UNWANTED EFFECTS OF COSMETICS AND DRUGS USED IN DERMATOLOGY

Second edition

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Notice The authors and publisher of this work have made every effort to ensure that the drug dosage schedules herein are accurate and in accord with the standards accepted at the time of publication. Readers are advised, however, to check the product information sheet included in the package of each drug prior to administration to be certain that changes have not been made in either the recommended dose or contra-indications. Such verification is especially important in regard to new or infrequently used drugs.

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Preface

While preparing the manuscript for the first edition of this book on side effects of cosmetics and (local and systemic) drugs used by the dermatologist, we intended it to become a reference work with the following characteristics: comprehensiveness, easy to use, easy location of relevant information, copiously referenced, and up to date.

We did not know whether and how this 'encyclopaedic approach', providing many alphabetically listed tables while keeping the text to a minimum, so fundamentally different from the major textbooks in this and adjacent areas, would be appreciated. Several reviews in some major dermatological and cosmetical periodicals, as well as many letters from readers proved this 'formula' to be well accepted, and encouraged us in our view that the data provided in this way filled a need.

Stimulated and encouraged by this response and realizing that the fastly increasing amount of information in this field makes it difficult for any reference book to remain up to date, we hereby present a second, enlarged edition, two years after the first edition was released. This second edition has been revised according to new experiences, new publications and helpful advice from many users of the book. Apart from updating and completing the existing text, some important subjects have been added. Chapter 13, 'Drugs used on the oral mucosa', has been extended to the discussion of topical and systemic side effects of drugs used on the vulvo-vaginal mucosa and drugs used in ophthalmological practice. This chapter has accordingly been renamed 'Drugs used on the mucosae'.

Many more topical drugs and cosmetics which were found to have caused systemic side effects are discussed in Chapter 16. We found it appropriate (though it seems somewhat paradoxical) to include in this chapter a section on 'Transdermal drug delivery systems', where percutaneous absorption of topically applied drug, is exploited for therapeutic purposes. Examples are nitroglycerin, scopolamine and clonidine.

Chapter 19 has been updated with a comprehensive survey on adverse effects of oral retinoids. Although there can be no doubt that this group of vitamin-A analogs, notably etretinate and isotretinoin, is a very valuable addition to the therapeutic armamentarium of the dermatologist, he should be conscious of the fact that many side effects, some serious, may occur. Also new in this chapter are ketoconazole and acyclovir, drugs which, thus far, appear to have relatively low toxicity profiles.

Throughout the text, many more patch test concentrations and vehicles have been listed, thus facilitating adequate investigation in cases of suspected contact allergic reactions.

Approximately 800 new references have been added. This should enable easy access to further relevant information for any one wanting to know more about a particular drug or side effect.

Last but not least, an extensive alphabetic index of all compounds mentioned in the text has been compiled, including synonyms and trade names.

The authors wish to acknowledge their indebtedness to the many dermatologists, whose observations have been incorporated in this volume. We hope that the users of this book will continue to share their criticisms and suggestions for improvements with us.

J.P. Nater
A.C. de Groot

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1. Contact dermatitis

INTRODUCTION

1.1 Dermatitis and eczema are names used to indicate a special inflammatory state of the skin; when caused by external agents, this reaction is termed contact dermatitis or contact eczema.

1.2 Contact dermatitis may be classified as follows:

- Acute toxic contact dermatitis
- Irritant contact dermatitis
- Allergic contact dermatitis
- Phototoxic contact dermatitis
- Photoallergic contact dermatitis

MORPHOLOGICAL ASPECTS OF CONTACT DERMATITIS

1.3 An *acute allergic* contact dermatitis is characterized by polymorphy of the eruption; in the acute phase the skin reddens, clusters of minute papules, non-umbilicated vesicles and swelling occur, as well as weeping and exudation leading to the formation of crustae. The eruption is usually accompanied by itching, which may vary from moderate to quite severe. In cases of strong reactions the process may be noted to spread. In the subacute phase the polymorphy of the eruption diminishes: the skin becomes dry and scaly and fissures may be noted.

When the eruption becomes chronic, areas of the epidermis thicken, with deepening of the normal skin lines (lichenification); erythema and papules are less prominent. Multiple excoriations indicate the process to itch.

1.4 *Irritant* contact dermatitis often starts with dryness, itching and scaliness of the skin; papules and vesicles may develop later. In some cases it is impossible, on clinical examination, to distinguish between acute irritant dermatitis and acute allergic contact dermatitis.

2. Toxic and irritant contact dermatitis

ACUTE TOXIC CONTACT DERMATITIS

2.1 Acute toxic contact dermatitis may be provoked by single or repeated contacts with strongly toxic substances. The association between the injury and the toxic substance is usually quite obvious from the patient's history.

This type of reaction occurs frequently as a result of, mostly accidental, contacts with acids, alkalis, cleansers, solvents, etc.; only very rarely, however, is it caused by drugs.

IRRITANT CONTACT DERMATITIS

2.2 Irritant contact dermatitis is a term used to describe a localized, superficial, exudative, non-immunological inflammation of the skin, which is due to the direct influence of one or more external factors [15]. Many substances, including drugs, may after repeated contact with the skin cause irritant dermatitis by a direct action. This occurs without previous sensitization; immunological processes are not involved.

During and after the first contacts no visual alterations may be observed. After repeated contact, the skin gradually becomes erythematous; drying and cracking occurs, and later, an eczematous reaction with papules and vesicles may develop.

An irritant substance will cause dermatitis if it is permitted to act in sufficient intensity and quantity and for a sufficient length of time. Irritant reactions may develop in all persons, though the individual susceptibility varies greatly. This probably depends on the thickness of the epidermis. Irritant reactions are more easily provoked under occlusion, e.g. under adhesives and polyethylene, or in skin folds.

Differential diagnosis

2.3 The condition of an already eczematized skin (from whatever cause) is quickly worsened by the application of a mild irritant medicament; the resulting exacerbation may be mistaken for an allergic reaction. In such cases irritant and allergic reactions are often difficult to distinguish. The differential diagnosis between irritant and allergic contact dermatitis must be made by means of patch testing. This is sometimes rather difficult, as patch tests with mild irritants (if insufficiently diluted) may cause false positive patch test reactions, especially when they are performed on patients with an eczematous eruption elsewhere on the skin. In such circumstances even standard test substances in routine concentrations may elicit false positive reactions. The problem of false positive reactions is further discussed in § 3.18.

Topical drugs that have caused irritant dermatitis are listed in § 2.4.

2.4 Irritant dermatitis due to topical drugs

Drug	Use	Ref.
6-aminonicotinamide	psoriasis therapy	29
ammonium persulfate	hair bleaches	7
benzalkonium chloride	antiseptic	9
benzoyl peroxide	acne therapy	18
cantharidin	wart treatment	6
carmustine (BCNU)	topical cytostatic drug	39
chrysarobin	psoriasis therapy	11
citral	fragrance material	35
clioquinol	antiseptic	12
colchicine	treatment of condylomata acuminata	26
diethyltoluamide	insect repellent	41
dimethyl sulfoxide (DMSO)	solvent	14
dinitrochlorobenzene (DNCB)	treatment of alopecia areata and warts	16
dithranol (cignolin, anthralin)	psoriasis therapy	30, 33
ether	solvent	17
5-fluorouracil	topical cytostatic drug	10, 42
hexachlorophene	antiseptic	2, 28
hydroquinone	skin bleaching agent	24
6-hydroxy-1,3-benzoxathiol-2-one	psoriasis therapy	22
iodine tincture	antiseptic	13
mechlorethamine hydrochloride	treatment of mycosis fungoides	38
mesulfen	scabicide	31
monobenzyl ether of hydroquinone	skin bleaching agent	23
phenol	antipruritic	4, 21
podophyllum resin	treatment of condylomata acuminata	25
propylene glycol	vehicle constituent	27, 34, 36
quaternary ammonium compounds	antiseptics	9
resorcinol	antipruritic, peeling agent	3
retinoic acid	acne therapy	19, 40
salicylic acid	keratolytic drug	11

(continued)

2.4 Irritant dermatitis due to topical drugs

(continuation)

Drug	Use	Ref.
selenium sulfide	dandruff therapy	1
sodium lauryl sulfate	vehicle constituent	8, 32
tar	psoriasis and eczema therapy, in cosmetics	20
urea	keratolytic drug, enhances penetration of chemicals through the skin	5, 37

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