pig   | 59 ± 15.5   | 83 ± 6.5     | 41 ± 11.9 |
| Human        | 14 ± 6.6    | 62 ± 8.7     | 27 ± 6.3 |

Abbreviations: PAH, polycyclic aromatic hydrocarbons; B[a]P, benz(a)pyrene.

species tested in Table 1. Although several site locations were sampled and dermal absorption was assessed as part of a collaborative project with the Ontario Ministry of Environment, only data from one site (#174) is reported in Table 1.

The data in Table 1 demonstrate significant absorption of all three PAHs from Great Lakes basin sediment in guinea pig skin over the 24-hr treatment period. The observation of a lower degree of absorption of B[a]P than for naphthalene and phenanthrene may be due to the filtering of the correlation between lipophilicity and $K_{ow}$ for compounds with a log $K_{ow}$ above a certain optimal level. The $K_{ow}$ for the two ringed compound naphthalene would be less than that for the three-ringed phenanthrene, which in turn would be much less than that for the five-ringed B[a]P, as $K_{ow}$ is additive by ring substituent (81). The observation of much less absorption through human skin than for guinea pig skin is consistent with the general paradigm for animal species-related skin permeabilities: rodent skin is usually thought to be more permeable than human skin.

Using the method of Wester et al. (8) to calculate the absorbed dose, we can substitute into Equation 2 the value in Table 1 of 14% human dermal absorption, the concentration in the sediment of approximately 1 µg/ml of wet sediment (the sediment concentration of the 14C-radiolabel), an exposed skin surface area of 0.64 cm², and a wet sediment volume in the donor chamber of approximately 0.1 ml to calculate an absorbed dose of phenanthrene over the 24-hr exposure period as follows:

$$(1 \text{ µg/ml}) \times (0.1 \text{ ml/0.64 cm}^2) \times (17,000 \text{ cm}^2/1) \times 0.14 = 372 \mu\text{g}$$

We note that a 24-hr swimming exposure would only occur following a marathon race. Further, the present study was conducted with a dense slurry of lake sediment exposed to the skin in a sediment/water ratio far surpassing that usually encountered in Great Lakes basin lake water by swimmers. It is interesting to mention that a control study conducted with 14C-phenanthrene applied to human skin without sediment demonstrated a higher degree of dermal absorption (24 ± 3.8%) than with sediment present (14%), hence preferential partitioning to sediment may decrease the ecovailability of water contaminants as discussed previously (Figure 2). Since the in situ lake water sediment/water ratio would be lower, the 372 µg calculated in Equation 3 may be an underestimate. It is recommended that this study be repeated employing the flow-through donor solution procedure depicted in Figure 3 and that environmental conditions (e.g., sediment/water ratio, donor flow rate, temperature, pH, solar [UV] illumination) be appropriate for exposure situations encountered in the Great Lakes basin.

**Bathing and Showering Exposure**

This review would not be complete without considering exposure to water contaminants in tap water during bathing and showering situations. Tap water derived from wells may become contaminated by chemicals leaching into wells from groundwater. For example, atrazine, a widely used herbicide, has been detected in tap water from wells used for obtaining bathing and shower water. Ademola et al. (82) have reported that 16% of the atrazine applied in vitro to human skin was absorbed from a finite dose (68 nmol/cm²) and that some dermal metabolites of the herbicide were identified. Although 16% may appear to be a low degree of dermal absorption, in a bathing or showering situation, exposure of large body surface areas is involved, and a small flux of a compound exerted over a large area may provide a significant transdermal dose of the chemical. In fact transdermal delivery of methyl salicylate and salicylate has been investigated in a bathing situation to determine whether this could provide a therapeutic dose for the treatment of rheumatoid arthritis. 6.7 mg of methyl salicylate and 4.3 mg of salicylate were observed to be dermally absorbed by human subjects following 20 min bathing in water containing 0.03 g/l and 0.3 g/l, respectively (83). Such therapeutic concentrations are very high in comparison to usual environmental contaminant levels in the Great Lakes basin waters (< ppb); however, several reports have suggested that the degree of dermal absorption of chemicals applied to the skin at low concentrations may surpass that observed at higher concentrations (44,84,85). Hence, it is important that exposure conditions mimic environmental contaminant levels as closely as possible when conducting dermal absorption tests.

The studies of Jo et al. (86,87) and Bogen et al. (44) concerning the dermal absorption of chloroform during showering are excellent reports to consider for estimating the importance of the dermal route of absorption in relation to the ingestion and inhalation routes. Jo et al. (86) measured chloroform levels in the breath of human subjects following shower exposures to chlorinated tap water. Their data demonstrated that 48% of the total chloroform absorbed was due to dermal absorption and the remainder was attributed to inhalation. Jo et al. (87) proceeded to analyze this data to determine the risk of cancer that might result from such exposure. They reported that the lifetime risk of cancer from one 10-min shower per day was 122 per million and that this was less than that calculated for a daily ingestion of 2 liters of tap water (180 per million). Further, the lifetime cancer risk of 122 from a 10-min shower could be divided into a risk per million of 62 that resulted from dermal absorption of chloroform and a risk of 60 that resulted from inhalation of chloroform. The latter risk was proposed to result from the fact that chloroform is volatile, especially from heated shower water, and is readily inhaled. An important consideration in the Jo et al. (86,87) studies was that risk of exposure must be calculated as the sum of all exposure routes and that the dermal route is seldom considered. Jo et al. (87) concluded that if people are advised not to drink water contaminated with VOCs, then they should be advised not to bathe or shower in such water as well. Hence, by analogy we would suggest that if people are advised not to drink Great Lakes basin water due to water contamination, then they should similarly be advised not to bathe or shower with lake water pumped in without treatment or to use contaminated well water for this purpose. It should be mentioned that it is common practice for cottagers to use untreated lake water for bathing and showering.

Bogen et al. (44) have conducted an in vivo dermal absorption test with hairless guinea pigs three quarters immersed for 72 min in water treated with 20 to 110 ppb concentrations of three VOC compounds. They reported $K_a$ values of 0.13, 0.23 and 0.37 ml/cm² hr for chloroform, trichloroethylene, and tetrachloroethylene, respectively. They also calculated a $K_a$ of 0.16 from the human shower data of Jo et al.
(86) and reported the close agreement of this value with their $K_a$ for chloroform of 0.13. To put their data in perspective, Bogen et al. (44) calculated that for a reference 70-kg human with a body surface area of 18,000 cm$^2$, 80% immersed for 20 min in bath water, dermal absorption would amount to an exposure equivalency of ingesting about 0.6, 1, and 2 liters of water, respectively, for chloroform, trichloroethylene, and tetrachloroethylene. Bogen et al. (44) also observed that the $K_a$ for chloroform was constant through 3 to 4 orders of magnitude of the water concentration of this VOC (up to 100,000 ppb). This latter point is important since, as mentioned previously, other reports have indicated that the degree of dermal absorption is higher at lower dose concentrations and a constant $K_a$ over the dose range as reported by Bogen et al. (44) would suggest that calculations of exposure could be made from earlier literature data where high-dose concentrations were employed. It also suggests that the $K_a$ values calculated from high-dose concentrations could be used to predict the maximum risk of exposure to low-level water contaminant exposure.

**Oral versus Dermal Exposure**

As well as the inhalatory route discussed previously for volatiles such as chloroform, the oral route of exposure would be expected to play a significant role in determining the total impact of water contaminants in the Great Lakes basin ecosystem. Much concern has recently been given to the health effects of ingesting fish contaminated with lead and mercury. For the purpose of the present review, it is instructive to compare the exposure to food contaminants resulting from the ingestion of an average 250-g meal of fish to that resulting from a 1-hr swimming exposure in polluted water. In an extensive pesticide monitoring program conducted from 1980 to 1981, the United States Fish and Wildlife Service reported the levels of several organochlorine pesticide residue levels in fish species sampled from 107 stations across the country (23). From their report, we can see that the total DDT residues (1,1-dichloro-2,2-bis(p-chlorophenyl)ethane + 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene + DDT) present in lake trout taken from Lake Huron (station #106) in 1981 amounted to 1.04 μg/g fresh weight of fish. Hence for an average meal of 250 g, one would be exposed to 260 μg (250 × 1.04) of DDT residues. Using a value for dermal absorption of DDT of 15% determined in our laboratory (Moody et al., unpublished data) with human skin (28 year-old female) *in vitro* (0.64 cm$^2$ surface area) and the same water sediment concentration of DDT (1.04 ppm) as present in the fish, we can calculate from Equation 2 that in 1 hr a swimmer would absorb

\[
(1.04 \mu g/ml) \times (0.05 ml/0.64 cm^2) \\
\times (17,000 cm^2/l) \\
\times 0.15 = 207 \mu g
\]

Although this 15% dermal absorption value was determined from a 48-hr *in vitro* study, it can be applied here as a worst-case scenario in which a swimmer is exposed for 1 hr and then fails to wash off the skin deposit of water sediment until the next day. This is the case, since a 24-hr skin wash was used in the *in vitro* study with DDT. Further, this *in vitro* study was performed with DDT dissolved in fuel oil #2 and, in reference to our prior discussion, it is interesting to view this exposure as a swimmer encountering a DDT contaminated oil slick on the water surface. Hence, at equivalent exposure concentrations, the exposure from a 1-hr swim (207 μg) would approximate that from ingesting 250 g of fish (260 μg), thus demonstrating that in this case, the dermal route is as significant as the oral. Of course this is for a worst-case situation and the likelihood of swimmers encountering DDT concentrations as high as 1 ppm in surface slicks is remote. Nevertheless, mixtures of lipophilic contaminants may partition to a combined high communal concentration in slicks and water sediment and they may have additive or even synergistic effects on human health. Also, exposure via the dermal route should be viewed more vigilantly since the risk of toxicity resulting from skin absorption is potentially greater due to the lack of hepatic detoxification (first pass effect) for percutaneously absorbed compounds.

**Conclusions and Recommendations**

It is certain that people who use the Great Lakes for occupational or recreational purposes and permit the lake water to contact the skin will be dermally exposed to a wide variety of low levels of water contaminants. It is probable that these water contaminants will be absorbed dermally to some degree and hence become bioavailable [for recent review, see Wester and Maibach (88)]. It is possible that after prolonged exposure of the skin, especially under conditions that may enhance skin permeability (such as peeling of the stratum corneum following sunburn), toxicologically significant amounts of certain water contaminants could be absorbed via the dermal route. It is unlikely, however, with the possible exception of the marathon swimmer, that an unreasonable degree of risk would result from such exposure. It is recommended that suitable precautions be taken to minimize exposure such as confining swimming to public beaches, discouraging swimming by children for extended periods if they exhibit sunburn, and to wash the skin thoroughly with soap and water as soon as possible following swimming. Considering the paucity of directly relevant literature reports in this area, it is highly recommended that future research investigations be conducted to examine the dermal absorption of water contaminants of concern in the Great Lakes basin. These studies should focus on the development of accurate models of the swimming-exposure scenario where environmental and physiologic conditions that mimic those present *in situ* are employed.

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