

Staphylococcus aureus in the lesions of atopic dermatitis

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SUMMARY

Quantitative aerobic cultures were obtained from fifty patients with chronic plaques, and from twenty with exudative lesions of atopic dermatitis. In the former, *Staphylococcus aureus* was isolated from 90% and the density exceeded $1 \times 10^6/\text{cm}^2$ in 45% of the samples. In the exudative form, *Staph. aureus* was recovered in every case with a mean density of 14×10^6 organisms per cm^2 . *Staph. aureus* was the dominant organism not only in the lesions but in nearby clinically normal skin. Despite these high numbers, clinical signs of infection were lacking. Systemic and topical antibiotic therapy produced a profound decrease in *Staph. aureus* density.

It is proposed that high numbers of *Staph. aureus* may aggravate the underlying lesion and be the source of *Staph. aureus* infections in contacts.

Although patients who suffer from atopic dermatitis have been shown to be peculiarly at risk to infection with herpes simplex and vaccinia viruses, overt bacterial infections are not very common (Baer, 1955; Sulzberger, 1971). Local signs of infection, such as suppuration, heat, oedema and crusting, occasionally occur, but systemic signs, such as fever, leukocytosis and lymphadenopathy, are extremely uncommon. Nonetheless, the lesions of atopic dermatitis have been recognized to carry *Staphylococcus aureus*, by students of hospital cross-infection (Hare & Cooke, 1961; Noble & Davies, 1965). For example, *Staph. aureus* was found in fifty-six of 113 patients with eczema (Selwyn, 1965). Only twenty-four of these patients were clinically judged to be infected, and seventeen of the unsuspected carriers served as *Staph. aureus* dispersers. Similarly, in another report *Staph. aureus* was demonstrated in forty-four out of 106 patients with 'eczema' who were judged not to be infected on clinical grounds (Selwyn, 1963). In these studies, no quantitative assessment of *Staph. aureus* density was made. The purpose of this study was to quantify *Staph. aureus* in both the chronic plaques and the acute exudative lesions of atopic dermatitis.

METHODS

Seventy patients ranging in age from 4 months to 19 years were studied. The majority were children between 2 and 10 years, with a prolonged history of the disease. In fifty, the lesions were atypical, pruritic, chronic, lichenified, non-exudative plaques of atopic dermatitis. The antecubital fossa was

the site usually sampled. Sixty-six lesions in these fifty patients were evaluated in a quantitative fashion for aerobic bacteria. In twenty-seven, clinically normal skin 5 cm or more away was similarly sampled. At the time of sampling none was using bacteriostatic soaps, or topical or systemic antibiotics. In another twenty, acute exudative lesions were sampled during an acute exacerbation of the disease. Again the majority of lesions sampled were in the antecubital fossa. The afflicted skin showed erythema, oozing, microvesiculation and occasionally slight crusting. Frankly infected lesions were not sampled. No patient had fever, lymphadenopathy or leukocytosis. In fourteen of this group of patients, clinically normal skin 5 cm away was also sampled.

Bacteriological samples were obtained by the detergent scrub technique (Williamson & Kligman, 1965). Single drops from a tenfold dilution series were plated on (1) Trypticase Soy Agar (TSA), a non-selective medium, and (2) TSA with lecithin as a detoxicant and with polysorbate 80 to enhance growth of *Staph. aureus*. In addition, streaks were made on Marshall & Kelsey's medium. The plates were incubated aerobically at 35°C for 2 days. The total aerobes per cm² and the proportion comprised by *Staph. aureus* were then determined.

Thirteen of the patients with chronic lichenified lesions were treated with a 1% neomycin cream twice daily for 7 days, followed by bacteriological evaluation on the eighth day. Another eleven received erythromycin, 250 mg four times daily. We sought primarily to compare oral and topical treatment with respect to elimination of *Staph. aureus*. Additionally, we examined the possibility of relating antibacterial efficacy to clinical response. The effect of treatment was evaluated by observing changes in erythema, lichenification and excoriation. Using these indicators, the response was designated as 'improved', 'no improvement' or 'worse'. No other therapy was given during the 1 week of antibiotic therapy.

RESULTS

Cultures from dermatitic skin

In chronic, lichenified plaques the mean density of sixty-six samples was 593,800 organisms per cm². *Staph. aureus* was recovered from sixty sites (91%) with a mean density of 403,900/cm². In the twenty acute, exudative lesions, the mean density of aerobes was 18,417,000/cm². *Staph. aureus* was recovered in all twenty (100%), with a mean density of 15,122,000/cm². In both types of lesions, therefore, *Staph. aureus* was overwhelmingly the predominant organism. In chronic plaques, pure cultures of *Staph. aureus* were obtained in nine patients; the density exceeded 10⁶/cm² in thirty-one (45%). In the exudative lesions, ten patients yielded pure cultures of *Staph. aureus*; thus exudative lesions carried a tremendously greater number of total aerobes ($t=3.77$, $P<0.01$) and of *Staph. aureus* ($t=3.33$, $P<0.01$).

Comparison of normal and dermatitic skin

Staph. aureus was isolated from all fifteen paired cultures of normal and dermatitic skin in the patients with exudative lesions, in twenty-one out of twenty-seven cultures of normal skin, and in twenty-four out of twenty-seven cultures from the chronic lichenified plaques. This difference was not significant. The density of *Staph. aureus*, however, was very much greater in dermatitic skin. Lichenified plaques had a mean density of 554,300 *Staph. aureus* per cm², compared to only 1,358/cm² on normal skin ($t=6.23$, $P<0.001$). Likewise, the total aerobic flora was considerably larger in dermatitic skin, 718,900 against 2624/cm² ($t=10.5$, $P<0.001$) (Fig. 1). In patients with exudative lesions, a mean density of 14,505,000 *Staph. aureus* per cm² was found, compared to a mean density of 182,352/cm² on normal appearing skin ($t=8.8$, $P<0.001$). Likewise, the total aerobic flora was again considerably larger in dermatitic skin, a mean density of 16,646,428/cm² in lesions compared to 232,307/cm² in normal skin ($t=9.2$, $P<0.001$) (Fig. 2).

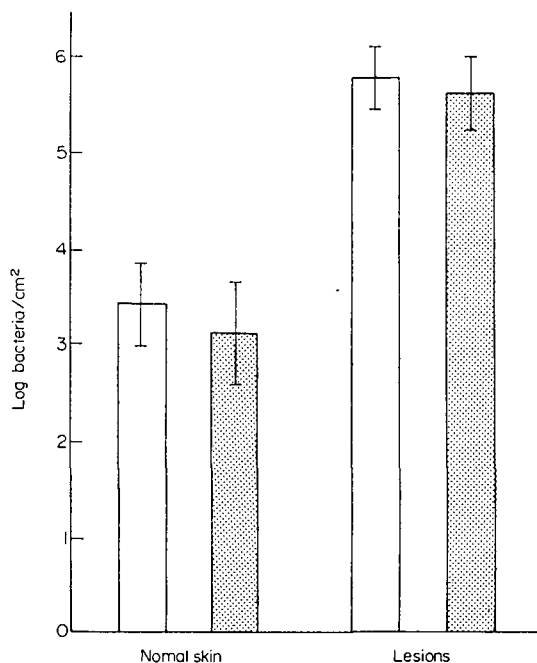


FIGURE 1. Chronic lichenified plaques support both a greater density of total aerobic organisms and *Staph. aureus* than normal skin. *Staph. aureus*, however, is the predominant organism in both normal and dermatitic skin. Open columns, total bacteria; stippled columns, *Staph. aureus*.

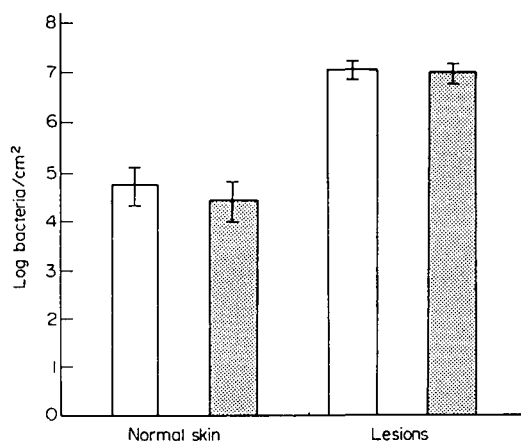


FIGURE 2. Acute, exudative lesions support extremely high numbers of aerobic organisms. Again *Staph. aureus* is the predominant organism. Open columns, total bacteria; stippled columns, *Staph. aureus*.

Effect of antibacterial treatment

All thirteen patients treated with neomycin cream twice daily had *Staph. aureus* prior to treatment, the mean density being 360,000/cm² (range 8,421,000–232). Eight had 1,000,000 or more organisms per cm²; the mean was unduly lowered by four patients who had only 200,000 organisms per cm² or

less. After 1 week of neomycin, *Staph. aureus* was completely eradicated in six. In the remaining, the mean density was a mere 388/cm². The total aerobes fell from 721,000/cm² to 342/cm². In the eleven treated with oral erythromycin, the mean density of *Staph. aureus* before treatment was 1,700,000/cm². After a week of therapy, *Staph. aureus* was totally eradicated in three and the mean count was 1890/cm² in the rest. The total aerobic count was reduced from 3,334,000 to 6,180/cm² (Fig. 3).

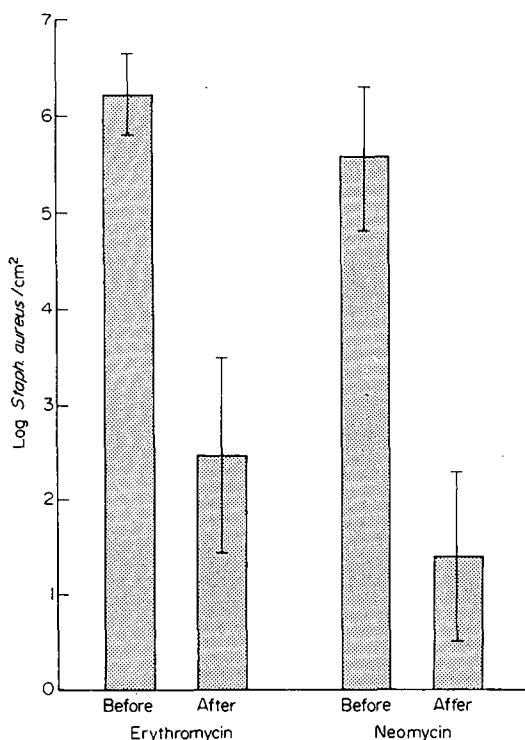


FIGURE 3. Both topical and systemic antibiotic therapy significantly lower the total aerobic flora and the density of *Staph. aureus* in the chronic lichenified plaques.

DISCUSSION

Atopic dermatitis is thought to be a multifactorial disease. *Staph. aureus* overgrowth appears to be a neglected component. More than 90% of patients with chronic lichenified plaques carried this pathogen. Indeed, *Staph. aureus* was overwhelmingly the dominant species with counts exceeding 10⁶/cm² in about half of the patients. The affinity of *Staph. aureus* for atopic dermatitis was even more pronounced in the acute, exudative form of the disease. *Staph. aureus* was recovered 100% of the time with a mean density of 18,417,000 organisms per cm² in acute lesions. In only five of twenty patients was the density less than 10⁷/cm². Despite these huge numbers, the lesions did not look infected. Only in the acute exudative form was there any hint of a harmful effect of *Staph. aureus*, visible as a slight serous exudate and thin crust.

A question of major importance is whether these extraordinarily high numbers of *Staph. aureus* represent secondary infection or harmless colonization. *Staph. aureus* is not a customary member of the cutaneous microflora except for occasional resident status in the perineum (Allen *et al.*, 1972).

Noble *et al.* recovered *Staph. aureus* nine times in 201 samples from normal skin and in only one was there more than six colonies (Noble, Valkenburg & Wolters, 1967). Retrospective analysis of the clinical notes revealed that those patients who were judged to have improved on the basis of less erythema, fewer excoriations, diminution of serous exudation and a subjective decrease in the amount of pruritis, initially had more than a million *Staph. aureus* per cm². This beneficial response was associated with a reduction of *Staph. aureus*. A clinical improvement accompanied by a drastic drop in the quantity of this virulent organism is presumptive evidence for the presence of infection. In our view, which we are still elaborating, secondary infection may be defined in quantitative terms in much the same way as urinary tract infections. Densities above 10⁶/cm² suggest that the organism is likely to be aggravating the underlying dermatosis. We refer here to secondary infections only and hasten to point out that antibiotic treatment in such cases produces improvement but certainly not clearing of the dermatitis. The high frequency of *Staph. aureus* in clinically normal skin was also somewhat surprising. Even though the density was low, the recovery rate was the same as for the lesions. It remains an open question whether this reflects continual dispersion from lesions (contamination) or actual colonization with continued multiplication. The uninvolved skin of patients with atopic dermatitis may be inherently favourable to colonization by *Staph. aureus*. Atopic dermatitis, for example, is distinctly different from psoriasis. In psoriatic plaques, the density of *Staph. aureus* uncommonly exceeds 10³ organisms per cm² with a prevalence rate of 50% (Marples, Heaton & Kligman, 1973).

These findings do, however, provide a plausible explanation for the practice of including antibiotics in the initial therapy of atopic dermatitis, even in the absence of the usual signs of infection. Antibiotics are best administered for only a 1 week period, for by that time *Staph. aureus* can be lowered to a harmless level. Prolonged antibiotic therapy may invite colonization with resistant organisms or new pathogens, which could lead to clinical relapse (Leyden & Marples, 1973a, b).

The unexpectedly high numbers of *Staph. aureus* raises the question of how corticosteroids work so well in atopic dermatitis. We are currently conducting a series of experiments with various regimens of local and systemic steroids with quantitative bacteriological monitoring. To date it appears that their action is solely anti-inflammatory; suppression of inflammation leads to unfavourable conditions for *Staph. aureus*. We have not seen any patient develop clinical signs of infection during corticosteroid therapy.

High numbers of *Staph. aureus* may not only intensify pre-existing lesions but may have great importance in relation to public health. Inflamed skin has been recognized as a major source of dissemination of *Staph. aureus* in hospital wards (Davies & Noble, 1962; Selwyn & Chalmers, 1965). Fatal infections have been traced to dermatitic skin. We witnessed one such epidemic of *Staph. aureus* wound infections in a gynaecology ward, the source in this instance being atopic dermatitis in the resident physician. Phage typing and antibiogram established the identity of the organism in each wound with that of the atopic lesion. On several occasions, we observed primary pyoderma (furuncles) in members of families of patients with atopic dermatitis, the identity of the organism being validated as above.

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