Those interested in reducing the appalling number of deaths on the road might do well to press for a radical revision of the present system of granting driving licences to professional drivers.

Summary

Civilian medical board records of 1,276 professional drivers were examined for causes of rejection from military service. Physical defects and impairment of vision found were considered in relation to the declaration of physical fitness made on the application form for a driving licence.

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HYDROCORTISONE OINTMENT IN THE ECZEMAS

BY

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Cortisone has been used with dramatic effect in diseases of the skin. Unfortunately, the side-effects of cortisone therapy are hazardous and limit its use in dermatological practice to potentially fatal illnesses such as pemphigus, disseminated lupus erythematosus, and exfoliative dermatitis. The local application of cortisone has little or no anti-inflammatory effect on the skin, though it has been of value as an ophthalmic application, being readily absorbed through the conjunctiva.

Hydrocortisone has been found to exert anti-inflammatory effects when applied to the skin as well as when administered systemically. No systemic effects have been reported in the hundreds of patients who have used hydrocortisone ointment, and Smith (1953) found no significant change in the circulating eosinophil count when ointment containing 150 mg. of hydrocortisone was applied to normal or diseased skin.

Literature

Sufficient reports on the use of hydrocortisone ointment have been published for some assessment of the type of case in which it is of most value. With one exception (Goldman and Preston, 1953) the accounts have been enthusiastic.

There is general agreement that the ointment is of no value in psoriasis, lichen planus, pemphigus vulgaris, generalized exfoliative dermatitis, and alopecia areata. Evidence of the response of chronic discoid lupus erythematosus is conflicting; Sidi and Bourgeois-Gavardin (1953) report improvement or healing in seven cases, while Sulzberger *et al.* (1953) found only slight improvement in one of five cases, and other observers have observed the same lack of response.

The effect of hydrocortisone ointment in atopic eczema has been extensively studied (Sulzberger and Witten, 1952; Sulzberger *et al.*, 1953; Robinson, 1953; Sidi and Bourgeois-Gavardin, 1953; Malkinson and Wells, 1954; Witten *et al.*, 1954), and the results have shown a remarkable uniformity, about two-thirds of the cases responding in each series. McCorrison (1954), in a series of 104 cases, obtained even

better results and records a good response in each case. Most observers found that response was apparent within a week and that benefit was sometimes visible within 24 to 48 hours from the beginning of treatment.

Several series were controlled by the use of the "symmetrical paired comparison" method, and it was noted that some improvement often occurred on the side of the body on which the inert ointment was used. Also in cases using hydrocortisone on one area only, improvement was observed in remote areas. Systemic absorption or contamination with hydrocortisone has been suggested as the cause, but a more likely explanation is the "sympathetic" improvement which is also seen with other forms of local treatment.

McCorrison found that 60% of cases of atopic eczema maintained improvement on stopping treatment, but others (Robinson, 1953; Malkinson and Wells, 1954) have observed a relapse in most cases, or even an exacerbation.

The treatment has been found most effective in eczema or dermatitis affecting the eyelids, pinnae, and ano-genital regions (Sidi and Bourgeois-Gavardin, 1953; Alexander and Manheim, 1953; Malkinson and Wells, 1954), probably because of improved absorption from these areas. Acute contact dermatitis, lichen simplex, nummular eczema, and seborrhoeic dermatitis are also reported as responding to hydrocortisone ointment. Sidi and Bourgeois-Gavardin (1953) warn against the danger of secondary infection in acute contact dermatitis; they also state that the antipruritic effect is slight in cases in which much lichenification is present.

The American work has been criticized on the grounds that the patients were selected private patients who knew they were having some special remedy applied. In the present series the patients were hospital patients who were aware that they were receiving a special remedy, and the control cases were, of necessity, under a similar impression. Those patients were selected whose diagnosis was firmly established and in whom the areas affected were not too extensive.

Method

A series of 105 cases of various types of eczema and dermatitis were treated with an ointment containing 1% hydrocortisone acetate; in a few of the more resistant cases 2½% hydrocortisone was used. The base consisted of anhydrous lanolin, petrolatum, and mineral oil ("cortef" ointment).

A further 23 cases of eczema were used as controls, at the beginning of the trial alternate patients being issued with the ointment base in a similar packing and given the same instructions.

Patients were instructed to use a thin smear of the ointment twice daily, to avoid soap and water on the affected areas, and to use liquid paraffin or olive oil for cleaning.

Results

Nummular Eczema.—This was separated from other endogenous forms of eczema on account of its distinctive pattern. Of the 25 cases treated, 18 had had previous treatment with x rays and tar preparations without healing. Ten healed completely, most within one week, 11 improved but did not heal, three showed no response, and one became worse under treatment. Five cases which had healed or improved relapsed within seven to ten days of stopping treatment. Three of the 10 controls showed some improvement, and the remaining seven became worse.

Eczema.—This group contained an assortment of cases of eczema which were considered to be endogenous and which affected various areas of the body. Of the 24 patients treated, 17 had had previous treatments without healing. Eight healed completely, eight improved, three showed no response, and five became worse; one of the last-named appeared to be aggravated by the ointment. Of the six controls, one healed, two remained static, and three became worse. Half of those not responding to treatment had

eczema of the hands which involved the palmar surface, and it seems probable that lack of penetration of the thickened horny layer may have contributed to failure. In another of the failures, infection, which was present when treatment began, spread rapidly. Of the cases which improved, four relapsed within seven to ten days of stopping treatment.

Atopic Eczema.—This group comprised 30 patients varying in age from 1 year to 50 years. Twenty-five were old patients, the majority of whom had been difficult to control with the usual treatments. Three patients were treated during admission to hospital. Nine healed completely, 13 improved, six showed no response, and two became worse. Of the four controls, three showed no response and one became worse. Most of the cases which responded to treatment showed maximum improvement within a week. The more lichenified and chronic the eczema the less effective was the treatment, and in these resistant cases 2½% hydrocortisone ointment did not seem to be more effective than the 1% ointment.

Lichen Simplex.—Of the 10 patients treated, nine had very long-standing lesions which had resisted the usual occlusive and x-ray therapies. Three healed completely after three to four weeks of treatment, and have remained healed. Three improved and gained relief from itching, but despite the use of 2½% ointment their lichenified patches remained, to be scratched again when treatment ceased. Four showed no response to 2½% ointment. Of the three controls, two became worse and one remained static.

Contact Dermatitis.—Six new cases of acute and weeping contact dermatitis were treated. All were due to medications. One did not respond. Improvement in the others was dramatic, the lesions drying and subsiding almost completely within two to three days.

Pruritus Ani.—Ten cases of pruritus ani were treated; six of them had resisted various therapies, including x rays. Four healed and remained symptom-free, four improved but did not lose all their irritation, and two derived no benefit. No controls were included in this series, and it is recognized that a fairly high proportion of these cases derive benefit from any new treatment. Nevertheless, knowing the chronic cases which admitted improvement, one is impressed with the therapeutic effect.

Comment

Improvement or complete healing was observed in 76% of the 105 treated cases and in 17% of the 23 controls. Deterioration occurred in only 7.5% of the treated cases and in 56% of the controls. It is evident that the psychological effect of the "new treatment" (packed in impressively small 5-g. tubes) was slight. Although there was an overall high rate of improvement certain conditions improved more readily than others.

Those which improved most rapidly were cases with a raw weeping skin lesion which allowed rapid absorption of the hydrocortisone. Acute contact dermatitis responded dramatically and almost healed in two or three days. Two of the treated patients presented with an acute weeping dermatitis of the face a few days before they were due to go for their summer holiday. With the usual bland applications recovery might have taken 10 to 14 days. In three days after application of hydrocortisone the rash was almost healed in each case and these patients did not miss their holiday.

A high proportion of cases of nummular eczema healed completely in a week; and here, too, the more acute and weeping the eczema the better the response. Relapse followed cessation of treatment in some cases, but application of a minute amount of ointment every day, or even every second to third day, was sufficient to prevent recurrence. In some cases healing was not complete, but hydrocortisone was useful in rapidly controlling exudation and rendering the eruption suitable for applications of tar pastes.

Patients suffering from an acute skin eruption may be prepared to endure messy applications with the prospect of recovery in sight, but the atopic eczema subject spends a lifetime fighting unpleasant attacks of eczema with almost equally unpleasant remedies. The freedom from sting, stain, and stench (as Sulzberger puts it) makes hydrocortisone a welcome treatment for the "atopic." Unfortunately the results are variable and unpredictable. Some cases healed completely in less than a week and derived complete relief from itching. Others improved more than with any other local application. Healing or improvement occurred in two-thirds of the cases treated. Those which did not respond well had very lichenified eczema that was not easily penetrated by the ointment. Patients in whom excoriations were more marked than eczema did not respond well, possibly because their scratching had become a habit. In some of the milder cases the patients still complained of itching, though the skin had apparently returned to normal; this may explain the continuation of scratching. Infection tended to be spread by the ointment, and should be regarded as a contraindication until it has been controlled by appropriate antibiotic therapy. The types of eczema outlined can easily be recognized and hydrocortisone avoided in these cases, but there remained in this series a few cases which were not improved by the ointment, though clinically indistinguishable from cases in which it worked like a charm.

Most cases of atopic eczema relapsed when treatment was stopped. It has been suggested that 2½% hydrocortisone ointment may be useful for controlling the eczema and that 1% can be used for maintenance therapy. In this series it was found that cases either responded to 1% ointment or not at all. Maintenance therapy is possible, but may prove expensive when large areas are affected. Once the rash was controlled the patient could revert to the usual tar applications with every hope of maintaining improvement; only when treatment was stopped completely was there a severe relapse. It seems likely that hydrocortisone may prove most useful as something on which the atopic eczema subject can rely to control the exacerbations to which he is so prone. The very knowledge that he has this weapon available will probably make its use less often necessary.

In other cases of localized areas of eczema the results depended largely on the site and nature of the eruption, raw and exuding areas responding well to treatment and lichenified chronic cases deriving little benefit. Eczema of the hands which involved the palmar surface responded poorly, presumably because of lack of penetration of hydrocortisone through the thickened horny layer.

Similarly, lack of penetration probably explains the poor results in lichen simplex. The 2½% ointment was used on all cases, and treatment was maintained for three to eight weeks, but only 30% of the cases healed.

In pruritus ani the degree of improvement depended on the extent and nature of the perianal dermatitis. Those patients with an active eroded and excoriated eruption experienced rapid relief, which in several chronic cases proved lasting. Those with much lichenification derived some relief from itching but did not heal. Persistent cases with intractable itching but with little or no abnormality of the skin did not respond to hydrocortisone therapy, presumably because the site of origin of their irritation was in the head rather than the seat.

From these results it is evident that hydrocortisone is not the complete answer to the treatment of eczema and dermatitis. It is, however, a potent weapon whose value can be compared to that of x-ray therapy, provided that it is used with the same circumspection.

Summary

A series of 105 cases of eczema and dermatitis were treated with 1% and 2½% hydrocortisone ointment. A further 23 cases were treated as controls with an inert ointment. Improvement or healing occurred in 76% of the treated cases and in 17% of controls.

Response appeared to depend on the ease of absorption of hydrocortisone, eroded and exuding eczema and dermatitis healing rapidly, while lichenified eczema showed little improvement.

Good results were obtained in acute contact dermatitis, nummular eczema, atopic eczema, and perianal dermatitis. Lichen simplex, lichenified atopic eczema, and lichenified cases of ano-genital pruritus responded poorly. Infection was spread by the ointment unless controlled before its use.

Relapse occurred in many chronic cases on stopping treatment, and could be prevented by using the ointment less frequently as maintenance therapy or by reverting to the use of tar applications.

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A SEARCH FOR ABNORMAL HAEMOGLOBINS IN SOME SOUTHERN SUDANESE PEOPLES

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Sickle-cell Tests

Nilotic peoples are found in two main areas—the southern Nilotes in Uganda and round the eastern shores of Lake Victoria, the northern Nilotes in the Southern Sudan. During the course of investigations among the northern Nilotes of Upper Nile Province, Sudan, the blood of a large number of individuals was examined for sickling. Some specimens were sent to laboratories for testing; in London, where positive specimens from West Africa could be used as controls, 344 specimens were tested, 83 by one of us (H.L.) and 261 by Dr. J. N. M. Chalmers, of St. George's Hospital; in Khartoum 215 were examined by Professor Dean Smith of the Kitchener School of Medicine.

These specimens were obtained from unrelated adult individuals; details of the sampling methods employed are given elsewhere (Roberts, Ikin, and Mourant, 1955). In the field, testing was largely restricted to specimens from children, 10 adults and 170 children of all ages being examined by D.F.R.; these children constituted the major part of the child population of one Dinka and two Shilluk villages, and the individuals from each village were therefore not all unrelated. As regards technique, in London and in the field, 2% solutions of potassium

metabisulphite were used, freshly made up on each occasion with distilled water; in Khartoum, each specimen was carefully enclosed bubble-free under a cover-slip ringed with petroleum jelly, and examined after 24, 48, and 72 hours.

Altogether specimens from 739 individuals were examined, representing the different indigenous peoples as follows:

People	Adults	Children
Northern Dinka	217	103
Shilluk	204	67
Nuer	100	
Mabaan	34	
Dinka/Shilluk/Nuer-hybrids ..	14	

Since in no individual of this large sample was the sickle-cell trait observed, it is concluded that the absence of the trait is a characteristic typical of the northern Nilotic peoples. This finding is similar to that of Foy *et al.* (1954).

Examination by Electrophoresis

Seventy-five specimens were further examined by paper electrophoresis according to the procedure described by Lehmann and Smith (1954). Of these, 64 specimens were from northern Dinka individuals, 4 were from Mabaan, 3 were from Dinka/Nuer hybrids, and 4 from Dinka/Shilluk hybrids.

All blood specimens contained nothing but normal adult haemoglobin. No haemoglobin S (or D), C, E, or G was found. The results of this survey are in striking contrast to those obtained in the Gold Coast (Edington and Lehmann, 1954a, 1954b), where out of 211 West Africans examined 41 were found to possess haemoglobin S, 29 haemoglobin C, and 1 haemoglobin G. On the other hand, in Tanganyika (Dar es Salaam) 100 out-patients of mixed tribal origin but mainly Bantu were recently examined by us through the kindness of Dr. Mackey; although 12 individuals with a haemoglobin showing the electrophoretic properties of S were noted, no haemoglobin C or any of the other known variants was found.

Discussion

In several recent publications the view has been advanced that the sickle-cell gene provides an example of balanced polymorphism in man. Neel (1953) discussed the possibility that the balance was attained through increased fertility on the part of the heterozygote. Allison's (1954a, 1954b, 1954c) experiment in Kampala, and his examination of the geographical distribution of the sickle-cell trait in East Africa, with high and low frequencies respectively confined to endemic and non-endemic malarious areas, provide some evidence, implementing that of Brain (1952), Mackey and Vivarelli (1952, 1954), and others, that possession of the trait confers selective advantage in malarious regions. He postulates a condition of balanced polymorphism, selection acting against the sickling homozygote through sickle-cell anaemia, against the non-sickling homozygote through malarial susceptibility, the heterozygote, however, being at an advantage over both homozygotes through the protection afforded by the sickle-cell trait against malaria, especially subtertian.

The role of malarial endemicity in determining sickle-cell frequency once the gene is introduced, however, should not be exaggerated. Many tribal areas are not sufficiently local in extent to be assigned to a single category of endemicity: the range of flight of the mosquito may admittedly be greater than the limit of several hundred yards generally quoted; but it is essentially local, and many "hyper-endemic" tribal territories must consist of intensely malarious and less malarious districts. Hence differences in selection pressure will occur within the territory, and if mating tends to be to any extent local differences in gene frequency will result. The actual value found for any sample will depend on a combination of social and ecological factors, the mating system of the people, the