Haitian and Chilean Quakes: By the Numbers

- **Haiti**
  - Magnitude: 7.0
  - Epicenter: 10 miles from Port-au-Prince; 8 miles below surface
  - Death toll: ~220,000
  - Poverty: Extreme (#180 out of 210)
  - Earthquake preparedness: Non-existent

- **Chile**
  - Magnitude: 8.8 (500 times stronger)
  - Epicenter: 200 miles from Santiago; 21 miles below surface
  - Death toll: 800+
  - Poverty: Middle income (#76)
  - Earthquake preparedness: Long history of experience

Image

A Chilean overpass after the quake. Note the re-bar.
Skin

• The skin plays an important role in:
  – Physical protection from environmental agents
  – Hydroregulation through both passive and active mechanisms
  – Thermoregulation to maintain core body temperature
  – Absorption of clinically important pharmaceutical preparations
  – Chemical synthesis of vitamin D
  – Immunological surveillance and function
  – Sensory reception of pain, temperature, touch, and pressure

Skin

• Part of an active defense strategy; designed to prevent widespread internal or cutaneous damage
• The heaviest organ in the body (~15% of total body weight)
• Average exposure surface area of 1.5–2.0 m².
• From a toxicological viewpoint, the skin is of concern because it is a:
  – Route of exposure for systemic toxicants
  – Direct target for toxicity
  – Xenobiotic metabolizing organ
  – Minor pathway for the elimination of certain toxicants

Structure of the Skin

• The skin can be divided into three basic regions:
  – Epidermis
  – Dermis
  – Hypodermis
• Skin “thickness” relates to the epidermal layer
  – Thin skin covers most of the body
  – Thick skin is found on the palms, fingertips, and soles of the feet
    • Lacks hair follicles and sebaceous glands
  – Epidermal thickness varies from 0.06 mm to several millimeters, as does moisture and lipid content in different regions of the body.
Skin Absorption of Chemicals

- Systemic toxicity: the chemical moves from the epidermis to the dermis
  - Movement is by passive diffusion and is called **percutaneous absorption**.
  - The major barrier is the stratum corneum (outermost layer of epidermis)
  - Conditions that alter the structural integrity of the skin such as lacerations or abrasions can enhance the absorption of xenobiotics.

Skin Absorption of Chemicals (2)

- The rate of penetration is largely related to the lipophilicity of the chemical (the more lipophilic, the greater its penetration rate)
  - Lipophilic substances (nonpolar substances) essentially diffuse through the nonaqueous lipid matrix of cells and extracellular space.
  - Hydrophilic substances (polar substances) diffuse through any available aqueous channels within the epidermis, including epidermal appendages such as sweat glands.
Factors Affecting Skin Absorption

– Applied dose
– Chemical concentration
– Duration of exposure
– Surface area involved
– Physical integrity of stratum corneum
– Regional variations of skin
– Degree of hydration (↑ hydration → ↑abs)
– Temperature (↑ temp → ↑ abs)
– Presence of other substances

Factors Affecting Skin Absorption (2)

• Location of chemical contact is an important consideration
  – Relative rates of absorption:
    • Plantar foot arch = 1
    • Forehead = 43
    • Scrotum = 300

Skin Absorption of Chemicals

<table>
<thead>
<tr>
<th>Chemicals</th>
<th>System Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organophosphates</td>
<td>Cholinesterase inhibition</td>
</tr>
<tr>
<td>Benzidine</td>
<td>Bladder cancer</td>
</tr>
<tr>
<td>Carbon tetrachloride</td>
<td>Kidney, liver, central nervous system</td>
</tr>
<tr>
<td>Hydrofluoric acid</td>
<td>Electrolyte derangement, kidney</td>
</tr>
<tr>
<td>Methyl-ethyl ketone</td>
<td>Peripheral neuropathy</td>
</tr>
<tr>
<td>Aniline</td>
<td>Methemoglobinemia, bladder cancer</td>
</tr>
<tr>
<td>Acrylamide</td>
<td>Peripheral neuropathy</td>
</tr>
<tr>
<td>Carbon disulfide</td>
<td>Coronary artery disease, central and peripheral nervous system</td>
</tr>
<tr>
<td>Glycerol ethers</td>
<td>Aplastic anemia</td>
</tr>
<tr>
<td>Hexachlorophene</td>
<td>Encephalopathy</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>Coronary dilatation</td>
</tr>
<tr>
<td>Mercury</td>
<td>Renal toxicity</td>
</tr>
<tr>
<td>Arsenic</td>
<td>Neurotoxicity</td>
</tr>
<tr>
<td>Bicarb acid</td>
<td>Gastrointestinal lesions</td>
</tr>
</tbody>
</table>
Skin Toxicity

• Local effects include:
  – Acute irritant dermatitis
    • A single exposure to a “strong” irritant causes immediate inflammation (and worse)
  – Chronic irritant dermatitis
    • Repeated exposure to a “weak” irritant causes cumulative inflammation
  – Allergic contact dermatitis
    • An immunological response (a delayed hypersensitivity response) to an exposure; no direct injury to the skin by the substance
  – Corrosion
    • Exposure causes fairly immediate, irreversible tissue damage

Skin Toxicity (2)

• Hands, wrists, forearms are most at-risk
• Factors that influence the skin exposure – outcome link:
  – Pre-existing skin conditions
  – Allergies
  – Age
  – Humidity
  – Temperature

Contact Dermatitis

• The most common occupationally-induced skin condition (90% of all workplace skin problems)
• Results from direct or indirect exposure to the chemical
  – Direct: produces a skin inflammatory response (primary irritant response)
    • Example: exposure to an organic solvent, which dissolves the lipids of the skin
  – Indirect: due to the allergic sensitization of the individual upon re-exposure to the offending agent
    • An allergic response triggered by the immune system
    • An inflammatory response results in either case
Contact Dermatitis (2)

- Direct and indirect share common symptoms
  - Itching
  - Burning
  - Discomfort
  - Erythema (redness or rash)
  - Edema (swelling)
  - Induration (sclerosis or hardening)
  - Vesiculation (blistering)
  - Oozing
  - Scaling

Contact Dermatitis (3)

- Responsible for 80% of all contact dermatitis cases
- The extent of irritant action of chemicals on the skin is determined by factors such as:
  - the duration and repetitiveness of contact
  - concentration
  - pH
  - temperature

Contact Dermatitis (4)

- Primary irritants include:
  - Solvents
  - Surfactants
  - Strong inorganic and organic acids and alkalis
  - Cement
  - Soaps and detergents
  - Metals such as chromium, antimony, and nickel
Skin Corrosion

- An extreme form of direct skin damage by chemicals
  - An immediate and irreversible response from a single exposure to an agent
  - Results in epidermal and dermal necrosis
- Corrosion or contact dermatitis?
  - Largely a function of concentration

Skin Corrosion (2)

- Examples of corrosives include:
  - Concentrated acids and bases
  - Ammonia
  - Chlorine
  - Isocyanates
  - Phenol
  - Phosphorous
  - Ethylene oxide
  - Hydrogen peroxide
  - Calcium oxide

Allergic Contact Dermatitis

- Represents approximately 20% of reported contact dermatitis cases
  - A cell-mediated (T-cell) immunological reaction in individuals who have become sensitized to the offending agent
  - Key factors:
    - A genetic predisposition to sensitization
    - A sensitizing event
    - Contact after the sensitization
Allergic Contact Dermatitis (2)

• Unlike the primary irritant response, where the extent of injury is proportional to the magnitude of the exposure, in contact allergic dermatitis even a small amount of chemical in the sensitized individual can result in a significant dermatitis.

Examples of Occupational Skin Sensitizers

<table>
<thead>
<tr>
<th>Substance</th>
<th>Uses</th>
<th>Occupation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disinfectants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glutaraldehyde</td>
<td>Health care, cleaners, papermaking</td>
<td></td>
</tr>
<tr>
<td>Fragrances</td>
<td>Cleaning agents</td>
<td>Cleaning personnel, hairdressers</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics</td>
<td></td>
<td>Health care</td>
</tr>
<tr>
<td>Preservatives</td>
<td>Metal cutting fluids, cosmetics, wood preservatives, water-based paints, glues</td>
<td>Metal workers, beauticians, manicures, hairdressers, woodworkers</td>
</tr>
</tbody>
</table>

Phototoxicity

• Light and chemicals on the skin can interact to produce a phototoxic skin response.
• Ultraviolet (UV) radiation in the 280 to 320 nm range (UVB) penetrates the dermis and can cause:
  – A short-term inflammatory response (erythema)
  – Long-term changes upon chronic exposures, such as actinic keratosis, basal and squamous carcinomas, and malignant melanoma
  – A decline in immunocompetence due to a depletion of Langerhans cells (cells in the skin that signal the immune system)
Phototoxicity (2)

- Sunlight also facilitates normal (positive) biochemical reactions such as formation of vitamin D.
- It is thought that the combination of UV light and skin exposure to certain chemicals results in the production of free radicals that produce effects that are similar to contact dermatitis.

Phototoxicity (3)

- Both natural light and artificial light have the ability to induce skin changes.
  - The minimal erythremic dose refers to the minimum exposure (intensity and time dependent) required to produce skin redness.
  - UVA light (320–400 nm) has greater penetrative power compared with UVB light (280–320 nm).
  - Is this odd?
- Exposures to certain plant products such as the furocoumarin 8-methoxy psoralen found in limes and polyaromatic hydrocarbons (PAHs) can produce a “phytophotodermatitis.”
- A photoallergic response can result from exposure to sulfanilamide (an antibiotic).

Acne

- Can be induced by contact with chemicals such as coal tars and chlorinated hydrocarbons.
- Acne venenata.
- The chemicals capable of producing acne venenata are termed comedogenic.
  - Papules, cysts, pustules, and scars may also result.
Acne (2)

- Hair follicles can become inflamed as a result of exposure to chemicals (or infection)
  - Folliculitis
    - Typically presents on the face, neck, forearms, backs of hands and fingers, lower abdomen, buttocks, and thighs.

Chloracne

- An uncommon refractory form of acne caused by halogenated hydrocarbon exposure
- Contact produces persistent yellow or straw-colored cysts along the side of the forehead, lateral eyelids, and behind the ears.

Chloracne (2)

- The chemicals that produce chloracne are referred to as chloracnegens and include:
  - Polychlorinated biphenyls (PCBs)
  - Polybrominated biphenyls (PBBs)
  - Hexachlorodibenzo-p-dioxin (HCDD)
  - Tetrachlorodibenzo-p-dioxin (TCDD)
  - Polybrominated dibenzo-furans
  - Polychlorodibenzofurans
  - Polychlorodibenzofurans
  - Tetrachlorobenzene
  - Tetrachloroazobenzene
  - Polychloronaphthalenes
Examples of Skin Effects from Chemical Exposures

- **Urticarial reactions:** Type 1 allergic reactions cause the release of histamines and other local inflammatory mediators
- **Cutaneous granulomas:** Inflammatory response to insoluble materials
- **Physical dermatitis:** Fiberglass

Examples of Skin Effects from Chemical Exposures (2)

- **Hair loss:** Destroy hair-producing cells in the follicle or in the hair matrix due to exposures to depilatories, thallium, ionizing radiation, cancer chemotherapeutic agents
- **Hypopigmentation:** Inhibition/destruction of melanocytes (e.g., phenolic preparations, hydroquinones)
- **Hyperpigmentation:** Heavy metals, acridines
- **Color changes:** for example, orange/yellow from picric acid, green from copper dust, black from osmium trioxide

Case Study #3: Dark and Lovely?

Refer to the handout provided (Part 3).

Questions:
1. Now that you know a little more, what are the risk factors that increase a person's chances of having melanoma?
2. How does sunlight contribute to the development of melanoma?
3. What does it mean to be predisposed to getting cancer? If you inherit a mutated cell cycle gene, does that automatically mean that you will get cancer some day? If you inherit a mutated cell cycle gene and participate in risky behaviors such as sunbathing, does that mean that you will automatically get cancer some day?