It was found that the kidneys' concentrating ability is often impaired, particularly in children with radiological evidence of pyelonephritis or vesicoureteric reflux. This defect is reversible with effective chemotherapy.

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Treatment of Infected Surface Lesions with Sulfamylon Acetate Cream

Established infection in large cutaneous lesions presents many problems apart from the obvious hazard of septicaemia; the presence of vast numbers of Gram-negative bacteria in infected burns tissue was reported by Lindberg and his colleagues (1965), and this serious complication is also common with large pressure sores and with exposed subcutaneous tissue after excision of neoplastic lesions. They listed the properties of an ideal medication for the treatment of infections involving extensive burned surface, suggesting that the agent

should be active against Gram-negative and Gram-positive bacteria, be readily applicable and non-irritant to raw surfaces, and permit the free formation of granulation tissue. It should be stable in the presence of tissue exudates and serum and, if absorbed, be rapidly excreted or converted to a non-toxic derivative. Clinical studies by these workers suggested that sulfamylon acetate cream met their criteria, and subsequent laboratory investigations by Holt, Murphy, and O'Donnell (1968) confirmed that the drug had a broad anti-bacterial spectrum and other desirable properties. These observations suggested to us that sulfamylon acetate cream could play a valuable role in the control of infection of extensive skin lesions in children and permit successful grafting onto these areas, and we report below details of representative cases.

Methods

(1) **Cultures from infected surfaces.** Swabs moistened in broth were applied to selected sites and subsequently cultured aerobically and anaerobically on horse blood agar, gentian violet blood agar, MacConkey agar, Czapek-Dox agar for the isolation of *Candida* spp. and fungi, and in Robertson's cooked meat broth. On occasions replica pad cultures (Holt, 1966) were made of some areas.

(2) **Sensitivity tests.** Bacterial sensitivity to sulfamylon acetate was tested by the methods reported elsewhere (Holt *et al.*, 1968).

(3) **Sulfamylon acetate cream.** This contained 11.2% w/w in a smooth, stable, hydrophilic cream base; it was spread daily on infected surfaces with sterilized flexible steel pastry spatulae, after removal of the previous cream layer. Though the manufacturer recommends layers of about 1.5 mm depth, a greater depth (3.5 mm) was found necessary in this series to ensure that the cream remained on the moist surface; Moncrief (1970) used even thicker layers (6 mm).

Case Histories

Case 1 (male child, age 23 months). Admitted with deep weeping burns of feet, lower limbs, buttocks, external genitalia, and lower abdomen caused by sitting in a bath to which scalding hot water had inadvertently been added. About 50% of the body surface was burned, mostly to full thickness depth. The burns were treated in the first instance by exposure. Skin and blood cultures during the first week were sterile, but by the third and fourth weeks cultures yielded a profuse growth of *Pseudomonas aeruginosa* with scanty *Esch. coli* and enterococci.

The pseudomonas and *Esch. coli* were fully sensitive to sulfamylon acetate, requiring minimal inhibitory concentrations (MIC) below 1 mg/ml of the drug. The enterococci were less sensitive, requiring an MIC between 2 and 5 mg/ml.

Three weeks after the accident, split skin 'postage stamp' grafts were planted on all surfaces; the skin was taken from the anterior abdominal wall and a small area of unburned thigh, and was held in place by pressure dressings. Within a few days it became apparent that pus was forming at the graft sites and that the grafts were detaching; cultures of exudate from the grafted areas gave a profuse growth of *Ps. aeruginosa*. Sulfamylon acetate treatment was started, during which the child was sedated, and nursed in a hammock bed.

The grafts showed very satisfactory progress after two weeks of this treatment, none had sloughed, and epithelialization had occurred under the sulfamylon cream layer to fill the spaces between grafts; repeated cultures revealed only scanty Gram-negative bacilli sensitive to sulfamylon. Further split skin grafts to the heels and dorsum of the left foot were made at 8 weeks, again under heavy layers of sulfamylon cream.

The child was discharged at 15 weeks with complete and successful grafting and has since continued to make excellent progress; normal skin flora gradually colonized the healed surfaces after application of the cream was stopped.

Two complications occurred during the period that the child was in hospital; at 4 weeks he developed *Salm. typhimurium* enteritis, eradicated by an 8-day course of paromomycin. At 7 weeks an abundant growth of *Candida albicans*, believed to have originated from his faeces, was isolated from the thigh surfaces. Nystatin powder, to which the *Candida* was fully sensitive, was applied with sulfamylon cream and the *Candida* was rapidly eliminated.

Case 2 (male, aged 20 months). Admitted with 60% of the body surface burned to full thickness after his clothes had caught fire; the areas involved included his trunk and neck, the anterior aspects of the upper limbs, and left thigh. Within a few days the debrided burn surfaces became heavily infected with *Ps. aeruginosa*, *Klebsiella*, and *Proteus mirabilis*, all of which were sensitive to sulfamylon acetate. Continuous coating of the burned areas with sulfamylon acetate cream was maintained for four weeks, and three small area skin grafts were successful; grafting was limited because only one healthy leg was available as a donor site. During therapy the burned areas rapidly became sterile, though there were two brief episodes when scanty growths of *Candida* and *Staph. aureus* were cultured; these organisms disappeared rapidly. Eventually the whole area was epithelialized with healthy tissue and normal skin microflora became established.

Case 3 (female). The baby was born with a huge haemangiomatic mass extending from the shoulder to the finger tip of her right arm. At 2 months, peripheral circumcision was performed, with deliberate scarring by suturing and diathermy to limit the spreading lesion. At 7 months, partial excision was attempted on the upper arm scar; after this the whole area became infected with *Ps. aeruginosa*, *Esch. coli*, and *Proteus mirabilis*. Eusol irrigation and polybactrin spraying

did not control this infection, and split skin grafts were unsuccessful. Since all the infecting organisms were sensitive to sulfamylon acetate, further split skin grafts from the right thigh and left side were made three weeks apart, and the whole lesion was covered daily with sulfamylon cream for three days before grafting and for the next six weeks. The surface infection was drastically reduced, the grafts were successful, and at the age of 14 months the child was discharged with the arm covered with healthy tissue.

Case 4 (female, age 9 years). This girl had a meningocele, hydrocephalus, and neurogenic bladder, with frequent urinary tract infections; she was paraplegic from the waist downwards. At the age of 9 the left anterior superior spine was incised and all muscle freed from the outer side of the spine to allow free internal rotation and hip extension. Nine days after operation she burst the external stitches. The wound broke down and a large trophic ulcer developed over the greater trochanter of the left femur. Despite Eusol irrigation, the sore enlarged and deepened into the buttock tissue. Four months after the original operation the ulcer was incised down to the lateral aspect of the trochanter, from which a necrotic bone disc was removed. By this time, and during the next year, the large deep ulcer became successively infected with *Staph. aureus*, *Streptococcus pyogenes*, *Ps. aeruginosa*, *Proteus* sp., enterococci, *Esch. coli*, and *Klebsiella*. The *Strep. pyogenes* was eliminated by ampicillin and benzylpenicillin, but despite the continued Eusol irrigation and therapy with cloxacillin, fucidin, fucidin tulle, polymyxin, ampicillin, and polybactrin, the other bacteria persisted and the ulcer showed no signs of healing; it remained a deep, foul smelling, weeping lesion, about 8 cm long, 3 cm wide, and 5 cm deep. 16 months after the original operation the ulcer was infected with *Staph. aureus*, *Ps. aeruginosa*, *Esch. coli*, *Klebsiella*, and *Proteus* sp., all of which were fully or moderately sensitive to sulfamylon acetate. The ulcer was packed twice daily from the bottom upwards with sulfamylon acetate cream, care being taken to remove the cream from previous applications as far as possible. After three months of treatment the lesion was sterile, the tissue looked much healthier, granulation was evident for the first time at the bottom of the deep cleft, and epithelialization was spreading from the skin edges; 30 months after the operation the wound healed.

Discussion

Where large raw cutaneous or subcutaneous surfaces are heavily colonized with bacteria, healthy tissue regeneration is very unlikely. This proposition must be accepted as axiomatic, and topical therapy for these areas is logically directed towards eliminating all the bacteria and then maintaining a virtually sterile state in which epithelialization can proceed to cover the area; autografts may help to hasten this but will fail on an infected area.

After application of the cream several workers have reported pain, assessed by Moncrief (1970) as mild to moderate in a proportion of patients, and by Lowbury and Jackson (1970) as moderate to severe in several cases. I. F. K. Muir (personal communication, 1971) found that most patients experienced a burning sensation on application, but this was bearable and passed off rapidly; in only about 5% was pain severe enough for treatment to be discontinued. In none of the small series treated here was there evidence of pain after application, or of skin rash which might well have been expected with young hypersensitive skin. In our children the complete lack of tissue toxicity was demonstrated by the ease and speed with which grafts took and new areas of epithelialization extended under the cream blanket to cover the exposed subcutaneous surfaces; daily improvement was often noted when the previous cream layer was carefully removed before fresh application. Skilled and patient care is necessary in removal of the previous cream layer, which was frequently caked and yellow from absorption of serous exudate into the hydrophilic cream base. We found that the depth of cream at each application was very important; too thick a layer caused cream to coalesce into large blobs as it warmed to body heat, and these tended to run down curved body surfaces, leaving almost uncovered zones. Spread more thinly, to a depth of 3–5 mm, the cream usually remained where applied for the next 24 hours. The baby with the arm haemangioma was unusually active, and a light external gauze dressing was essential; no absorptive dressing was placed outside. The exceptionally deep pressure sore was packed with cream and the whole area covered with an occlusive dressing.

There can be no doubt sulfamylon acetate cream is a most valuable topical agent for infected burn surfaces; this is apparent from the series of 12 cases reported by Muir, Owen, and Murphy (1969) and from 2 cases reported above. The success achieved in the chronic trophic ulcer suggests that sulfamylon may also be of value in the treatment of pressure sores in which infection of the devitalized

tissues plays an important part in prevention of healing. The bacterial flora in these ulcers is usually similar to that in the cases described here, and application of sulfamylon cream may well produce results better than hitherto attainable.

Summary

Sulfamylon acetate cream was used to treat extensive burns heavily infected with *Pseudomonas aeruginosa* and *Enterobacteriaceae*; it was also successful in the control of heavy infection of a large deep trophic ulcer and of the excision site of a large congenital haemangioma. Details are given of the bacteriological flora at different stages during therapy. It is suggested that use of this preparation should be extended from the treatment of infected burns to the treatment of large chronically infected pressure sores in geriatric and orthopaedic practice.

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