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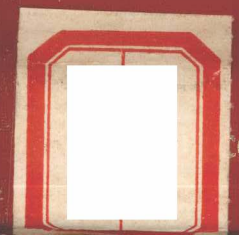
Occupational Contact Derma



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Occupational Contact Dermatitis

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OCCUPATIONAL CONTACT DERMATITIS

This book is dedicated to
LORENE, CYNTHIA, AND GREGORY

FOREWORD

An old saying about dermatologists goes something like this: "A dermatologist must know more than anyone else about the skin and its contents."

Soon after I had become especially interested in contact dermatitis and in occupational dermatoses, back in 1920, I realized that the old expression was too limiting—and I added a tag of my own: "A dermatologist must know more than others, not only about the skin and its contents, *but about everything that surrounds the skin.*" I believe these statements are pardonable exaggerations. For man's skin is the limiting interface, the membrane between his internal structures and the world around him. As such, it is constantly reacting to the substances and impulses coming from the interior, born of the other organ systems and borne by the blood and nerves. And it is equally and constantly exposed and reacting to the substances and influences coming from the external environment.

In this modern world of proliferating man-made plastics and chemical combinations which are added daily to nature's products, the number and diversity of the skin's external exposures rival those of the skin's internal environment.

Dr. Robert M. Adams' book *Occupational Contact Dermatitis* takes full account of these facts. Its early chapters analyze the indigenous or host factors—the genetic, metabolic, enzymatic, immunologic, and other contributors to susceptibility and resistance. Dr. Adams then proceeds to analyze and describe in careful and, above all, in useful detail the numerous occupational environments which act upon the skin. In greater profusion than in any previous work with which I am acquainted, he describes the chemical and physical irritants and the allergens of modern occupations. These are not mere lists which he gives, but expositions showing what the substances are, both quantitatively and qualitatively, and in what forms and in what occupations they are likely to be encountered. He describes in practical detail the techniques by which harmful substances can be discovered and how tested to establish their guilt or innocence. And finally, Dr. Adams discusses how the damaging exposures can be reduced or eliminated, and how occupational skin diseases should be prevented or treated.

I know that Dr. Adams has for many years read and studied, skin-tested, diagnosed and treated, and visited and surveyed plants, industrial combines, large and small workshops, agricultural and mining activities, and so on. He has personally investigated many of the thousands of exposures which more or less commonly cause occupational skin troubles, and his book analyzes in detail 100 occupations and the potential contact sensitizers of each.

I cannot recall any modern medical text so encyclopedic and complete which was the work of a single individual and not of a group of authors. The result, despite the volume and diversity of its subject matter, is a unified, well-planned book.

Some portions of the text are designed for reading, some for study, and some for reference. But in its entirety it will serve as a useful tool for practically every indi-

vidual and group concerned with occupational skin diseases (which are, as is well known, by far the most common of all occupational diseases).

Those who will profit most include not only the workers themselves, and not solely dermatologists, allergists, industrial physicians, preventive medicine and rehabilitation experts, but also, among others, immunologists, toxicologists, plant superintendents, industrial hygienists, public health officials, industrial nurses, insurance experts, safety engineers, lawyers, compensation court referees, labor and union leaders, business tycoons, owners of large and small plants, and the self-employed.

I predict that *Occupational Contact Dermatitis* will become one of the most dog-eared volumes on any shelf, and suggest that the publishers and printers make it of strong material.

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PREFACE

Because of the need for more detailed and precise information on the ingredients of commercial and industrial products for use in patch testing, I decided several years ago to gather together as much of this information as possible. The work was later expanded to provide a ready source of reference for the following information: (1) the ingredients, both primary irritants and allergic sensitizers, in many commercial and industrial products; (2) a list of approximately 250 contact allergic sensitizers and where they may be found; and (3) the possible contact allergens encountered in approximately 100 occupations.

With this material, the study of patients with contact dermatitis became more rewarding, frequently enabling the investigator to discover the etiologic agent with little delay. The teaching of contact dermatitis assumed greater significance and emphasized to students of skin disease the importance of the environment in the causation and aggravation of dermatitis. In addition, the information provided the industries of northern California, especially those in the San Francisco Bay Area, with a source for more accurate, detailed analysis of their dermatologic problems than was previously available to them.

Chapters 1 through 17 grew out of a desire to present some of the basic knowledge already acquired about occupational contact dermatitis. Much of this information derives from the experience of the author and his colleagues, as well as from the literature on the subject. A significant part also comes from a month-long course, given at Wayne State University, Detroit, by Dr. Donald J. Birmingham during May, 1967. Hopefully the teachers of this course will recognize some of their material in the text.

The ingredients of commercial and industrial products were derived from many sources, including works by Gosselin and by Dreisbach, the *Encyclopedia of Chemical Technology, The Condensed Chemical Dictionary,* the Poison Control Center publications, the American Conference of Governmental Industrial Hygienists, and, not least, from the manufacturers themselves, who in many instances generously provided detailed information. Since much of this is confidential in nature, trade names cannot be provided; therefore only the *possible* composition of each substance is recorded. Not all ingredients are present in each substance, of course. However, when confronted with a positive result from patch testing, the physician himself can obtain the exact ingredients of a given product by writing to the company manufacturing it.

Undoubtedly there are omissions in this section, as I have tried to include only those ingredients definitely known to be present. Asterisks appear only next to those chemicals commonly acknowledged to be contact allergic sensitizers. Undoubtedly other ingredients will be found to be sensitizers as this information is put to wider clinical use. I hope many readers of this book will become their own investigators and make additions, deletions, and modifications to these lists from evaluation of their own contact dermatitis patients.

I must emphasize that not all the substances listed in the section on contact allergens are common or potent sensitizers. Some may not be allergens at all, such as acacia, tragacanth, and others. I have included many substances with a nod to tradition. Experience will probably make it necessary to delete a considerable number from this list, at the same time adding other substances.

In general, I have given the concentrations recommended by previous authors, but in some instances, notably pine oil, hexylresorcinol, and several others, my experience indicates that the traditional concentrations are too high and therefore irritating to the skin. Hence I have reduced the concentrations to nonirritating levels. White petrolatum has been employed as the vehicle in as many instances as possible, because when water or volatile substances are used, evaporation and subsequent augmented concentration of the test substance occur.

The physician will find it difficult to acquire many of these chemicals in pure state. However, local chemical laboratories, pharmacies, retail stores, and the Hollister-Stier Laboratories located in various sections of the country can provide many of them. The manufacturers themselves are often helpful in this regard.

The section on possible allergens encountered in 100 occupations is offered as a guide to patch testing. Of course not all of them should be used on each patient suspected of having allergic contact dermatitis. The history must provide the clues for testing; only the most likely substances should be employed in the testing procedure. One must remember that when large numbers of test chemicals are used, the number of false positives bearing no relation to the existing dermatitis will increase accordingly. Unless this possibility is recognized, the examiner may become hopelessly confused by the results. This emphasizes the critical importance of the medical history, especially the initial history as given by the patient, the formulation of which requires sufficient time for careful and detailed analysis.

Robert M. Adams, M.D.

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It has been my good fortune in recent years to be a member of the Dermatology Department of Stanford University School of Medicine, headed by the able and imaginative Dr. Eugene M. Farber, who has supplied much encouragement in the preparation of this book. I have also received substantial support from Drs. Alvin J. Cox, Jr., George Kulchar, Herschel Zackheim, Faye Arundell, and Harold M. Schneidman of the Stanford faculty.

I am greatly indebted to the eminent Dr. Marion B. Sulzberger for reading and clarifying many chapters and for providing the introduction. He devoted considerable time to working over parts of the manuscript with me, and I greatly value his confidence and encouragement. I also wish to acknowledge Dr. Donald J. Birmingham of Detroit, who read not only one, but two, drafts of this work and provided invaluable advice. His excellent and unique 28-day course on occupational skin disease, presented in May 1967 at Wayne State University School of Medicine, Detroit, under the auspices of the U. S. Public Health Service, provided many ideas and a sizable amount of relevant material.

To Dr. Jay T. Bartlett and his staff, including W. P. Townes and R. W. King of the Division of Occupational Health, Santa Clara County, California, I owe much gratitude for their assistance in arranging plant visits and in gathering data and material. I also extend my thanks to Dr. Thomas H. Milby and Robert Mendell of the State of California Division of Occupational Health for their help and advice, and to Jack Washkuhn of the San Mateo County, California, Division of Occupational Health, for his assistance.

Drs. Robert Armbruster and George Wood of the Department of Industrial Medicine, Palo Alto Medical Clinic, I thank for reading the manuscript and for providing the opportunity to study many plants in the area, as well as for referring numerous interesting and challenging patients. Drs. Marcus Krupp and Robert Jamplis of the Palo Alto Medical Research Foundation and the Palo Alto Medical Clinic also read the manuscript and offered valuable suggestions and help.

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Richard Thompson of the Department of Photography, Palo Alto Medical Clinic, prepared most of the photographs and deserves commendation for his careful and skillful work. Mrs. Winifred Vetter of the Palo Alto Medical Research Foundation, who typed the manuscript through many revisions, deserves special recognition for her devotion and for sacrificing most of her free time for many months. She also deserves praise for her efficiency, accuracy, and speed.

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To the superb editorial staff of J. B. Lippincott Company, especially Brooks Stewart, J. Stuart Freeman, and Miss Elin Robbins, I owe a special debt of gratitude for their skill, precision, and indefatigable efforts to help make this book a significant contribution to the medical literature.

CONTENTS

CHAPTER 1

PRIMARY IRRITATION

The skin's basic and vital function is protection, which it achieves through a variety of properties. Having remarkable tensile strength and resiliency, the skin provides a defense against physical injury, especially shearing stress. The armor of keratin acts as a barrier against irritating chemicals, while the presence of melanin furnishes protection against the damaging effects of ultraviolet light. The unremitting upward movement of the cellular epidermis provides continual renewal, and at the same time discourages the colonization of microorganisms. Highly integrated, complex biochemical reactions go on every minute of the day and night to make these activities function smoothly and efficiently.

But in spite of the ability of human skin to protect itself and withstand the onslaughts of a frequently hostile environment, the skin is still the most commonly injured organ in industry today. Comprising more than 65 per cent of all occupationally-related diseases,[1-3] approximately 800,000 cases of skin disease are reported to workmen's compensation insurance companies annually in the United States. Including cases which fail to be reported, the total undoubtedly exceeds one million persons each year, resulting in enormous financial losses to employers and workers alike.

Most occupational skin disease results from contact with a chemical substance, more than 6,000 of which are in current use in industry throughout the United States.[4] The majority either are harmless or are primary irritants to varying degrees. A small number are potential allergic sensitizers. Fairly complete toxicity data are available on about 400,[5] but, unfortunately, detailed information regarding cutaneous toxicity is lacking on a great many of the remainder.

Approximately 80 per cent of all cases of occupational contact dermatitis result from contact with primary irritants.[6] For this reason an understanding of the patterns and mechanisms of skin irritation is of considerable importance to practicing physicians.

Primary Irritant—Definition

A primary irritant may be defined as any agent which produces a cutaneous inflammatory response by direct action at the point of contact on any person's skin, provided the concentration and duration of action are sufficient. The agent acts directly, through a mechanism which damages the skin; allergic sensitization is not a factor, although many contact allergens are also primary irritants.

Most primary irritants are chemicals, but a morphologically similar or identical reaction may be produced by certain living organisms, ultraviolet and x-irradiation, and thermal injury.

Primary irritants can be divided into two types: (1) *absolute irritants* and (2) *relative irritants.*

Absolute irritants are intrinsically damaging, corrosive substances that injure any person's skin immediately following first

FIG. 1-1. Chronic dermatitis from repeated contact with surface of abrasive wheel and detergent-type coolants.

contact. Examples are strong acids and alkalies, certain metallic elements and their salts, and many essential oils. The response is nearly identical in all persons, and the only factors of importance besides the nature of the chemical itself are the concentration and duration of contact. Thus the substance and its ability to damage skin are of primary concern, not the individual, because almost all persons respond in similar fashion.[7]

Relative primary irritants comprise less toxic substances which, to produce inflammation, require either repeated, prolonged contact with the skin or the presence of certain ancillary factors. Commonly-encountered relative primary irritants are soaps, detergents, and most organic solvents. These substances in "normal" use by the average person will not damage intact skin, but, following repeated or prolonged use, the skin of any person eventually becomes irritated.

Factors contributing to irritation are shown in Table 1-2. Most important are trauma, especially friction and pressure, presence and degree of occlusion, and certain individual characteristics including dryness of the skin, amount of pigment, and the presence of other skin diseases.

In most cases several of the factors shown in Table 1-2 set the stage for the development of dermatitis, but sometimes one factor alone may determine the outcome. For example, most organic solvents, when spilled on an uncovered area of normal skin, produce only a brief erythema accompanied by a sensation of coldness. If spilled on clothes, however, and permitted to remain in contact with the skin for a period of time, a bullous eruption resembling a burn may result.

Perhaps in no other disease, with the possible exception of acne vulgaris, is an evaluation of all the contributing factors more important than in dermatitis due to contact with relative primary irritants.

Exact diagnosis is also important because success in therapy depends upon complete avoidance of contact with the irritant and elimination, if possible, of all contributing factors. Too often an incorrect diagnosis of "allergy" is made, which results in unwarranted expense for employer and insurance company, as well as unnecessary time lost for the employee. When a diagnosis of allergy is made, not uncommonly the em-

FIG. 1-2. Severe bullous lesions from acrolein, accidentally spilled into a glove. Inhaling the vapors of this substance from contaminated clothing may cause irritation of nose and throat, as well as narcosis.

ployee is forced to change jobs, sometimes sustaining a considerable decrease in pay.

It is important to remember that when an outbreak of dermatitis occurs in a factory and many workers are involved, it usually, but not always, signifies that a primary irritant rather than an allergic sensitizer is responsible. It also frequently means that adequate protective measures are not being used, and/or that the chemical substance, especially if recently introduced, possesses unusual or unrecognized irritant properties.[6] Occasionally the outbreak indicates the existence of a potent allergic sensitizer.

Clinical Appearance of Primary Irritant Dermatitis

The clinical appearance of dermatitis due to primary irritation varies from slight erythema at the point of contact to large bullae with necrosis and ulceration. Bullous, destructive, ulcerative lesions suggest contact with a strong primary irritant such as a caustic alkali or a strong acid. Such lesions follow immediately upon contact with the irritant and the relationship is obvious.

Relative primary irritants, however, produce a clinical picture which is embodied in the condition know as *eczema*, a term derived from a Greek word meaning "boiling over." An eczematous dermatitis is one which shows vesiculation and oozing of the skin surface at some time during its development. It must be remembered that the clinical picture produced by relative primary irritants is not different from that of many other skin diseases, and differentiation from allergic sensitization is impossible from gross inspection alone.

The earliest change produced by relative primary irritants is erythema, usually limited to the area of contact with the irritant. Soon edema develops, with the appearance of various-sized vesicles and papules upon the reddened area. After several days, crusts and scales form, and if contact with the irritant ceases, the process is completed in one to three weeks. Pruritus is always associated to a variable degree.

The usually affected sites are exposed areas of skin. In most occupations, the hands and forearms have the greatest contact with irritants, particularly the dorsal aspects of hands and fingers. The palms and soles are partially protected by the presence of a thick stratum corneum on their surfaces.

A substance in clothing produces dermatitis at the region of greatest contact, such as the anterior thighs, the upper back, and the soles of the feet. Dusts collect in flexural areas, under the collar and belt, and at the tops of shoes.

The scalp is rarely involved with contact dermatitis, because of the protective mantle of hair. The male genitalia are a common site of involvement from transfer of the irritant by the hands. Contact dermatitis also tends to appear in areas not always

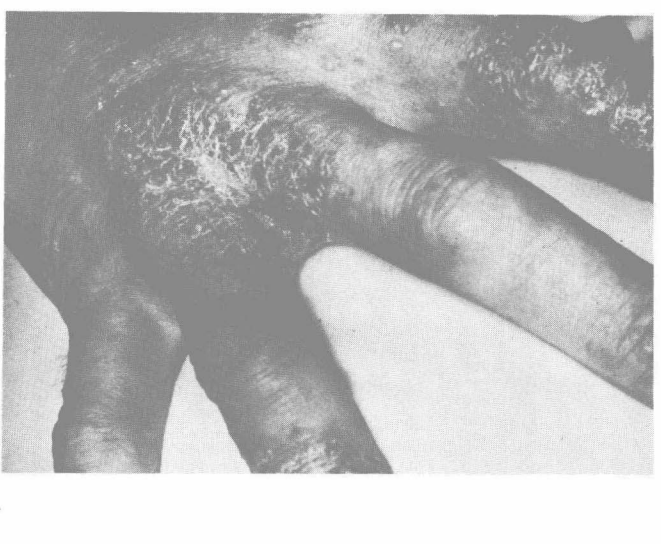

FIG. 1-3. Chronic hand dermatitis due to the primary irritant effects of soaps and solvents in a man working as a "spotter" in the dry-cleaning industry. Note secondary bacterial infection with fissuring between the third and fourth fingers.

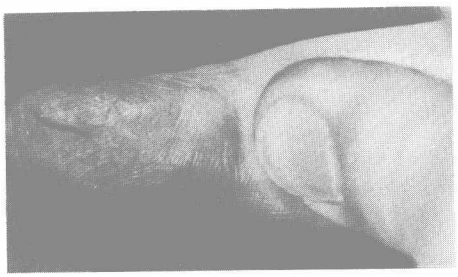

FIG. 1-4. Typical example of the painful fissures which readily develop on the volar surfaces of palms and fingers from prolonged irritation.

thoroughly cleaned, such as under rings, between the fingers, and intertriginous areas.

In subacute and chronic dermatitis, after seven or more days of continuing irritation, the skin becomes thickened, has a firm, "infiltrated" feel, and later shows lichenification with spotty areas of hyperpigmentation.

The initial appearance of the dermatitis is always at the site of contact with the irritant, and prompt disappearance usually occurs following its removal, provided the treatment is not irritating or sensitizing. Spreading to other regions of the body rarely occurs in primary irritant dermatitis, unless allergic sensitization or autoeczematization ensues.

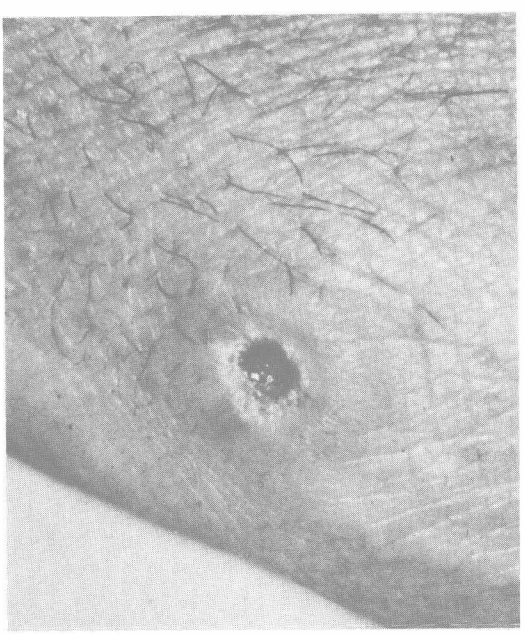

FIG. 1-5. Close-up of ulceration produced by chromic acid in an electroplater. Such lesions are commonly known as "chrome holes." (Dr. Allen Lyell, Glasgow, Scotland)

Each recurrence of primary irritant dermatitis requires the same number of contacts, and identical, or almost identical, conditions as were necessary for the development of the original dermatitis. This is an important point in differentiation from dermatitis due to allergic sensitization, which requires a single and often trivial exposure to the allergen for the full-blown disease to recur in fully-sensitized persons.[7]

Occasionally certain features are present which strongly suggest the nature of the irritant:

1. Ulcerations	Chrome[8] Arsenic[9] Lime[10]
2. Folliculitis Acneiform lesions "Chloracne"*	Petroleum, tar, asphalt,[11] chlorinated naphthalenes and diphenyls,[12] arsenic[9]
3. Miliaria	Occlusive clothing and dressings, adhesive tape, ultraviolet, heat and cold, aluminum chloride, phenol, chloroform[13,14]
4. Alterations in pigmentation	Any irritant or allergen, e.g., post-inflammatory pigmentary changes, monobenzyl ether of hydroquinone[15]
5. Alopecia	Chloroprene dimers[16]
6. Granulomas	Keratin,[17] silica,[18] beryllium,[19] talc, cotton bacteria, fungi, parasites.

* It is entirely possible that the acnegenic properties of the chlorinated naphthalenes and diphenyls may be totally unrelated to their irritating action.[29]

Histopathologic Appearance

In most cases it is impossible histologically to differentiate primary irritant reactions from those due to allergic sensitization. However, experimental studies have shown the following changes to be fairly characteristic of primary irritant reactions:[20]

1. There is epidermal necrosis with separation of the epidermis from the dermis.

2. Predominantly polymorphonuclear leukocytes are present in the vesicle fluid.

3. The intraepidermal vesicles and bullae are usually located high in the epidermis, and contain a mixture of neutrophils and lymphocytes.

Action of Primary Irritants

For many years irritant substances have been arbitrarily separated into various categories depending upon some of their known actions: *keratin solvents* include alkalis, soaps, and most organic solvents; *fat solvents,* organic solvents and most detergents. *Dehydrators* include inorganic acids, anhydrides, and alkalis such as calcium oxide; *oxidizers,* bleaches, chlorine, peroxides, and perborates; *reducing agents,* salicylic acid, oxalic acid, and formic acid; *keratogenic agents,* coal tar, petrolatum, and arsenic.

The above is purely descriptive and tells us little about basic pathologic mechanisms. Unfortunately, more is known about the healing of wounds than how skin is damaged by chemical agents, especially mild irritants.

In general, skin irritation is increased if the agent is somewhat unstable, possesses the ability to react with living tissues, and is water-soluble and capable of ionization. Relatively insoluble chemicals react less readily with cellular components of the skin, and may act instead as foreign bodies. However, many water-insoluble, non-polar compounds, such as fat solvents, may react with the aqueous cellular constituents because of the presence within the surface film of emulsifiers such as cholesterol and wax alcohols.[13]

The physiologic stability of the epidermal cell, as of all cells, is dependent upon enzymes which control the rate of such reactions as oxidative phosphorylation and the Krebs cycle, both of which occur within mitochondria. It is known that enzymes are altered by changes in their amino acid sequence, as well as by disruption of the spatial configuration of protein molecules. Strong irritants containing heavy metals such as Lewisite,[21] for example, when brought into contact with an enzyme molecule, usually bind at -SH, $-NH_2$, or -OH groups. The resulting union with metal causes the cessation of enzyme function, leaving the cell without power. Nitrogen mustard appears to act in the same fashion.[22]

At least one of the enzymes most vital to cell respiration, glucose-6-phosphatase, seems to require an intact cell membrane to operate.[23] When non-polar lipid solvents such as chlorinated hydrocarbons (chloroform, carbon tetrachloride, etc.) alter the stereochemical structure of the lipoprotein cell membrane, severe damage to the cell results. Lipid solvents also disrupt the mitochondrial limiting membrane and thus destroy the structural relationship of the electron transfer particles within the membrane, causing a breakdown of energy-dependent functions within the cell, so that complete disintegration of the entire cell quickly occurs.

In general, however, chemicals which damage the skin most severely are those which are water-soluble and ionize readily.

It can be seen that chemical agents which change the molecular arrangement of the structural components of the cell also alter specific enzymes which maintain the cell's function,[24] leading to disruption of the dynamic equilibrium of the cell and the stability of the system. If the restorative mechanisms cannot limit the damage, cellular death ensues. Cellular equilibrium is not static, however, as numerous autoregulatory mechanisms constantly operate within the cell's machinery to maintain a fine balance.

Application of this information to the action of mild irritants is somewhat more difficult than its application to strong irritants. Following mild injury, the earliest sign of damage to the skin is the formation of edema between the epidermal cells, which leads later to the development of intraepidermal vesiculation. But this reaction is also seen following application of a large number of different stimuli, including mechanical trauma and contact with microorganisms, and even after the interaction of antigen and antibody in delayed hypersensitivity reactions. The fundamental event is disruption of the bonding forces between epidermal cells, apparently