LOCAL DIBROMPROPAMIDINE IN THE TREATMENT OF BURNS

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Claims for the value of local dibrompropamidine in burns and wounds have been put forward by several writers (Kohn and Cross, 1948; Arden, 1949 and 1954; Champion and McDowall, 1949). Our experience with the compound (see Bull et al., 1948; Lowbury et al., 1952) and the report of its toxic action on leucocytes by Wien et al. (1948) led us to abandon its use in favour of other agents which were found to be safer and also more effective (Jackson et al., 1951 a, b).

We report below four groups of observations in support of our opinion that dibrompropamidine is unsuitable as a routine application for burns.

1. The Clinical Effect.—Dibrompropamidine delays the separation of sloughs, as described by Arden (1954). One of the main features of treatment with dibrompropamidine, according to this writer, was a dry eschar which sometimes took many weeks to separate; it was adherent and often disguised the depth of burning; and furthermore, removal prior to skin grafting was often difficult, the eschar appearing to be intimately blended with the living tissues. These details, well illustrated in Fig. 4 of Arden's account, coincide exactly with our own observations on burns treated with 0.15 per cent. dibrompropamidine in a carbowax base (M & B 1270). The seriousness, however, of these unfavourable features was perhaps appreciated more by us, since over 80 per cent. of our inpatients have full-thickness skin loss lesions in contrast to 33 per cent. of Arden's series. It is well known that superficial burns will heal rapidly in spite of a moderately unfavourable environment.

Agreement is universal that deep burns should be grafted as soon as possible. Any first-aid dressing which makes the diagnosis of the depth of burning more difficult must be detrimental. If, moreover, the application delays the separation of the slough as well as obscuring the depth of necrosis, the healing time will inevitably be lengthened and the risks of infection and scarring will be increased.

2. The Histology of Burns treated with Dibrompropamidine. Histological sections made from burned skin of five patients after treatment with dibrompropamidine cream indicated that the drug produced a thicker dermal slough which separated slowly, and that there was inhibition of the regenerative activity of dermal epithelium. The effect of dibrompropamidine is shown, for example, by comparing the histology of two three-to-four-week-old severe scalds, one treated with penicillin and the other with dibrompropamidine. At this time very little of the post-burn dermal slough remained in the penicillin-treated skin, and the dermis had been converted into a very cellular and vascular granulation tissue. The dermal epithelium was in the process of regeneration, and even the sweat coils had been transformed into narrow solid columns of angular squamous epithelium which were pushing their way to the skin surface. In the dibrom-
propamidine treated scald, the swollen altered collagen still remained in the upper half or more of the dermis as a prominent acellular slough densely attached to the poorly developed granulation tissue beneath it. This appearance is well shown in Fig. 5 of Arden’s article. Deeply placed sweat coils remained histologically viable, but their lumina were still present and regenerative activity was absent or delayed.

3. The Toxic Effect on Skin Tissue Culture. The toxicity of antibiotics and chemicals likely to be of use for the local treatment of burns can be conveniently tested *in vitro* upon cultures of skin. Tests on dibrompropamidine were carried out by the same general method as described by Cruickshank and Lowbury (1952). It was found that dibrompropamidine at a concentration of 0.1 mg. per ml. was toxic to skin, while growth was permitted at a concentration of 0.01 mg. per ml. These concentrations compare unfavourably with the toxicity of antibiotics such as penicillin and polymyxin, the highest concentrations of which free from toxic effects are 0.6 mg. per ml. and 2 mg. per ml. respectively; such concentrations are higher than those used in creams applied to burns. The concentration of dibrompropamidine advocated by Arden (1.5 mg. per g.) was considerably in excess of the level found to be toxic to skin cells *in vitro*.

4. The Effect of Dibrompropamidine on the Bacteriology of Burns.—In view of the unfavourable effect of dibrompropamidine on burns demonstrated during the pilot studies, no controlled trial of the compound was made. We did, however, obtain the following information during a period of ten weeks when M & B 1270 was applied to all burns (in fifty-six patients). The bacteriology of these burns was compared with that of a series treated with penicillin.

The added infections with *Staphylococcus aureus*, *Streptococcus pyogenes*, *Pseudomonas pyocyanea*, and coliform bacilli which occurred during these periods are shown in the table; with the exception of *Str. pyogenes*, which was infrequent in both series, all of these organisms were more frequent in the burns treated with dibrompropamidine than in those of the series treated with penicillin. The penicillin treated burns were controls from a nine-months' prophylactic trial of polymyxin, the results of which are also included in this table and show significant protection by polymyxin against *Ps. pyocyanea* and coliform bacilli (see Jackson *et al.*, 1951a).

During the period when dibrompropamidine was used as a routine there was a slight increase in the resistance to dibrompropamidine of most strains of *Staph. aureus* isolated from burns; these strains were four to eight times as resistant as the Oxford strain of *Staph. aureus*, which showed the average level of resistance of staphylococci isolated from burns before and again after the ten weeks' trial of dibrompropamidine.

**DISCUSSION AND SUMMARY**

The contraindications to the use of local dibrompropamidine are described above. Most important perhaps are the delay in the separation of burn slough and toxic effects on leucocytes and epithelium.

There is no evidence that local dibrompropamidine 0.15 g. per cent. is more effective than local penicillin 1,000 units per g. in preventing added bacterial infection of burns.
The possible advantages of local dibrompropamidine in preventing or treating small superficial streptococcal infections in wounds other than burns has not been investigated; but in these, too, the toxic effect on leucocytes and epithelium might be expected to limit its usefulness.

Organisms acquired by Burns initially free from them

<table>
<thead>
<tr>
<th>Routine Cream applied at Dressings</th>
<th>Staphylococcus aureus</th>
<th>Streptococcus pyogenes</th>
<th>Pseudomonas pyocyanae</th>
<th>Coliform Bacilli</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dibrompropamidine isethionate (0.15 per cent)</td>
<td>72</td>
<td>57</td>
<td>1.6</td>
<td>62</td>
</tr>
<tr>
<td>Polymyxin (0.1 per cent.) + penicillin (1,000 units per gram)</td>
<td>60</td>
<td>120</td>
<td>3.0</td>
<td>151</td>
</tr>
<tr>
<td>Penicillin (1,000 units per gram) (controls in polymyxin trial)</td>
<td>63</td>
<td>164</td>
<td>3.0</td>
<td>203</td>
</tr>
</tbody>
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REFERENCES

-- (1951 b). Lancet, 2, 705.