Drug Treatment of Disease

UNCOMPLICATED PSORIASIS

BY

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The cause of psoriasis is unknown; therefore treatment is based on observation and the knowledge accumulated from clinical experience and experiment. Recent work indicates that the malady may be associated with some fault in one or more of the enzyme systems of the skin, those concerned with protein metabolism having particularly attracted attention; but the systems presumably are not autonomous, and their activities, one suggests, must be controlled or at least greatly influenced by some higher system more closely integrated with the corporate life of the individual. Many of us would like to inculcate an endocrine factor, which would be an easy way to explain such known facts as the tendency for the eruption first to appear when the patient is between 8 and 15 years old, the tendency for the rash to clear during pregnancy and relapse soon after parturition, the potent effect of emotional stress in producing an outbreak of psoriasis in susceptible individuals, and so forth. But as yet there is little evidence to support such a hypothesis.

General Management

There are many cases, perhaps the majority, in which, when the zenith of each attack is reached, the eruption is only a very minor affair, but there are others in which every outburst of the eruption is widespread and severe. A common fault, which we all make, is to mishandle these severe cases by dealing too casually with them. The result in some—but not all—individuals is that each recurrent attack becomes more resistant as the patient becomes older, until a stage is reached when he is seldom free from an extensive eruption. It is wise to remember that, if any viscus or joint was as badly inflamed as is the skin in severe psoriasis, not only would the individual be at rest in bed but he would be lucky if he could crawl into that haven unaided. Why then, when dealing with the skin, do we deny that organ the treatment based on a cardinal principal of therapeutics which is rigidly applied to all other inflammations? The answer, of course, is that the patient with psoriasis is not ill: he does not want to go to bed, but he does want to get rid of the eruption. One should emphasize this latter fact, and remember that in many cases a week in bed, during which period mild sedation and mild topical remedies are given, may make a great deal of difference to the immediate and remote outcome of the case.

The next point to consider is the precipitating factor. Can one find a cause, emotional or somatic (including toxic) which precipitated the attack? If so, can treatment be undertaken either immediately or later so that further attacks can be limited in frequency or in severity or both? It is disputed whether a toxic episode will precipitate an attack of psoriasis, but there are at least a few cases which seem to improve when, at a convenient opportunity (*not* during the efflorescence of the eruption), some septic focus is removed.

It is particularly in the domain of the general practitioner to follow up cases of this malady, and the patients can be helped if they are kept for relatively long periods under friendly and not too onerous observation.

Systemic Treatment

For the sake of convenience the drugs which can be used internally in the treatment of psoriasis will be considered alphabetically.

Aminopterin.—This is one of the group of compounds, known as folic-acid antagonists, which block the action of folic acid in nucleic-acid metabolism and cytopoiesis. It is extremely toxic and, *inter alia*, can cause a rapid fall in the leucocyte count, aplasia of bone marrow, gastro-intestinal ulceration, alopecia, and dermatitis. However, it can cause improvement in many cases of psoriasis, though, as with all known treatments, the eruption recurs sooner or later. It is only in the most exceptional cases that the remedy should be considered, and expert opinion is so strongly biased against its use that details of dosage will not be given here. References in the literature include Gubner (1951), Levi (1954), Rees *et al.* (1955), and Cohen (1958a).

Arsenic.—Once widely prescribed, arsenic is now in disfavour. There are four reasons for this: the first is that if given in the stage of efflorescence arsenic may aggravate the eruption; secondly, in many cases the drug does not confer benefit; thirdly, multiple cutaneous carcinomata not infrequently develop in later years in patients who either have taken the drug for long periods or have had recourse to it on numerous occasions; fourthly, it may cause hepatitis. Usually it is given in doses of 2–8 minims (0.1–0.5 ml.) of Fowler's solution (arsenical solution *B.P.*, 1953) and traditionally is given thrice daily in a simple mixture with a few grains of sodium or potassium bromide. Few persons can take more than 4 minims (0.2 ml.) thrice daily in this way. If used at all it is best reserved for those who have somewhat chronic, resistant lesions, and not given at all frequently.

Cyanocobalamin.—Ruedemann (1954) gave 1,000 μ g. of vitamin B₁₂ intramuscularly daily for 10–20 days to 34 psoriatic persons. The eruption disappeared from 11, nearly disappeared from 10, and slowly improved in 6. Since then reports have been published in several countries confirming that the treatment is beneficial, even in stubborn cases. I have not seen any ill-effect from its employment. We do not yet know how to choose the cases which are likely to benefit. It is interesting to note that, while aminopterin is a folic-acid antagonist, cyanocobalamin and folic acid are involved in the synthesis of nucleoproteins.

Cystine.—Casabianca (1953) claimed good results from the administration of cystine given in a cachet thrice daily; each cachet contained 0.5 g. of the amino-acid. Fowler's solution was given, and ointments of the

traditional type containing oil of cade were used concurrently. This treatment has not been widely acclaimed.

Thiacetazone.—Thiosemicarbazone is a toxic anti-leprotic drug which can cause anaemia, agranulocytosis, and hepatic dysfunction. Reports on its effects in psoriasis have kept appearing in recent years; a few dermatologists abroad are enthusiastic, but the majority are sceptical. De Gregorio and Cisneros (1957) gave very large doses up to 1 or even 1.5 g. daily for periods of at least three months, and believe it to be the most effective drug in the treatment of psoriasis; but few of us would care to take the risk involved in such a scheme of dosage.

Triamcinolone.—The chief importance of this drug lies in the fact that for reasons yet unknown (Shelley *et al.*, 1958) it is the only corticosteroid yet introduced which can quickly remove psoriasis in the majority of cases. What seems to have been overlooked is that the relapse rate is extremely high, and not only does recurrence often occur when the steroid is withdrawn but it may be worse than the attack for which the steroid was given. At St. Bartholomew's Hospital our investigations indicate that the relapse rate is greater with old-standing cases of psoriasis than with adult patients who have only had a few episodes of the malady, but further experience might change this tentative opinion. Shelley *et al.* (1958) treated 60 patients suffering from psoriasis. In 36 the response was prompt and unquestionable and within 2–4 weeks the psoriasis had, in some cases, entirely disappeared. When the treatment ceased, or sometimes when the dose was reduced, the psoriasis rapidly recurred. In 24 cases there was no response. The side-effects include flushing, hyperidrosis, purpura, vertigo, fainting, epigastric distress, and nausea. These rapidly disappear when treatment ceases. But triamcinolone is a potent stimulator of hirsuties, and can cause moon face and buffalo humping. Shelley and his colleagues believe that the drug should be given only for acute extending psoriasis not controllable by other means, or for very extensive and severe chronic forms of the eruption. It is not to be given for the relief of a few scales from the elbows. When benefit follows administration this must be regarded as purely palliative. The use of triamcinolone cream is discussed below.

Treatment, for the average adult, should begin with 16 mg. daily in divided doses. When the lesions are fading, after about 10–14 days (though such generalization is scarcely permissible), one can reduce the amount to 12 mg. each day, and then slowly, step by step, taking several days between each change, the patient can be weaned off the drug. Meanwhile, records must be kept of his weight (some patients lose weight on triamcinolone), blood pressure, the results of urine testing, and, if facilities are available, of serum electrolytes.

General Remarks on Systemic Treatment

Aminopterin is extremely dangerous. Arsenic and thiacetazone are not recommended. Cystine is probably safe enough, but its effects have not been assessed by many persons. Triamcinolone brings many disappointments; it should be used only in very carefully selected cases. Vitamin B₁₂ is one of the few internal remedies which is reasonably efficacious, relatively inexpensive, and apparently safe. Rest in bed is of considerable importance. In many stages a reasonable amount of sedation is important. Possibly—although this is hypo-

thetical—the main action of the sedative is to reduce the patient's anxiety about his eruption. I have been much less impressed by the action of tranquillizers than of sedatives.

Radiation Therapy

Grenze is the German word for "border," and *grenz* rays are so named because they lie in the border between ultra-violet and conventional x rays in the electro-magnetic spectrum. They are very soft x rays which have wave-lengths of 1–3 Å and are generated at 8–12 kilovolts. Their particular advantage is that, as they do not penetrate the tissues deeply, they are very much safer than ordinary x rays, but they tend to cause pigmentation, and this may be unsightly. Some cases of psoriasis respond very satisfactorily to *grenz* rays; in others the lesions are aggravated and may spread.

The use of conventional x rays in psoriasis is becoming increasingly unpopular because of the genetic and other hazards involved. While they may produce rapidly a very beneficial effect when first applied, in most cases the recurrences of the eruption become more resistant, so that the dosage has to be increased, and the hazards thus are increased likewise.

Ultra-violet rays are of very great importance in the treatment of psoriasis and their use is discussed later. Here one should note that they must not be used if the patient has tuberculosis, as there is considerable risk of aggravating his infection.

Local Treatment

The old rules which one learned as a student still apply and for the sake of brevity may be stated dogmatically: strong remedies are not to be used when the eruption is efflorescing, for they will aggravate the malady; oily lotion of calcium hydroxide, soft paraffin, hydrophilic ointment *U.S.P.*, perhaps calamine cream, or an ointment made by mixing equal parts of glycerin of starch and salicylic acid ointment *B.P.* are preferable. Do not aggravate psoriasis by over-treatment: the least hazard of this is the production of resistant lesions, the worst the development of exfoliative dermatitis. Ointments containing chrysarobin, dithranol, pyrogallol, or other substances which in a few persons produce violent inflammatory reactions must be used only on small areas at first until the patient's sensitivity to them has been assessed.

There is one new observation: lotions and ointments containing corticosteroids with or without antibiotics serve only to relieve itching; they seldom benefit the psoriasis. There is one exception to this: Jarrett and Spearman (1959) in a preliminary report have stated that benefit may follow the frequent application of a preparation made of 0.1% triamcinolone cream containing 12,500 units of water-solubilized vitamin A per gramme. Unfortunately the preparation of vitamin A is not easily obtained in England.

Fundamentally the local treatment of psoriasis still depends on the use of preparations of tar, salicylic acid, mercury, or sulphur. Resorcin and pyrogallol are still employed, but much less frequently; dithranol has won its place in the *British Pharmacopoeia*. Chrysarobin is less popular and remains in the *British Pharmaceutical Codex*; being obtained by extraction from a vegetable product (goa powder) its effects are less predictable than those of dithranol, its potency varies from batch to batch, and it has a more deleterious effect on clothing.

As a generalization, which applies to the majority of cases, one can say that the skin of a psoriatic subject benefits considerably from heliotherapy or from exposure to ultra-violet rays. Some patients find that if they purchase an ultra-violet-ray lamp and use it sensibly several times a week the tendency to recurrence of the eruption is minimized. But in time the skin becomes somewhat resistant to the effects of ultra-violet rays and patients seldom continue to use a lamp for very long periods. Possibly this is a good thing, for long-continued exposure to the rays might in time produce cutaneous epitheliomata. Yet it is one of the strange things about the psoriatic subject—who often has received so much treatment that he should be particularly prone to cutaneous cancer—that, if therapy with arsenic is excluded, epitheliomatous changes arising as a direct consequence of treatment are not common.

It is believed that the beneficial effect of tar in the malady is largely due to its photo-sensitizing effect. Certainly many years' experience has shown that for routine purposes there are few more reliable methods of treatment than that devised by Goeckerman (1925).

Modified Goeckerman Regime

This treatment is particularly of use in stubborn cases which are not in the stage of efflorescence. Except for the periods of daily treatment the patient is kept in bed under mild sedation—for example, phenobarbitone $\frac{1}{4}$ gr. (16 mg.) thrice daily and a sedative at bed-time. Ointment is cleaned off with liquid paraffin and a very thin smear of this is left over the affected areas. He is then exposed to ultra-violet rays, receiving enough to cause a mild erythema, and has a weak tar bath made by adding 2 oz. (60 ml.) solution of coal tar to 25 gallons (114 l.) of water. He may use a bland non-medicated soap in the bath. After drying, his lesions are dressed with zinc oxide and coal tar paste *B.P.C.* modified to contain only 4% of crude coal tar. (As treatment progresses the amount of tar in the paste can be increased slowly in accordance with his tolerance; it is seldom necessary to exceed a concentration of 10%.) He then returns to bed. Lesions in the scalp may be treated with emulsifying ointment to which ammoniated mercury 5% and salicylic acid 3% have been added. The scalp is washed twice a week.

If properly carried out, one can rely on the regime to clear most cases of psoriasis within 21 days. For mild cases the system can be modified, the patient is not kept in bed, uses the ointment only at night, has a bath in the morning and ultra-violet rays at a convenient opportunity through the day. Autohaemotherapy is often used as an adjunct, but in many cases is not necessary.

Alternative Formulae

If the Goeckermann regime is not employed, local inunction can be carried out with tar ointments fortified by the addition of salicylic acid, sulphur, or mercury. It is usually believed that the acid merely acts as a keratolytic and removes scales, but possibly it has some further effect of which little is known. Recent research indicates that the traditional use of sulphur may be scientifically justified, but the use of mercury is based more on tradition than on any pharmacological reason.

Two formulae may be mentioned:

Coal tar solution	..	..	..	12.5%
Salicylic acid	..	..	..	2.0%
Ammoniated mercury	..	..	..	2.0%
Aqueous cream (<i>B.P.</i>)	..	..	to	100%

This formula is usually more acceptable to the patient than the ammoniated mercury, coal tar, and salicylic acid ointment of the *B.N.F.* If the skin fissures easily, the active ingredients should be blended into paraffin ointment instead of simple cream.

This formula is satisfactory for treating the scalp:

Coal tar solution	..	..	..	12.5%
Precipitated sulphur	..	..	..	4.0%
Salicylic acid	..	..	..	2.0%
Oil of lavender	..	..	..	q.s.
Coconut oil	..	..	to	100%

Cohen (1958b) drew my attention to a fact which I can now corroborate—namely, that “tar biosone G.A. ointment” gives much relief to pruritic psoriasis eruptions. It is available in a greasy and also in a non-greasy form, the antipruritic element presumably being the glycyrrhetic acid which is incorporated.

Resorcinol with tar is useful in the treatment of stubborn localized patches (but some patients react briskly to it):

Resorcinol	..	..	..	2.0%
Zinc oxide	..	..	..	12.0%
Oil of birch tar	..	..	..	6.0%
Emulsifying ointment	..	..	to	100%

Pyrogallol is almost forgotten. It has the disadvantage of being black in colour, and fell into disfavour because if absorbed from large areas it can be very toxic. However, pyrogallol ointment 5% is useful for small areas.

Chrysarobin and dithranol are so widely known that they will not be considered, except to note that a proprietary preparation, “chrysocrema,” which contains 2% chrysarobin, is satisfactory, and patients report that it stains clothing less than they would normally expect. Recently “alphosyl” lotion, which contains allantoin 2% and an extract of coal tar 5% in a vanishing-cream base, has become available: its cleanliness in application makes it very acceptable to the patient.

Conscientious Treatment

Failure in the local treatment of psoriasis is much more often due to the fact that an ointment is improperly used than to any fault in the ointment itself. In nearly all cases, only small amounts of ointment gently but thoroughly worked into the skin are required. Lacking instruction, the average patient takes large amounts of the preparation, rubs it in casually, and leaves himself smeared thickly with the unguent, so that he feels sticky and ruins his clothing. He should be told that “it is what goes into the skin, not what stays on the surface, that matters,” and, provided he is sufficiently sensible to avoid over-treatment, the ambulant patient should be encouraged to take plenty of time every evening and, in a warm room, apply the remedies gently but conscientiously. Three treatments a week done thoroughly will often do more good than casual twice-daily applications.

In general, I would advise that, provided the caveats stated above are heeded, treatment should be by the Goeckerman regime for severe cases and by means of an ointment of tar, mercury, and salicylic acid in mild cases. The sulphur ointment for the scalp is always useful. Tar biosone G.A. ointment is valuable when itching is troublesome.

Only when a patient is not doing well on these methods should one explore the possibilities of treatment with dithranol or chrysarobin. Pyrogallol is to be used only for limited areas, and the same rule can safely be applied to the use of resorcinol.

Finally, we have still got to say, "There is no cure for psoriasis"; but there is some hope that within the lifetime of many of us the aetiology will be discovered and either a cure or else adequate preventive measures may become available.

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REFERENCES

- Casabianca, J. (1953). *Bull. Soc. franç. Derm. Syph.*, **60**, 172.
 Cohen, E. L. (1958a). *Practitioner*, **181**, 618.
 — (1958b). Personal communication.
 De Gregorio, E., and Cisneros, T. (1957). *Clin. y Lab.*, **63**, 411.
 Goeckerman, W. H. (1925). *Northw. Med. (Seattle)*, **24**, 229.
 Gubner, R. (1951). *Arch. Derm. Syph. (Chicago)*, **64**, 688.
 Jarrett, A., and Spearman, R. I. (1959). *Brit. J. Derm.*, **71**, 267.
 Levi, L. (1954). *G. ital. Derm. Sif.*, **95**, 55.
 Rees, R. B., Bennett, J. H., and Bostick, W. L. (1955). *Arch. Derm. (Chicago)*, **72**, 133.
 Ruedemann, R. (1954). *Ibid.*, **69**, 738.
 Shelley, W. B., Harun, J. S., and Pillsbury, D. M. (1958). *J. Amer. med. Ass.*, **167**, 959.

NOISE AND THE PATIENT IN HOSPITAL

A PERSONAL INVESTIGATION

BY

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The study and control of noise in the modern world have received much attention, varying from attempts at suppression of the tremendous noise of jet planes to that of noise in hospitals.

The following report is of a personal study carried out in the Royal Northern Hospital, London, of the views of adult patients on noise, correlated with their home background and tenor of their work. Each patient was asked verbally what noise, if any, disturbed, worried, irritated, or kept him or her awake while in hospital; whether their home and work lay in a quiet or noisy neighbourhood; the number of young children living with them; the type of housing (flat, council house, or own home); and, lastly, the relation of their home and place of work to railways, main roads, etc.

The subjects interviewed were mostly in-patients during the period of investigation, but some had been discharged and were attending out-patient clinics.

The hospital buildings stand in a non-industrial but very busy traffic region in London, and face the main road carrying heavy lorries continually.

Of the 114 patients questioned, many were in large wards (25–30 beds), some were in small wards (up to six beds), and a smaller number were in single rooms. More than half those in single rooms were private patients. The patients questioned came from all walks of life and occupations: professional men and women, housewives, clerks, bus-drivers, labourers; in fact, their work varied from that of a busy mayor of a large provincial city to a mortuary attendant; the latter had perhaps the quietest occupation of them all, and a blacksmith one of the noisiest. The most tranquil home belonged to a solicitor living in an isolated part of North Wales. At the other extreme, a wife with three

energetic young children lived over the incessant clatter of a large dairy factory in central London.

The length of stay of these patients in hospital ranged from a few days up to about four months. Their ages fell between 17 and 82 years. All had normal hearing and none were under prolonged or heavy sedation. About 63% were in surgical wards and the remainder in medical wards.

On analysis of answers given at the personal interviews on direct questioning, the outstanding findings were as follows: 50% of patients had no complaints of noise at all; and 50% complained of noises which disturbed or worried them. This figure is in complete accordance with that given by King Edward's Hospital Fund for London (1958) in its report on the number of complaints of noise in eleven London hospitals.

Of the total number studied 50% of males and 50% of females made complaints of noise. Fewer single than married patients complained; patients with noisy surroundings, either in the home or at work, made fewer complaints than those with quiet backgrounds. Patients with quiet homes and quiet occupations thus complained much more than those with a noisy environment.

Patients under 21 years of age and over 65 complained much less than those in the middle group—that is, from 21 to 65.

Patients admitted to single rooms complained much more than those admitted into wards. Of these patients 63% complained, but only 44% of those in wards. This difference is, I think, explained by the fact that patients in a general ward are interested in ward activities. The patient in a single room usually has no such distractions, and thus his reaction to noise is accentuated. Slightly more patients in medical wards complained than did those in surgical wards.

Patients interviewed after their discharge from hospital, and subsequently attending as out-patients, gave a similar story. 50% also complained of noise while in hospital.

Noises in Hospital

The noises which disturbed patients were predominantly those made by other people, especially by patients talking, snoring, calling out, etc., particularly at night and early morning, and to a slightly less extent by the voices of the nursing staff. Almost 50% of the noises complained of were therefore made by the human voice.

Of the "internal" hospital noises (those occurring within the building from any source) the following were the most disturbing, apart from voices, and constitute approximately 25% of the noises complained of: doors banging; bedpans clanking; articles dropped in wards or corridors; squeaking trolley-wheels; bells and buzzers; the scraping sound of moved bedside tables and chairs, and finally the crashing of lift gates. The hospital plumbing system—for example, dripping taps, etc.—caused very few complaints.

"External" noises (those from courtyards, grounds, or roads) caused about 25% of the complaints, especially of traffic—in particular, the sudden explosive acceleration of motor-cycles and, to a less extent, the noise and movement of ambulances and staff cars in the hospital car park.