

best person to diagnose and manage most sleep disorders. He is in the best position to recognise those of his patients who need support through their middle and later years, when complaints about sleep will be only part of a larger picture, which he is the most likely person to understand.

IAN OSWALD

Professor of Psychiatry,
University of Edinburgh

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Transdermal drug administration—a nuisance becomes an opportunity

Skin is not as impenetrable an organ as is often believed: while it forms an effective barrier against invasion of the body by micro-organisms and protects against loss of body water, it will allow transdermal permeation of topically applied creams and ointments¹ in quantities sufficient to have a systemic action. Topical steroids have been a major advance in dermatology² but their systemic side effects are potentially serious because of their disturbance of the pituitary-adrenal axis.³⁻⁵ Systemic side effects have also been reported with the use of 1% gamma benzene hexachloride for scabies and pediculi,⁶ and from bismuth-containing creams,⁷ phenylephrine,⁸ salicylic acid,^{9 10} and hexachlorophane.¹¹

What factors, then, govern the transdermal permeation of drugs through skin? What is the relative permeation through intact and damaged skin? and Why are these systemic reactions manifest only occasionally and often not at all? The scientific basis for current understanding of the permeability of skin to different solutes was laid by Scheuplein.¹²⁻¹⁵ Many substances with adequate solubility in oil and water and molecular weights below 800-1000 can permeate across skin.¹⁶ Definition of the factors responsible for variable and apparently unpredictable transdermal absorption was essential before the skin could be used as a dependable route for absorption of drugs. Absorption varies within and between individuals in response

to alterations in the concentration of the solute applied to the skin, the use of a different vehicle, the intactness of the stratum corneum, the extent of inflammation of the skin, the age of the skin, ethnic skin differences, regional skin differences in permeability, and the areas of skin covered.¹⁷

Systemic drug administration by the transdermal route is now part of therapeutics. In the United States and various European countries preparations of nitroglycerin,¹⁸ etofenamate,¹⁹ and 17-beta-oestradiol²⁰ are now available for application to the skin for systemic treatment. The rate of systemic drug absorption from these preparations is variable, mostly because of the wide range in the area of application by the patient. In the absence of specific directions patients are left to apply the drug to enough skin to obtain the effect sought, but not to so much skin as to result in a rate of absorption that causes side effects. The duration of systemic action is mainly controlled by the thickness of the layer of the ointment or cream applied.

The pharmaceutical industry is now focusing interest on drug-delivery systems that provide a defined rate of drug release over a prescribed time—so-called therapeutic systems.²¹ Adhesive drug-containing films of defined surface area deliver the drug to the surface of the intact skin at a preprogrammed rate. This rate is such that the system, and not the skin, determines the rate for drug absorption. These transdermal therapeutic systems provide a predictable rate of giving drugs systemically and will maintain that rate for extended periods and so eliminate many of the variables associated with ointments and creams.¹⁷

The first transdermal therapeutic system, recently introduced in the United States, administers hyoscine at the predetermined rate of 0.5 mg over three days for the prevention and treatment of motion sickness. Hyoscine is the most effective agent for the prevention of motion sickness²²: given transdermally it prevents motion sickness in 75% of susceptible patients.²³ The flow of saliva is transiently reduced, but other recognised parasympatholytic effects of the drug are infrequent or rare. In contrast, giving hyoscine hydrobromide by mouth for the prevention of motion sickness usually produces tachycardia, profound reduction in salivary flow, drowsiness, and occasionally effects on the central nervous system.

This new dosage form is a small, circular, adhesive film 2.5 cm² in area and 18 mm in diameter. It is designed for application behind the ear, where favourable skin permeation properties ensure that the rate of the drug released from the system determines the rate of entry into the circulation.²⁴ The inner adhesive face of the product is applied to the skin after removal of a protective liner, as with an ordinary adhesive bandage. The crucial control of the rate is provided by a microporous membrane interposed between the drug reservoir and the adhesive. Though the system looks like a single-layered film, it consists of four layers laminated together: from outside in, an impermeable flesh-coloured surface, a reservoir of drug, a microporous, rate-controlling membrane, and an adhesive, which contains a small quantity of drug for immediate absorption. The system's design is based on knowledge of the skin-permeation properties of hyoscine. Release of the drug occurs by diffusion from the reservoir, through the rate-controlling membrane and adhesive to the skin surface, which can absorb the drug at rates many times higher than that at which the system's membrane allows the drug to be released. For full efficacy, the system should be applied several hours before exposure to motion, but it may also halt motion sickness, because the drug is effectively absorbed even if the patient is vomiting.

Therapeutic system forms of nitroglycerin are being developed and undergoing clinical evaluation, though no data have yet been published. Current technological methods make transdermal systems of reasonable size practicable for drugs active at a daily parenteral dose of 10 mg or less.²⁵ Development of such dosage forms should complement the traditional route for advancement of treatment—namely, the new chemical structure.²⁶ The therapeutic system will broaden the charter for new drug seekers, for they now can think in terms of drugs with short biological half lives or narrow therapeutic indices.

JANE E SHAW

Vice-president, product research
and development

JOHN URQUHART

Chief scientist

Alza Corporation,
Palo Alto,
California 94304,
USA

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Signed editorials

Good arguments may be found for printing either signed or unsigned editorials. Signing gives readers the name and standing of the writer whose views are printed. Conversely, anonymity allows the author to express unpopular opinions and readers to criticise the views and not the person behind them. It allows the editor to choose relatively junior authors, to change the English style considerably for the sake of clarity, and, on occasion, to combine one editorial with a second written by another author.

Until now the *BMJ* has acknowledged the latter arguments and printed anonymous editorials—over 90% of which are drafted by experts outside the editorial office—holding that the correspondence columns are always open for alternative views. We believe the time has come to change this policy. The current trends in science are towards more open decision making. Too many decisions in science are still being taken anonymously yet, on the criterion of the heavy investment of public money in research alone, the public has a right to be told who took them and on what basis. Similarly, among the factors taken into account in assessing arguments for a particular policy of clinical management, readers should also be able to know the status of the author. A second substantial argument is that unsigned editorials are seen as a statement of the orthodox, established view on a topic; authors writing an unsigned article tend to play safe and avoid controversy. The author of a signed article, in contrast, should be—and often is—prepared to argue strongly for a fresh, original viewpoint, pointing out where his views diverge from the orthodox. Signed editorials should be closer to the growing edges of medicine.

Unsigned, consensus editorials may seem to have more “authority” than signed ones—but such additional authority is exaggerated and comparable with that of an article that has not undergone assessment by peer review but appears authoritative merely because it is printed. Nevertheless, a need for the occasional unsigned editorial remains, in discussing some social or medicopolitical issues (when the view is a consensus one of the *BMJ* editorial staff), and when the expression of legitimate opinions would threaten the author’s job. Hence in future we shall print the occasional unsigned editorial but most of them will bear their author’s name and appointment.

STEPHEN LOCK

Editor,
British Medical Journal