

Koushik Lahiri
Editor

A Treatise on Topical Corticosteroids in Dermatology

Use, Misuse and Abuse

Foreword by
Jerome Z. Litt

 Springer

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To,

My

Parents,

Professors,

Partner,

Progenies,

Peers,

Patients,

And everyone else from whom I have learned something

Foreword

Topical Corticosteroids: The Boon and the Bane

We have been blessed with the use of topical corticosteroids. And we have been cursed by the use of topical corticosteroids.

For more than 60 years, first by dermatologists, then by general medical practitioners, and then by pharmaceutical companies and pharmacists, these creams, lotions, ointments, solutions, gels, sprays, and pastes have been prescribed and promoted for a variety of cutaneous disorders and ailments, mainly pruritus, atopic dermatitis, psoriasis, and other corticosteroid-responsive cutaneous afflictions, and used by the general public, indiscriminately, for itching, redness, swelling, hyperpigmentation, and lately as a panacea for all their skin woes. This has been reinforced by all the publicity that we see on television and read in ladies' magazines and supported, advertised, promoted, and endorsed by the pharmaceutical industry. It is egregious and unconscionable to advertise these ever-increasing potent and damaging products to an unsuspecting, gullible public.

The first reported use of a topical corticosteroid, hydrocortisone, was by Sulzberger and Witten in 1952 in the *Journal of Investigative Dermatology* (J Invest Dermatol. 1952 Aug; 19(2):101–2). Since then, a plethora of warnings has been launched on a trusting but ignorant public, to no avail. Some of these corticosteroids are powerful enough to cause irreparable damage not only to the skin but to internal organs as well. These steroidal ointments, creams, lotions, gels, solutions, aerosols, sprays, shampoos, foams, drops, and other vehicles can be found in drugstores and pharmacies and can often be purchased without a doctor's prescription.

There are myriad side effects to many of the stronger, more potent, varieties of topical corticosteroids, some of which are serious and hazardous and can lead to permanent damage. Fluorinated steroids, particularly the ointment varieties, when used under occlusion, should be used cautiously and not for any length of time.

Steroid atrophy is a serious side effect of protracted applications of topical corticosteroids. Steroids are absorbed at different rates depending on the thickness of the stratum corneum. The eyelids and the genital areas absorb about 25%, the palms and soles about 0.1%, the upper and lower extremities about 2%, and the face about 7%. The absorption rate is much greater when the steroid is used in an ointment base.

It is almost criminal to recommend or to prescribe corticosteroids, particularly the high potency varieties, for mild to moderate dermatoses, for long periods of time, for infants and children and for the elderly where the ravages of time coupled with prolonged exposure of the sun have already caused some skin impairment.

The present obsession with fairness!

Did you ever consider that skin color did not determine the social status in ancient Greece and Rome? The preferred skin color has varied by culture and time. The Maasai people of Kenya have associated pale skin with being cursed by evil spirits. Many cultures have historically favored lighter skin in women. Before the Industrial Revolution in Europe, pale skin was a sign of high social status. The poor classes worked outdoors and got dark from exposure to the sun. The idle rich stayed indoors and had lighter skin. Slavery and colonization in Europe inspired racism and led to the belief that darker-skinned people were inferior and uncivilized; the lighter-skinned black people were more beautiful and more intelligent. These people were often preferred to be house slaves and given an education; the darker people worked in the fields in the sun. The preference for fairer skin among blacks was noteworthy and still is. A light skin signifies a higher social status in some countries and suggests that person is wealthier.

Like other Asian countries, in India, fairness mania is very much evident. Steroid containing bleaching creams are misused by many to get fair, resulting in devastating consequences. Suggestion: stop all sales of these OTC products!

Population in India as of today is on the order of 1,400,000,000. (No. I did not get the number of zeroes wrong!) In the United States, there are roughly 330,000,000 people. Both countries have almost the same number of dermatologists: 9000... Go figure!

“Fairness” and whitening are major problems. They must be dealt with as we speak.

Jerome Z. Litt, MD

Author of Litt’s Drug Eruption and Reaction Manual, updated yearly for 23 years. CRC Press. Also the website: Litt’s DRUG ERUPTION and REACTION DATABASE

Preface

When the proposal of publishing a book with one of the leading publishing houses reached me, spontaneously, this topic came to my mind.

Over almost the last seven decades, topical corticosteroids have significantly influenced the dermatologist's capability to effectively treat several difficult dermatoses. During this period, they have completely changed the face of therapy of dermatological disorders. The available range of formulations and potency gives flexibility to treat all groups of patients, different phases of disease, and different anatomic sites and made it almost inseparable from the practice of dermatology anywhere in the globe. But, these are supposed to be used in various dermatological disorders based on evidence-based knowledge and expertise.

It was indeed surprising that in spite such important locus in the practice of dermatology, a complete discourse dedicated only to this subject of topical corticosteroids in its entirety has never been attempted in an exhaustive manner.

Most of the time, at least initially, dermatological disorders are largely managed by family physicians and general practitioners. Inadequate awareness about the potency-based classification and insufficient acquaintance about the mechanism of action, indications, and contraindications of topical corticosteroids have given rise to the rapid incidence of the improper use of these drugs which threatens to bring disrepute to the entire group of these remarkable drugs.

As we had to deal with an extremely specialized topic and as this was the first book entirely dedicated to a single topic, topical corticosteroids, we had to select experts from all over the world for this ambitious project.

They are all working on specific topics assigned to them for many years, and some have contributed articles in journals.

The benefits of rational and ethical use and the harm of overuse and misuse for nonmedical, especially for cosmetic, purposes should be clearly conveyed before penning a prescription involving topical corticosteroids. Despite being the most useful drug for such treatment, they are known to produce serious local, systemic, and psychological side effects when overused or misused.

A separate book dedicated to topical corticosteroids has never been planned or executed.

This treatise aims to fill up that lacuna and to contribute significantly to the dissemination of knowledge about the indication/contraindication,

mechanism of action, ethical use, side effects, and various other facets related to topical corticosteroids.

In order to give shape to this ambitious vision, we tried to rope in the best global experts on this topic.

Knowing some of the authors helped us draw on their personal experience as well as scientific evidence in these chapters.

The final result is a never before compilation on this subject authored by fifty top thought leaders in the field.

This is an astonishing treatise, a collective wisdom of key academic opinion leaders bejeweled with rich illustration from the extensive and priceless clinical arsenal of the authors.

We hope this comprehensive compendium will be of value to all dermatologists whether postgraduate students, senior practitioners, or academicians in India, Asia, and the globe. General practitioners/family physicians would also immensely benefit from this book.

This is our sincere and humble effort to bridge gaps in the subject while presenting the latest advances to our fellow dermatologists. We know the road ahead is still long, but a beginning was necessary.

We look forward to your feedback.

Kolkata, India

Koushik Lahiri

Acknowledgments

Even after working closely on the nuances of topical steroid use and misuse for well over an entire decade, I was a little apprehensive when I first agreed to take-up the project.

My apprehension was partly for the fact that I did not have a charted track before me and partly because of such overwhelming importance of topical corticosteroids in the practice of dermatology. It was intriguing that a complete discourse dedicated only to this subject of topical corticosteroids in its entirety has never been attempted in an exhaustive manner.

These initial concern and consternation turned into pleasure and enthusiasm when all esteemed contributors whom we approached responded in a very positive way. They are virtually the topmost key opinion leaders in the field. I would like to personally thank each author who contributed for the project. No words of appreciation are enough for them. In spite of their very busy schedule, they have done a stupendous job in writing so meticulously.

All the credit of the book goes to the brilliant contributors only.

Astonishing polymath Professor (Dr.) S Premalatha, Dermamom, as she is fondly known in India, helped me to divide the chapters and topics. I sincerely appreciate her invaluable contribution.

JoAnne VanDyke, the volunteer president and executive director of International Topical Steroid Awareness Network (ITSAN), was a source of constant encouragement behind this project.

I must thank Springer, the world's leading publisher of scientific, technical, and medical e-Books, for inviting me to publish with them.

Eti Dinesh, senior editor, Medicine Books and Journals, Springer India, took personal care of this project. I owe a lot to her.

Kumar Athiappan, the assigned project coordinator for this project, was there with us with his sincere and professional competence.

Rajesh Sekar, the project manager, worked tirelessly during the last lap of this journey who oversaw the production from manuscript to final print and online files.

The icing on the cake was the foreword from a real living legend, Professor Jerome Z. Litt. His priceless foreword has certainly enhanced the credibility and definitely added value and recognition to our humble effort.

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About the Editor

Biography

Dr. Koushik Lahiri is the editor of the *Indian Journal of Dermatology*, Vice President of the *International Society of Dermatology*, and the immediate past president of the *Association of Cutaneous Surgeons of India*.

Dr. Lahiri is a foundation fellow of the Asian Academy of Dermatology--Venerology, fellow of IADVL Academy of Dermatology, International fellow of American Academy of Dermatology, and founder council member of the Asian Skin Foundation and Asian Society for Pigment Cell Research (ASPCR).

He is a fellow of all the three Royal Colleges of Physician of England, FRCP (London, Edinburgh and Glasgow), and a member of the Royal College of Physicians and Surgeons, MRCPS (Glasgow).

Dr. Lahiri is an editorial board member or reviewer for the *British Journal of Dermatology*, *International Journal of Dermatology*, *Dermatology Online Journal*, *Egyptian Dermatology Online Journal*, *IJDVL*, *IJSTD*, etc.

Dr. Lahiri has published more than *100 articles* in several indexed journals in the last two decades and contributed several chapters in different textbooks. He has compiled an extremely popular megaproject *100 Interesting Cases in Dermatology* and edited a highly acclaimed exhaustive compendium *Pigmentary Disorders* and the first *Textbook of Lasers in Dermatology*.

He has received various national and international awards, including the two highest oration awards for Indian dermatologists, the *Dr. B M Ambady memorial oration* and *Dr. P N Behl oration*.

As the former honorary national general secretary of IADVL, Dr. Lahiri conceptualized and proposed the *IADVL Academy of Dermatology*, which has now become the academic lifeline for Indian dermatologists. *ACSI Academy of Dermatosurgery* was also his brain child.

Today his name is inseparable with an extremely familiar entity among the dermatologist community in India, *TSDF* or Topical Steroid-Dependent/Damaged Face—a term he coined.

As a tireless protagonist in the fight against the misuse of topical corticosteroids in India, Dr. Lahiri has worked relentlessly to sensitize other doctors (even dermatologists), government agencies, chemists, media, and the common people regarding this shameful practice. As the founder chairperson of

the countrywide *IADVL Taskforce Against Topical Steroid Abuse (ITATSA)*, he became the face of a historic and epoch-making movement of Indian dermatologists.

He is the sixth Indian who has received the *International League of Dermatological Societies (ILDS) prestigious Certification of Appreciation (CoA)* award. He was the first Indian to be honored for *outstanding leadership, with special recognition from the Rutgers State University of New Jersey and New Jersey Medical School Chapter of Sigma Xi, the Scientific Research Society*.

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Evolution and Development of Topical Corticosteroids

1

Sandip Mukhopadhyay and Gagandeep Kwatra

Abstract

Corticosteroids are the steroidal compounds derived from the adrenal gland or prepared synthetically. Topical corticosteroids are mainly glucocorticoids. The first use of corticosteroids was in the form of adrenal extracts which was reported in 1930 by Swingle et al. In the same year, Tadeus Reichstein in Zurich; Edward Kendall at the Mayo Clinic, USA; and Oskar Wintersteiner at Columbia had been able to isolate small amount of active steroid from the adrenal gland. Systemically it was used successfully to treat rheumatoid arthritis in 1948. Reichstein, Kendall and Hench received a 'Nobel Prize' for their work with adrenal steroids. The first successful use of topical hydrocortisone in human dermatoses was reported in 1952 by Sulzberger and Witten. This landmark event opened up the avenue for the search of newer molecules with more potency and desirable properties. Gradually, the fluorinated compounds like flumethasone, flurandrenolone and triamcinolone were developed by early 1960. All these preparations were more potent than cortisone and hydrocortisone. The third generation of topical corticosteroids, betamethasone, beclomethasone or fluocinolone, found their places in the early 1960s which gradually extended their presence from systemic to topical therapy. Betamethasone, a remarkable one, after primarily systemic use, was placed successfully in the topical world in 1964. Betamethasone valerate was prepared by 1967 by esterification which further added to the potency of the parent

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compound. With the increase in the number of topical corticosteroid preparations, the World Health Organization classified such agents into seven groups. Several assay methods were developed for assessment of potency and activity of topical corticosteroids. Human vasoconstrictor assay, described by McKenzie and Stoughton in 1962, was one of the methods which has been very common for years.

Keywords

Topical steroids • Adrenal extracts • Hydrocortisone • Betamethasone • Dermatoses • Sulzberger and Witten

Learning Points

1. First systemic corticosteroid use was reported by Swingle et al in 1930 and it was in the form of adrenal extract. In the same year some small amount of corticosteroid were isolated from the adrenal gland by Tadeus Reichstein, Edward Kendall and Oscar Wintersteiner.
2. Evolution of topical corticosteroids was sincere efforts by the scientists during the World War ravaged world.
3. First successful use of topical corticosteroid in dermatoses was reported by Sulzberger and Witten in 1952 in the form of hydrocortisone.
4. Though first fluorinated compound was 9- α -fluorohydrocortisone acetate and it was successfully used in topically in 1954, the real success came with the flumethasone, flurandrenolone and triamcinolone in 1960s which were much more potent than hydrocortisone.
5. Betamethasone was a significant discovery and the first topical use was reported in 1964. Betamethasone valerate was prepared by 1967 which was more potent than the parent compound.
6. Human vasoconstrictor assay was successfully used for screening of the compounds with topical activities.

1.1 Introduction

Corticosteroids are steroid hormones produced either from the cortex of the adrenal gland or synthetically derived from it. These are subdivided as glucocorticoids, mineralocorticoids and sex steroids. These are essential hormones for the body which found their potential in the therapeutics long back. We are still witnessing newer roles of corticosteroids in the endeavour to restrain the diseases. Newer molecules with more desired properties, duration and actions for different disease conditions are now exposed to the world. Topical corticosteroids are primarily glucocorticoids. Now a long list of topical steroids is enlisted in the classification of the World Health Organization [1]. However, the beginning of this journey was not smooth.

1.2 The Early Stages: A 'Planned Serendipity'?

The world was yet to come out of joy of the discovery of serendipity – the penicillin in 1928; the 'Great Depression' of the history started (1929) to spread the shadow of its paw on civilization. The share market was yet to recover from the 'crash' following the 'Great Depression'. People of the USA were stunned with the brutality of 'St. Valentine Day Massacre' by the 'Al Capone' gang in February of 1929 in the city of Chicago [2].