Percutaneous Absorption and Age
Implications for Therapy

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Summary
Human skin changes dramatically with increasing age. Morphological, physiological, and biochemical changes within the tissue have been investigated and documented. Considerable interest in transdermal drug delivery to produce systemic effect has occurred in recent years. However, it is not known whether the penetration barrier of aged skin changes. Morphological and physiological changes in aged skin may affect the percutaneous absorption of compounds and thus their potential for localised, as well as systemic, efficacy. This article reviews the published literature on skin aging changes from adulthood to old age, collates these changes with clinical implications pertinent to the practising dermatologist, reviews the existing data supporting a change in the barrier function of human skin with increasing age, and comments on the relevance of conclusions previous investigators have drawn from their studies.
An important function of the skin is to act as a barrier between the body and the environment. Body water is kept in, and noxious chemicals and drugs are kept out. Topical application of drugs has been the basis of therapy in dermatology, and here it was assumed that drugs applied to the skin will exert their effects locally and not be appreciably absorbed. Although adult skin is relatively impermeable to drugs, some percutaneous absorption does take place and transdermal drug delivery for systemic effect has received increased attention in recent years. For these reasons, the permeability of human skin to various compounds has been an area of active interest by several laboratories (Bucks et al. 1988b; Chandrasekaran & Shaw 1978; Feldmann & Maibach 1969; 1970; Guy et al. 1987; Schaefer et al. 1982; Scheuplein & Blank 1971).

Pre-term infants have incompletely developed skin, and in the most immature babies, the epidermis is thin and histologically almost devoid of stratum corneum (Evans & Rutter 1986; Harpin & Rutter 1983), the major barrier to the ingress of foreign compounds. These properties reduce the barrier function of the skin, rendering the infants vulnerable to deleterious effects from inadvertent percutaneous absorption of noxious substances; many examples are found in the literature and include aniline dyes (Kagan et al. 1949), hexachlorophene (Curley et al. 1971; Powell et al. 1973), and alcohol (Harpin & Rutter 1982). At least one group of researchers is investigating the potential for transdermal absorption as a potential route for delivery of drugs to the neonate (Cartwright et al. 1990). By contrast, the full term infant has a well developed epidermis with excellent barrier properties; reasonably good experimental percutaneous absorption data exist and have been recently reviewed (Fisher 1985; Harpin & Rutter 1983; McCormack et al. 1982; Wilson & Maibach 1982).

There is also a substantial body of literature describing in vivo percutaneous absorption in normal healthy adults (Feldmann & Maibach 1969, 1970). However, in the elderly (> 65 years), the quantitative evaluation of skin barrier function has been addressed only minimally.

Physiological changes in aging skin may affect the percutaneous absorption of compounds and thus their potential for both localised as well as systemic efficacy. Thus the objective of this article is to review and outline the possible structural and physiological alterations associated with normal human skin aging and how this impacts on percutaneous absorption.

1. Rationale

Despite much research into the mechanisms of skin aging (Gilchrist 1984), the effect of this process on the percutaneous absorption of drugs and other chemicals has received scant attention. Hence, it is not intuitively obvious how the significant age-related biological changes in human skin impinge upon its ability to maintain a barrier to the ingress of foreign compounds into the body (Barry 1983).

Rationale for this review article has emanated from 3 areas. First, the population shift to higher age ranges has produced, and will continue to result in, major healthcare-related repercussions. The proportion of elderly citizens in our population has more than doubled in the US in this century. In 1900, 4% of Americans were over 65 years old; in 1980 approximately 11% (Besdine 1980), and in the year 2030 it is estimated that 20% of the population. 50 million Americans, will be over 65 years of age (Kovar 1977).

Secondly, most clinical studies are conducted using male subjects between 18 and 40 years of age. Information obtained from this general sampling may be inappropriate for prediction in or use toward a specific population such as the elderly.

Finally, the elderly are not exempt from skin disease or systemic disease requiring topical drug administration. Therefore, the question of whether the efficacy of percutaneous drug therapy is a function of skin age must be addressed. The answer to this question has relevance not only in dermatology and the treatment of local skin problems, but also in the application of transdermal drug delivery (TDD) for systemic effect. There has been an enormous growth of interest in TDD recently (Guy & Hadgraft 1986). This administration route offers