Today's Treatment

Diseases of the Skin

Present and Future Trends in Approaches to Skin Disease

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The articles in this series have dealt with the management of common skin conditions, and readers must have realized how much this depends on the same drugs used in other branches of medicine. Antibiotics and steroids have changed the pattern of dermatological practice. Tuberculosis and syphilis are now seldom seen in British skin clinics and a student can even complete his training without seeing a patient with impetigo. Antibiotics have meant that infective dermatoses are often not recognized because they are rare.

Nevertheless, skin ecology is a recent science which is concerned with the pollution of human skin by man-made agents such as deodorants, antiseptics, and antibiotics. Resistant bacteria are beginning to emerge: pseudomonas and other Gram-negative organisms cause most of the deaths in burns units after the use of antibiotics aimed at the staphylococcus. Some units have even had a drop in the death rate when they stopped treating these infections; apparently the staphylococci themselves lead to less morbidity.

Steroids have also had a dramatic influence; in dermatology they may be used in local preparations and, sensibly prescribed, they are the mainstay of the treatment of many skin diseases. Today patients with eczema rarely have to stay in hospital over a fortnight. A skin doctor without steroids is like David without his sling. But—as their overuse in generalized pustular psoriasis and perioral dermatitis ought to have shown—the Devil without his horns could be a better simile.

During the last 20 years other less dramatic, but still important, advances in treatment have been made. Griseofulvin for ringworm infections makes the previous treatments of tinea capitis seem barbaric. Immunosuppression for pemphigus, venesection for porphyria cutanea tarda, and systemic cytotoxic agents for severe psoriasis and local ones for solar keratoses help with other problems.

Advances in treatment are achieved by luck, as the result of careful research, or by a mixture of both. Not surprisingly, jobbing physicians and full-time research workers differ on the importance of each but fortunately they are not mutually exclusive. There is no easier way to be wrong about the future

than building on current growing points. Trends are always petering out but it is still worthwhile trying to extend them.

Psoriasis

More work on cell turnover and its regulation will give the clue to psoriasis. Tissue-specific chalones may control the replication of keratinocytes, but the chalone theory has recently been questioned by those who think that epidermal turnover is regulated through the cyclic AMP mechanism. They think that chalones from tissue homogenates may simply represent cyclic AMP and molecules which increase its intracellular levels. Activation—for example, by adrenaline—of adenylyl cyclase in keratinocyte membranes increases intracellular levels of cyclic AMP and depresses mitotic activity. Voorhees thinks that psoriasis may result from a defect in this mechanism, and that low epidermal intracellular levels of cyclic AMP (causing increased mitotic activity) can be explained by imbalances in enzymes responsible for the formation (adenylyl cyclase) and degradation (cyclic phosphodiesterase) of cyclic AMP. If this is confirmed there are exciting possibilities for therapeutic agents acting through this mechanism.

Acne

Only a multidirectional approach can solve the problem of acne. The answer is unlikely to come from trying out more antibiotics and peeling agents, but from substances which lower the sebum-excretion rate. Continued research on systemic and topical antiandrogens is inevitable. Recolonization of the skin with lipase-deficient strains of *Corynebacterium acnes*, if it worked, would be a logical development of bacteriological research.

Eczema

At last the emphasis has switched from quibbles about the classification and morphology of the eczemas. The International Contact Dermatitis Research Group are defining the common allergens and will surely see that the dangerous ones are outlawed. Or will contact dermatitis be treated by getting rid of clones of sensitive lymphocytes, or by specific desensitization, rather than by antigen avoidance? Our present-day treatment of atopic eczema is often ineffectual and only palliative. Cutting out certain foods in the earliest months of life may be a promising approach in children at high risk; prevention rather than cure.

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Dermatitis Herpetiformis

There is encouraging news that the skin and gut lesions of dermatitis herpetiformis improve with a gluten-free diet. This is an uncommon disease but research has snowballed since the discovery in 1966 that about 70% of patients have a jejunal mucosa similar to that of coeliac disease. Multiple small intestinal biopsy specimens have shown that this enteropathy is patchy, mostly affects the proximal small intestine, and is present in nearly all patients.

The association of dermatitis herpetiformis with thyrotoxicosis and pernicious anaemia prompted further immunological investigations. Raised IgA concentrations have been found in the serum and jejunal aspirates of patients. Nuclear, thyroid, and gastric autoantibodies occur more often than in controls. Fixed IgA deposits in unaffected skin are a diagnostic feature, and complement (C3) is found in the skin lesions. Circulating immune complexes are found in 80% of patients on a diet containing gluten and in only 40% of those on a gluten-free diet. The final explanation must relate gluten sensitivity to the chain of events leading to a complement-dependent reaction in the dermal papillae. Circulating anti-reticulin antibodies have been found in 20% of patients, and their cross-reaction with gluten helps to explain the localization of the skin lesions to that part of the dermis—just deep to the basal lamina—rich in reticular fibrils.

Tumours

The role of the herpes virus in cervical cancer and of DNA repair in xeroderma pigmentosum makes it easier to understand some aspects of cancer. There is also great interest in immune responses to tumours. The point of this research is to find out whether host reactions can be changed to encourage tumour regression. Promising results after the immunotherapy of leukaemia suggest that this treatment may help in other conditions. It is a pity that viral warts and keratoacanthomas, both self-limiting skin tumours, attract so little attention.

The detection of the T and B cell lymphocyte populations is leading to a rational classification of the reticuloses. Mycosis fungoides, and its rare cousin the Sezary syndrome, seem to be T-cell diseases. This might be important therapeutically as methods of causing systemic depletion of lymphocyte subpopulations are already being investigated.

Slow motion epidemics, of the sort suggested for Hodgkin's disease, will be detected only by advanced computer-record linkage systems. Punch cards will become as out of date as are names like pityriasis lichenoides et varioliformis acuta.

Genetic and Immunological Disorders

There is a glimmer of hope in the rarer genetic disorders and the gap between the clinical morphologist and biochemist is narrowing. Enzyme grafting has already shown its worth in renal transplants for Fabry's disease (α -galactosidase deficiency). Only the dermatologist can recognize the fine clinical points which distinguish such single gene defects.

Histocompatibility antigens will be investigated in diseases ranging from parapsoriasis and mycosis fungoides to vitiligo and pemphigus. Immune responses to certain antigens are controlled by immune-response determinants in or near the major histocompatibility region of the chromosome. The clinical implications are slowly becoming clearer—for example, multiple sclerosis may result from an inherited immunodeficiency of T cells making the patients incapable of eradicating an infectious agent. There are plenty of skin diseases whose causes are not known which are candidates for mechanisms of this sort.

Immunological research will increase. It has already supported the clinical distinction between dermatitis herpetiformis and pemphigoid. Few would have thought ten years ago that circulating basement membrane antibodies would now be used

to clinch the diagnosis or monitor treatment in pemphigus. Immunology now covers topics as different as contact dermatitis, vasculitis, urticaria, and lupus erythematosus. It could provide answers to diseases ranging from leprosy to the rare halo naevus.

General

Pharmacology as applied to skin problems will also expand. Prostaglandins are beginning to emerge as important in the skin, and the safety and uses of new vehicles, particularly dimethyl-sulphoxide, urgently need study. Sun screens will halt the epidemic of skin cancer in sun worshippers and outdoor workers. If lotions are to be used, they must combine with the horny layer so that one or two applications could cover a fortnight's holiday. Perhaps natural protective mechanisms will be mimicked. A suntan will be self-prescribed (using melanocyte-stimulating substances) before holidays.

A greater understanding of the behaviour of normal skin is essential. Ageing, with its atrophy, pruritus, and minor cosmetic problems causes much distress but gets little attention. To understand cellular interactions in the skin all tissues must be studied together. The lymphatics and peripheral nerves, and their role in the control of tissue behaviour in skin disease, must be investigated. Interdisciplinary reading and international meetings are first steps in this direction. Most dermatologists know little of current research on lymphatics or of the Pavlovian concepts of neurovegetative control so popular in the Russian literature. Already it is known that the autonomic nervous system may be linked with the control of epidermal turnover via the adenylyl cyclase-cyclic AMP system. This may be important in psoriasis.

There must be further research into the mechanisms by which mental processes affect the skin. The placebo effect is largely ignored but it can control some skin diseases better than any drug available at present. It is the least damaging of all therapeutic agents as it depends on, rather than interferes with, normal tissue behaviour.

Some diseases are due to a failure to remove micro-irritants and to repair injury. There will be an increasing recognition that the skin is continually being injured by physical agents, infection, and nervous and immune phenomena. Failure to combat such insults results in disease. This is the Koebner phenomenon in its broadest sense. For instance, multifactorial diseases, such as high blood pressure and psoriasis, may succeed a variety of stresses. Early prevention is more important than treatment in the later stages of a disease.

Patient Care in the Future

Improved treatment for patients will depend on new discoveries; on better teaching of doctors and nurses; on closer co-operation between doctors, nurses, and the public; and on greater involvement and education of the public. Through organizations such as the Psoriasis Association the public are becoming better informed than some doctors about diseases which concern them. The Health Service must realize that if the public is to get the best from dermatology instruction is needed as much as treatment, and, if advances in treatment are to be made, departments will have to be enlarged.

Traditional care is no longer sufficient. Night beds should be used more for those who wish to continue to work by day. Properly supervised nurses, technicians, and informed lay people could look after patients with skin diseases (especially the elderly) in day-care centres. Local authorities must provide alternative work for patients whose dependence on national assistance shames our programme of health care within the community. The outpatient treatment of psoriasis, pioneered in Leeds many years ago, has still not spread to most centres. Clinical and administrative inertia rather than a lack of research is now stopping progress.