investigations carried out by the department of chemistry; and to H.M. Coroner, Penang, for permission to see the report on the inquest.

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TRIAL OF DEQUALINIUM FOR SKIN INFECTIONS

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Despite the many preparations now available for the treatment of infective skin conditions, none are universally acceptable. The older agents, particularly the heavy metals, will occasionally irritate or cause sensitization, and the dyes—though effective and still widely used—are cosmetically unattractive. Sulphonamides and penicillin, used locally on the skin, are particularly apt to sensitize, and on this account are avoided by dermatologists.

Although the modern polyvalent or "wide-spectrum" antibiotics are very efficient and rarely irritant, their dangerous influence on the adaptable staphylococcus raises new problems. The skin infections may be improved at the price of increasing the cadre of existing staphylococci and of subjecting the patient to a subsequent, and more serious, attack by the resistant strain thus created.

Antibiotics that are not generally used parenterally—such as neomycin, framycetin, tyrothricin—have been preferred for local applications. Even so, resistant strains are already developing to some of these and may well become more prevalent. This potential danger of outrunning the future supply of antibiotics suitable for skin treatment, and to which the staphylococcus remains sensitive, justifies the search for suitable alternatives. There are sufficient grounds, therefore, for assessing any new synthetic bacteriostatic agent which seems likely to fulfil the necessary criteria. Many such synthetic chemicals are widely used by surgeons for the sterilization of wounds, burns, grafts, and other abraded surfaces, but in these instances the problem of epidermal sensitivity is not of great importance and they are not all suitable for use on the skin itself.

The qualities required of such a preparation are: (1) freedom from irritant action, (2) a low rate of sensitization, (3) a wide range of bactericidal or bacterio-

static activity, (4) ease of application and cosmetic acceptability, and (5) cheapness. Monilicidal or fungicidal activity would be an additional advantage.

We have recently carried out a preliminary clinical investigation of a new preparation claimed to have a wide spectrum of activity against pyococcal organisms, *Candida albicans*, and some fungi. This substance, dequalinium (decamethylene bis-(4-aminoquinaldinium) chloride), is marketed by Allen and Hanburys Ltd. as "dequadin."

The wide antibacterial activity of dequalinium *in vitro* was reported by Babbs *et al.* (1956), who found that it inhibited the growth of all of 21 species of pathogenic bacteria tested, including Gram-positive, Gram-negative, penicillin-resistant, and acid-fast bacteria; and some fungi. In a concentration of 100 µg. per ml. at 20° C. it destroyed within one hour 99.99% of organisms in a suspension of *Staphylococcus aureus*. Its activity was not inhibited by serum.

The local antiseptic action was demonstrated by injecting dequalinium solutions intraperitoneally into mice half an hour after lethal doses of bacterial suspensions had been injected into the same site. When streptococci were used, a dose of 0.9 mg. of dequalinium per kg. of body weight protected all mice from death, and when staphylococci were used 4 mg. per kg. was fully effective.

Clinical reports of the use of dequalinium for its local antibacterial action have been published by Trotter (1956) and by Fowler and Jones (1957). The former used dequalinium chloride in gelatin sponge as a bacteriostatic and haemostatic dressing after dental extractions in over 900 patients, and found it effective in counteracting and preventing sepsis and promoting healing. Fowler and Jones used a powder containing dequalinium chloride 0.1% as a wound dressing in veterinary practice. The powder was applied topically to accidental and surgical wounds in over 100 animals and was effective in controlling infections due to the common bacterial contaminants occurring in infected wounds in animals.

Clinical Investigations

We have used dequalinium on 241 patients suffering from various skin conditions. Of these, seven defaulted, and 234 clinical trials were completed on the remaining 234, 20 of whom suffered from two separate conditions or took part in two separate trials. The preparations used were dequalinium cream, containing 0.4% dequalinium chloride, and dequalinium paint (propylene glycol base) containing 0.5% dequalinium chloride. Dequalinium lozenges were used in a few cases.

In order to satisfy ourselves of the absence of toxic or irritant effects on the human skin, we first used these preparations on 12 patients with acute or extensive epidermal damage—eczematous, bullous, and ecthymatous. No adverse effects were encountered after a minimum of two weeks' treatment, and it was therefore considered justifiable to continue with a full trial. The trial was conducted in three parts.

Range of Activity

First, we applied dequalinium to a wide variety of skin diseases in order to determine its range of activity. The results are shown in Table I.

124 trials were carried out, the preparation being used for a period of two weeks in most cases and from four to six weeks in paronychia and *Trichophyton rubrum* infections. Cure, or considerable improvement, resulted in 43

TABLE I.—Response of Various Conditions to Dequalinium

Diagnosis	Improved	Not Improved	Worsened
Pyococcal conditions:			
Impetigo	16	1	0
Folliculitis. Furunculosis	5	3	0
Neonatal staphylococcal infection ..	22	2	2
	43	6	2
Mixed infective conditions of various types:			
Intertrigo	10	4	0
Angular cheilitis	2	1	0
Paronychia (chronic)	8	0	0
Infectious eczematoid dermatitis and infected eczema	7	3	0
	27	8	0
Tinea infections:			
<i>Tinea cruris</i> and <i>T. pedis</i>	6	1	0
Cattle ringworm	1	1	1*
<i>Trichophyton rubrum</i> infections ..	1	2	0
	8	4	1
Other conditions:			
Stomatitis (aphthous, erythema multiforme, etc.)	4	4	0
Eczema (not infected)	3	6	2*
Non-infective ulcers and non-infective bullae	3	2	1
	10	12	3

* Sensitization reactions.

out of 51 trials in staphylococcal skin infections of various sorts, usually within a week. Good results were also obtained in conditions of mixed aetiology in which staphylococcal or monilial infections played an important part. A small number of ringworm lesions were treated, and in 8 out of 13 cases these cleared or improved. It is accepted, of course, that cattle ringworm in particular tends to remit spontaneously. Various conditions not primarily due to infective causes responded indifferently.

Therapeutic Effects

In order to establish that the therapeutic effects obtained were due to the active agent itself and not merely to the

TABLE II.—Comparison of Dequalinium With Inert Base

Diagnosis	More Effective	No. Difference Between dequalinium and Base	Base More Effective
Infective conditions (e.g., impetigo, folliculitis)	12	3	1
Mixed conditions (e.g., intertrigo, infected eczema)	5	2	0
Non-infective conditions (e.g., acne, psoriasis, eczema)	3	8	2
	17	5	1

TABLE III.—Comparison of Dequalinium With Standard Treatment

Diagnosis	Better than Standard Treatment	Same as Standard Treatment	Inferior to Standard Treatment
A. Conditions in which dequalinium was as effective as, or more effective than, standard remedies			
Staphylococcal impetigo	8	7	1
Boils and folliculitis	1	2	2
Infected eczema and otitis externa ..	13	6	5
Angular cheilitis	2	0	1
Intertrigo	7	3	1
Chronic paronychia	5	3	0
	36	21	10
B. Conditions in which dequalinium was less effective than standard remedies			
Gravitational ulcers	3	4	5
Eczema	0	2	4
"Pustular bacterid"	0	0	3
	3	6	12

base or to spontaneous resolution, a second series of 36 patients were treated with both substances—that is, base and the base with dequalinium incorporated. Whenever possible, opposite sides were treated at random. Where this was not practicable the preparations were each used consecutively for a minimum period of five to seven days. The active preparation and the base were labelled and dispensed by the pharmacist or ward sister and applied "blind." The results are shown in Table II.

In addition, six cases of "idiopathic" black hairy tongue were treated (see below). There was a significant difference in the activity of the two preparations.

Table II shows that the preparations containing dequalinium, when used in conditions where infection was present, were more effective than the bases alone.

Finally, dequalinium cream or lotion was used in comparison with preparations normally used by us—for example, dyes, neomycin ointments, hydrocortisone, etc. The two preparations were again allocated to sides at random, wherever possible. Where similar lesions could not be treated concurrently, however, the preparations were used consecutively. The results are given in Table III.

Comment

In conditions of pyococcal origin the results were the equivalent of those obtained with antibiotics and dyes, but a particularly gratifying effect was noticed in cases of secondarily infected eczema and infective eczematoid dermatitis around the ears and in the body folds. On the hairy areas, the beard, and scalp the paint was especially useful.

We have not yet had enough experience of the routine treatment of dequalinium in ringworm infections to assess its comparative effect against standard remedies; further trials are proceeding.

A small group of six patients with idiopathic black hairy tongues were treated. They had all had much previous treatment and had suffered from the complaint for more than six months. A variety of organisms and yeasts had been cultured from the mouths. These were probably of secondary significance only. In two cases where dequalinium paint was applied thrice daily, there was no difference between it and the base; in four cases the patients noticed an improvement in the appearance and taste while using dequalinium, but in only two of these did complete clearance take place. The four patients still affected were then given dequalinium lozenges in addition; one of these improved. The condition is subject to curious irregular remissions, and no firm conclusions can yet be drawn.

Bacteriology

As this was primarily a clinical trial bacteriological results are not discussed in any detail. If the clinical efficacy of dequalinium is confirmed, properly controlled bacteriological trials should be conducted separately. There are certain material difficulties inherent in a combined assessment, particularly in skin infections. For instance, the *in vitro* behaviour of the staphylococcus under controlled conditions is frequently different from that *in vivo*; the effective local concentration of a bacteriostatic depends upon tissue exudates and immunological mechanisms, and the problem of superinfection change of staphylococcal type in hospital material must be allowed for. We did not attempt, therefore, to control the results of treatment bacteriologically. But routine swabs were taken from the skin before and during treatment in a number of cases, and it may be of interest to mention the results of these.

From the affected area of skin 65 swabs were taken before treatment. Routine cultures grew no organisms, or commensals only, in 14 cases. A coagulase-positive staphylococcus was grown in 27 cases. In 15 of these the culture was sterile at the end of the first week of treatment, and, in a further 3 cases each, at the end of two and four weeks respectively. In the remaining 6 cases a staphylococcus was

still present. In 10 cases of leg ulcers, various Gram-negative organisms were grown, and these cleared in only four cases. Beta-haemolytic streptococci were cultured in an insufficient number of cases to merit comment.

From these routine bacteriological findings it seems likely that, at any rate so far as the staphylococcus is concerned, the clinical improvement obtained in most cases is reflected in the results of routine cultures from the skin.

Findings

In general we found dequalinium to be non-irritant even when applied to mucous membranes and the skin of infants. However, three cases of allergic sensitization were encountered. One of these was to the base and two to the active ingredient. The latter showed positive patch tests to the active cream and no reaction to the bases applied alone. This figure of 1.2% is low enough to be acceptable in practice, but occasional cases of sensitization will probably arise, as with other antibiotic and antiseptic agents.

Our findings may be listed as follows.

1. *Impetigo*.—Dequalinium is a clean and useful agent in this condition, and it has the great advantage of not creating antibiotic-resistant strains of staphylococci. The paint is particularly valuable in impetigo of hairy areas.

2. *Staphylococcal Neonatal Infection*.—Dequalinium constitutes an effective and most useful application in all forms of neonatal sepsis.

3. *Intertrigo*.—This condition, in which monilial or pyococcal infection is an important factor, responds well to dequalinium. (It was also very effective in a case of monilial balanitis.)

4. *Paronychia*.—Chronic paronychia of pyogenic or monilial origin responded well. (In all cases advice about keeping the fingers dry was given in addition to treatment with dequalinium.)

5. It may be used with safety and success in conditions in which infection is present together with eczematous changes in the skin. It has no specific value in non-infective conditions, but the cream appears to be soothing and is pleasant to use. It may have some value as a prophylactic in such conditions as acute cheilopompholyx, eczematized ringworm of the feet, and eczema of the scalp, all of which are particularly prone to secondary infection.

Summary

A new antibacterial agent, dequalinium, has been used on 241 patients suffering from various skin conditions. In the form both of cream and of paint it was used alone, in comparison with the inert bases, and in comparison against standard routine measures of treatment.

Dequalinium was found to be of considerable value in pyococcal infections of the skin, notably impetigo and neonatal staphylococcal infections. It was also of considerable value in skin conditions in which pyococcal or monilial infection played a predominant part. It also appeared to be of value in tinea infections in a relatively small number of patients.

Non-infective conditions did not respond, but were not made worse.

Dequalinium appeared to be as effective as antibiotic preparations and dyes and is pleasant to use, colourless, and relatively cheap. No irritant or toxic properties were observed, and it can be used on the mucous membranes and on the skins of infants. However, three cases of sensitization occurred, an incidence of 1.2%. In one of these the base was responsible.

We believe dequalinium to be a useful valuable preparation against pyococcal and monilial infections of

the skin, and one that represents a welcome addition to dermatological therapy.

ADDENDUM.—Since writing this paper we have been supplied with a quantity of dequalinium cream containing 0.5% prednisolone. Some 37 cases of atopic eczema, pruritus ani et vulvi, intertrigo, and neurodermatitis have been treated with this preparation. This prednisolone-dequalinium mixture showed a superior effect to the plain dequalinium cream, when used in these states, where itching and reflex rubbing are very pronounced. There were no failures in this short series, nor was any sensitization seen.

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SIZE OF THE ADRENALS IN JAMAICANS

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Not only does the pattern of disease in Jamaica differ from that encountered in Europe but the response of the Jamaican to shock is poor. Because a difference in endocrine make-up may be concerned, the weight of the adrenal glands in the Jamaican was compared with that of the European.

Variations in total adrenal gland weight may be due to cortex or medulla or both, and for this reason the weight of both components was estimated in 10 glands covering the full range of gland weights. In 20 more glands the cortical thickness was measured.

Materials and Methods

The adrenal glands from 105 (67 male and 38 female) adult Jamaicans of all racial groups were examined. The glands, obtained from routine necropsies, included material from 10 male cases of sudden and usually violent death.

The glands were dissected clean of fat and connective tissue, blotted dry with filter paper, and immediately weighed in grammes to two places of decimals on an analytical balance before fixation in 10% formol-saline solution. Ten of the glands, covering the whole range of weights, were selected and the cortical and medullary masses estimated by a modification of the methods of Swinyard (1940) and Allbrook (1956). Frozen sections were cut at intervals of 2 mm. and the unstained sections projected at eight diameters enlargement on to photographic paper. The photographic enlargements were cut out and the cortical and medullary components weighed separately to give a ratio. From this ratio and the weight of the whole gland the cortical and medullary weights were calculated.

In 20 more glands the thickness of the cortex was measured by means of a micrometer eyepiece. Each gland was divided by three parallel cuts made lengthwise. Frozen sections were cut from three of the surfaces and four different fields measured on each section, giving 12 measurements of cortical thickness in each gland.