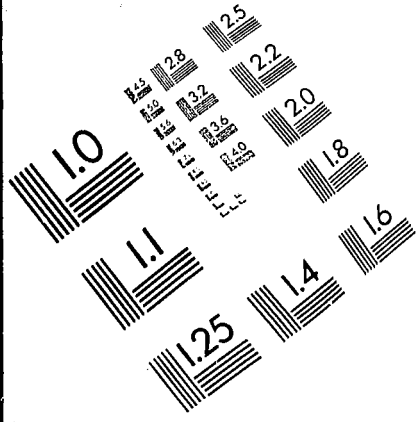

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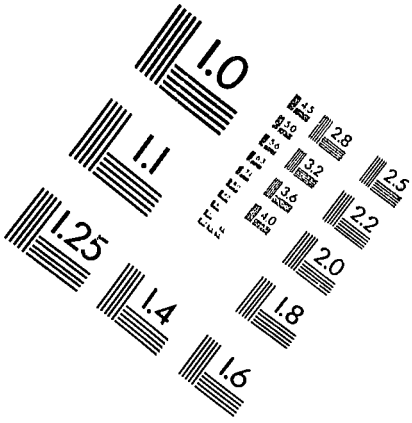

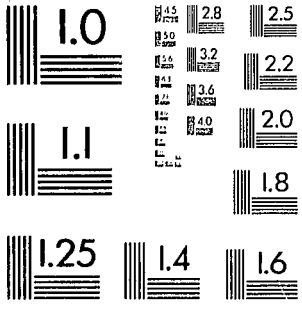

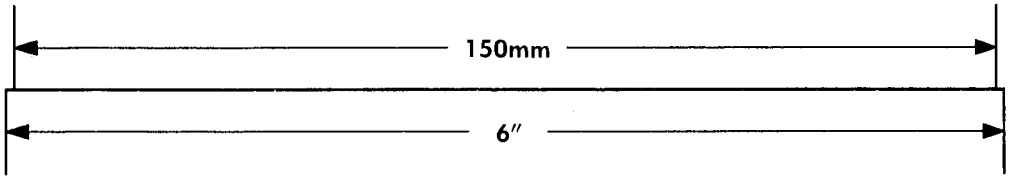

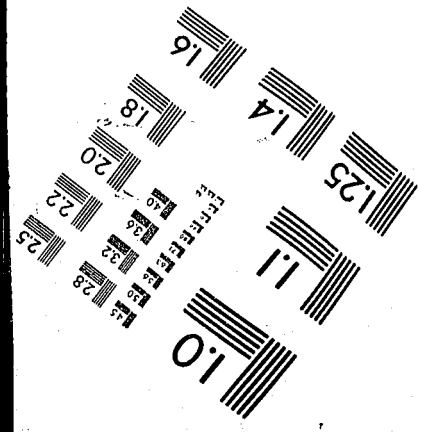

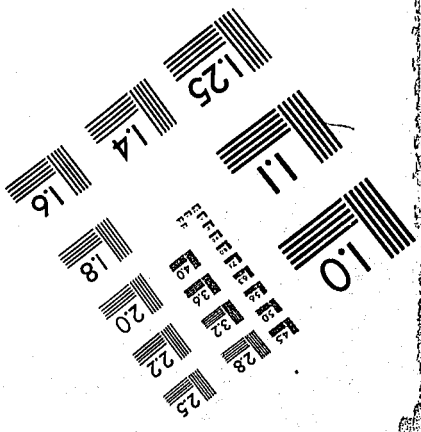

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10

Occupational Dermatoses

C. G. Toby Mathias, M.D.

HISTORICAL ASPECTS

In 1700 A.D., Bernardino Ramazzini[99] called attention to diseases of workers in his classic text, *De Morbis Artificium*. This work contained explicit descriptions of a variety of occupational skin diseases which remain true even today. Examples included fissuring dermatitis of the hands from lye, leg ulcerations among salt miners, and grain mite dermatitis. As noted by Schwartz et al.,[109] this latter observation was remarkable, since Ramazzini was able to deduce the probable cause as an "invisible parasite" on the basis of his clinical observations alone, without the aid of a microscope.

In 1775, Percival Pott published the first detailed description of occupationally induced cancer of the scrotum in chimney sweeps, which he correctly attributed to soot penetrating through clothing and being rubbed into scrotal skin as the sweep descended within the chimney. The potent carcinogenic properties of tars were later verified by numerous authorities, and have proved to be an important research tool in the experimental induction of cutaneous neoplasm.

However, it was not until the Industrial Revolution that substantial medical attention was given to diseases of occupational origin. Robert Willan and Thomas Bateman described occupational contact dermatitis from shoe wax among cobblers and from sugar and spice among bakers. Thackrah noted contact dermatitis in tobacco handlers. Potton described dermatitis in silk winders. In 1859, Hespian reported dermatitis induced by coal tar. Becourt and Chevalier correctly identified chromate as an important cause of industrial dermatitis in 1859, and Halforto described mercury dermatitis in craftsmen. Occupationally acquired skin infections from fungus, vaccines, and anthrax were reported among animal and hide handlers by the distinguished French physicians Alibert, Rayer, and Ibresilc.[109]

The first major treatise devoted solely to occupational skin disease, *The Dermatergoses*, initially published in 1915 and subsequently revised, was written by Robery Prosser White, an energetic English general practitioner.[98] The detailed clinical descriptions of a wide variety of skin disorders contained in this text remain remarkably accurate.

Following the dramatic growth and expansion of the chemical and petroleum industries in the United States after World War I, interest in occupational skin disease became so great that the U.S. Public Health Service organized the Office of Dermatoses Investigations in 1928. This effort culminated in the publication of *Occupational Diseases of the Skin* by Schwartz, Tulipan, and Peck in 1939.[107] The last revised edition of this excellent and comprehensive text was published in 1957.[109] Although dramatic technologic changes within industry since then have either made portions of this text obsolete or have created new causative agents, recent smaller texts provide excellent but limited supplemental information on these subjects.[2, 42, 74]

EPIDEMIOLOGY

Clinical Types

Occupational skin disease accounts for only a small portion (1%–2%) of all occupational injuries or illnesses. Excluding injuries, however, which account for 96%–97% of all cases, skin disease accounts for 40%–50% of all remaining occupational illnesses (Table 10–1).

Approximately 80%–90% of all types of occupational skin disease may be classified as contact dermatitis, while another 5% is due to infection. California data (Table 10–2) illustrate that only a small percentage of skin disease cases are due to disorders other than contact dermatitis or skin infection (e.g., urticaria, acneiform

TABLE 10–1.
Occupational Injuries and Illnesses, 1975*

TYPE OF CASE	TOTAL CASES	INCIDENCE†	PERCENT OF TOTAL
All	4,983,100	0.91	100
Injuries	4,819,000	0.88	96.7
Illnesses	163,000	0.03	3.3
Skin disease	74,400	0.014	1.5

*Adapted from Wang CL: The problem of skin disease in industry. Office of Occupational Safety and Health Statistics, US Dept of Labor, 1978.
†Rates per 1,000 full-time employees.

TABLE 10–2.
Types of Occupational Skin Disease (California, 1977)*

TYPES	PERCENT
Contact Dermatitis	92.2
Skin Infections	5.4
All Others	2.4

*Modified from California Department of Industrial Relations, Division of Labor Statistics and Research: *Occupational Skin Disease in California (With Special Reference to 1977)*. San Francisco, California Department of Industrial Relations, 1982.

eruptions, or pigmentary disorders). Approximately 80% of all cases of contact dermatitis are believed to result from skin irritation rather than contact allergy.

Causative Agents

Causal agents of occupational skin disease are ranked in Table 10–3. The data probably reflect the large numbers of employees in the workforce who are exposed to these agents, more than any inherent risk from exposure to the individual causal agents themselves. The large percentage of cases attributable to poison oak is unique to California.

The most frequently identified solvents causing occupational skin disease in California have been acetone, chlorinated hydrocarbons (freon and methylene chloride), toluene, xylene, petroleum distillate, and alcohols. Fiberglass accounted for 70% of all cases attributable to dust, while rock wool (and other insulating materials), dried cement and plaster dust, paper dust, and sawdust accounted for most of the remainder. Fruits and vegetables caused almost two thirds of all cases of dermatitis attributable to food products. Epoxy resins accounted for the largest percentage of cases to various plastics and resins. Causal agents will vary in importance within various industry classifications. The most important causal agents within selected industries have been listed in Table 10–4.

TABLE 10–3.
Causal Agents of Occupational Skin Disease and Percent Distribution (California, 1977)*

CAUSAL AGENT	PERCENT
Poison oak	23.7
Soaps, detergents, cleaning agents	6.1
Solvents	5.0
Fiberglass and particulate dusts	4.7
Food products	4.2
Plastics and resins	3.9
Petroleum products (nonsolvent)	3.3
Plant and animal products (inedible)	3.3
Agricultural chemicals	3.0
Infectious agents	2.5
Metals and their salts	1.7
Cutting oils and coolants	1.3
Environmental conditions	1.1
Textiles, fabrics, materials	0.9
Rubbish, dirt, sewage	0.3
Miscellaneous chemical agents	17.9
All others	0.9
Unspecified	16.2
Total	100

*From California Department of Industrial Relations, Division of Labor Statistics and Research: *Occupational Skin Disease in California (With Special Reference to 1977)*. San Francisco, California Department of Industrial Relations, 1982. Used by permission.

TABLE 10–4.
Important Causal Agents of Occupational Skin Disease by Selected Industry Classifications*

INDUSTRY CLASSIFICATION	PERCENT
Manufacturing	
Electronic equipment, components	
Solvents	12.8
Plastics and resins	10.2
Acids	8.8
Fiberglass	6.9
Metals and metallic salts	6.6
Machinery	
Cutting oils	14.2
Solvents	10.7
Petroleum products (nonsolvent)	10.7
Fiberglass	8.2
Plastics and resins	4.9
Fabricated metal products	
Petroleum products (nonsolvent)	17.1
Solvents	10.1
Metals and metallic salts	8.0
Acids	7.7
Cutting oils	5.9
Chemicals and allied products	
Solvents	12.7
Plastics and resins	8.4
Rubber and plastic products	
Plastics and resins	18.9
Fiberglass	14.9
Solvents	5.9
Stone, clay, glass products	
Fiberglass	8.7
Cement, mortar, plaster (wet)	8.7
Plastics and resins	8.4
Dusts	6.8
Solvents	5.0
Food products	
Fruits, vegetables, meats	32.2
Soaps, detergents, cleaning agents	8.2
Caustics	4.6

(continued)

TABLE 10–4. *Continued*

INDUSTRY CLASSIFICATION	PERCENT
Lumber and wood products	
Poison oak	39.7
Fiberglass	13.3
Glues, pastes, adhesives	7.3
Plants (inedible)	5.0
Agriculture	
Poison oak	35.5
Agricultural chemicals	16.2
Fruits, nuts, vegetables	11.8
Plant and animal products (inedible)	9.8
Construction	
Poison oak	54.3
Cement, mortar, plaster (wet)	8.8
Fiberglass and other dust	6.1
Hospitals/health services	
Soaps, detergents, cleaning agents	26.6
Infectious agents	16.7
Medicines, disinfectants	6.2
Restaurants	
Soaps, detergents, cleaning agents	48.6
Food products (miscellaneous)	10.6
Fruits, nuts, vegetables	4.8

*Adapted from California Department of Industrial Relations, Division of Labor Statistics and Research: *Occupational Skin Disease in California (With Special Reference to 1977)*. San Francisco, California Department of Industrial Relations, 1982.

Rates and Risks

Because large surface areas of skin are directly exposed to the environment, this organ is particularly vulnerable to occupationally induced disease. Excluding injuries and accidents, the skin accounts for a disproportionately large percentage of all remaining occupational illnesses. Surveys conducted by the National Bureau of Labor Statistics (BLS) from 1972 to 1976 consistently demonstrated that the skin accounted for approximately 40% of occupational illnesses, with an incidence of 1.7 per 1,000 full-time employees in the private sector.[120] Although the proportion of occupational illnesses attributed to skin disease has remained relatively constant, the annual incidence figures have been steadily declining. By 1982, the incidence had fallen to 0.7 per 1,000 full-time private sector employees, a drop of over 50%.* With over 100 million people now employed in the private sector workforce,[115] one can conservatively estimate that there are at least 70,000 new cases of occupational skin disease annually.

The precise reason for this decline in annual incidence is unclear. Automation and new technology have almost certainly reduced the total numbers of individuals within industry directly exposed to potential cutaneous irritants and allergens, and they have contributed to a larger percentage of the workforce being employed in lower-risk, service-oriented occupations. However, there is reason to suspect that part of this decline has resulted from exploitation of a "loophole" in the Occupational Safety and Health Administration (OSHA) reporting system, from which the BLS statistics are derived. "Injury" is defined by OSHA as a condition resulting from a "one-time exposure," an unfortunately vague term. Injuries do not have to be recorded in the OSHA log unless they result in time lost from work, but regulations mandate that *all* illnesses be recorded, regardless of whether these cases result in lost work time. By considering an illness to have resulted from a "one-time injury," employers may be able to classify these as injuries, e.g., chemical burns. This is particularly advantageous if no lost work time has occurred, since the case would not have to be recorded in the OSHA log. In California's semiconductor industry, the annual incidence for occupational illness fell from 1.3 per 100 workers to 0.3, possibly due to this loophole.[69] Additionally, if an injury or illness is treated only with "first aid," the condition does not have to be reported. The employment of occupational health nurses and other safety personnel by large companies to administer "first aid" may not only reduce the overall costs of occupational disease, but also the incidence statistics.†

The difficulty in accurately determining the true incidence of occupational skin disease is compounded by the ultimate dependency of all reporting systems on reliable recognition by treating physicians, employers, or employees in the first place. Inadequate training in occupational dermatology and busy office work schedules may leave physicians unprepared to make a proper diagnosis or too busy to complete the proper reporting claims. Insufficient monitoring of the work environment and inadequate training of health and safety personnel may lead to underrecognition by management. If neither management nor physicians recognize occupational disease, the responsibility settles on the employee, who requires adequate job health education to do so. If a survey by Discher and associates[34] is correct, only 2% of occupational illnesses had been correctly diagnosed and entered into the BLS statistics. This observation led these investigators to conclude that the true incidence of occupational illness was probably 10–50 times greater than its reported incidence.

The incidence of occupational skin disease may vary from one geographic location to another. In 1977 skin disease accounted for 40% of all occupational illnesses in California, with an incidence rate of 2.7 per 1,000 full-time employees.[22] In South Carolina from July 1978 to June 1979, however, skin disease accounted for 83% of all the occupational illnesses, with an incidence rate of 1.1 per 1,000 workers.[62]

Manufacturing and agricultural industries have fourfold higher relative risks for development of occupational skin disease (Table 10–5). The incidence of occupational skin disease among agricultural workers is 4.1 per 1,000 employees, compared to an approximate average incidence of 1.3.

Disability

Bureau of Labor statistics from 1972 through 1976 indicate that approximately 23.7% of all occupational skin disease cases lost an average of 11 days from work.[124] Data from California and South Carolina have been similar, with 25% and 21.6% of all skin

*C. Wang, U.S. Dept of Labor, Division of Labor Statistics and Periodic Surveys: Personal communication.

†Joseph LaDou, MD, Peninsula Medical Clinic, Palo Alto, California. Personal communication.

TABLE 10–5.

Incidence Rates and Relative Risks for Occupational Skin Diseases by Major Industry Classification*†

INDUSTRY	ALL CASES	LOST WORKDAY CASES	LOST WORKDAYS PER LWC‡	RISK
Agriculture§	5.1	1.0	6.4	4.1
Manufacturing	2.6	0.6	11.7	4.1
Construction	1.0	0.3	7.3	0.8
Transportation	0.8	0.2	7.0	0.6
Services	0.7	0.2	6.5	0.5
Wholesale trade	0.5	0.2	20	0.4
Mining	0.4	0.2	7.5	0.3
Retail trade	0.4	0.1	15	0.2
Finance, insurance, real estate	0.1	<0.05	>18	0.1

*Adapted from Wang CL: *The Problem of Skin Disease in Industry.* Office of Occupational Safety and Health Statistics, US Dept of Labor, 1978.
†Rates per 1,000 full-time private sector employees.
‡Lost workday cases.
§Includes forestry and fishing.

TABLE 10–6.

Causal Agents of Occupational Skin Disease and Lost Workday Cases*

CAUSAL AGENT	LWC†	TOTAL	PERCENT
Poison oak	761	4,147	18.4
Soaps, detergents, cleaning agents	261	1,071	24.4
Solvents	161	880	18.3
Fiberglass and particulate dusts	127	780	16.3
Food products	219	739	29.6
Plastics and resins	146	681	21.4
Petroleum products (nonsolvent)	99	577	17.2
Plant and animal products (inedible)	108	575	18.8
Agricultural chemicals	136	526	25.9
Infectious agents	108	445	24.3
Metals and their salts	46	294	15.6
Cutting oils and coolants	24	235	10.2
Environmental conditions	36	189	19.0
Textiles, fabrics, materials	31	164	18.9
Rubbish, dirt, sewage	11	45	24.4
Miscellaneous chemical agents	645	3,113	20.7
All others	26	163	16.0
Unspecified	466	2,828	16.5

*Adapted from California Department of Industrial Relations, Division of Labor Statistics and Research: *Occupational Skin Disease in California (With Special Reference to 1977).* San Francisco, California Department of Industrial Relations, 1982.
†Lost workday cases.

disease cases losing an average of 9 and 10.2 days per lost workday case, respectively.[22, 62] Lost workdays are not normally distributed among these lost workday cases. In California, 25% of all lost workday cases lost more than one week (California Department of Industrial Relations). In South Carolina, 26% lost more than one week but accounted for 82% of all lost workdays; the median number of lost workdays was only 2.3.* Lost workday cases among female workers are not higher than among male counterparts, but there is a trend toward a greater number of lost workdays among women employed in manufacturing per lost workday case than among men.[22]

Lost workday case incidence and lost workdays per lost workday case are depicted in Table 10–5. Lost workday cases have been listed by causal agent from California data in Table 10–6.

Demographics

Data from California[22] indicate that, although more than 40% of the workers employed in 1977 were female, only 28% of occupational skin disease cases occurred among women. Excluding all cases among outdoor workers (primarily men), this figure rose to only 34%. This lower overall rate may be attributable to a larger proportion of women having been employed in occupations at lower risk for development of occupational skin disease. In manufacturing, the incidence rate for women was actually higher (4.7 per 1,000 women) compared to men (3.8 per 1,000 men). Whether this difference was due to an enhanced susceptibility of female skin to irritation or a relative inexperience among female workers has not been established.

Inexperience contributes to the development of occupational skin disease. California employers corroborate the opinion that recently hired employees are more likely to develop dermatitis than those with a longer period of employment. Approximately 25% of all disabling occupational skin diseases occurred within the first three months of employment, and 45% occurred within the first year. In contrast, only one out of six workers disabled for injuries or illnesses other than dermatitis had been employed for three months or less.[22]

The hands and wrists are the most frequent body sites on which occupational skin disease develops, while covered areas are involved in only a small percentage of cases. The hands were involved in one third of California cases,[22] while 80% of cases from South Carolina affected the hands.[112] Personal experience suggests that the latter percentage is a better estimate.

Costs

Reliable determinations of annual costs directly attributable to occupational skin disease are difficult to achieve, but some reasonable estimates may be obtained from published data. Assuming a private sector work force population of 100 million in 1984 and minimum incidence of 0.7 per 1,000 employees, there are at least 70,000 new cases of occupational skin disease annually. Based on South Carolina data, the average medical cost per case is $67.50 for an annual total of $4,725,000. The average compensation payments for lost wages are $1,590 per compensated case (i.e., only those cases losing more than seven workdays). Assuming 22.5% of all cases lose time from work and 25% of these lost-workday cases receive disability payments, the annual indemnity costs for compensated cases total $6,360,000.[85] Assuming 10.5 lost workdays per lost-workday case, an average eight-hour workday, and an average hourly wage of $8.28 in 1984, annual costs attributable

*Source: Ed Shmunes, Department of Dermatology, University of South Carolina.

to lost worker-productivity exceed $11 million. This brings the total annual costs of medical treatment, disability payments, and lost worker-productivity to $22 million. If the Discher report estimates of underreporting are correct (and there is good reason to believe they are), this figure needs to be inflated 10- to 50-fold, bringing annual cost estimates into the range of $220 million to $1 billion dollars annually.

STRUCTURE AND FUNCTION OF SKIN[41, 87]

The skin (Fig 10–1) is composed of two principal layers, the epidermis and dermis. Each layer contains structural elements which are important not only in regard to their function but also in regard to disease processes which may affect them.

The epidermis is approximately 100–200 μ thick. The innermost layer is composed of a thin layer of germinative basal cells, which reproduce every 14 days. The bulk of epidermal thickness is comprised of metabolically active squamous cells, which are connected to each other by numerous desmosomal junctions. Squamous cells synthesize keratinous filaments and keratohyaline granules, destined to become the principal structural proteins of the outermost protective stratum corneum as well as membrane-coating granules composed of complex lipids. As the squamous cells are pushed upwards by dividing cells from below, they enter a zone of transition (the granular layer) and undergo a process of maturation called *cornification,* in which cytoplasmic contents are condensed, nuclear contents disintegrate, and the membrane-coating granules are extruded into the intercellular spaces, where they contribute to the intercellular barrier. Intercellular tight junctions increase in number in the granular layer. The end result of this maturation process is a densely packed layer of relatively impermeable, cornified "dead" cells, the stratum corneum, which constitutes the principal protective barrier against penetration by exogenous chemical substances and microorganisms.

Some protection against exposure to alkaline substances is also afforded by virtue of the buffering action of lactic acid, amphoteric amines, and weak bases deposited on the stratum corneum surface by eccrine sweat, outward diffusion of carbon dioxide through the skin, or decomposition of the most superficial layer of cells. Free fatty acids, on the skin surface, derived from enzymatic degradation of sebaceous gland lipid, possess some antifungal and antibacterial activity, and offer further chemical protection against invasion by cutaneous microorganisms. Odd-numbered C5 through C13 fatty acids have more potent antifungal activity than even-numbered chains, while long-chain unsaturated fatty acids have limited bacteriostatic activity.

Melanocytes are located along the basal cell layer and synthesize a protective pigment, melanin. This pigment is packaged within melanocytes into granules (melanosomes). Under suitable

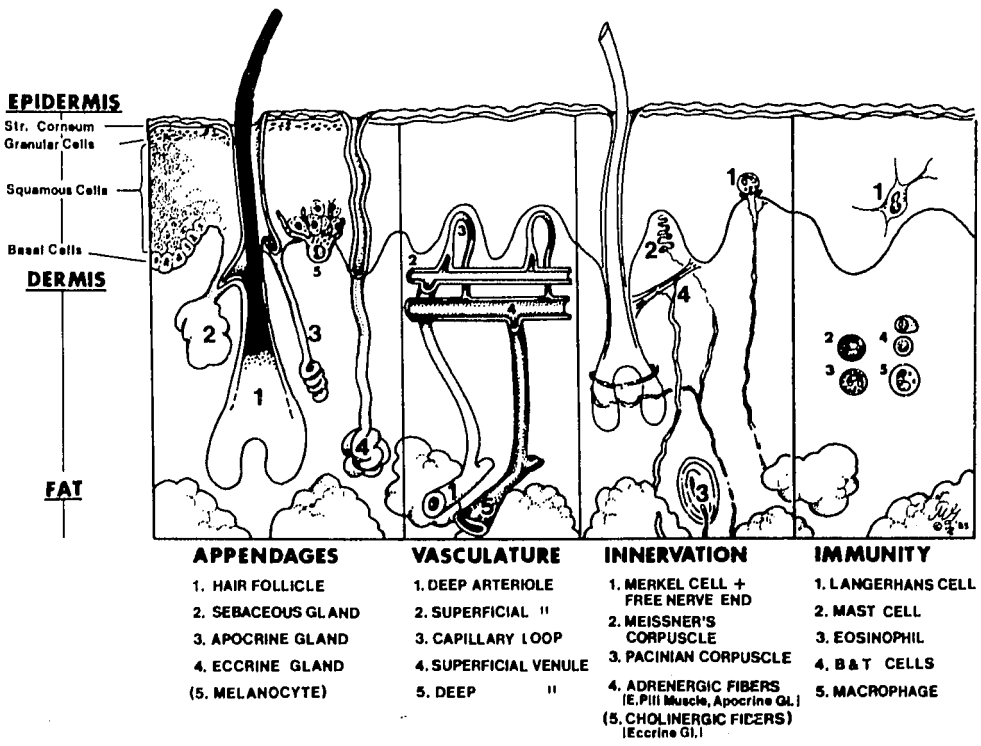

FIG 10–1.
Anatomical structures and components of skin. (Illustration courtesy of Dr. Marc Goldyne.)

stimulation from ultraviolet radiation, these granules are dispersed into neighboring keratinocytes through dendritic extensions of cytoplasm, resulting in the darkening of skin complexion and enhanced protection from ultraviolet radiation. The starting point of melanin synthesis is the amino acid tyrosine, which is converted by the copper-dependent enzyme tyrosinase into dihydroxyphenylalanine (dopa). Melanin synthesis subsequently proceeds through a number of intermediary steps before the final melanin polymer is formed. Melanocytes may be selectively inhibited or destroyed by the toxic effects of phenolic substances structurally resembling tyrosine, resulting in cutaneous depigmentation.

Langerhans' cells are present in the basal and suprabasal layers of the epidermis. These dendritic cells possess immunochemical surface markers similar to macrophages and histiocytes. Accumulated evidence strongly suggests that these cells actively participate in cutaneous immune regulation and surveillance and are responsible for antigen processing and presentation to circulating T lymphocytes. Selective uptake of simple contact antigens by Langerhans' cells has been demonstrated.[110] T lymphocytes subsequently circulate through dermal lymphatic channels to the paracortical areas of regional lymph nodes, where further antigen processing occurs.

Densely intertwined nerve tissue fibers, the dermal nerve network, transverse the superficial dermis and dermal papillae and function as the principal sensory receptors. Merkel cells, most numerous in the suprabasalar epidermis of fingers, oral mucosa, and outer sheaths of hair follicles, are closely associated with terminal neuronxons derived from these myelinated cutaneous nerves. These cells contain densely cored cytoplasmic granules similar to monoamine-containing granules in other neuroreceptor cells and probably function as mechanoreceptors. Vater-Pacini corpuscles, which are found deep in the dermis of hair-bearing skin, are encapsulated, specialized nerve tissue organs responsible for the sensation of pressure. Other specialized nerve tissue elements found in the skin include mucocutaneous end organs, found most abundantly in superficial dermal tissue of mucous membranes, and Meissner's corpuscles, found only in the volar dermal tissue of the hands and feet. No specialized cutaneous sensation has been ascribed to these latter nerve endings.

Blood is distributed within dermal tissue through a highly developed, interconnected network of superficial and deep dermal vessels. Capillary loops extend from dermal arterioles to interface with the overlying epidermis within the dermal papillae. Cutaneous blood flow is regulated by constriction of metarterioles and precapillary sphincters, and a large volume of circulating blood may be brought close to the skin surface. The masses of interlacing small vessels function primarily for thermoregulation and tissue nutrition. Mast cells are often arranged around the walls of small vessels. These cells contain granules within which pharmacologically active substances (histamine, heparin, serotonin, and leukotriene precursors) are found. Upon appropriate physical, chemical, or antigen stimulation, mast cells release their granules, the contents of which participate in a number of diverse pathologic reactions resulting in vasodilation.

The bulk of perceptible skin thickness is due to a loose matrix of dermal connective tissue, composed of fibrous proteins (collagen, elastin, and reticulin) embedded in an amorphous ground substance. The tensile strength and elasticity of the dermis help protect the body from mechanical injury, while the permeability characteristics of ground substance allow diffusion of nutrients from dermal blood vessels to fibroblasts and other cellular elements of the dermis, as well as to the epidermis. Dermal connective tissue may participate in a number of pathologic reactions, including excessive scar tissue formation in response to cutaneous trauma.

Eccrine sweat glands are found on all cutaneous surfaces, but are most numerous on the palms and soles. The ducts of these coiled appendages transverse the epidermis and deposit their contents on the skin surface. Sweat glands are innervated by cholinergic nerve terminals and respond principally to thermal stimulation and emotional stress. Local heating of skin lowers the threshold response of sweat glands to cholinergic stimulation. Acclimatization of sweat glands to thermal stimulation also occurs, and repeated daily exposures to heat eventually produce a marked increase in the rate of sweating. Although the primary function of eccrine sweat glands is to provide evaporative cooling when the body is stressed by heat, secondary buffering of the skin surface against alkaline substances may be provided by lactic acid, amphoteric amines, and weak bases contained in sweat.

Sebaceous glands are intimately associated with hair follicles and share a common ductal opening, lined with stratified squamous epithelium, to the skin surface. The oily content of the sebaceous gland (sebum) is composed chiefly of triglycerides, wax esters, and squalene. Sebum production and secretion is principally due to androgenic stimulation. The glands are largest on the forehead, face, scrotum, and anogenital skin. In some locations, sebaceous glands may open directly onto the skin surface, for example, onto the meibomian glands of the eyelid margins and the glands of the areolae. In mammals, the general function of sebum is that of a sexual attractant (pheromone), but its function in man is unclear. The fatty acids derived from sebum have some bacteriostatic and fungistatic properties and may have a limited function in this regard once deposited on the skin surface. Apocrine glands, found in the axillae and anogenital skin, possess no known useful function in man, but their secretions may be responsible for sexual attractiveness in lower primates.

Hair follicles are found on all cutaneous surfaces except the palms, soles, and mucous membranes. The roots (bulbs) extend below the level of the sebaceous glands, with which they share a common duct. Hair grows cyclically, with alternating periods of growth (anagen phase) and quiescence (telogen phase); the transitional phase between growth and quiescence is termed catagen. The hair follicles of man grow and rest independently of one another, and some shedding of hair occurs continuously. Although the duration of the growth phase may be extremely variable, depending on the body regions in which the hairs are located, the quiescent phase generally lasts only one to three months. During this period, the hair bulbs shorten and retract, the outer root sheath in the bulb becomes detached, and "club" hairs are shed before new growth begins. Although hair has some protective and insulating functions in other animals, this function is relatively unimportant in man. Instead, the principal function of hair, with its richly innervated bulbs, appears to be that of a secondary sensory organ. Alterations in the hair growth cycle may lead to sudden and increased loss of hair.

The nail plates on the tips of the digits overlying the thick-

ened, stratified epidermis of the nail beds are composed of tightly packed, keratinized cells. The germinal cells from which the plate is derived are found in the nail matrix, an oblique wedge of tissue located beneath the proximal nail fold. The cuticle, a cornified epidermal extension from the proximal nail fold over the nail plate, protects the nail matrix and underlying tissue of the proximal nail fold from exogenous chemical substances and microorganisms. Although man has adapted his nails for a number of uses, the primary function is to assist in the grasping and manipulation of small objects. The nail folds, matrices, and beds are susceptible to a number of environmental insults, resulting in dystrophic growth, infection, or separation of the plate from the nail bed.

The structure and function of the various cutaneous components, as well as their susceptibility to occupational disease, have been summarized in Table 10–7.

CLINICAL ASPECTS

Contact Dermatitis

General Considerations

Contact dermatitis is by far the most common occupational dermatosis. The term refers to the induction of cutaneous changes, usually accompanied by inflammation, from direct skin exposure to exogenous chemical or physical substances. Inflammation is provoked by either (or both) of two mechanisms, irritation or allergy. The end result of either reaction pathway is a progression of clinical changes inevitably accompanied by transudation of serum through the epidermis. These changes range from slight dryness, chapping, and redness of the skin surface to frank vesicles or blisters. At least 80%–90% of contact dermatitis cases are secondary to irritation rather than allergy, and the majority (another 80%–90%) are caused by chemical substances.

The inflammatory cutaneous changes that occur from skin irritation result from a direct, local, toxic effect on cellular elements in the skin, leading to cell death, release of lysosomal enzymes and soluble inflammatory mediators, recruitment of inflammatory cells, and further tissue destruction. Although substantial tissue destruction may quickly occur following relatively brief skin exposure to strong caustics or corrosives (i.e., chemical burns), the majority of cases of irritant contact dermatitis result from cumulative and repetitive exposures to "weak" irritants, substances which are not likely to produce visible cutaneous injury following only brief or limited exposure. Two points deserve repeated emphasis here: (1) virtually any substance, under the right set of circumstances, is potentially capable of causing irritant contact dermatitis,[66] and (2) clinical irritant contact dermatitis often results from multiple, cumulative exposures to several potential skin irritants, rather than from just a single substance. Irritant dermatitis generally remains confined to the primary areas of skin exposure and

TABLE 10–7.
Structure, Function, and Occupational Disorders of the Skin

STRUCTURE	FUNCTION	OCCUPATIONAL DISORDER
Stratum corneum	Barrier against chemical diffusion & microorganisms	Chapping from low humidity, chemical stains
Squamous and basal cells of epidermis	Cell regeneration, synthesis of stratum corneum, wound repair	Infection, contact dermatitis, neoplasms
Melanocytes and melanin	Absorption of ultraviolet radiation	Toxic vitiligo, melanoma, hyperpigmentation
Langerhans' cells, lymphatics, dermal macrophages	Immune regulation & surveillance	Delayed hypersensitivity reactions
Merkel cells, nerve tissue elements	Perception of environment	Toxic neuropathies
Blood vessels, mast cells	Thermoregulation, nutrition of tissue	Heat stroke, contact and systemic urticaria, flushing reactions, vibration "white" finger
Connective tissue	Mechanical protection against trauma, wound repair	Infection, granulomatous reactions, scleroderma, solar elastosis, scar
Eccrine sweat glands	Thermoregulation, buffering of skin surface	Miliaria, "rusting"
Sebaceous glands	Synthesis of skin surface lipids, chemical barrier against microorganisms	Oil acne, chloracne
Hair, follicles	Insulation and protection, secondary sensory organs, social appearance	Folliculitis, traumatic or toxic alopecia
Nails	Grasping & manipulation of small objects	Paronychia, dystrophy, oncholysis

does not spread to other parts of the body where the affected individual is not aware of direct exposure.

The factors which predispose to the development of cutaneous irritation are summarized in Table 10–8.[81] While the inherent caustic or corrosive chemical properties of a substance obviously influence whether cutaneous irritation will develop, other considerations are important. Physical properties such as molecular size, weight, ionization, and polarity affect the ability of a chemical substance to penetrate the protective barrier and provoke inflammation. Large (molecular weight greater than 1,000), polar, ionized molecules are poor penetrants in general, and thus are less likely to cause irritation. In the case of solid substances, the physical properties that determine the coefficient of friction against the skin are important determinants of frictional dermatitis. Quantitative aspects of exposure are modulated by the concentration of the potential irritant and the duration, frequency, or number of cutaneous exposures; the lower the concentration and the shorter or less frequent the exposure, the less likely cutaneous irritation will develop. The permeability of the protective barrier may be further compromised by other qualitative aspects of exposure. Occlusion or entrapment of chemical substances against the skin surface by water-impermeable membranes such as clothing increases the hydration and skin surface temperature of the stratum corneum, thus increasing its permeability; quantitative aspects of exposure may also be enhanced by preventing evaporation or wash-off of a potential irritant from the skin surface (Fig 10–2). When the temperature of the protective barrier is increased, it becomes more permeable; warm or hot potential irritants (such as dishwashing detergents) will transfer heat to the stratum corneum, enhance their own permeability, and increase their irritant potentials. If the potential irritant contacts the skin surface where the protective barrier is defective, as, for example, when the skin is dried or chapped, or there are traumatic scratches or lacerations or preexisting inflammatory skin disease, clinical irritation is more likely to develop. The anatomical skin site contacted by a potential irritant also influences the outcome; the eyelids, face, and genital skin (where the protective barrier is thinnest) are most susceptible to clinical irritation. Atopy is the single greatest risk factor determining host susceptibility to the development of clinical irritation, and the relative risk of developing occupational atopic dermatitis has been estimated to be 13.5%.[112] It is often stated that black

TABLE 10–8.
Factors Predisposing to the Development of Cutaneous Irritation

Potential irritant(s)
Chemical properties
Physical properties
Quantitative aspects of exposure
Concentration
Duration of exposure
Frequency and number of exposures
Qualitative aspects of exposure
Occlusion of substance against skin
Temperature of substance or skin surface
Preexisting skin damage to protective skin barrier
Anatomical skin site
Host susceptibility
Atopic disease
Race(?)
Sex(?)
Age(?)

FIG 10–2.
Irritant contact dermatitis on the thigh of a machinist. The lesion developed from inadvertently placing a rag still moist with solvent in the pocket of work trousers.

skin is more resistant to irritation than white skin. Although this statement is supported by limited experimental data, there is no convincing evidence which indicates that these subtle differences are clinically important. Similarly, no strong body of experimental data supports the frequently alleged claim that women are more susceptible to cutaneous irritation than men. Increasing age may be an important determinant of susceptibility to cutaneous irritation, but this issue has not been thoroughly studied to date.

The development of allergic contact dermatitis requires that the affected individual first become immunologically sensitized to the offending substance. The sensitization process involves delayed hypersensitivity mechanisms, which require a period of one to three weeks following first exposure before sensitization can occur. Generally, the allergenic substance must first complex with skin tissue protein, following which this hapten protein conjugate is processed by cutaneous Langerhans' cells and subsequently transported by circulating T lymphocytes to regional lymph nodes, where further antigen processing and cell proliferation occur. Once sensitized, an affected individual will react within several hours to one or two days following cutaneous reexposure to extremely low concentrations of the offending substance. Unlike irritant contact dermatitis, allergic contact dermatitis frequently extends to other body surfaces remote from the primary site of direct skin contact with the allergen.

With the exception of poison oak, most potentially allergenic substances are relatively "weak" antigens and require either a damaged skin barrier (e.g., preceding irritant contact dermatitis) or repetitive skin contact to facilitate immunologic exposure. For these reasons, sensitization frequently occurs from long-standing exposure rather than exposure to a substance recently introduced into a worker's environment. Allergens that are also irritating are more likely to produce clinical sensitization. When the exposure to a potential allergen occurs only at low concentrations, there is often a history of preceding dermatitis suggestive of irritation. Unlike irritant contact dermatitis, however, where atopy is a clear predisposing risk factor, there do not appear to be any unique risk factors determining host susceptibility to allergic contact dermatitis.

As stated earlier, contact dermatitis accounts for most cases of occupational skin disease, and at least 80%–90% of all cases of contact dermatitis result from irritation rather than allergy. Excluding poison oak (where virtually all cases result from allergy) and skin infections, the list of causal agents in Table 10–3 becomes a reasonable rank order approximation of the most common cutaneous irritants. Possible exceptions to this rank order are plastic resins and metallic compounds, where many of these cases are probably allergic.

Common causes of occupational allergic contact dermatitis are listed in Table 10–9. Since exposure to many of these common sensitizers may occur from the domestic as well as occupational environments, the source of exposure should be clearly identified. Not uncommonly, a contact allergy in the workplace results from inadvertent sensitization from rubber gloves, first-aid cabinet preparations, or skin-cleaning preparations usually considered as preventive measures rather than causes of dermatitis.

Follow-up studies (lasting three to ten years) of occupational contact dermatitis indicate that only approximately 25% experience complete resolution of dermatitis and are symptom-free, while 50% are improved but continue to have periodic flares; the remaining 25% develop chronic, persistent eczema which is as severe (or worse) as the initial dermatitis.[20, 43, 54] Almost 30%–40% of persons with occupational contact dermatitis have their jobs changed or modified, but surprisingly only 25% experience complete clearing despite a job change. The prognosis is slightly, but not strikingly, better for allergic than for irritant contact dermatitis. The factors influencing prognosis are not well understood.

Contact dermatitis must be differentiated from endogenous inflammatory dermatoses, particularly atopic dermatitis, dyshidrotic eczema, and psoriasis, with which it may be confused by the unwary. Regardless of type (irritant or allergic), the principles of management include minimization or elimination of the causative exposures and liberal use of topical corticosteroid preparations. Allergic contact dermatitis usually requires complete elimination of exposure to the allergen. For extensive contact dermatitis (more than 20% of the body surface) or limited but severe involvement of the face, genitalia, or palms, systemic corticosteroid therapy is

TABLE 10–9.
Common Causes of Occupational Allergic Contact Dermatitis

*Poison oak/ivy**
Metallic Compounds
Nickel*
Chromate*
Gold
Mercury
Rubber products
Accelerators*
Antioxidants*
Plastic resins
Epoxy resins,* hardeners, reactive diluents
Phenolic resins
Formaldehyde resins
Acrylic resins
Rosin (colophony)*
Organic dyes
Paraphenylenediamine*
Numerous others
Topical first-aid medications
Neomycin*
Thimerosal*
Benzocaine*
Biocides and germicides
Formaldehyde*
Parabens*
Quaternium-15*
Formaldehyde releasers
Isothiazolin-3-one derivatives
Miscellaneous product ingredients
Fragrances*
Ethylenediamine*
Antioxidants

*These substances commonly produce sensitization from exposure in the domestic environment as well as the occupational environment.

preferred. A usually successful regimen is an initial dose of 70 mg of prednisone, tapering 5 mg per day over a two-week period. If 5 mg tablets are dispensed (total number of 105), the patient may be conveniently instructed to take 14 tablets on day 1, then to take one less tablet per day for the next 13 days.

Chemical Burns

Chemical burns may be considered as a special form of irritant contact dermatitis in which substantial skin necrosis and inflammation result from a one-time, usually brief, exposure to a chemical substance. Chemical burns may be divided into first-, second- or third-degree chemical burns, depending on the degree of tissue destruction, and are analogous to thermal burns. Some of these are of special interest either because of unique challenges of management or the potential threat of systemic toxicity from percutaneous absorption.

Chemical burns most frequently result from accidental exposure to a diverse number of organic and inorganic acids and alkalies. Acids generally damage tissue by coagulating protein through oxidation, reduction, desiccation, or salt formation mechanisms. Alkalics not only coagulate tissue protein by desiccation or salt formation, but they also saponify fats and cause liquefaction necrosis. In all cases, management includes copious lavage of the affected skin surface with water, debridement of necrotic skin, and application of a topical antibiotic preparation (usually silver sulfadiazine) followed by a nonadherent surgical dressing. Although neutralization of acids (dilute solutions of sodium bicarbonate, aluminum hydroxide gel, or milk of magnesia) or alkalics (dilute solutions of vinegar) have been recommended by some authorities immediately following water lavage, most consider this unnecessary.[59]

Burns from hydrofluoric acid (HF) (used as a rust remover, metal surface cleaner, etching agent in the semiconductor industry, and a reagent in numerous fluorination processes) typically cause intense pain and erythema which may not become clinically apparent for several hours following cutaneous exposure. Clinical symptoms tend to correlate with the concentration of the acid; signs and symptoms are likely to be immediate if the strength of the acid is greater than 20%, but are often delayed in onset when the exposure is less than 20%. Extensive tissue destruction occurs in part from the high affinity of the fluoride ion for calcium, and extensive destruction of underlying bone may occur from burns on the fingers. Following copious water lavage, treatment is directed at inactivation of the fluoride ion. The affected skin may be soaked with iced 25% magnesium sulfate (Epsom salts), 1%–2% benzalkonium chloride (Zephiran) or 1%–2% benzethonium chloride (Hyamine) solutions. Alternatively, 10% calcium gluconate gel may be applied repeatedly over burned skin. If pain persists, local injection of 10% calcium gluconate into the burned tissue is recommended.[59, 111] For HF burns of the fingertips, the nail may have to be avulsed to facilitate injection of calcium gluconate. If skin burns are extensive, potentially fatal decreases in serum calcium and magnesium concentrations may occur and require supplemental intravenous administration.

Alkyl mercury compounds, used as disinfectants, wood preservatives, and fungicides, are strong skin irritants and may cause second- or third-degree chemical burns. They are extremely toxic to the central nervous system, and fatal neurotoxicity may develop from continued absorption of the alkyl mercury compound still present in blister fluid or necrotic tissue. Blisters and necrotic tissue should therefore be debrided as soon as possible.[11] Despite the paucity of information on chemical burns from other substances which have important systemic toxic effects, immediate debridement of blisters and necrotic tissue should be considered in all similar situations (e.g., chemical burns from methyl bromide).

Phenol (carbolic acid) is highly corrosive to skin and is absorbed rapidly into the body. Systemic toxicity associated with phenolic burns has included cardiac arrhythmias, cardiopulmonary arrest, convulsions, and coma. Lavage with water is not particularly effective in removing residual phenol from the skin surface, and polyethylene glycol (PEG) 300 or 400 in 2:1 mixtures of PEG and alcohol have been recommended for skin decontamination.[17]

Among all chemical burns, white phosphorus is unique in that it ignites upon contact with air and may cause thermal burns if it is in contact with the skin. Used in the manufacture of munitions, explosives, and fireworks, white phosphorus is usually stored under water in underground holding tanks. In order to minimize the risk of continuing thermal burns, the skin surface should be kept wet while mechanical debridement of residual white phosphorus particles is performed. Irrigation of the skin surface with 1%–2% aqueous solutions of copper sulfate has been recommended, since copper sulfate combines with white phosphorus and forms a colored complex which facilitates the visual location of residual particles to be debrided.[32]

Chromic acid is widely used for surface treatment of metals, electroplating, etching, glass cleaning, photoengraving, and a variety of other industrial processes. It is a strong tissue-oxidizing agent and may produce small, usually painless ulcers ("chrome holes") of the fingers and hands. Inhalation of its vapors has produced ulceration and perforation of the nasal septum. Management includes frequent rinsing with a fresh aqueous solution of 10% ascorbic acid, which reduces the hexavalent chromate.[105]

Solvents

Dermatitis from solvents almost always results from contact irritation rather than allergy. Exceptions to this general rule are the naturally derived solvents, such as turpentine. Although most solvent vapors are irritating to the mucous membranes and respiratory tract, frank dermatitis from exposure to solvent vapors alone is extremely rare. Dermatitis most commonly results from repeated, direct skin contact with solvent rather than just an occasional brief exposure. Based on chemical and physical properties alone, the ten most potentially irritating solvents have been listed in Table 10–10. The irritant action of solvents is based on the dissolution of skin surface, stratum corneum, and cell membrane lipids. In general, an inverse correlation between the boiling point of a solvent and its irritant potential has been observed, with lower boiling point solvents generally being more irritating.[64] The ability of any solvent to produce clinical irritation may be modified by other circumstances or conditions of exposure, as discussed above. A more detailed description of dermatitis from specific solvents may be found elsewhere.[2]

Soaps and Detergents

Excluding poison oak, the second most common cause of occupationally acquired dermatitis in California, ranking only behind

TABLE 10–10.
The Ten Most Potentially Irritating Solvents, in Decreasing Order of Severity*

Carbon disulfide
Petroleum distillates (diesel, gasoline, kerosene)
Coal tar solvents (xylol, toluol)
Turpentine
Chlorinated hydrocarbons (methylene chloride, trichloroethylene, Freon)
Alcohols (methyl, ethyl)
Glycols (propylene glycol)
Esters (methyl acetate, butyl acetate)
Ketones (acetone, methylethyl ketone)
Dimethyl sulfoxide

*Adapted from Pirila V, et al: Legislation on occupational dermatoses of the International Contact Dermatitis Research Group. *Acta Derm Venereol* 1971; 51:141–150.

solvents, is soaps, detergents, and other industrial cleaning agents. Contact dermatitis may result not only from excessive or inappropriate exposure associated with the correct use of such products but also from incorrect or inappropriate use of these agents to clean skin.[83]

Soaps and detergents are usually dispersed in water for the purpose of removing dirt and stains from a variety of surfaces. The first step in the cleansing process is the wetting of the surface to be cleaned. All detergents contain surface active agents which lower the surface tension of water and facilitate its spread. Second, a layer of detergent must be absorbed at the interface of the cleaning solution and the soiled surface. Detergent molecules generally have hydrophobic ends which solubilize into the soiled surface. Third, the stain or soil must be removed from the surface to be cleaned and dispersed into the water. This is facilitated by mechanical agitation, heating the wash solution, and the addition of foaming agents to the cleaner. For special cleaning purposes, such as removal of proteinaceous stains or burned organic material, other additives such as enzymes or sodium hydroxide are required to facilitate surface cleaning. Finally, the removed soil or dirt must be prevented from redepositing on the cleaned surface. This is usually accomplished by addition of emulsifiers or antiredeposition agents. Most industrial detergents also contain builders (usually salts of phosphate or silicate) to prevent scum buildup. Liquid soap solutions containing organic compounds will have a biocidal preservative added. Formaldehyde is still sometimes used as a preservative in industrial liquid soaps marketed for skin cleaning.

Depending upon the cleaning task, a variety of special additives may be contained. Detergents which also disinfect inert surfaces usually contain phenolic substances (e.g., p-tert-amylphenol) which may occasionally sensitize. "Waterless" hand cleaners, marketed for cleaning the skin of mechanics, contain 15%–20% petroleum distillates. These are not truly waterless, since the solvent is formulated into a water washable cream base with a mild detergent action. They remove oil and grease stains reasonably well from most skin surfaces except the palms and palmar fingers, where the deep skin creases make the stains less accessible to the cleaning action of these agents. Since they contain a substantial amount of petroleum distillate, waterless hand cleaners may cause irritant contact dermatitis if used excessively.

Abrasive soaps contain inorganic minerals (borax, sand, pumice) or hard plant material (sawdust, ground vegetable matter) which produce mechanical friction and agitation on the surface to be cleaned, assisting in the removal of difficult dirt or grease stains. Abrasives may be found in scouring powders, but are also popular in powdered soaps marketed to clean mechanics' skin. Mechanics often prefer abrasive soaps to waterless hand cleaners, particularly for cleaning palmar skin. Excessive use of abrasive soaps may cause frictional dermatitis of the forearms or dorsal hands, but the palms (where the stratum corneum is thickest) tend to be resistant.

Contact dermatitis from soaps and detergents usually results from the irritating effects of alkalinity and delipidization of the skin surface, rather than sensitization. On those infrequent occasions when dermatitis results from sensitization, the biocidal preservative (e.g., formaldehyde) or germicidal disinfectant (e.g., p-tert-amylphenol), or lanolin (cream soaps) is usually responsible. Rarely, some other additive (optical whitener, dye, perfume) may sensitize.

Some general guidelines apply for prevention of dermatitis from soaps and detergents. Cleaning agents designed for inert surfaces, which are generally much harsher than toilet soaps and workplace solvents, should never be used to clean skin. Protective gloves should be worn whenever cleaning with industrial detergents; gloves should be removed and the skin immediately rinsed if detergent accidentally enters the gloves. The temperature of any wash solution should be kept at the lowest possible level that will get the job done. Waterless hand cleaners should be rinsed off the skin surface with mild soap and water following each use and should never be used on inflamed skin. The use of abrasive soaps should generally be restricted to palmar skin cleansing.

Cement

Cement is a mixture of mineral-like oxide compounds, similar in composition and structure to the naturally occurring silicates. It is made by burning together limestone (calcium carbonate) and a natural carrier of silicates and aluminum oxides (clay or shale) in a fired kiln, to which iron is usually added. The resulting kiln product ("clinkers") is subsequently cooled and ground into fine particles. Gypsum (calcium sulfate) is added at this stage to retard the setting time. The resultant mixture (cement) derives its industrial properties from the ability of its anhydrous compounds to react with added water to form hydrates, which increase in strength as the amount of free water decreases by progressive hydration and evaporation. The strength of cement can be further increased by the presence of inert fillers such as sand and rock (e.g., concrete).

Severe burns and ulcerations can result from prolonged skin contact with wet cement, and onset of symptoms is typically delayed several hours after exposure. Burns usually occur on the knees from kneeling on wet cement or on the ankles from cement splashing inside workboots. They probably result from the extreme alkalinity of calcium hydroxide in cement formed when water reacts with calcium oxide, combined with the effects of pressure and occlusion against the skin.[102]

Contact dermatitis from cement usually results from skin irritation secondary to the alkaline, hygroscopic, and abrasive properties of cement, and typically presents as a dry but only slightly inflamed dermatitis of the hands and arms. Occasionally, dermatitis results from allergic sensitization to water-soluble chromate present in cement. Chromate is not normally present in the raw materials used in cement, but it is inadvertently added when these materials are processed and fired in the kiln. The primary source of contamination is felt to be the bricks lining the kiln.[23] In such cases, the dermatitis usually has a more pronounced inflammatory component than is seen with irritant cement dermatitis. Cements manufactured in the United States have generally been found to contain only very small amounts of water soluble chromate (less than 5 ppm) compared to European cements, and true contact allergy from chromate in cement is correspondingly rare.[95] Nickel and cobalt, implicated in some European cases of cement dermatitis, are not present in American cements.

Water-soluble hexavalent chromate may be reduced to trivalent chromate by the addition of ferrous sulfate to cement[44] and is felt to reduce the risk of having contact allergy develop from chromate. Although this practice is now being followed in some European countries, it has not been adopted in the United States.

Fiberglass

Fiberglass has extensive application in thermal and acoustic insulating material, industrial textiles, and reinforcement fillers for plastics. The popularity of fiberglass is due to its virtually total resistance to thermal, chemical, or microbial degradation.

Spicules of fiberglass may produce a mechanical irritation which results in severe skin itching. The intensity of symptoms is inversely proportional to fiber length and directly proportional to fiber diameter; short fibers, less than 3.5 μ in diameter, are least likely to produce any symptoms.[53] Pinpoint excoriations are the principal clinical findings, although occasional inflamed papules may be present. Frank eczematous dermatitis is unlikely to be due to fiberglass. Individuals with underlying dermographism (i.e., skin that urticates following scratching, pressure, or friction to the skin surface) are most likely to be severely affected. Although strands of fiberglass may be coated with various plastic resins which may theoretically sensitize, allergic contact dermatitis from fiberglass does not appear to be a serious concern.[97] Dermatitis from fiberglass must be differentiated from scabies, which it may resemble.

Plants and Vegetation

The oleoresins found in poison oak *(Toxicodendron diversilobum)* and poison ivy *(Toxicodendron radicans)* are powerful skin sensitizers. The active sensitizing principle is a substituted catechol with a 15-carbon (pentadecacatechol in poison ivy) or 17-carbon (heptadecacatechol in poison oak) unsaturated side chain. The resin dries quickly on skin, clothing, shoes, or tools, and will maintain its allergenic potency for long periods of time unless oxidized. Partially oxidized resin appears black, and black stains may occasionally be detected on the skin or clothing of affected patients (Fig 10–3). Clinical dermatitis is usually characterized by areas of linear or streaked eczematous patches, where portions of the crushed or broken plant were dragged or pulled across the skin surface. Dermatitis may be spread or exacerbated following repeated exposures to fomites contaminated with resin, as work clothes or tools. Blisters of poison oak/ivy dermatitis do not contain any allergenic oleoresin, however, and skin contact with blister fluid from an affected individual will not precipitate dermatitis in another sensitized person.[65]

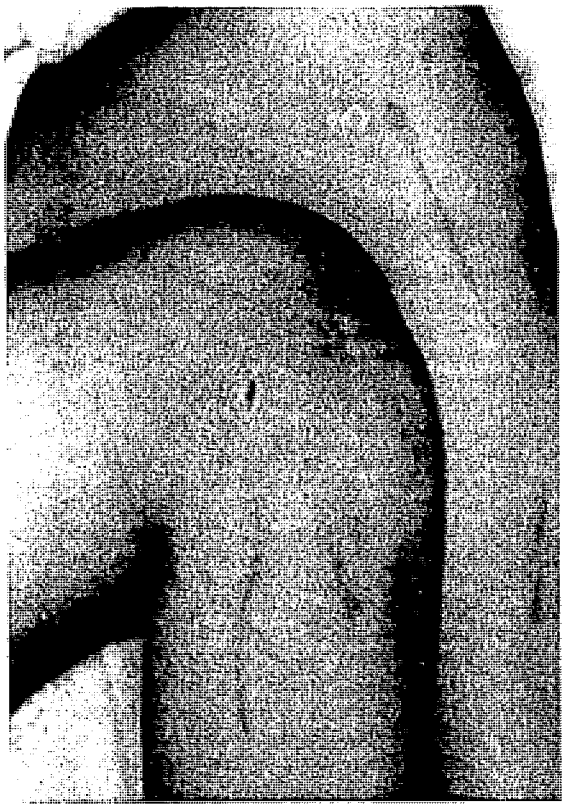

FIG 10–3.
Poison oak dermatitis, showing typical linear eczematous streaking where plant contacted the legs. A small black stain, representing dried oleoresin, is present near the knee.

Poison oak and ivy are members of the *Anacardiaceae* plant family, many of which contain identical or similar cross-reacting antigenic oleoresins. Individuals allergic to poison oak/ivy may inadvertently develop contact dermatitis when exposed to these other plant species or their products. Important members of this family include the mango tree, cashew nut tree, Japanese lacquer tree, and the Indian marking nut tree. A resinous oil derived from cashew nutshells has had extensive utilization in plastic resins and coatings, brake linings, and miscellaneous lubricants and occasionally precipitates dermatitis in exposed individuals previously sensitized to poison oak. Varnishes or lacquers derived from the Japanese lacquer tree, or objects coated with them, can cause similar occurrences of dermatitis.

Skin cleaning with soap and water following contact with poison oak/ivy is generally unsatisfactory in terms of removing oleo-

resin from the skin, unless it is performed within the first few minutes. Recent interest has centered on the possible prophylactic use of protective creams containing polyoxypropyleneamine salts of a linoleic acid dimer, which seem to bind to the resin and inactivate it.[92] Hyposensitization through oral administration of oleoresin extracts is effective experimentally in animals and under rigidly controlled conditions in man.[40] The efficacy of hyposensitization at a practical clinical level, unfortunately, is far from convincing. Variations in antigenic potency of extracts by different manufacturers (or between lots from the same manufacturer), problems of patient compliance, accidental reexposure to the plant before the recommended course of immunotherapy is complete, and side effects (e.g., perianal itching) all limit the likelihood of successful induction of tolerance. Hyposensitization treatment must begin three to four months prior to anticipated exposure, and maintenance dosages may have to be continued indefinitely.

Dermatitis from most other plants and woods is usually secondary to irritation from essential oils or juices in the stems, leaves, flowers, fruit, or wood. Important plants and woods which may occasionally sensitize the skins of forestry workers, gardeners, nursery workers, or wood workers are listed in Table 10–11. Next to poison oak/ivy, chrysanthemums and other *Compositae* species probably cause the greatest number of cases of contact allergy, particularly in nursery workers. In many instances of dermatitis from woods among forestry workers, contact allergy results from liverwort or lichens on the bark rather than from the wood itself. Exposure to potentially allergenic substances in the heartwood occurs when the wood is cut or sawed. Clinical dermatitis frequently occurs on exposed surfaces of the body indirectly exposed to allergens in pollen or sawdust (e.g., the face and neck) and may mimic photodermatitis. A characteristic dry, fissured dermatitis of the fingertips may occur among nursery workers or gardeners as a result of handling tulip or hyacinth bulbs.

TABLE 10–11.

Important Plants and Woods That May Cause Allergic Contact Dermatitis, Excluding Poison Oak/Ivy*

PLANTS	WOODS
Compositae (sesquiterpene lactones)	Cedar (thymoquinone)
Chrysanthemums	
Ragweed	
Sagebrush	
Feverfew	
Liverwort	
Lichens (usnic acid)	Cocobolo (dalbergiones)
Algerian/English Ivy (helenin)	Ebony (naphthoquinine)
Primrose (primin)	Mahogany (anthothecol)
Tulips (tulipaline A)	Pine and Fir (Δ-pinene, 3-carene)
Hyacinths	Rosewood (? quinone)
Garlic (diallyldisulfide)	Satinwood (?)
Onions	Teak (deoxylapichol)

*Sensitizing agent, where known, is included in parentheses.

Metals and Metallic Salts

Nickel is the most frequent metal which induces allergic contact sensitization and accounts for approximately 10% of all positive patch tests in North America. Occupational exposures occur mainly from metallic alloys or electroplating solutions containing nickel. In the case of solid metals, prolonged skin contact is generally required; heat, moisture, sweating, and friction probably facilitate the leaching of nickel from the metal and its subsequent absorption by the skin. Occasionally, sensitization occurs from contamination of industrial fluids (e.g., cutting fluids) with nickel leached from metal surfaces contacting the fluids. Sensitization is much more frequent in women, who tend to wear costume jewelry and to have pierced ears, than in men, who are more likely to be sensitized through occupational exposure.

Water-soluble hexavalent chromate may be both an irritant and a sensitizer. Alkaline solutions are more caustic to skin than acid solutions and typically cause "chrome ulcers" (see Chemical Burns). Occupational exposures occur from metals alloyed with chrome, electroplating solutions, tanning agents, paint and printing ink pigments, and industrial solutions or products to which chromate has been added as a corrosion inhibitor. Trivalent chromate has extremely low water-solubility, is poorly absorbed through the skin, and does not usually contribute to the development of clinical contact dermatitis. Trace amounts of chromate in cement probably do not contribute to cement dermatitis in the United States (see Cement).

Cobalt hypersensitivity frequently accompanies nickel or chromate allergy. Presumably, this occurs because cobalt is closely associated with these other metallic elements in the periodic table, and one metal is almost always contaminated with the other. Independent sensitization may occur from occupational exposures to cobalt in electroplating solutions, paint driers or cobaltous pigments, catalytic reagents, or hard metal grindings (containing approximately 90% tungsten and 10% cobalt).

Gold and its salts are strong potential experimental sensitizers, but clinical allergy is relatively rare. Metallic gold resists attack by water and oxygen and is virtually insoluble except in aqua regia; hypersensitivity from metallic gold objects is correspondingly and exceedingly rare. Soluble gold salts may occasionally produce allergic sensitization, but many are extremely irritating to the skin as well, such as gold potassium cyanide salts used in electroplating solutions.[40]

Beryllium salts are irritating and may cause painless skin ulcerations similar to chrome ulcers. Allergic contact dermatitis has also been reported. Both beryllium and zirconium salts, when inoculated into the skin, have produced allergic, delayed hypersensitivity granulomas. Awareness of severe respiratory disease from beryllium has led to the implementation of preventive measures to eliminate exposure, and clinical skin disease from beryllium is now exceedingly rare.

Inorganic arsenicals and platinum salts may occasionally cause allergic contact dermatitis, but sensitization from other metals is extraordinarily rare.

Rubber Products

Rubber products are manufactured from natural rubber latex or synthetic polymers of styrene-butadiene (SBR rubber), acrylonitrile-butadiene (ABR rubber), neoprene, isobutylene-butadiene (butyl rubber), polysulfides, polyurethanes, or silicone. With the exception of silicone and polysulfide rubbers, the other types all require addition of accelerators to speed the rate of cure and antioxidants to preserve the elasticity and flexibility of the rubber product. Other additives may include pigments, reinforcers, fillers, softeners, plasticizers, and phenolic resins (used as tackifiers).

In the manufacture of rubber, irritant contact dermatitis may occur from a variety of acids, alkalies, detergents, and solvents used in the process. Allergic contact dermatitis occurs not infrequently and is almost always due to an organic accelerator or antioxidant. While the list of potential sensitizing accelerators and antioxidants is enormous, common allergens include tetramethylthiuram disulfide, mercaptobenzothiazole, zinc dimethyldithiocarbamate, n-isopropyl-n-phenyl-p-phenylenediamine (IPPD) analogues, phenyl-β-naphthylamine, diethylthiorurea, and other related thiurams, mercapto compounds, p-phenylenediamine analogues, carbamates, naphthyl compounds, and thioureas.[2]

Clinical dermatitis from finished rubber products generally results only when the rubber item contacts the skin for long periods of time. Wearing apparel, especially protective gloves, rubber workboots, and facemasks, accounts for most of the occupational cases. Heat, sweat, and moisture are important cofactors, since the sensitizing accelerators or antioxidants must first be leached out of the solid rubber item. Preceding irritant dermatitis is common in cases of contact allergy to rubber gloves or boots. Often, the worker has ignored the wearing of appropriate protective gloves or boots until clinical irritant dermatitis has developed. The subsequent wearing of gloves or boots over inflamed, dermatitic skin may predispose to contact sensitization.

Germicides and Biocides

Industrial solutions or products that contain water and organic compounds generally require the addition of a biocidal agent to prevent decomposition of the product and prolong its shelf life. Examples include cutting fluids and emulsions, latex paints, liquid industrial hand soaps, first-aid creams, and water-based adhesives. When encountered in sufficient concentrations, virtually all biocides may be irritating or caustic, and most may sensitize. The likelihood of sensitization increases as the concentration of the biocide increases, and individuals who handle undiluted biocides (e.g., formulation of industrial products) are at greatest risk. Important biocidal agents are listed in Table 10–12. Formaldehyde and organic mercurials were formerly the most important causes of contact allergy in this group, but they have largely been replaced by other less-toxic agents; many of these may still release small amounts of formaldehyde or cross-react, causing dermatitis in formaldehyde-sensitive individuals. Formaldehyde may still be found, somewhat paradoxically, in industrial liquid hand soaps at up to 0.1% concentrations, although its use as a biocide in other industrial products has substantially decreased. Isothia-

TABLE 10–12.
Important Biocides Which May Irritate or Sensitize

TRADE NAME	CHEMICAL NAME
Formalin, Formol	Formaldehyde solution
Grotan BK*	Hexahydro-1, 3, 5-tris (2-hydroxyethyl) -sym-triazine
Grotan HD-2	2-chloro-N-hydroxymethylacetamide
Grotan K	Chloro-2-methyl-4-isothiazolin-3-one
Proxel CRL	1, 2-benzisothiazolin-3-one
Bioban p-1487	4-(2-nitrobutyl) morpholine and 4, 4-(2-ethyl-2-nitrotrimethylene) dimorpholine
Kathon CE, Kathon 886 MW	5-chloro-2-methyl-4-isolthiazolin-3-one and 2-methyl-4-isothiazolin-3-one
Skane M-8	2-N-octyl-4-isothiazolin-3-one
Quaternium-15,* Dowicil 75,*	1-(3-chloroallyl)-3,5,7-triaza-1-1-azoniaadamantine chloride
Tris Nitro	2-(hydroxymethyl)-2-nitro-1,3-propanediol
Dowicide 1, Dowicide A	O-phenylphenol
Sodium or Zinc Omadine	Sodium or zinc 2-pyridylthio-N oxide
Preventol D-2	Benzyl hemiformal
Preventol D-3	Chloromethylacylaminomethanol
Benzytol, Dettol, Ottasept Extra	Chloroxylenol, p-chloro-m-xylenol
Ottafact	Chlorocresol
Merthiolate	Thimerosal
Phermernite	Phenylmercuric nitrate
Captax, Dermacid, Mertax, Thiotax	Mercaptobenzothiazole

*Formaldehyde-releasing biocides.

zolin-3-one derivatives are emerging as an important new class of sensitizers.

Pesticides

The term *pesticide* designates any toxic chemical used against rodents, insects, fungi, weeds, or other pests. Skin disease among agricultural workers is relatively common and frequently attributed to pesticide exposure, although a direct causal relationship may be difficult to establish. Pesticides commonly implicated as causes of occupational skin disease are listed in Table 10–13. Dermatitis is most often observed, although several other adverse reactions have been reported (porphyria, urticaria, chloracne, erythema multiforme). Chemicals used as pesticides may have industrial applications outside agriculture (e.g., thiurams are used as rubber accelerators) or are used as biocides in industrial products. Irritant dermatitis is the rule and may be due to the vehicle in which the pesticide has been formulated, while true allergic contact dermatitis is relatively rare. The following classes of pesticides have consistently been among the most common contact allergens, in those few instances where pesticide-associated dermatitis has been evaluated by appropriate patch testing: carbamates, thiurams, captans, organomercurials, triazines, and pyrethrums. Formerly, contact allergy from pyrethrums was common and was caused by sensitizing sesquiterpene lactones contained in the crude extract (derived from a chrysanthemum species). Today, the extraction and purification process is such that the active insecticidal principle (pyrethroids) present in modern pyrethrum-containing insecticides should not contain any sensitizing sesquiterpene lactone. Contact allergy from pyrethroids or synthetic pyrethrins (derived from petrochemical sources) has not been observed. Skin disease attributable to pesticides sprayed on vegetation must be distinguished from skin disease caused by the vegetation itself, with which it is frequently confused. Pesticide-associated skin disease has been extensively reviewed by Adams.[2]

Plastics, Resins, and Coatings

A plastic is any substance, solid in its finished state, which has the capacity to be molded into various shapes. Plastic resins may be derived from either natural or synthetic sources. Contact dermatitis may occur when the plastic is in its liquid or unpolymerized state, but generally does not result from solid plastic products or coatings unless substantial, free, unpolymerized resin is still present.

Rosin (colophony) is the most important natural resin which may cause allergic contact dermatitis. Wood rosin is obtained by distillation of a crude extract from the wood of the pine tree *(pinus palustris)*, while distillation of turpentine yields a more highly purified gum rosin. Rosin is a brittle material which becomes sticky when heated, thus lending it to a number of adhesive applications, e.g., hot melt glues and adhesive tapes. Rosin is also hydrophobic, nonconductive, and noncorrosive, properties which make it extremely useful for electrical soldering operations. It is frequently combined with other synthetic resins or natural drying oils to form new plastic substances with a variety of physical properties. Rosin contains many potential skin allergens, the two principal ones being abietic acid and alcohol. With the exception of rosin and resinous products derived from plant species related to poison oak/ivy (see Plants and Vegetation), contact dermatitis from other naturally occurring resins is extraordinarily rare.

TABLE 10–13.
The Most Common Causes of Pesticide-Associated Skin Disease (California, 1977–1981)*

Sulfur
Propargite
Creosote
Benomyl
Glyphosphate
Weed oil
Methyl bromide
Captan
Difolatan
Dyrene

*Courtesy of Dr. Michael O'Malley, National Institute for Occupational Safety and Health.

Epoxy resins are synthetic resins which all share in common a highly reactive epoxide group contained within the molecular structure. Over 90% of commercial epoxy resins are based on the reaction of epichlorohydrin and Bisphenol A, producing monomers or polymers of the diglycidyl ether of Bisphenol A. Other types of epoxy resins are formed by reacting epichlorohydrin with hydantoin or other phenolic compounds. Epoxy resins uniquely combine the physical properties of strength, adhesiveness, and electrical and chemical resistance. Thus, they are extensively used in industrial paints, coatings, adhesives, and laminates, and may also be used to modify other resins. Reactive diluents (usually monoglycidyl ethers of alkanes or phenolic compounds) are frequently added to decrease the viscosity of the resin and to increase its flexibility. Polymerization requires addition of a curing agent (hardener), usually a polyfunctional aliphatic or aromatic amine, polyamide, or acid anhydride. The aliphatic amines will produce curing at room temperature, but the aromatic amines and anhydrides require addition of heat before curing can occur. Although the diglycidyl ether of Bisphenol A is a potent skin sensitizer, the epoxy reactive diluents or hardeners are responsible for approximately 10% of allergic contact dermatitis caused by epoxy resins. Dermatitis may be particularly severe when the epoxy resin is either sprayed or heat cured, since extensive skin contact from aerosolized particles or volatilized vapors can occur. Although the extremely alkaline aliphatic amine hardeners are potential skin irritants, clinical dermatitis from irritation is not very common, possibly because skin contact with the hardener is seldom prolonged. In this author's experience, careful investigation of contact dermatitis due to epoxy resin almost always demonstrates sensitization to the epoxy resin, reactive diluent, or hardener.

Phenolic resins are manufactured by reacting phenol (or some other phenolic) with an aldehyde (usually formaldehyde). The most important commercial phenolic resins are phenolformaldehyde, melamine formaldehyde, resorcinol formaldehyde, parater tiarybutylphenol formaldehyde, furfuryl formaldehyde, and cardolite (the condensation product of formaldehyde and a phenolic extract of cashew nutshell oil). Phenolic resins find extensive applications in plywood laminations, binders for foundry sand,

impregnation of wood or plastic to increase insulation, and combination with other adhesives (e.g., neoprene glue) to increase moisture resistance. Although phenolic resins release formaldehyde, morethan 90% of cases of allergic contact dermatitis to phenolic resins occur from the resin itself rather than released formaldehyde.[28] Since industrial processes employing phenolic resins are usually heat cured, exposure to the vapors may cause severe dermatitis in sensitized individuals.

Acrylic and methaerylic acid are strong solvents and potential skin irritants. A number of useful thermoplastic acrylic resins can be derived by esterification, modification, or copolymerization of these acids. These include Plexiglas (polymerized methyl methacrylate), latex paints, coatings, inks, dental or bone cement, anaerobic sealants, and floor polishes. Recently, polyfunctional acrylates that rapidly cure upon exposure to ultraviolent light have been employed in printing inks, dental adhesives, and miscellaneous coatings; these resins require addition of an ultraviolet light absorber such as benzophenone to effect cure. Irritant contact dermatitis may occur from prolonged skin contact with any acrylic resin; cyanoacrylate vapors are particularly irritating to the mucous membranes. An unusual form of delayed skin irritation caused by polyfunctional acrylates has been observed, the onset of which was delayed 12–24 hours but which was frequently bullous or painful.[77] Esters of methacrylic acid, particularly methyl methacrylate, are the most important skin sensitizers, but allergic contact dermatitis has been reported from polycthyleneglycol dimethacrylate in anaerobic sealants,[82] and polyfunctional acrylates and methacrylates.[38, 91]

Polyurethane resins are formed from the reaction of a polyalcohol with a diisocyanate (e.g., toluene diisocyanate). Although the volatile diisocyanates are extremely irritating to the skin or membranes, allergic contact dermatitis occasionally occurs from the diisocyanate or a polyamine euring agent.

Organic Dyes

Most organic azo dyes are potential skin sensitizers, the most important of which are paraphenylenediamine and its analogues. Water-soluble azo dyes are more likely to cause clinical sensitization than insoluble dyes. Beauticians exposed to paraphenylenediamine derivatives in hair dyes, workers dyeing textile resins, and photographic film developers exposed to color developing solutions not infrequently become sensitized to azo dyes. In addition to allergic eczematous contact dermatitis, color developing solutions have caused lichen planus-like eruptions.[46]

Cutting Fluids

Cutting fluids are used in virtually all industries that cut, grind, or machine metals. These preparations are formulated with vegetable or mineral oils, water, and high-pressure additives (sulfur and/or chlorine). Cutting fluids are used to cool and lubricate the cutting tool and parts, to flush away metal chips during the cutting or grinding operation, and to prolong the work life of the cutting tool. Neat oils are most commonly employed for low-speed grinding or honing operations, while oil-water emulsions are employed for high-speed cutting or grinding, where higher temperatures are encountered. Irritant contact dermatitis is most commonly produced by the cutting fluid emulsions, which contain water, detergents, and emulsifiers as well as potentially irritating sulfurated or ehlorinated oils; it is more likely to occur in machinists who must continually immerse their hands in cutting fluids throughout the work shift. Machinists frequently complain that "used" cutting fluid is harsher to their skin than "fresh" fluid, pointing to the possible role of contaminants or breakdown products in the development of irritation. Allergic contact dermatitis occasionally develops, and it is usually due to the biocide contained in the water-based emulsion, although metallic salts from the machined metal (e.g., nickel) or other additives (dyes, perfumes) are rare causes.[100] Some industries have recently adopted the practice of purchasing full-strength biocides and requiring employees periodically to add small amounts of fresh biocide to recirculating cutting fluid, in order to preserve its work life. The potential for becoming sensitized is markedly enhanced when skin contact to an undiluted biocide occurs, as opposed to the dilutions of biocide normally encountered in commercially formulated cutting fluid concentrations; this author has already observed several such cases.

Photodermatitis

Photodermatitis requires activation of a chemical substance on the skin surface by ultraviolet radiation (290–400 nm wavelength) for its clinical expression. Chemical substances capable of causing photodermatitis generally contain aromatic rings in their molecular structure and absorb ultraviolet radiation emitted by the sun. Most compounds that can absorb sufficient ultraviolet energy can cause phototoxic reactions if exposure occurs at sufficiently high concentrations, and some of these may also produce allergic photosensitization. Substances that do not have an absorption spectrum in the ultraviolet wavelength range are not likely to cause clinical disease. In all cases, inflammation develops on body surfaces normally exposed to sunlight (dorsal hands, arms, neck, face), provided that the responsible photosensitizer also contacts those anatomical areas. Covered skin, the eyelids, submental chin, and upper ears covered by hair are characteristically spared.

Phototoxic reactions, analogous to irritant contact dermatitis, are typically accompanied by immediate burning, stinging, or "smarting" of the skin shortly following sun exposure, and clinical inflammation appears more like an acute sunburn than an eczematous dermatitis. Inflammation is the result of a toxic photodynamic effect and is not mediated by immunologic mechanisms. Coal tar, pitch, creosote, and other products derived from coal tar may cause severe stinging and burning ("tar smarts"), the wavelength of activation being 340–430 nm.[29] Once this reaction has been initiated, much smaller amounts of ultraviolet light exposure can reproduce the stinging and burning sensations for several hours, even though a larger exposure was required to initiate it.[33] Phototoxic reactions are common in outdoor workers exposed to coal tar or its crude extracts, such as railroad workers who must handle creosote-impregnated ties. Coal tar epoxies contain up to 25% crude coal tar, and phototoxic reactions in outdoor workers exposed to this coating must be distinguished from epoxy resin allergy.

Furocoumarins are phototoxic substances found in various members of the ***Rutaceae*** and ***Umbelliferae*** plant families which may cause severe, painful, bullous reactions in any worker who

must handle or harvest these plants or their essential oils. Important species include limes, lemons, figs, celery, carrots, parsley, parsnip, dill, rue, bergamot, and the gas plant. Indoor workers who handle furocoumarin-containing fruits or vegetables are susceptible as soon as they leave their employment and are exposed to sunlight (e.g., bartenders who squeeze limes), but the cause may go undetected without careful questioning. Celery harvesters are particularly susceptible to severe reactions, since a common fungal parasite ("pink rot") dramatically increases the furocoumarin content in infested plants.[12] Postinflammatory hyperpigmentation characteristically follows furocoumarin-induced phototoxic reactions and may be the only clinical manifestation in mild cases.

True occupational photoallergic dermatitis is relatively rare and clinically presents as an eczematous dermatitis in sun exposed areas. Formerly, halogenated salicylanilides produced large numbers of cases as a result of their use as antibacterial agents in toilet soaps. Their use has been banned in toilet soaps for years, but they may be occasionally encountered in janitorial cleaning agents or first-aid creams. Pharmacists, nurses, physicians, veterinarians, or individuals employed in pharmaceutical manufacturing may develop phototoxic or photoallergic reactions from photosensitizing drugs. Photoallergic reactions may sometimes be followed by a persistent state of light reactivity (persistent light reactor) where clinical dermatitis recurs following exposure to sunlight alone, in the absence of exposure to the original photosensitizing chemical. This has typically occurred following topical reactions to halogenated salicylanilides or systemic reactions to chlorothiazides, but it has recently been observed following photosensitization to epoxy resin.[4]

Occupationally acquired photodermatitis must be differentiated from endogenous photosensitivity disorders, including porphyria cutanea tarda, polymorphous light eruption, solar urticaria, and systemic lupus erythematosus. Outdoor employment, however, may substantially aggravate an underlying endogenous photosensitivity disorder or precipitate a reaction in individuals taking potentially photosensitizing medication for some other medical problem. Rarely, porphyria cutanea tarda may be precipitated by exposure to chlorinated aromatic hydrocarbons (e.g., hexachlorobenzene).

Topical and systemic therapy is the same as for contact dermatitis. Preventive measures must include avoidance of the provocative agent or sunlight (or both), or the use of broad-spectrum sunscreens that effectively shield throughout the entire ultraviolet spectrum (e.g., sunscreens containing p-aminobenzoic acid esters or cinnamates combined with benzophenones, usually having a protection factor rating of 15 or greater).

Important causal agents of phototoxic or photoallergic reactions are listed in Table 10–14.

TABLE 10–14.
Some Important Causes of Occupational Phototoxic or Photoallergic Reactions

Coal tar products	*Drugs*
Crude coal tar	P-aminobenzoic acid and esters
Pitch	Chlorothiazides
Creosote	Diphenhydramine
Dyes	Phenothiazines
Acridine	Griseofulvin
Eosin	Nonsteroidal anti-inflammatories
Fluoroscein	Benzophenones
Rhodamine	Nalidixic acid
Rose bengal	Quinine
Plants	Tetracyclines
Carrots	Sulfonamides
Celery	*Antimicrobials*
Bergamot	Halogenated salicylanilides
Dill	Bithional
Figs	Hexachlorophene
Lemons	*Miscellaneous*
Limes	Saccharin
Parsley	Cyclamates
Parsnip	Optical whiteners
Rue	Epoxy resin
Gas plant	
Angelica	
Buttercup	
Mustard	
Goose foot	
Scurfy pea	
St. John's wort	
Essential oils and fragrances	
Angelica root oil	
Bergamot oil	
Lemon oil	
Lime oil	
Orange oil (bitter)	
Rue oil	
Cedarwood oil	
Sandalwood oil	
Lavender oil	
Musk ambrette	
6-methyl coumarin	

Pigmentary Disorders

Toxic Vitiligo

Depigmentation resembling idiopathic vitiligo (Fig 10–4) can be caused by cutaneous exposure to a variety of phenolic or catecholic derivatives which structurally resemble tyrosine, an amino acid precursor of melanin synthesis.[47, 76] At low doses, these substances simply inhibit melanin synthesis, but at higher doses they may be cytotoxic to melanocytes, resulting in irreversible pigment loss. Phenolic or catecholic derivatives are frequently employed as antioxidants or germicidal disinfectants and may be encountered in rubber products or manufacture, photographic developing solutions, lubricating oils, plastics or adhesive manufacture, and institutional or industrial disinfectant cleaning solutions. Depigmentation may be preceded by inflammation of the affected skin and is frequently associated with allergic contact sensitization to the same chemical responsible for the loss of pigment. Important causes of toxic vitiligo are listed in Table 10–15. The essential chemical requirement of melanocyte toxicity appears to be a nonpolar side chain in the para position on the phenolic or catecholic ring structure.[14, 48]

Postinflammatory Changes

Hyperpigmentation may follow any episode of cutaneous inflammation, but it is more likely to occur in darkly complexioned

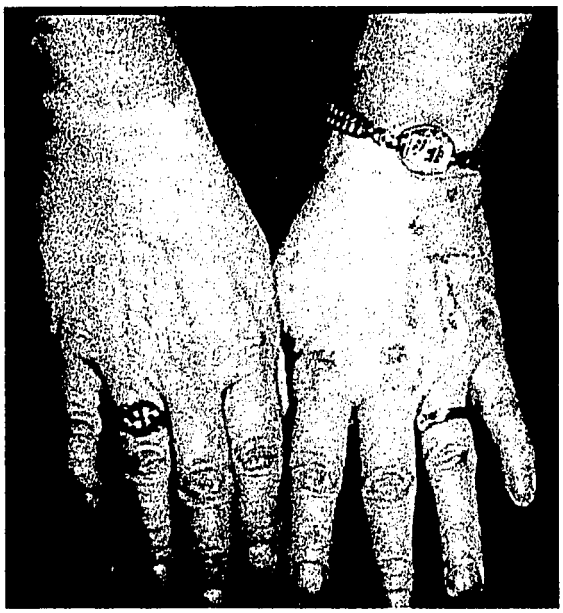

FIG 10–4.
Toxic vitiligo in a hospital custodial worker secondary to p-tert-amylphenol in a disinfectant cleaning solution.

individuals. Cutaneous darkening is due to accumulation of melanin from injured melanocytes or hemosiderin from extravasated red blood cells in dermal tissue. Pigment deposition may persist for years, particularly in black persons, although there is some tendency toward spontaneous improvement. Postinflammatory pigmentation may also follow reactions to photosensitizers (see Photodermatitis), but in these instances the increased pigment results from melanocyte stimulation (i.e., "tanning") rather than injury.

Loss of cutaneous pigment may occur when tissue injury is severe enough to destroy melanocytes, such as chemical or thermal burns.[108] This must be distinguished from toxic vitiligo.

TABLE 10–15.
Important Chemical Causes of Toxic Vitiligo

Hydroquinone
Monobenzyl ether of hydroquinone
Monomethyl ether of hydroquinone (4-hydroxyanisole, 4-methoxyphenol)
Paracresol
Para-tertiary butylcatechol
Para-tertiary butylphenol
Para-tertiary amylphenol
Ortho-phenylphenol
Ortho-benzyl-para-chlorophenol
4-Isopropylcatechol

Discolorations and Stains

Chronic intoxication from heavy metals, particularly silver, mercury, or arsenic, may produce diffuse slate-gray, blue-gray, or melanotic discoloration of skin. The nail beds may be similarly affected. Discoloration results either from metallic deposition within the skin or stimulation of melanin synthesis and is often accentuated in sun-exposed areas.

Numerous industrial substances may stain the skin. These stains serve as useful markers of cutaneous exposure and may be particularly helpful when symptoms of systemic toxicity are present without an obvious history of exposure. Nitrosylated compounds, including nitric acid, trinitrotoluene, dinitrophenol, and metaphenylenediamine, produce yellow to orange cutaneous stains. Many of these nitrosylated substances are initially colorless, and the characteristic stains appear only after oxidation occurs on the skin surface, or after nitration of the nuclei of various aromatic amino acids incorporated into cutaneous protein.[45] Explosive or abrasive forces may adventitially tatoo the skin with pigmented foreign particles.[3] "Coal miner's tatoo," produced by inoculation of coal dust into the skin, is such an example.

Acneiform Disorders

Environmental Acne

Preexisting acne vulgaris may be substantially aggravated by various occupational stresses. Heat and high humidity favor swelling of the keratinous ductal epithelium, with subsequent poral occlusion ("tropical acne"), which may precipitate substantial flares in acne-prone individuals employed in tropical climates or excessively hot work environments, such as foundries. Rubbing, pressure, or friction against the skin may provoke new acne lesions in susceptible anatomical areas ("acne mechanica"). Occupational causes of acne mechanica include face masks, belts, straps, tight-fitting work clothing, and pressure from seat backs.[86]

Oil Acne

Heavy, lubricating petroleum greases, oils, and pitch fumes may cause follicular plugging and pustular folliculitis (oil acne) and is seen not infrequently in machinists and automotive mechanics.[30] Lesions occur most frequently on body surfaces maximally exposed to the causative petroleum products, such as the dorsal fingers, hands, and extensor surfaces of the forearms, and may be particularly severe on parts of the body covered by oil-soaked clothing, such as the thighs. The mechanism of induction involves stimulation of follicular keratinization followed by ductal occlusion. Comedones (blackheads) are invariably present, but inflamed follicular papules and pustules are often numerous. The pustules of oil acne are usually sterile, but occasionally secondary bacterial infection may be present.

Chloracne

Chloracne (Fig 10–5) describes an acneiform disorder caused by either polychlorinated or polybrominated aromatic hydrocarbons, and the term "halogen acne" has been suggested as a more appropriate name.[30, 31] Chemical substances which may cause chloracne are listed in Table 10–16. Toxicity and acneigenic potential depend more on the stereoisomeric positioning of the halo-

FIG 10–5.
Chloracne. Note preponderance of noninflammatory comedones and cysts. Sites of predilection are the malar crescents and posterior auricular folds. (Photo courtesy of Dr. James S. Taylor. Cleveland Clinic Foundation, Cleveland, Ohio.)

gen atoms than on the degree of halogenation itself.[2] The mechanism by which all chloracneigens produce disease involves induction of squamous metaplasia of the sebaceous gland ducts, followed by atrophy of the underlying sebaceous glands and subsequent formation of keratin-filled cysts.[115] The chemical responsible for inducing chloracne, however, cannot be detected in the cystic contents.[93] There is a rough correlation existing between acneigenic potential and ability to stimulate the aryl hydrocarbon hydroxylase microsomal enzyme system, with 2,3,7,8-tetrachlorodibenzodioxin being the most potent.[31]

TABLE 10–16.
Chemical Causes of Chloracne

Polyhalogenated biphenyls
Polyhalogenated dibenzofurans
Polyhalogenated naphthalenes
Polyhalogenated contaminants
Dioxin (trichlorophenol, pentachlorophenol)
Tetrachlorazobenzene and tetrachloroazoxybenzene (dichloroaniline and related chemicals)

The basic dominant clinical lesion is a small cystic swelling resulting from plugging of the pilosebaceous duct, ranging in size from a pinhead to a small pea. The follicular openings of many lesions become obscured, and the swellings begin to assume a characteristic pale yellow color ("straw colored cyst"). The locations in which lesions first begin to appear are the malar crescents (that is, the skin just lateral to the eyes) and the retroauricular folds, and in mild cases these may be the only areas involved. The nose is frequently spared. As the severity of the disease increases, cystic lesions become more numerous on the face, inflammatory lesions appear, and involvement spreads to the posterior neck, trunk, buttocks, and scrotum. The most severe cases may resemble cystic acne, although the number of inflammatory lesions is considerably less. Extensive scarring may occur as inflammatory lesions involute. Some degree of spontaneous improvement is the rule within a few months after cessation of exposure, and approximately 80% resolve completely within two to three years. In the most severe cases, residual lesions may persist for many years, but usually only in the malar regions and behind the ears.[31]

Dusky hyperpigmentation of the face may develop in chloracne cases as the severity of facial involvement increases. Meibomian gland swelling and a peculiar pigmentation of mucous membranes and nail beds occurred in the Yusho and Taiwan PCB (polychlorinated biphenyl) poisonings, where the route of exposure was by ingestion,[68, 126] but it has not been observed in cases caused entirely by cutaneous exposure. Erythema and dermatitis may develop following exposure to the sodium salts of chlorophenols,[31] but is not likely to occur from exposure to trace amounts of chloracneigens.

Chloracne must be distinguished from acne vulgaris, which may appear virtually identical in mild cases, solar elastosis with comedones (Favre-Racouchot syndrome), and other forms of environmental acne. The malar crescents and posterior auricular folds are almost always involved in chloracne cases. The occurrence of numerous, noninflamed, cysts outside the typical areas of distribution for acne vulgaris, documented substantial exposure to known chloracneigens, and absence of other external causes all favor a diagnosis of chloracne. Although histologic examination of chloracne cysts usually demonstrates squamous cell metaplasia and plugging of the infundibular ducts with atrophy of the underlying sebaceous glands,[30] its usefulness in establishing a diagnosis of chloracne has been questioned.[93] Treatment is generally unsatisfactory, but there is anecdotal evidence that topical or oral treatment with cis-13 retinoic acid has been helpful in selected cases.

Vascular Reactions

Urticaria

In comparison to occupational asthma, true occupationally induced urticaria is rare. The overwhelming majority of cases of generalized urticaria are either idiopathic in origin (almost two thirds) or are provoked by exposures outside the work environment (e.g., food or drug allergies). When caused by occupational factors, the route of exposure is almost always inhalation, and episodes of urticaria are invariably accompanied by other symptoms of inhalant allergy (asthma, rhinitis, or conjunctivitis). Some chemical sub-

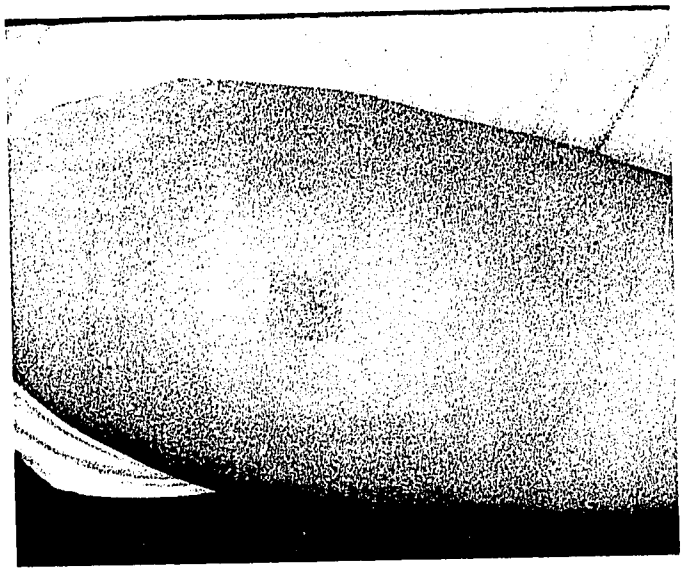

FIG 10–6.
Contact urticaria from carbon paper. The patient complained of swelling and itching of the fingers. A moistened piece of carbon paper produced this intense urticarial reaction after 20 minutes of occlusion against the skin.

stances are also capable of producing localized erythema or wheal and flare responses following skin contact, provided that sufficient penetration through the skin has occurred. This latter phenomenon has been dubbed "contact urticaria"[19] (Fig 10–6).

Urticaria may be provoked by either immunologic or nonimmunologic mechanisms, and its occurrence is not always synonymous with allergy. Urticaria from nonimmunologic mechanisms is caused by direct stimulation (chemical irritation) of the vasculature, indirect provocation of mast cell degranulation, or neural reflex vasodilation. Immunologic mechanisms generally involve IgE-mediated immediate hypersensitivity; more rarely, urticaria may be caused by immune complex-mediated vasculitis, due to activation of the complement cascade and generation of C3a and C5a anaphylotoxins.

Localized contact urticaria requires that the provocative agent first penetrate into the skin. In the case of small molecules, penetration may occur through intact skin. Vasoactive chemical substances capable of inducing localized erythema (rubefacients) have been employed medicinally for centuries as promoters of healing. Contact urticaria from immediate allergy to large proteinaceous molecules generally requires that the normally intact skin barrier be first compromised, since these large molecules would not normally be expected to penetrate intact skin. Atopic persons are more prone to develop immunologic contact urticaria, and they generally give histories of reacting to the provocative substance by inhalation or ingestion as well. Atopic persons who are employed in wet work occupations where skin irritation commonly occurs and who are simultaneously exposed to potentially allergenic proteinaceous molecules, are particularly susceptible, since the skin barrier is compromised by preceding contact dermatitis.[84] Occupations in which allergic contact urticaria is most likely to occur include gardening, food handling, and veterinary medicine, where the occurrence of clinical disease generally reflects a previously documented inhalant or food allergies.

The clinical eruption of urticaria consists of evanescent, pruritic, erythematous macules or wheals ("hives"), usually erupting within 15–60 minutes following exposure. Individual lesions usually subside within 24–48 hours after cessation of exposure. Contact urticaria, by definition, always occurs at the site of primary skin contact with the provocative substance; subjective stinging and burning suggest nonimmunologic mechanisms, while pruritus and swelling characterize immunologic contact urticaria. Generalized urticaria following a localized reaction is rare, but should also suggest IgE-mediated hypersensitivity. A peculiar clinical variant of contact urticaria, termed "protein contact dermatitis," may occur in food handlers or other workers with dyshidrotic or irritant hand eczema.[56] Immediate symptoms of itching, swelling, and redness are rapidly followed by increased vesiculation of the skin, which is more characteristic of delayed hypersensitivity reactions. Whether this biphasic response represents an interaction of humoral and cell-mediated immune mechanisms, or results from nonspecific accumulation of serum released by the urticarial reaction within preexistent microvesicles, has not been resolved.[19]

Causes of occupational urticaria are listed in Table 10–17. Outdoor workers are susceptible to ordinary inhalant allergies to grass, trees, or pollen, for example, which may be accompanied by generalized urticaria. With the exception of proteinaceous dust and molds, inhalant allergies with urticaria among indoor workers are extremely uncommon, and case reports attributing urticaria to chemical fume allergy are mostly anecdotal[63] and difficult to prove. One exception is "platinosis," a syndrome among workers exposed to fumes of platinum salts, consisting of conjunctivitis, rhinitis,

TABLE 10–17.
Some Common Causes of Occupational Urticaria

INHALANTS	SKIN CONTACTANTS
Dust	Dairy products
Molds	Fish
Grasses, trees, pollen	Citrus fruits
Castor bean pomace	Grains
Coffee bean dust	Meats
Platinum salts	Nuts
Penicillin	Spices
Formaldehyde(?)	Vegetables
Pesticides(?)	Medicinal rubefacients
Ammonia(?)	Animal hair and tissues
Sulfur dioxide(?)	Plants and grasses
Aliphatic polyamines(?)	Dimethylsulfoxide
	Alcohols
	Numerous other chemicals

asthmatic symptoms, urticaria, and angioedema.[15] This syndrome has been clearly demonstrated to involve IgE-mediated hypersensitivity to platinum compounds.

Diagnostic evaluation requires prick, intradermal, or epicutaneous provocative tests, with appropriately prepared extracts and sufficient numbers of controls; clinical challenge tests may be necessary in some cases. Confirmation of immunologic mechanisms involves RAST or passive transfer tests. Management consists of avoiding exposure to the provocative substances, and adequate doses of antihistamines. Care should be taken when the patient operates heavy equipment or machinery, since oversedation represents a safety hazard; antihistamines with the least sedating properties (e.g., tersenadine) should be selected in such circumstances. Nonsteroidal anti-inflammatory agents have benefited some cases of nonimmunologic contact urticaria.

Flushing Reactions

Flushing is a transient redness of the skin that occurs primarily on the face but occasionally on the neck and upper chest. It results from a temporary shunting of blood flow to the face into the superficial dermal blood vessels. In the occupational setting, exposure to several different chemical substances may trigger unpleasant flushing reactions.

Rubber industry workers exposed to tetramethyl- or tetraethylthiuram disulfide (disulfiram; Antabuse), which is used to accelerate rubber curing, may experience severe flushing reactions and headaches, along with nausea and vomiting, if alcohol is ingested shortly after work. In part, it was the observation of these unpleasant reactions in rubber workers in the 1920s and 1930s that led to the introduction of disulfiram as a treatment for chronic alcohol addiction.[13] Disulfiram inhibits the enzymic alcohol dehydrogenase, blocking the normal catabolism of alcohol, leading to an accumulation of acetaldehyde in the body, which is thought to be responsible for the reaction.

"Degreasers' flush" has been described in workers who subsequently ingested alcohol following exposure to trichloroethylene vapors.[10, 114] Trichloroethylene also inhibits the normal catabolism of alcohol.[89] Disulfiram-like reactions in industry workers have also been reported following exposure to N,N-dimethylformamide[73] and N-butyraldoxime.[72]

Rosacea is an acneiform disorder of the face characterized by erythema, telangiectasia, and a tendency toward papule and pustule formation. Connective tissue hypertrophy, particularly of the nose, may also occur. Flushing reactions are common in rosacea, may be accompanied by burning and stinging sensations in the skin, and are usually the earliest component of the condition to be identified. Although rosacea is generally considered to be an endogenous condition, transient flushing reactions may be triggered by a host of nonspecific environmental stimuli. These include sunlight, heat, alcohol, organic solvent vapors, and emotional stress. When these nonspecific stimuli are encountered in the workplace, considerable diagnostic confusion may result.

Connective Tissue Disorders

Vibration White Finger

Physiologic changes induced by vibration are reviewed in detail in Chapter 21. Operators of vibratory tools, such as chain saws, rock drills, chipping hammers, grinders, and many other power tools, may experience episodic numbness, tingling, and blanching of one or more fingers, identical to the cold-induced vasospastic changes of Raynaud's phenomenon. This disorder has been variably called "vibration-induced white finger disease," "traumatic vasospastic disease," or the hand-arm vibration syndrome. The latent interval between exposure to vibration and onset of symptoms is inversely related to the acceleration of the vibrating tool and the cumulative hours of daily exposure to vibration.[16] Frequencies above 60 Hz are capable of inducing vasospasms at threshold acceleration values in the range of 75 m/sec^2.[16] Since the Pacinian corpuscles respond most sensitively to frequencies in the 125 Hz range, reflex linkage of Pacinian corpuscles to the sympathetic innervation of the cutaneous vasculature has been suggested as a possible mechanism for induction of the vasospastic phenomena.[57] Other etiologic factors believed to be important are biodynamic forces involved in the holding or operation of the tool and individual host susceptibility (for example, smoking or preexisting vascular disease may increase susceptibility).[116]

The first symptoms consist of persistent numbness and tingling, developing within several minutes of commencing operation of a vibratory tool, followed by variable degrees of swelling of the fingers. With further exposure, blanching of the fingertips begins to occur and is generally most severe in the fingers exposed to the most intense vibration. At first, these symptoms may totally subside on weekends or vacations, but later they may be precipitated upon exposure to cold. The ischemia is followed by reactive hyperemia and cyanosis, and in advanced cases persistent cyanosis of the fingers is present. Ischemic ulcerations of the fingertips may develop, but the latter complication is fortunately rare. Paresthesias and neurosensory deficits are also the rule. The disease may be particularly severe in forestry workers operating chain saws who are simultaneously exposed to damp cold.[70]

Vibration-induced white finger disease must be differentiated from Raynaud's phenomenon that is associated with underlying connective tissue disease, occlusive vascular disease, brachial ar-

tery compression syndromes, dysglobulinemia, and neurogenic disorders. Spontaneous remission is not likely, except in mild cases, and moderately to severely affected workers must usually change occupations. Warm, protective clothing is necessary in cold climates. Pharmacologic therapy formerly consisted of vasodilatory agents such as reserpine, but recent interest has focused on calcium channel blockers. Although reportedly effective in the management of Raynaud's phenomenon associated with underlying collagen vascular disease, their effectiveness in vibration-induced white finger disease remains to be established.

Collagen Vascular Disease

Cutaneous changes similar to those observed in scleroderma or progressive systemic sclerosis have been reported in association with various occupational exposures,[52] which are listed in Table 10–18. Workers exposed to unreacted vinyl chloride monomer, used to manufacture polyvinyl chloride, have developed Raynaud's phenomenon, papular cutaneous sclerosis, sclerodactyly and fibrosis of the lungs, liver, and spleen, accompanied by lytic lesions of the middle distal phalanges (acroosteolysis).[78] These changes mostly revert to normal following cessation of exposures, but an increased incidence of angiosarcoma of the liver has been observed. Other than vinyl chloride disease, the vast majority of other reported cases of occupational scleroderma have occurred from exposure to silica dust (silicosis), but unlike vinyl chloride disease, the cutaneous sclerosis has been diffuse rather than papular.[101] A new sclerodermatous disorder has been recently described in Japanese workers exposed to epoxy resin, consisting of severe, diffuse cutaneous sclerosis and muscle weakness.[127] This latter disorder was attributed to a cyclohexylamine hardener (bis(4-amino-3-cyclohexyl)methane), which produced sclerodermatous skin changes, with increases in type 1 collagen, following intraperitoneal injections into mice. Reports attributing scleroderma to various solvent exposures are largely anecdotal and require further observation and confirmation.[104, 113, 128]

Peripheral Neuropathy

This subject is discussed in detail in Chapter 50. Although most cases are due to ingestion or inhalation exposures, the skin is an important potential route of exposure. Following absorption through the skin, peripheral conversion by the liver to a toxic metabolite may be necessary before neurotoxicity can develop (e.g., in exposures to n-hexane, methyl-n-isobutyl ketone). Occasionally, a few chemical substances which are directly neurotoxic may have a selective effect at the primary site of skin contact, such as acrylamide. Recently, synthetic pyrethroids have been shown to elicit cutaneous paresthesias in workers handling this insecticide.[67]

TABLE 10–18.
Occupational Causes of Scleroderma-Like Disorders

Vinyl chloride
Silica
Epoxy resin hardener (bis(4-amino-3-cyclohexyl)methane)
Perchloroethylene(?)
Trichloroethylene(?)
Miscellaneous organic solvents(?)

Neoplasms

Radiation

Considerable clinical, epidemiologic, and experimental evidence has established ultraviolet (UV) solar radiation to be one of our most potent and important environmental carcinogens. Despite the large number of individuals occupationally exposed to sunlight, and the relatively frequent occurrence of skin cancers in outdoor workers,[51] little effort has been expended to protect workers' skins adequately from carcinogenic UV radiation.

Squamous cell carcinoma (Fig 10–7), a neoplasm of epidermal squamous cells, occurs most frequently on areas of the body that are chronically exposed to sunlight, namely the head, neck, and dorsal hands and forearms. Within areas of chronic exposure, there is a further clustering on regions that receive the maximum amounts of UV exposure: the cheeks, nose, forehead, lower lip, and tops of the ears. Squamous cell carcinoma seldom arises spontaneously on normal appearing skin, and involved sites generally show other signs of extensive actinic damage. These latter changes include: thickened, yellowish, furrowed skin (solar elastosis); abundant cutaneous wrinkles; multiple, dilated, superficial cutaneous blood vessels (telangiectasiae); solar-induced lentigines (freckles); and flat, erythematous, scaling, premalignant actinic keratoses.

Basal cell carcinoma, a tumor of epidermal basal cells, demonstrates a similar, strong clinical predilection for anatomical areas chronically exposed to sunlight. Unlike squamous cell carcinoma, however, up to one third of basal cell carcinomas may develop within skin which is not chronically exposed, and there is a further tendency to cluster in periorbital skin and the nasolabial folds, which receive considerably less UV radiation than other facial sites, suggesting that additional factors other than sunlight contribute to its development.[120] Except for lentigo maligna melanoma, a clinical variant occurring in chronically sun-exposed skin of elderly individuals, the evidence linking malignant melanoma to chronic UV exposure suggests a complicated inter-relationship.[71]

Epidemiologic surveys have clearly demonstrated an increased risk for the development of squamous cell, basal cell, or melanoma skin cancers among white populations as one moves closer to the equator.[51, 119] When geographic locations at similar latitudes are corrected for the cumulative yearly amount of UV radiation actually reaching the earth's surface, the association becomes even stronger. Within any geographic location, a similar correlation between skin cancer incidence and cumulative individual exposure to UV radiation may be demonstrated. Host susceptibility and pigmentary skin differences also influence the development of skin cancer; while persons with Irish, English, or Scottish origins who sunburn easily have the greatest relative risks.[123]

Squamous cell carcinoma may be easily produced in hairless rodents by repeated exposures to artificial UV radiation, with the

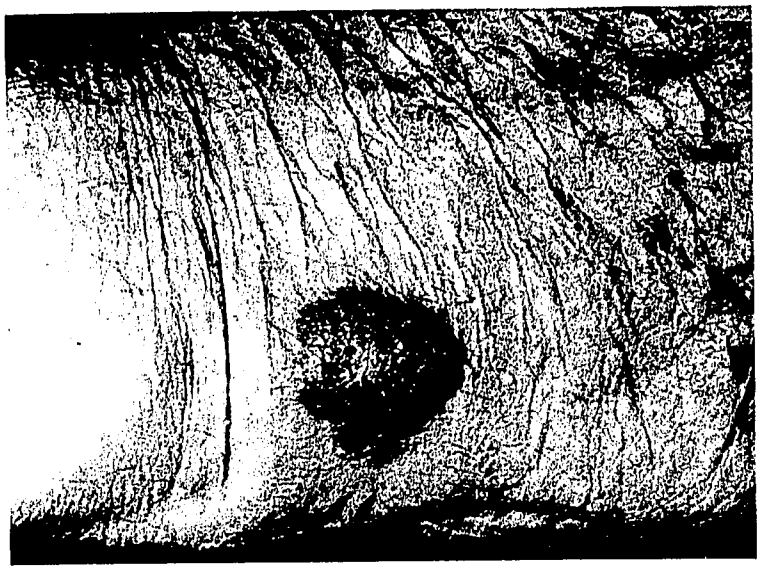

FIG 10–7.
Squamous cell carinoma arising within sun-damaged skin on the dorsal hand of a farmer.

primary carcinogenic wavelength being in the 290–320 nm range. Concomitant exposure to longer wavelength UV radiation, or environmental climatic changes induced by heat, wind, or excessive humidity, may augment carcinogenesis in the laboratory. Cutaneous chemical carcinogens, such as polycyclic aromatic hydrocarbons and nitrosourea compounds, have additive effect when combined with UV radiation. Furthermore, chemical irritants which are not primarily carcinogenic (e.g., croton oil) may promote the development of UV-induced squamous cell carcinomas. To date, neither basal cell nor melanoma skin cancer has been experimentally reproduced in laboratory animals following UV irradiation alone, but malignant melanoma has been reproduced following UV exposure only after benign melanocytic tumors have been first induced by topical application of dimethylbenzanthracene.[39]

Prevention of solar-induced skin cancers should be generally aimed at reduction or elimination of UV exposure. Hats and tightly knit clothing may substantially reduce sunlight exposure, but workers often cannot tolerate such protective clothing in hot climates. The most practical and efficient method of reducing UV exposure in outdoor workers should be the regular use of broad-spectrum sunscreens, preferably with a solar protection factor of 15 or greater. The selected sunscreens should also resist wash-off by sweating and should probably be reapplied several times during the work shifts.[94]

Cutaneous neoplasms may arise in areas of chronic radiodermatitis resulting from excessive exposure to ionizing radiation. Numerous cases have been observed in physicians, dentists, and other medical personnel who were inadvertently exposed while operating x-ray machines. The histologic types include squamous cell and basal cell skin cancers, with sarcomas or melanomas developing more rarely. Squamous cell carcinomas indueed by ionizing radiation tend to be aggressive and metastasize early, compared to those of actinic origin.[25]

Polycyclic Aromatic Hydrocarbons

The role of polycyclic aromatic hydrocarbons in cutaneous carcinogenesis is well established. Squamous cell carcinoma of the scrotum of chimney sweeps was the first recognized occupational neoplasm and was later observed in mule spinners. Dimethylbenzanthracene and 3,4-benzyprine, found in coal tar and its derivatives (especially pitch, asphalt, creosote, and heavy mineral oil), are the most potent experimental carcinogens. After latent intervals of 6–20 years, keratotic papillomas ("tar warts") begin to appear on exposed surfaces. Sites of predilection include the face, forearms, hands, ankles, dorsal feet, and scrotum.[50] Other clinical signs of tar toxicity (oil acne, hyperpigmentation, phototoxicity) are usually present. Malignant degeneration into frank squamous cell carcinoma, however, probably occurs in only very few of the premalignant papillomas. Concomitant trauma and UV radiation exposure are generally considered important cofactors in tar carcinogenesis.[122]

Preventive measures are directed primarily at employee hygiene and education. Substitution of oils, free of carcinogenic polycyclic aromatic hydrocarbons, is desirable wherever possible and can substantially reduce the incidence of skin cancer.[37]

Arsenic

Despite the inability to induce experimental cutaneous tumor formation with arsenic, the circumstantial evidence implicating it as a cutaneous carcinogen is considerable. Numerous case reports have documented the development of arsenical keratoses and skin cancers in individuals who received Fowler's solution (sodium ar-

senite) for treatment of psoriasis. Taiwanese populations drinking water from artesian wells contaminated with arsenic have demonstrated a marked incidence of skin cancers compared to control populations.[117] One study of a group of factory workers exposed to inorganic arsenic demonstrated increased numbers of skin cancers in workers exposed to the highest levels of arsenic within the plant.[55]

Characteristic punctate, keratotic papules ("arsenical keratoses") develop on the palms and soles of individuals with chronic arsenic exposure. They generally range in size from 1 to 5 mm. Histologic examination usually shows varying degrees of nuclear atypia of the squamous cells, and degeneration into squamous cell carcinoma is sometimes observed. Arsenical keratoses must be distinguished from the punctate keratoses frequently seen on the palms or soles of black persons; these benign lesions remain confined to the palmar or plantar creases. Other signs of chronic arsenic exposure include a diffuse dusky pigmentation of the skin punctuated with white, slightly atrophic macules, giving the skin the appearance of "rain drops on a dusty road." Squamous cell carcinomas induced by arsenic exposure often occur on nonexposed skin surfaces; intraepidermal squamous cell carcinoma (Bowen's disease) is the most frequent clinical type and is associated with visceral malignancies. Basal cell carcinomas on nonexposed skin surfaces are also common.

Trauma

The role of trauma in cutaneous neoplasia remains controversial. Skin cancer arising directly within an area of cutaneous trauma has been documented on numerous occasions,[6, 35] but it should be considered a rare occurrence. Thermal burns with subsequent scar formation have been the most frequently observed form of associated trauma. In most cases, the skin fails to heal completely after the initial trauma, and malignancy develops after a variable latent period. If complete healing does occur, a causal relationship between the initial trauma and subsequent development of skin cancer should be suspected. Squamous cell carcinomas arising within burn scars on the legs from heating coals have been reported from India (Kangri ulcer) and Japan (Kairo ulcer), but they may be due primarily to polycyclic aromatic hydrocarbons in the coals rather than the actual trauma.[2] From a scientific viewpoint, evidence suggests that trauma is a co-carcinogen rather than a true carcinogen.[121]

Miscellaneous Neoplasms

A cutaneous T-cell lymphoma (mycosis fungoides) has been associated epidemiologically with work in construction and manufacturing industries and with pesticide and other miscellaneous chemical exposures.[106] Clinical observation suggests that in some cases, cutaneous T-cell lymphoma could develop from chronic bouts of allergic contact dermatitis and antigen stimulation, with subsequent malignant transformation of the stimulated clone of T cells.[120] These intriguing observations will require confirmation before definitive conclusions may be drawn.

Increased incidences of malignant melanoma have been observed in a number of occupations with diverse chemical exposures. At this time, no definite conclusions regarding causative exposures can be drawn on the basis of existing epidemiologic data.

Infections and Infestations

Individual workers employed in a diverse number of occupations may be exposed to a wide range of potentially infectious microorganisms. While virtually any kind of infection can occur as a result of some employment if conditions are favorable, some are considered to be specific risks for certain occupations and may have skin manifestations. Since a comprehensive review of infectious disease is well beyond the scope of this review, only those infections or infestations with primary or diagnostic cutaneous lesions will be considered here. Systemic infections with secondary skin manifestations will not be covered, although some (e.g., brucellosis) may be specific for certain occupations.

Bacteria

Abrasions, burns, and lacerations, particularly when combined with poor skin hygiene, may nonspecifically predispose a worker to a number of bacterial skin infections. Atopic workers are most susceptible to bacterial skin infections, particularly *Staphylococcus*. Excessive heat and humidity may predispose to bacterial folliculitis or furunculosis ("boils"), especially when work clothing is constrictive.

The primary lesion of anthrax, caused by *Bacillus anthracis*, is a small papule which rapidly enlarges to form a boggy, gelatinous, painless mass topped with a hemorrhagic or necrotic vesicle or pustule; satellite lesions may surround the primary lesion. Infection almost always occurs on exposed surfaces of the body (face, neck, arms, hands) from direct, accidental inoculation of spores from contaminated animal hair or hides, particularly sheep and goats. Later, regional lymph nodes enlarge and signs of systemic illness (fever, malaise, leukocytosis, tachycardia) appear. In the United States, strict animal controls and vaccination programs have virtually eliminated this disease among ranchers and farmers, and workers at risk are now primarily dock workers or freight handlers who unload animal hides imported from foreign countries, where strict controls do not exist. Anthrax may be fatal unless adequately treated with intravenous penicillin (4–6 million units daily) or tetracycline (2 gm per day) for two weeks. This diagnosis is established on gram stain and culture of exudate from the primary lesion.

Erysipeloid occurs in fishermen, butchers, or other handlers of raw meat or poultry products. It is an acute infection of traumatized skin, and usually occurs on the hands or fingers following puncture or laceration of the skin on bones or cutting utensils. The initial lesion usually occurs within one week following cutaneous trauma and consists of a painful, sharply marginated, raised edematous plaque which expands peripherally without ulceration or desquamation. Low-grade fever and malaise may develop, but serious systemic illness or complications are rare. The untreated lesion usually resolves spontaneously within three weeks but may occasionally relapse. The causative organism, *Erysiplothrix insidiosa*, is difficult to demonstrate on either gram stain or culture of infected tissue, and the diagnosis is established primarily on clinical grounds. Erysipeloid must be distinguished from streptococcal cellulitis. The disease responds to oral penicillin (equivalent to 2–4 million units per day) or erythromycin (1 gm per day) for seven to ten days.

Mycobacteria

Primary tuberculosis of the skin may be caused by accidental inoculation of material from infected human or animal tissues into traumatized skin. In individuals with no preexisting immunity to *Mycobacterium tuberculosis*, the initial lesion is a generally painless papule arising within two to four weeks at the site of initial trauma, which slowly enlarges and ulcerates (tuberculous chancre). Regional lymphadenopathy develops within one to two months following the appearance of the primary lesion. The clinical lesion of primary inoculation tuberculosis occurring in individuals with some degree of previous immunity is a slowly expanding, hyperkeratotic, verrucous appearing plaque with a purplish inflammatory halo (tuberculosis verrucosa cutis); the regional lymph glands are usually not enlarged. In the past, primary inoculation tuberculosis was considered an occupational risk of physicians, pathologists, and morgue attendants, and was sometimes called "prosector's wart." It is a relatively rare disease today. The diagnosis is established by biopsy and appropriate culture of infected tissue. Treatment consists of isoniazid in combination with rifampin or other antituberculous drugs.

Atypical microbacterial infections of the skin occur through primary cutaneous inoculation. The most common occupational infection is caused by *Mycobacterium marinum* and occurs in persons who fish or other workers who clean fish tanks. The clinical lesion is a firm, granulomatous nodule of the dorsal hand or finger with a tendency toward central ulceration. Multiple lesions of the hand and arm, oriented along lines of lymphatic drainage, may occur and resemble those of sporotrichosis. Diagnosis is established by tissue biopsy and appropriate culture. Spontaneous healing of untreated lesions normally occurs within two to three years, usually with residual scar formation. Small lesions may be surgically excised. Treatment with conventional antituberculous therapy may be limited by drug resistance. Minocycline, 100–200 mg per day, has been reported as an effective alternative therapy.

Viruses

Primary or recurrent herpes simplex infections of the hand or fingers (herpetic whitlow) has generally been considered an occupational hazard of dentists, nurses, physicians, or other health personnel exposed to oral secretions. The clinical lesions are often excruciatingly painful, and extensive edema of surrounding tissues may occur, resembling cellulitis. Lymphangitic streaking and tender enlargement of epitrochlear or axillary lymph nodes may develop. Virologic examination of blister fluid from the lesions of a recent series of patients with herpetic whitlow have challenged an automatic presumptive relationship to oral secretions, since 11 of 13 patients grew type 2 rather than type 1 virus.[49] The usefulness of acyclovir in primary inoculation herpes simplex infections remains to be established. Conservative management consists of limb elevation, analgesics, and any one of a myriad of topical drying agents.

Orf (echthyma contagiosum) is transmitted to human skin following contact with infected sheep or goats, in whom the disease is usually present as a weeping, crusted eruption around the mouth. It is caused by the orf virus, a member of the poxvirus group, and occurs primarily on the hands of farmers, ranchers, or veterinarians tending to sheep. The clinical lesion is most often solitary and generally evolves through six stages, each lasting about six days: the papular stage (erythematous, firm papule), the target stage (a central nodule surrounded by a halo of normal skin and an outer periphery of erythema), the acute stage (red, weeping surface on the nodule), the regenerative stage (thin, dry crust over surface of nodule), the papillomatous stage (tiny papillomatous growths over surface of nodule), and the regressive stage (regression of papillomas and reduction in overall size of lesion). Diagnosis is confirmed by electron microscopic examinations of infected tissues or specific viral antibody titers in serum. Complete resolution of the lesion without therapy is the rule.

Milker's nodule is a viral skin infection caused by paravaccinia virus, acquired by direct skin contact with infected cows, where lesions occur on the teats. Thus, it occurs most commonly in farmers or other dairy workers responsible for milking cows. The clinical lesion bears a striking resemblance to orf, with the nodule passing through similar stages of evolution. The diagnosis is confirmed by electron microscopy or viral culture of infected tissue. Spontaneous resolution without treatment occurs.

Fungi

The majority of superficial fungal (dermatophyte) skin infections are not work-related. Work environments which are hot and humid, such as foundries, may predispose certain populations of workers to development of superficial dermatophyte infections in a nonspecific fashion, particularly the groin and feet, since the presence of moisture, sweat, and heat promotes fungal growth. Dermatophytes may infect the fingernails and hands of those employed in wet work occupations. *Trichophyton rubrum* typically causes a dry, scaling, sometimes painful eruption of the palms, which for unknown reason is characteristically present on only one hand of the affected individual, but spares the other (Fig 10–8); evidence of *T. rubrum* infection can usually be found elsewhere on the body, particularly the toenails and soles. Wet work dries the skin of the affected palm even further, exaggerating the symptoms, and the worker often notices improvement when not working. A scaling eruption confined to the palm of one hand should immediately prompt an examination of the feet and search for fungus.

Zoophilic fungi (i.e., those with animal reservoirs) may specifically infect farm workers, veterinarians, or other animal handlers. Zoophilic *Trichophyton mentagrophytes* may be carried by a wide range of animals and frequently produces an intense inflammatory cutaneous reaction with pustule formation. Lesions caused by *Microsporum canis* (dogs and cats) more typically have a "ringworm" appearance. *T. verrucosum* is acquired from infected cattle and may produce a deep inflammatory reaction of the neck, beard, or scalp. Diagnosis is established by demonstration of fungal hyphae on potassium hydroxide examination of scales or hair from infected skin. Superficial dermatophyte infections on the general body surface may be treated with topical imidazole antifungal preparations. Infections of the palms, soles, and nails, or deep inflammatory reactions on hair-bearing surfaces, do not generally respond well to topical agents, and oral therapy (250–500 mg of micronized griseofulvin or its equivalent, two times per day) is preferred. Oral ketoconazole also has been used for treatment of dermatophyte infections.

Sporotrichosis is acquired from accidental inoculation of the fungus *Sporothrix schenkii* from contaminated vegetation. Rosebush

FIG 10–8.
Superficial dermatophyte infection of one palm, sparing the other, in a dishwasher.

thorns and sphagnum moss are favorite habitats of the organism, and the disease most frequently occurs in gardeners, florists, or nursery workers. The usual clinical presentation is an ulcerated nodule on the dorsal hand, followed by the appearance of similar cutaneous nodules spreading in a linear fashion along lines of lymphatic drainage. Definitive diagnosis by demonstration of the characteristic cigar-shaped organism in infected tissue is difficult, and culture is often required. Sporotrichosis must be distinguished from atypical mycobacterial infections caused by *M. marinum*, which it may mimic closely. The treatment of choice is 10–15 drops of a saturated solution of potassium iodide three times daily.

Warm, moist work environments may nonspecifically predispose to several clinical types of infection with *Candida albicans*. As with dermatophyte infections, *Candida* infections may develop in intertriginous body surfaces (the groin, axillae, and inframammary skin). Infection of the fingernail folds (paronychia) is perhaps the most frequent occupational infection caused by *Candida* and occurs in bartenders, beauticians, custodial workers, machinists, or virtually anyone else whose hands are constantly exposed to moisture while working. The clinical appearance is a red, swollen, mildly to moderately painful nail fold which does not suppurate, with local destruction of the cuticle. Erosive dermatitis from *Candida* infection occasionally occurs in the web spaces between the fingers. Treatment with topical mycostatin or antifungals is usually effective, but chronic paronychia may need to be treated for months.

Parasites

Outdoor workers are suseeptible to a host of biting insects or other infestations which may present with cutaneous lesions. Hookworm (cutaneous larva migrans) and schistosome (swimmers' or clam diggers' itch) infections may develop in workers maintaining beaches, lakes, or streams. Scabies, caused by the mite *Sarcoptes scabiei*, may infect employees of hospitals, nursing homes, or chronic care facilities who attend infested patients. The intensely pruritic eruption of scabies may occur anywhere on the body surface below the neck, but typically includes the axillae, buttocks, genital and periumbilical skin, wrists, ankles, and web spaces between the fingers, where pathognomonic burrows are classically seen. Diagnosis is established by microscopic demonstration of the mite, eggs, or feces from skin scrapings of a burrow. The treatment of choice is lindane or malathion lotion, applied to the entire body and left on for 8–12 hours; treatment may be reapplied in one week. Alternatively, preparations containing 5%–10% precipitated sulfur or crotamiton may be used. Other mite infestations generally considered to be specific risks for certain occupations include the poultry mite *(Dermanyssus gallinae)* and the grain mite *(Pheomotes ventricosus)*, which may cause pruritic papular eruptions in poultry workers or handlers of raw grain. The diagnosis must be established by demonstrating mites in the infected host, since they do not burrow or reside in human skin.

Disorders of Hair and Nails

Like the skin, the hair and nails are subject to a number of occupational afflictions, particularly infections, chemical discolorations, and abnormalities of growth.

Bacterial or fungal infection of hair follicles (folliculitis) has been previously discussed. Hair discoloration may result from accidental contact with industrial dyes and stains, but the cause is usually obvious. Workers with long hair who are employed around machinery with rapidly rotating parts are subject to traumatic hair loss (alopecia), if the hair accidentally becomes entangled in the machinery; the hair is literally pulled out by the roots, but complete regrowth in six to nine months is the rule and no treatment is indicated. When chemical or thermal burns severe enough to

cause scarring and destruction of the hair bulbs occur on hair-bearing surfaces, permanent hair loss results.

Diffuse hair loss has been associated with toxic exposures (toxic alopecia) to thallium-containing rodenticides, boric acid, arsenic, and chloroprene,[36] and is virtually always seen in association with other signs and symptoms of systemic toxicity specifically related to the causative exposure. Hair loss usually begins within two to four weeks of an acute toxic exposure, but onset may be more insidious in the case of chronic intoxications. Microscopic examination of hair shafts in toxic alopecia usually reveals a characteristic narrowing or tapering of the shaft near the hair root, due to arrest or inhibition of mitotic activity, and hair loss is caused by breakage of the structurally weakened shaft at this point. When toxic alopecia is due to thallium exposure, the hair shafts will also show some pigment darkening near the root. Circumscribed patches of hair loss suggest a diagnosis of alopecia areata, an autoimmune disorder of hair, and should not be confused with toxic alopecia. Toxic alopecia is a reversible disorder, and hair regrowth commences within a few months, provided that exposure to the provocative toxic agent has ceased.

The nails are similarly susceptible to a number of environmental and occupational afflictions,[9] listed in Table 10–19. Individuals employed in wet work occupations are commonly subject to subungual or paronychial infection of the nails from yeast, bacteria, or fungi. *Pseudomonas* infections characteristically cause a greenish pigmentation beneath the nail plates. Topical therapy can be extremely difficult if the affected individual continues to immerse the hands in aqueous solutions. Topical liquid antibiotic preparations marketed for eye or ear infections are suitable for treatment of subungual or paronychial infections, provided the organisms are susceptible to the selected antimicrobial agent(s). *Pseudomonas* is not sensitive to most of the available topical antibiotics, but preparations containing tobramycin (one of the few topicals to which *Pseudomonas* is sensitive) may be effective.

The nail matrix, located beneath the cuticle and proximal nail fold, contains the germinative cells which form the nail plate. The matrix is vulnerable to a number of occupational insults, all of which can result in dystrophic, abnormal growth of the nail plate. Physical trauma, ionizing or microwave radiation, and mechanical vibration, may all damage the matrix and induce longitudinal ridgings (Beau's lines), brittleness, or thickening of the nail plates. Inflammation of the overlying proximal nail fold, whether bacterial or chemical in origin, produces ridging, stippling, or pitting of the nail plate. Direct absorption of potentially toxic chemicals into the nail folds may occasionally affect the matrix, without causing paronychial inflammation, and alter the growth of the nail plates.[8] Frequent exposure of the nails to solvents may partially dissolve and weaken the formed nail plate, and workers handling solvents frequently complain of thinness and brittleness of the nails.

Onycholysis (separation of the nail plate from the nail bed) most often results from accidental trauma and can be excruciatingly painful. If severe, the entire nail plate may be lost or shed within a few weeks, but complete regrowth ensues. Despite its apparent hardness, the nail plate is not a totally impenetrable barrier and chemical substances may penetrate through or beneath the nail plate, provoking inflammation (contact dermatitis) of the underlying nail bed, with onycholysis, without necessarily provoking inflammation of the paronychial tissue. Similarly, infection beneath the nail plate causes separation of the overlying nail plate.

Discolorations of the nails generally accompany dermatophyte infections of the nail plate, and range from varying shades of yellow and white to brown and black. *Pseudomonas* infections produce greenish subungual pigmentation. Organic dyes, such as hair dyes and photographic solutions, and coal tar derivatives can produce virtually any shade of discoloration, but yellow-brown to black is the most common. Nitrosylated compounds characteristically cause a yellowish discoloration of the nail plates, as well as the skin. Silver intoxication is associated with a characteristic blue discoloration of the lunulae, while PCB intoxication has been associated with brownish pigmentation of the nail bed, but this has occurred only in oriental populations. Horizontal white bands in the nail plate may be caused by repetitive occupational trauma to the nails; distinctive, transverse white bands (Mees' lines) have been classically attributed to arsenic intoxication.

TABLE 10–19.
Common Causes of Occupational Nail Disorders

Paronychial Inflammation	*Onycholysis*
Infection	Trauma
Staphylococcus	Contact dermatitis
Pseudomonas	Infection
Candida	*Discoloration*
Dermatophytes	Infection
Contact dermatitis	*Pseudomonas* (green)
Dystrophic Growth	Dermatophytes (white, yellow, brown/black)
Trauma	Chemical stains
Radiation	Nitrosylated compounds (yellow)
Vibration	Coal tar derivatives (brown/black)
Infection	Organic dyes (brown/black)
Dermatophytes	Chemical toxicity
Candida	Silver (blue lunulae)
Contact dermatitis	PCB (brown)
Chemical toxicity	Arsenic (white bands)
	Trauma (white bands)

Climatic Disorders

Heat and Humidity

Hot, humid environments, or dry environments which are hot enough to provoke copious sweating, may promote blockage of the eccrine sweat glands and a subsequent inflammatory papulovesicular eruption, termed miliaria rubra or "prickly heat." The precise factors which precipitate clinical disease are not completely understood, but the sweat ducts become plugged in the mid to lower epidermis. Lesions begin to appear within a few months of beginning work in a hot environment. The affected individual notes a prickling or stinging sensation, particularly on areas covered by clothing, which may become more pruritic and is often provoked immediately when activities that promote sweating are performed; symptoms subside when the worker moves to a cooler shelter. Miliaria rubra must be distinguished from folliculitis and other cutaneous pyodermas that are also promoted by hot work environments. Although miliaria rubra subsides spontaneously within one week,

its disappearance may be aided by topical drying agents such as calamine lotion.

The combination of low humidity and low temperature promotes dryness and chapping of the skin, which quickly becomes pruritic ("winter itch"). When severe, frank eczematous changes develop, the extremities are the most frequently affected sites. Similar climatic conditions can be mimicked by refrigerated air conditioning systems and affect indoor workers during the summer time.[26] The condition responds to liberal use of topical moisturizers.

The combination of warm temperatures and low relative humidity (usually less than 35%) may produce subtle dryness of the skin and symptoms ranging from intense pruritic to low-grade eczema. Termed "low-humidity dermatosis,"[103] it may affect office workers exposed to warm, dry air from heating ducts, or employees engaged in manufacturing processes where low humidity is a necessary quality control measure, as in semiconductor manufacturing. The more vigorously the warm, dry air passes over the workers' skins, the more intense the symptoms. Urticaria has also been reported as an effect of low humidity, but it is unclear whether the phenomenon was simply redness secondary to the normal axon flare in response to scratching, or from underlying dermographism in a few affected individuals. Symptoms dramatically improve once the humidity is raised to 40% or greater and can also be ameliorated by topical moisturizers.

Rusters

A peculiar corrosive reaction of ferrous metals occasionally results from palmar sweat. Individuals capable of producing corrosion of metallic objects simply by touching their surfaces are known as "rusters."

The phenomenon occurs more frequently during the summer when sweating is greater, but it can also occur during winter months, since palmar sweating is also under emotional control. In addition to the unsightly cosmetic appearance of rusty fingerprints and blemishes, metallic products corroded by rusters may malfunction.

Once detected, such employees may lose their jobs. Most rusters give histories of excessive palmar sweating. Corrosion is generally thought to result from excessive concentrations of chloride ions in the palmar sweat of rusters,[18, 21] although this has been disputed;[60, 61] neither pH nor lactate concentrations in sweat appear to be of practical importance. Corrosion may be prevented by degreasing metallic objects in an appropriate solvent immediately after handling by rusters. Inhibition of palmar sweating with topical applications of aluminum chloride hexahydrate solutions has also been effective.[7, 61]

Percutaneous Absorption

Besides the lungs and the gastrointestinal tract, the skin may be an important route of entry for chemical substances that may produce systemic toxicity. For some exposures, such as chloracnigens and pesticides, the skin may be the principal or only route of exposure.[125] Chemical substances that are detoxified after first passing through the liver following intestinal absorption may be even more toxic when absorbed through the skin, since liver detoxification is bypassed.[5]

The development of signs and symptoms of systemic toxicity is determined not only by the inherent toxicologic properties of the chemical toxin, but also on its ability to penetrate through skin. Visible inflammation of skin is not a necessary prerequisite for significant percutaneous absorption, and many substances may produce serious systemic illness if enough is absorbed, without provoking clinical dermatitis. Obviously, a substance that may burn the skin or cause dermatitis, damaging the protective stratum corneum barrier, may enhance its own absorption and systemic toxicity. Factors that may promote percutaneous absorption include: prolonged skin contact with the potentially toxic substance; hydration of the stratum corneum beneath water-impermeable protective clothing, particularly when the potentially toxic substance is entrapped on the skin surface beneath the protective clothing; damage to the stratum corneum barrier from previous trauma (cuts or abrasions) or dermatitis; elevation of skin surface temperature, particularly from transfer of heat from warm or hot industrial liquids; and accidental contact with anatomical areas such as facial or genital skin, which are generally more permeable than the rest of the skin surface.[81]

Important occupational exposures that may produce serious systemic toxicity have been reviewed by Malkinson[75] and Birmingham.[12] Table 10–20 lists important exposures for which systemic toxic reactions have occurred as a result of skin absorption. Concerns regarding toxic exposures and percutaneous absorption have usually focused on relatively acute symptoms associated with exposure; long-term toxicities, particularly carcinogenicity, should also be considered.

ESTABLISHING THE DIAGNOSIS

History

In the course of taking the history from a patient who may have work-related skin disease, the following should be obtained: (1) an accurate chronologic sequence of events surrounding the onset of the skin disease, its subsequent clinical course, and associated work activities; (2) a description of the skin lesions and their initial anatomical locations and spread to other body sites; (3) disability caused by the skin disease; (4) identification of all relevant work exposures; (5) presence of similar skin disease in co-workers; and (6) response to previous medical treatment.

Work activities at the onset of skin disease often provide the most important clue for establishing the correct etiologic diagnosis since exposure to the responsible causal agent has likely occurred at that time. Note should be made as to whether the skin disease began while the patient was performing usual and customary work duties or while on modified assignment. Did the skin disease clear or improve while the patient was performing modified work duties or while not working, for example, during weekends, vacations, or lost work time due to illness? Did any specific activity or exposure exacerbate the skin disease? Care must be taken to distinguish clinical improvement that may be due to concomitant medical therapy from spontaneous improvement, which may occur when the worker is removed from the suspected causative work exposures.

While a clinical description of the skin lesions, obtained directly from the patient, is sometimes useful if no active lesions are present at the time of evaluation, this can be very unreliable, and

TABLE 10–20.
Some Chemical Substances That May Cause Systemic Toxicity Through Percutaneous Absorption

CHEMICAL	SYSTEMIC TOXICITY
Aniline, related azo dyes and derivatives	Methemoglobinemia, liver disease, bladder cancer
Arsenic	Malaise, weight loss, gastrointestinal disturbances, peripheral neuritis
Benzene	Aplastic anemia, myelofibrosis, acute myelogenous leukemia
Polyhalogenated aromatics (chloracneigens)	Gastrointestinal disturbances, liver disease, porphyria, cancer (?)
Cyanide salts	Diffuse cellular asphyxia, death
Mercury	Gastrointestinal disturbances, central nervous system intoxication, nephrosis
Organic solvents	Central nervous system depression
Organophosphates	Headache, diarrhea, increased urination, miosis and blurred vision, brachycardia, bronchorrhea and bronchospasm, muscle excitation and fasciculation, lacrimation, salivation, respiratory depression
Chlorinated hydrocarbons	Convulsion, delirium, central nervous system depression

a review of medical records (when available) is a preferable manner of obtaining a description of the initial clinical appearance. The initial skin site(s) to be involved are generally the areas of most direct skin contact with the causative agent; close attention should be paid to all potential exposures at the initial sites of cutaneous involvement. Dermatitis of the face and neck in a factory worker, for example, should suggest the possibility of an airborne exposure, such as a cutting fluid mist or overspray. The severity of the skin disease may be reflected in whether it has resulted in lost work time or job modification.

An accurate description of work duties and potential exposures is important, but it is not always possible to obtain reliable information directly from the patient; phone calls to supervisors or responsible health and safety personnel, as well as an occasional visit to the worksite, may be required. The evaluating physician should establish not only the identity of potential exposures, but also the quantitative and qualitative aspects of exposure. Have there been any new exposures introduced into the work environment prior to the onset of skin disease, or has there been an increase in amount or duration of skin contact with long-standing exposures, or a change in their circumstances? Protective clothing, such as gloves and work boots, and skin-cleansing products or techniques should be considered as potential causes of occupational dermatitis rather than solely as preventive measures. For example, did a potential irritant spill or splash inside work gloves, or were gloves put on before a potential irritant was properly cleansed from the skin? Environmental conditions, such as temperature and humidity in the workplace, should be established. All first-aid cabinet preparations used to treat the skin condition at the worksite should be identified as potential causes of, or contributions to, the skin disease.

The presence of similar skin disease in co-workers may provide another important clue to its occupational origin or etiology. Unfortunately, a history of similar skin disease based only upon the patient's account is notoriously unreliable. The physician is ill-advised to draw definitive conclusions regarding similar disease in co-workers unless he or she has personally evaluated them or reviewed appropriate medical records.

A thorough history should properly determine the presence of important risk factors, such as personal or family history of atopic allergies; antecedent skin disease or reactions, such as dermatitis from jewelry, cosmetic preparations, or hair dyes; and potential causative exposures in the domestic environment.

Physical Examination

Particular attention should be paid not only to the morphological appearance of individual skin lesions, but also to their distribution on the body surface. The search for a causative agent should be directed at chemical, physical, or biologic exposures actually occurring at the principal site(s) of involvement. Dermatitis that is confined only to palmar surfaces usually indicates that endogenous factors are probably operative.

The physical examination must help to differentiate occupational from endogenous dermatoses, principally psoriasis, atopic dermatitis, and dyshidrotic and various other forms of eczema. The entire skin surface should be examined for the presence of other characteristic skin lesions, particularly the feet. It is not unusual for an affected worker to deny the presence of skin lesions on covered parts of the body, especially if these other lesions are not asymptomatic. If the entire skin surface is not properly examined, the correct diagnosis may be overlooked.

Patch Testing

Although virtually any diagnostic procedure (blood tests, KOH examinations, skin biopsies) may be utilized in an evaluation of a suspected occupational dermatosis, the patch test is the most

frequently employed. A great deal of confusion and misunderstanding surrounds this remarkably simple but useful test. The fundamental purpose of the patch test is to establish a diagnosis of allergic (not irritant) contact dermatitis. Interpretation of the patch test rests on the assumption that a suspected allergen will cause a localized eczematous reaction, resembling the clinical eruption under evaluation, when occluded against the skin of a sensitized individual; no reaction should occur on the skin of a nonsensitized person.

Details of the methodology may be found in appropriate textbooks on the subject.[20] All materials to be tested must first be standardized so that no false positive inflammatory irritant reactions (chemical burns) occur when occluded on the skin of nonsensitized, nonexposed individuals (controls). In most cases, this requires dilution of the test material in a suitable vehicle (usually white petrolatum) to a concentration below its irritant threshold. Test substances (already standardized) may be purchased commercially or prepared by the investigator according to published guidelines. Where no reliable guidelines exist (which is often the case for many industrial substances), the investigator must be prepared to establish the proper test concentration by running a sufficient number of controls (usually about 20). Table 10–21 lists the substances contained in the "routine" battery screening series of the American Academy of Dermatology. Evaluating physicians should not forget that at best the patch test procedure only indicates whether or not the tested individual is allergic to any of the tested substances. No conclusions can be drawn regarding allergies to substances which were never tested in the first place. "Routine" screening series are aimed primarily at detecting allergies in the domestic environment and do not contain other allergens more commonly encountered in the workplace.

The test procedure itself is as carefully standardized as to the test concentrations, and it should be stressed that any deviations from the procedure may lead to false negative or positive results. A small amount of test substance (at proper concentration) is placed on a metallic disc or filter paper disc backed with aluminum foil. The disc is attached to adhesive tape and placed on the upper back or upper outer arms. Both the metallic disc and aluminum foil are totally impermeable to water, thus providing total occlusion of the test substance against the skin surface and maximum skin penetration. Test strips are removed two days following application, and the test sites evaluated. An unequivocal positive reaction should demonstrate the presence of numerous papules or vesicles. Weaker reactions (erythema and edema without papules or vesicles) cannot be reliably distinguished from false positive marginal irritant reactions on the basis of morphology alone. Test sites must be reevaluated 72–96 hours following initial application, since 30%–40% of all positive reactions will be negative or equivocal at the 48-hour reading.[79] Incorrectly testing with only partially occlusive test materials, such as Band-Aids, or on the

TABLE 10–21.

Routine Patch Test Screening Series, American Academy of Dermatology, 1984–1985.

Medicaments	
Benzocaine	5%
Neomycin	20%
Metals	
Potassium dichromate	0.5%
Nickel sulfate	2.5%
Resins	
Epoxy (diglycidyl ether of bisphenol A)	1%
Rosin (colophony)	20%
P-tert butylphenol formaldehyde	1%
Preservatives, germicidals	
Formaldehyde*	2%
Quaternium-15	2%
Thimerosal	0.1%
Amidozolidinyl urea	2%
Vehicles, stabilizers	
Wool lanolin alcohols	30%
Ethylenediamine HCl	1%
Flavorings and fragrances	
Balsam of Peru	25%
Organic dyes	
P-phenylenediamine	1%
Antioxidants	
P-tert-butylphenol	1%
Rubber Additives	
Thiuram mix 1%	
tetramethylthiuram monosulfide, tetramethylthiuram disulfide, tetraethylthiuram disulfide, dipentamethylenethiuram disulfide	
Carba mix 3%	
1,3-diphenylguanidine, zinc dimethyldithiocarbamate, zinc dibutyldithiocarbamate, paraphenylenediamine	
PPD mix 0.6%	
n-phenyl-n-1-cyclohexyl-p-phenylenediamine	
n-isopropyl-n-phenyl-p-phenylenediamine	
n, n-diphenyl-p-phenylenediamine	
Mercapto mix 1%	
n-cyclohexyl-2-benzothiazole-sulfonamide	
2,2-benzothiazyl disulfide	
4-morpholinyl-2-benzothiazyl disulfide	
Mercaptobenzothiazole 1%	

*Aqueous vehicle. All other substances tested in white petrolatum vehicle.

wrong skin surface, such as the ventral forearm, or failure to perform a delayed reading, may invalidate the results.

If a valid positive patch test is obtained, the evaluating physician must then decide whether the result adequately explains the dermatitis under consideration. Positive reactions may simply represent past exposure and sensitization to the allergen or reflect exposure from the domestic environment, and do not necessarily mean that exposure to the allergen is actually occurring at the workplace.

The patch test should not be used to diagnose irritant contact dermatitis, since the conditions of the test (total occlusion against the skin for 48 hours) seldom approximate the actual conditions under which exposure is occurring. For example, induction of a third-degree chemical burn by patch testing a mechanic to undiluted diesel fuel to which he is only intermittently and briefly exposed does not definitely indicate that diesel oil is responsible for clinical dermatitis; a better explanation may be cumulative and repetitive exposures to some other solvent to which the mechanic is exposed for several hours a day. In the ultimate analysis, the diagnosis of irritant dermatitis is a clinical judgment resting on a knowledge of the physical or chemical properties of the exposures, familiarity with the actual conditions or circumstances under which exposure is occurring, and some personal experience with similar exposures.

The complications of patch testing include scarring, pigmentary alterations, infections, and accidental induction of sensitization which did not exist prior to the test procedure.

Conclusions

In most cases, a causal relationship between an observed skin disease and a work exposure will be accepted by a workers' compensation board if the condition has been primarily caused or substantially aggravated by employment. Virtually any skin disease may be aggravated by unfavorable work conditions or exposures; the term "substantial aggravation" leaves considerable latitude for interpretation on the part of the evaluating physician. If, in the opinion of the physician, the skin disease would not exist in its present state, or to its present extent, were it not for a specific occupational exposure or activity, then it may be properly considered a work-related disorder. When no signs or symptoms of a primarily endogenous skin disease, such as psoriasis or dyshidrotic eczema, were present prior to an occupational exposure or activity, it may be considered an entirely occupational disorder if the physician believes that the endogamous condition would not likely have spontaneously arisen at that point in time were it not for the occupational exposure or activity which appeared to precipitate it.

PREVENTION

Awareness of the various types of occupational dermatoses and the agents that may cause them is essential to any successful preventive program. Exposures which may cause occupational skin disease within various occupational settings are listed in the Appendix.

Prompt recognition and precise etiologic diagnosis are necessary not only for management of individual cases, but also for prevention of further outbreaks of dermatitis. Contact dermatitis may occasionally be prevented simply by replacing the offending allergen or irritant with a suitable alternative equal to the task of the removed substance.[1, 24]

Protective measures that contain the industrial process and reduce workers' exposures have been the traditional preventive measures for reducing the incidence of occupational skin disease. Protective clothing, such as gloves, boots, and aprons, are available in a number of fabrics or materials; these should be carefully selected with regard to chemical and physical resistance to workplace exposures, and workers should be cautioned concerning entrapment and occlusion of potentially noxious substances against the skin beneath protective clothing. Good skin hygiene and cleansing are other important measures, but workers must be instructed not to clean or wash excessively with harsh substances.[83]

Barrier creams have been highly touted as effective deterrents, but from a scientific viewpoint, hard evidence of efficacy is lacking.[27, 92] Commercially available barrier creams may be divided into four general categories: (1) vanishing creams that simply facilitate skin cleansing; (2) water-repellent barrier creams that contain film-forming, hydrophobic substances (silicone, stearates, waxes, oils); (3) oil- and solvent-repellent barrier creams, which contain beeswax or lanolin to repel oil, or tragacanth and acacia to repel solvent; and (4) ionic exchangers that contain acidic or alkaline bases to buffer the effects of acids and alkalies. In most situations, white petrolatum (Vaseline) is as effective as any other type of barrier cream. In situations where barrier creams have seemed anecdotally effective, their success is more likely due to the lubricating or moisturizing effect of the cream formulation and their ability to facilitate skin cleansing, thus minimizing the need for excessive or vigorous washing, which may cause secondary irritation.

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Occupational Medicine

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