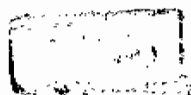


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# Retinoids in Dermatology



*An essay*

*submitted for the partial fulfillment of the*

*Master Degree in  
Dermatology and Venereology*

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**Wael Ebeid**

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the 1990s, the number of people in the UK who are employed in the public sector has increased from 10.5 million to 12.5 million, and the number of people in the public sector who are employed in health care has increased from 2.5 million to 3.5 million (Department of Health 2000).

There are a number of reasons for this increase. One of the main reasons is the increasing demand for health care services. The population of the UK is increasing, and the number of people who are aged 65 and over is increasing rapidly. This has led to an increase in the number of people who are in need of health care services, and this has led to an increase in the number of people who are employed in the public sector.

Another reason for the increase is the increasing demand for health care services from the private sector. The private sector is becoming increasingly important in the provision of health care services, and this has led to an increase in the number of people who are employed in the public sector. The private sector is also becoming increasingly important in the provision of health care services, and this has led to an increase in the number of people who are employed in the public sector.

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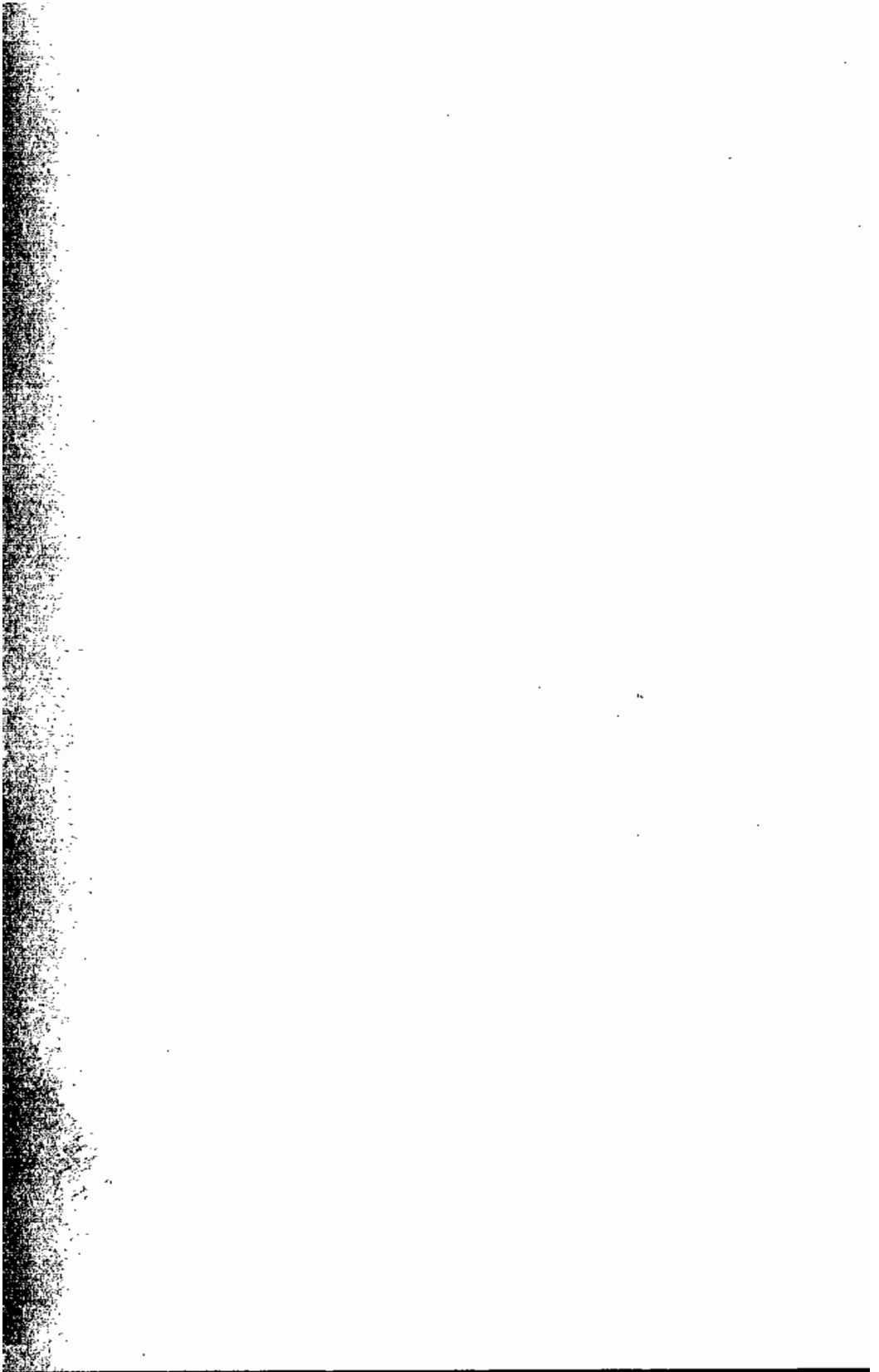
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# INTRODUCTION





## **Introduction**

Since their introduction 15 years ago, retinoids have been increasingly used for topical and systemic treatment of psoriasis and other hyperkeratotic and parakeratotic skin disorders. The term "retinoids" includes all synthetic and natural compounds that have activity similar to that of "Vitamin A".

Oxidative metabolites of vitamin A (retinol) are natural retinoids present at low levels in the peripheral blood. Synthetic retinoids are classified into 3 generations including nonaromatic, monoaromatic and polyaromatic compounds (*Elder et al., 1996*).

Retinoids affect epidermal cells growth and differentiation as well as sebaceous gland activity and exhibit immunomodularity and anti-inflammatory properties. Currently, tretinoin is used systemically for acute promyelocytic leukemia, etretinate and acitretin for psoriasis and related disorders, as well as other disorders of keratinization and isotretinoin for seborrhoea, severe acne, rosacea and acneiform dermatosis. Systemic retinoids are also applied for chemoprevention

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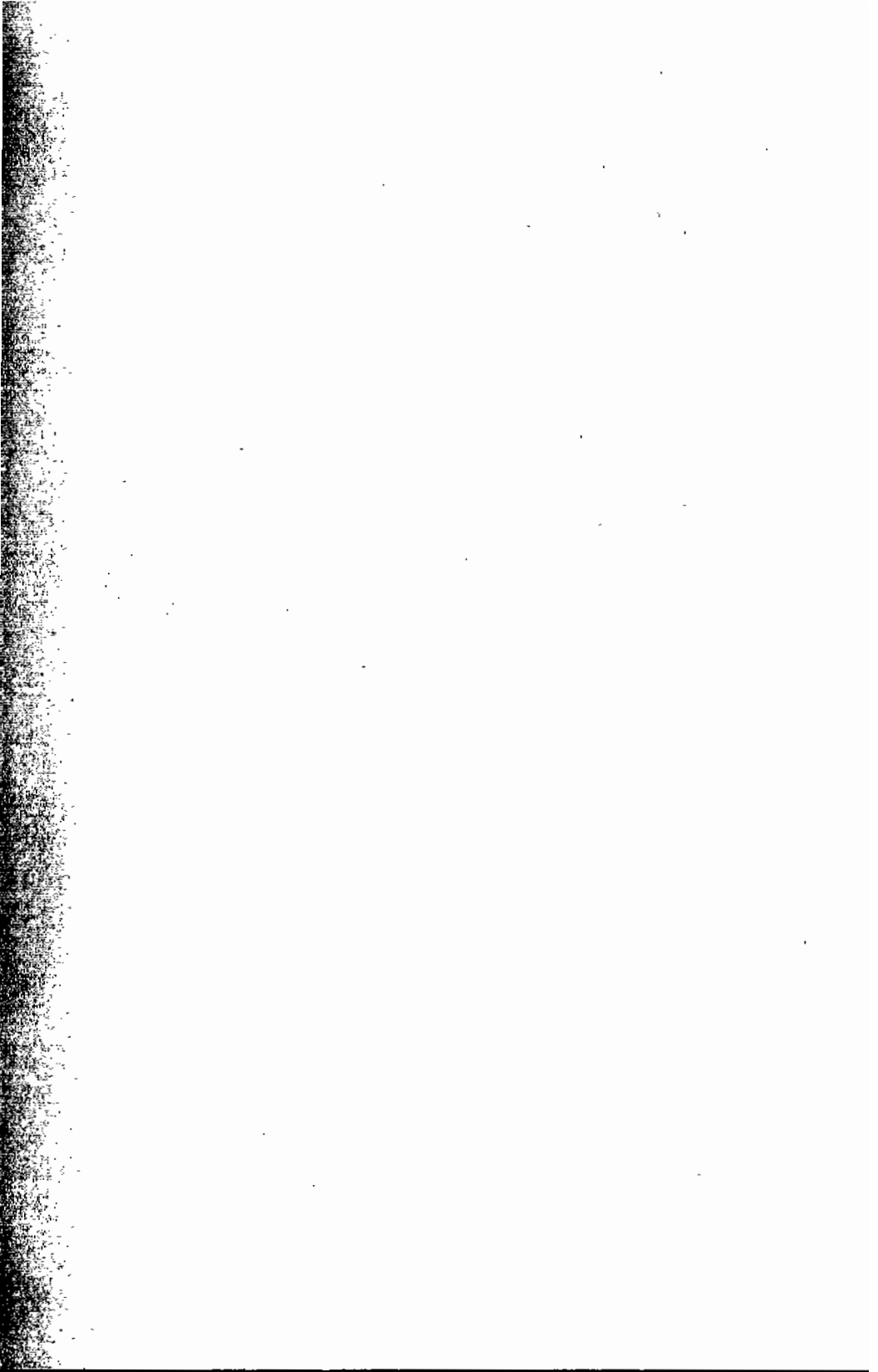
of epithelial skin cancer and cutaneous T cell lymphoma.

The major adverse effect of retinoids is teratogenicity; all other adverse effects are dose-dependant and controlable. Contraception is, therefore, essential during retinoid treatment in women of child-bearing age. Clinical monitoring requires physical examination for adverse effect every 3-4 weeks and proper laboratory investigations, also including analysis of retinoid bioavailability in selected cases. Topical retinoids are rapidly developing at present and seem promising for the future; their clinical applications includes acne, aging, photodamage, skin cancer and disorders of skin pigmentation. The development of receptor-specific retinoids for topical treatment may lead to interesting new compounds (*Orfanos et al., 1997*).

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**HISTORICAL PERSPECTIVES  
OF RETINOLIDS**



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## **Historical Perspectives of** **Retinoids**

Gunter Stutgen in 1986 summarized the main chronological developments of tretinoin, he traced the beginning of the story when topical vitamin A (retinol) did not produce any therapeutic results in dyskeratotic conditions. This led later to try metabolites of retinol topically. In 1969, the studies published showed that topical tretinoin was beneficial in ichthyosis, actinic keratosis and other hyperkeratotic conditions. Also, it was reported that topical tretinoin was effective in acne vulgaris, mainly by preventing and dislodging comedones. Subsequently, it was demonstrated that tretinoin produced a distinctive kind of hyperplasia of human epidermis that was associated with early shedding of horny cells. Having in mind that the keratinization process was being profoundly altered, researchers started to synthesize retinol derivatives (retinoids) that could be administered orally. The development of 13-cis-retinoic acid was one of the outcomes of this interest. In 1974, the antitumor effects of tretinoin were already demonstrated by showing that it produced

regression in many basal cell cancers. Today the cancer chemopreventive capability of retinoids is being intensively investigated in various organs. The year 1975 witnessed a rapid growth of basic knowledge about the pharmacology and therapeutic potential effects of retinoids. Clinical experience brought to attention the effectiveness of new applications for topical tretinoin. Positive results came from the treatment of plane warts, lichen planus, Darier's disease and retarding photoaging (*Gunter, 1986*).

### *Topical Tretinoin*

It was shown in 1962 by Hoffman that topical tretinoin was able to penetrate the epidermis, inducing definite erythema and sometimes considerable irritation of the skin, especially if occlusive dressings were used soon after the drug application. This phenomenon was particularly noticeable in cases of ichthyosis. The irritation caused by 0.17 tretinoin preparation was acceptable as compared to the therapeutic value in ichthyosis. Thus, the study was extended to include other conditions, such as actinic keratosis, seborrheic warts and basal cell carcinoma. At that time tretinoin preparations