*Drug Treatment of Disease***DRUG TREATMENT OF ECZEMA**

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Eczema, or eczematous dermatitis, is an eruption of the skin characterized primarily by pinhead-sized macules, papules, and vesicles and accompanied by intense itching or burning. Erythema may be a prominent feature, or oedema (as when the eyelids are affected) or blisters, as in the thick skin of the palms and soles in pompholyx. In the acute phase "weeping," or the exudation of serum from burst vesicles, is usual, and secondary infection may occur, with pustules and crusting. Excoriations are commonly seen, and in the more chronic phase there is scaling, and, as a result of friction, the skin becomes thickened or lichenified.

Eczematous dermatitis is a reaction of the skin to external or internal factors, usually to both. External factors may be primary irritant substances (e.g., acids, alkalis, turpentine, etc.) or sensitizing agents (allergens). It has been said that almost anything under the sun, and the sun itself, may provoke allergic sensitization in the skin. Certain drugs used in medical practice—the sulphonamides, penicillin, streptomycin, chloramphenicol, the antihistamine compounds, and other local anaesthetics such as the benzocaine group—if brought into contact with the epidermis for more than a few days are particularly apt to cause sensitization.

Internal or constitutional factors include heredity (for this reaction is often familial), age (for it is more common during infancy, puberty, the menopause, and senescence), and deterioration in health, both physical and mental. Emotional upsets are well recognized as a precipitating cause in some patients.

Eczematous dermatitis is therefore a general medical problem in which the patient as a whole must be considered as well as his family, his environment, and his past history. Unless the internal and external factors responsible for the condition are carefully analysed and dealt with, the mere application of various medicaments to the skin and the exhibition of drugs internally are likely to achieve little.

TOPICAL APPLICATIONS

Certain principles should guide the choice of topical applications. As the affected skin requires to be soothed and protected, bland, non-irritant substances should be used. In deciding whether to employ a lotion, a paste (containing a large proportion of solid matter), an ointment (whether greasy or not), a paint or liniment, the individual patient must be considered—his type of skin, the situation affected, and the phase of the eczema. Some patients are intolerant of grease on their skins. For the scalp or other hairy parts ointments containing emulsifying bases should be employed, as these can readily be washed out. Acute eczema must be treated gently.

No substances notorious as sensitizing agents should be applied to the skin. For this reason local anaesthetic and antihistamine creams (which are also local anaesthetics), though they relieve itching for a time, should never be used. Similarly, there is no justification for

the topical application of penicillin, chloramphenicol, streptomycin, or the sulphonamides. If their administration is indicated, they can be given internally. The possibility must be borne in mind of cross-sensitization, in which sensitization to one substance may induce sensitization to a number of other chemically related compounds. For instance, sensitization to sulphonamides may result in sensitization to aniline dyes—for example, gentian violet, acriflavine—and to other substances such as benzocaine and promethazine hydrochloride ("phenegan").

Lotions

Eczema in the acute weeping phase is best treated with watery lotions, of which calamine lotion is the best known. The *B.P.* lotion contains bentonite and phenol (about 0.42% w/v). Phenol, though an antipruritic, is an irritant, and in acute eczema the following lotion is likely to be more soothing:

Calamine	...	...	40 gr. (2.6 g.)
Zinc oxide	...	...	40 gr. (2.6 g.)
Glycerin	...	...	30 min. (1.7 ml.)
Aq. calcis	...	...	to 1 oz. (28 ml.)

On no account should one of the popular calamine lotions containing an antihistamine drug be prescribed.

Another useful and soothing lotion for acute eczema is:

Zinc oxide	}	Equal parts to 1 oz. (28 ml.)
Glycerin		
Talcum		
Aq. calcis		

These lotions should not be used as wet dressings but applied thinly with a brush or a pledget of cotton-wool and allowed to dry before covering with "tube gauze" or bandages. There should be a thin film of dry lotion over the area, and more should be applied only to make good deficiencies in this film. Thick plaques of dried lotion cause discomfort, especially on mobile areas such as the face and over the flexures.

When acute moist eczema shows evidence of secondary infection, the part may be soaked in a tepid solution of potassium permanganate (1 in 8,000) for ten minutes several times a day, or, if this is impracticable, it may gently be dabbed on. The patient with extensive eczema benefits from lying in a bath of this solution for a quarter of an hour once a day. The bath becomes stained and difficult to clean, but photographic sodium thiosulphate ("hypo") solution is effective for this purpose.

Silver nitrate (1–2%) or gentian violet (1%) in water is also helpful for acute infected eczema. Gentian violet is messy, but, like silver nitrate, tans the raw surface and is comforting. Rarely does the tanning cause sealing-up of organisms, with resulting lymphangitis, but this complication responds rapidly to oral sulphonamide. The use of steroid lotions is discussed later.

An oily lotion or liniment is useful for less acute eczema, but lot. calamin. oleos. *B.P.C.* is too oily and its contents separate readily. More satisfactory and more soothing is:

Calamine ...	40 gr. (2.6 g.)
Lanolin ...	40 gr. (2.6 g.)
Ol. arachis ...	Equal parts to 1 oz. (28 ml.)
Aq. calcis ...	

Pastes

Pastes differ from ointments in that they contain a large proportion of solid matter in the form of finely dispersed powder in a greasy base. Lassar's paste (past. zinc. oxid. et acid. salicyl.), probably the most beneficial local application we have, contains 50% bland powder in soft paraffin (optimum melting-point 46° C.). It should not be spread thickly with a knife on to linen or lint and applied to the skin unless the area is very moist, but with the finger-tips spread gently and thinly until a film covers the area. Although it is stiff it can be applied readily in this way without warming, and forms a soothing, protective covering which allows the skin to cool and perspire normally and which absorbs secretions. Often a dressing is not required when Lassar's paste is used in this way. More paste should only be applied to make good deficiencies in the film, which should not be removed before re-dressing.

If a softer paste is indicated, Lassar's paste may be mixed with an equal quantity of soft paraffin or emulsifying ointment *B.P.* A number of substances may be added to Lassar's paste—gentian violet ½%, or phenoxyethanol 2%, or ammoniated mercury 2% as antiseptics, and coal tar 2–6%, or ichthammol 2%, or podophyllin resin 0.1% as antipruritics. Tar and podophyllin should be applied only in chronic eczema.

Titanium dioxide paste *B.N.F.* is useful for exudative eczema, and it may be mixed with an equal quantity of emulsifying ointment to make a softer application.

Ointments and Creams

Ointments have greasy bases of which soft paraffin, castor oil, and wool fat are common examples. Creams are different in that they contain, in addition to greasy materials, emulsifying agents and water. The emulsion may be a mixture of oil in water or vice versa. Creams are indicated when the skin is inflamed, for the evaporation of water has a cooling effect, when there is an exudate, and when hairy skin requires treatment. Ointments, on the other hand, are useful for dry, hyperkeratotic, scaling, and fissured skin. With such conditions zinc and castor oil ointment *B.P.* is helpful.

A variety of active agents including coal tar, steroids, and antibiotics are added to ointments and creams.

Coal tar has already been mentioned as an antipruritic and is a valuable preparation for chronic eczema, in which, in addition to the relief of itching, it reduces lichenification. Even when used for long periods the risk of carcinoma is negligible. Comparison with experiments in mice is not valid. Kinmont (1957) showed that certain fractions of coal tar are more effective than prepared coal tar *B.P.* in the treatment of eczema, and ointments containing them are available.

It is convenient here to mention other ways in which coal tar may be used in the treatment of chronic eczema. Crude coal tar may be painted over the affected area and drying may be hastened by the use of an electric hair-dryer. It remains for a week or more as a

protective, antipruritic covering, though in places may have to be replaced daily. It can be removed by the application of Lassar's paste. Its colour is a disadvantage and it is useful only on the limbs and trunk. An alternative for the limbs is one of the proprietary linen bandages impregnated with tar (e.g., "coltapaste," "dalzoband No. 6").

Steroid preparations, as ointments, creams, and lotions, are valuable in the treatment of eczema, but their effect is temporary. Cost limits their use, and if large areas of skin are affected they are contraindicated for this reason. Steroid preparations, being cosmetically pleasant, are especially useful for eczema of the head and neck, and for eczema of the ano-genital region. It must not be thought that steroids are essential in the treatment of eczema; bland lotions and pastes are often preferable.

Steroid applications sometimes irritate the skin, and usually the base is responsible. The patient may be allergic to the base, or, when the latter is greasy, merely intolerant of oily materials.

The great variety of steroid ointments and lotions on the market to-day makes the choice difficult for the prescriber. He must decide whether to use an ointment, and if so whether greasy or otherwise, or a lotion. For moist, exudative areas a non-greasy preparation or a lotion is best, but for dry eczema, especially with fissuring, a greasy ointment is preferable. A lotion is often more suitable for the flexures.

There is no need to use hydrocortisone preparations in a strength greater than 1%, and often 0.5% is sufficient. Prednisolone is more effective and 0.25% or less is enough. There is little evidence that glycyrrhetic acid has a cortisone-like action.

The combination of steroids and antibiotics or antiseptics is usually unnecessary and may be disadvantageous. Often it means that a sensitizing agent or an irritant substance is introduced to no purpose. The belief that the treatment of eczema with steroids may encourage local infection is unsound. It is only when eczema is grossly infected, even impetiginized, that the combination is useful, except, occasionally, for eczema of the external auditory meatus (otitis externa). When infection is a prominent feature, it is best treated by antibiotics given internally.

If *antibiotic and antiseptic* ointments and creams are indicated, it is essential that neither irritant substances nor those apt to provoke allergic sensitization should be used. It is wise to employ antibiotics which are never prescribed for internal treatment, and for this reason ointments containing neomycin and gramicidin or bacitracin are popular. Useful antiseptic ointments are those which contain chlorquinaldol ("steroxin"), iodochlorhydroxyquinoline ("vioform"), chlorhydroxyquinoline ("quinolor"), and phenoxyethanol ("phen-oxetol").

INTERNAL MEDICATION

Sedative drugs are usually required for the tense, anxious, irritable patient with eczema, but large doses are unnecessary. Amylobarbitone ¼ gr. (16 mg.) two or three times a day is helpful and is less depressing than phenobarbitone in the same dosage. Potassium bromide is a valuable sedative and harmless if not prescribed for the elderly and not taken for more than a few weeks at a time. A dose of 7 gr. (450 mg.) twice or thrice daily is sufficient. Bromide eruptions are rare but must be watched for.

Antihistamine drugs play no part in treatment except as sedatives, because histamine is not released in the eczema reaction. In children as well as adults they are useful as hypnotics and help to reduce nocturnal irritation. They are, of course, contraindicated when the patient is allergic to certain antihistamines or chemically related compounds. The best antihistamines for use as hypnotics are diphenhydramine hydrochloride ("benadryl") 10-50 mg. and promethazine hydrochloride ("phenegan") 25-50 mg. given at night in capsules, tablets, or (for children) in an elixir.

Tranquillizing drugs have already been considered in this series of articles by Vogt (1958) and Sargent (1958). In this group of drugs hydroxyzine hydrochloride ("atarax"), which is also an antihistamine, seems to be the most effective in relieving the itchy patient, but it is expensive. Nevertheless, a small dose (10 mg. twice daily) is sufficient. Trimeprazine (10 mg. twice daily) is a good antipruritic.

Steroid drugs are rarely indicated for the internal treatment of eczema, and their chief use is in acute eczematous dermatitis provoked by sensitization to an allergen which can be identified and removed. Prednisone 5 mg. or triamcinolone 4 mg. or methyl prednisolone 4 mg. may be given four times a day for the first few days, and the dosage reduced gradually to one dose a day by the end of a further week, when treatment can usually be stopped. It is unsatisfactory to use these powerful and effective drugs for eczematous dermatitis of any type until a full assessment of the condition has been made, for the effects are suppressed without treatment of the cause.

Antibiotic drugs and sulphonamides, as has been indicated, are useful when eczema is secondarily infected, and they are better given internally than locally. *Staphylococcus aureus* is the most important organism to be dealt with, and sulphonamide for a few days is sufficient—for example, sulphasomidine 0.5 g. each morning.

REFERENCES

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HUMAN CHROMOSOMAL ABNORMALITIES

CONFERENCE AT KING'S COLLEGE HOSPITAL

[FROM A SPECIAL CORRESPONDENT]

A conference on human chromosomal abnormalities was held at King's College Hospital Medical School on September 18 and 19. In many ways this was a sequel to the symposium on nuclear sex held at King's two years ago. At that time it was realized that many of the problems connected with nuclear sex would be solved once satisfactory techniques for examining human chromosomes had been evolved, and it was forecast that that would be in the near future. Many of the technical difficulties have now been overcome. There have been some notable advances, principally in this country and Western Europe, and the conference brought together most of those who have contributed to this work.

Abnormal Sex Chromosomes

By examining cells in mitosis from *in vitro* cultures of bone-marrow and skin it has already been demonstrated that three conditions have chromosomal patterns differing

from the normal 46 chromosomes with XX in the female and XY in the male. In two of the disorders the sex chromosomes are at fault. Klinefelter's syndrome is characterized by 47 chromosomes, there being three sex chromosomes, XXY; in Turner's syndrome the majority of cases are "chromatin negative," and these have only 45 chromosomes, the Y being absent, giving an XO sex-chromosome pattern. The other chromosomal abnormality previously described involved the non-sex chromosomes or autosomes. In mongolism there are again 47 chromosomes, the extra autosome being one of the smallest.

These chromosomal abnormalities were discussed at length at the symposium by various speakers. Dr. C. E. FORD (Harwell), who developed the marrow-culture technique of chromosomal analysis, considered that some cases of Turner's syndrome might be "mosaics" showing two different chromosomal patterns in the marrow cells, some cells being XX with 46 chromosomes and the others XO with 45 chromosomes. There was much debate on this point, especially concerning the relationship with a previously described mosaic condition of sex-chromatin in the skin in a case of Turner's syndrome. Dr. Ford thought that the examination for colour-blindness of each eye separately in cases of Turner's syndrome might detect differences which would support the mosaic theory.

Colour-blindness Studies

Three speakers, Professor H. NOWAKOWSKI (Hamburg), Dr. J. S. S. STEWART (Dundee), and Dr. P. E. POLANI (London), described the results of colour-blindness studies in Turner's and Klinefelter's syndromes, from which it was possible to infer the mechanism of development of the chromosomal abnormalities. It appears that in Turner's syndrome no sex chromosome is inherited from the father and the single X comes from the mother, the supposition being that in spermatogenesis non-disjunction occurs during one of the meiotic divisions, so that XY gives rise not to one X and one Y spermatozoon, but to an XY and an O spermatozoon. Conversely, in Klinefelter's syndrome the defect is probably maternal, due to non-disjunction occurring in oogenesis so that XX and O ova are produced, and an XX ovum is fertilized by a Y spermatozoon, giving an XXY zygote. The speakers stressed the importance of further detailed studies of colour-blindness in patients with these disorders and in their relatives.

Miss PATRICIA JACOBS (Edinburgh) described a third type of abnormality of the sex chromosomes in a patient with secondary amenorrhoea and underdeveloped external genitalia, uterus, and vagina. The cells were characterized by the presence of 47 chromosomes and XXX sex chromosomes. This chromosomal pattern is analogous to the "super female" found in *Drosophila*. Some of the oral mucosal cells (and perhaps also some of the neutrophils) showed two sex-chromatin bodies, which should help in finding further cases by ordinary nuclear-sexing methods.

An abnormal sex-chromosome pattern has been postulated as the basis of the testicular feminization syndrome, but Dr. BERNARD LENNOX (Glasgow) showed that in cases he had studied the chromosome pattern was of normal male type—that is, 46/XY.

Abnormalities of the Autosomal Chromosomes

Dr. L. LEJEUNE (Paris) described the findings in a condition other than mongolism which showed changes in the autosomal chromosomes. In a child with polydyspondylism showing multiple bony abnormalities of the skull and spine and with low intelligence there were only 45 chromosomes. One of the smaller chromosomes was not seen perhaps because it had become attached to another chromosome.

Professor L. S. PENROSE, F.R.S. (London), demonstrated the correlation between increasing maternal age and the incidence of mongolism, and suggested that the same might occur in Turner's syndrome and Klinefelter's syndrome, but to prove this detailed data on more cases were needed.