Modulation of Comedonal Levels of Interleukin-1 in Acne Patients Treated with Tetracyclines

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To understand the basis for the anti-inflammatory activity of tetracyclines in acne, we compared the cytokine profiles [interleukin 1 (IL-1) alpha and beta, tumor necrosis factor (TNF) alpha, and IL-6] and bacterial flora of 66 open comedones removed from eleven patients before and after at least 8 weeks treatment with either tetracycline or minocycline.

Pre-treatment, the only cytokine regularly recovered from comedones was bioactive IL-1alpha–like material. The mean concentration of IL-1alpha–like bioactivity/mg comedonal material rose from 272.0 ± 88.6 pg to 844.3 ± 196.7 pg following treatment (p < 0.05, Wilcoxon matched pairs). All six minocycline-treated patients showed an increase in bioactive IL-1alpha–like material compared with three of five tetracycline-treated patients. The incidence (p < 0.001, X²) and concentration (p < 0.05, Wilcoxon) of immunochemical IL-beta were also raised post-treatment, although significantly more patients assigned to minocycline therapy had detectable levels of this cytokine before therapy was initiated. However, the mean concentration of IL-1beta/mg comedonal material post-treatment was similar in both groups (72.5 ± 23.3 pg for tetracycline-treated compared with 78.6 ± 41.9 pg for minocycline-treated patients). The other cytokines were either absent (IL-6) or present in <10% of comedones (TNFalpha) before and after therapy.

Following treatment, only three of 11 patients showed a decrease of ≥1 log₁₀ in propionibacterial numbers/mg comedonal material, whereas six patients showed an increase of >0.5 log₁₀ in numbers of staphylococci. In eight patients, the increase or decrease in staphylococcal numbers correlated with the change in concentration of IL-1alpha–like bioactivity.

This is the first study to show an effect of antibiotic therapy on cytokine levels in vivo. Increased levels of IL-1 in comedones destined to become inflamed may enhance resolution, and promote repair of the damaged follicular epithelium. Hence, these results provide further evidence of the augmentation of immune responses by tetracyclines and support the hypothesis that epidermal IL-1 plays a physiologic role in wound healing.


cne vulgaris is an inflammatory disease of the pilosebaceous follicles of the face, back, and chest, characterized by a variety of lesions showing various degrees of visible erythema [1]. Little is known of the inflammatory mediators other than complement [2,3] present in acne lesions. Two lines of evidence, namely, the histologic demonstration of non-random helper T-lymphocyte infiltration [4] and the secretion of pro-inflammatory cytokines by keratinocytes in vitro in response to a number of different environmental stimuli [5], suggested that the estimation of cytokines in acne lesions might yield information pertinent to the pathogenesis and treatment of the disease. We have recently shown that the majority of open comedones contain biologically active IL-1alpha–like material in concentrations sufficient to promote visible erythema if released into the dermis [6].

Successful anti-acne therapy with antibiotics is thought to be due, at least in part, to their inhibitory effect on the growth and metabolism of Propionibacterium acnes [7–9]. Micro-organisms, especially P. acnes, have been strongly implicated in the pathogenesis of acne [10,11] and may release microbial mediators of inflammation into the dermis or trigger the release of cytokines from ductal keratinocytes. However, despite clinical improvement, the numbers of propionibacteria do not always fall during antibiotic therapy [7]. Anti-inflammatory activity has been proposed as an alternative or complementary mode of action of antibiotics in acne [7] and has been demonstrated in vivo, for both tetracyclines and erythromycin [12]. There is currently much interest in the possible effects of antibiotics on cytokine production and upregulation of IL-1 and IL-6 production by monocytes has been observed in vitro [13–15].

The aims of this study were to determine whether oral acne therapy with tetracyclines altered the cytokine content of open comedones and to identify any concomitant changes in the comedonal microflora.

MATERIALS AND METHODS

Patients Open comedones (blackheads) were donated by 11 patients with mild to moderate acne vulgaris (grade 0.5 to 3.0 on the scale of Burke and Cunliffe [16]) before and after therapy for a minimum of 8 weeks with minocycline (four male and two female subjects, 15–29 years old, 100 mg/d), tetracycline (two male and one female, 13–26 years old, 500 mg twice daily) or Mysteclin (one male, 18 years old and one female, 15 years old, tetracycline 500 mg twice daily plus nystatin 500,000 units twice daily). Treatment was selected on the basis of clinical criteria only and two patients who had received tetracycline previously were given Mysteclin for reasons of compliance. No patient had received any anti-acne therapy

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for 6 weeks prior to, nor any natural ultraviolet irradiation during, the study.

**Recovery and Extraction of Comedones** Six open comedones were collected aseptically from the same sample site before and after therapy using a comedone extractor (Thackray) after swabbing the skin surface with isopropanol. Four patients were sampled from the face and seven on the back. No sample was obviously contaminated with blood. The wet weight of each comedone was determined prior to gentle homogenization for 1 min in a micro-tissue homogenizer (Thackray) in 250 µl of Dulbecco’s modified Eagle’s medium supplemented with 2 mM L-glutamine, 0.375% (w/v) NaHCO3, 20 mM Hepes, and 10% (v/v) fetal calf serum. The homogenate was centrifuged (10,000 x g; microfuge; MSE Microcentrufuge) for 10 min. The supernatant (approximately 230 µl) was removed and diluted 1:10 with base medium containing penicillin (100,000 U/l) and streptomycin (100 mg/l), aliquotted and stored at −20°C for the determination of bioactive and immunochromatographic IL-1 alpha and beta. The pellet was resuspended in 200 µl of wash fluid (0.075 M sodium phosphate buffer containing 0.1% v/v Triton-X100, pH 7.9) for microbiologic determinations.

**Cytokine Bioassays** Bioactive IL-1 alpha and beta were estimated as previously described using a modification of the CSH murine thymocyte proliferation assay in the presence of saturating levels of IL-2 [6]. Specificity was accomplished by pre-incubating the supernatants in the presence and absence of anti-IL-1 alpha and anti-IL-1 beta antibodies (British Biotechnology) separately and together prior to assay. For the dilution of the comedonal material in the assay, the sensitivity of the IL-1 bioassay was 10 pg/comedone. Bioactive TNF alpha was estimated using a conventional L929 cytotoxicity assay as previously described [6] and the lower limit of detection was 50 pg TNF alpha/comedone. Bioactive IL-6 was quantified by the method of van Oers et al [17] using IL-6-dependent B9.9 hybridoma cells and substituting MT2 conversion instead of 3H-thymidine incorporation as a measure of cell viability. All bioassays were validated “in house” for use with comedonal material as described in our previous report [6].

**Cytokine Immunochemical Assays** Immunochromatographic IL-1 alpha, TNF alpha, and IL-6 were determined using Quantikine enzyme-linked immunosorbent assay kits (British Biotechnology). The sensitivity of the kits varied between 17 and 31 ng/l (170–310 pg/comedone) for IL-1 alpha, and between 31–48 ng/l (90 pg/comedone) for TNF alpha and IL-6. IL-1 beta was determined using Cistron enzyme-linked immunosorbent assay kits supplied by T-cell Sciences. The sensitivity was 4 ng IL-1 beta/l (20 pg/comedone). All assays were carried out according to the manufacturers’ instructions.

**Enumeration of Microorganisms** Staphylococci and propionibacteria were enumerated in the pellets from the centrifugation of comedonal material as described in our previous report [6].

**Statistical Analyses** These were carried out according to the recommendations of Sokal and Rohlf [18].

**RESULTS**

**Effect of Therapy on Acne Grade** Acne is a slowly responding disease and the patients were deliberately sampled early (i.e., approximately one third of the way through a standard 6-month course of treatment) to determine the likely initial events leading to clinical improvement. At the time of sampling, two of the 11 patients had a 50% improvement in their acne grade (both on minocycline), four had an improvement of <50% (two on minocycline and two on tetracycline), one tetracycline-treated patient experienced a marked deterioration in acne severity that necessitated a change of therapy, and the remainder showed no detectable change. At the end of the standard 6-month course, four of six minocycline-treated patients were showing a >50% improvement in acne grade, one patient showed a <50% improvement, and one patient failed to return for their final assessment. Two of five tetracycline-treated patients were showing a <50% improvement at 6 months, one had withdrawn from the study (see above), and two failed to return for follow-up appointments.

**Effect of Therapy on Comedone Weight** There was no significant difference (Student’s t test) between the weight of the comedones before and after treatment with either minocycline or tetracycline although there was reduction of 30% in the mean comedonal weight following tetracycline treatment (Table I).

**Effects of Therapy on Bacterial Numbers** Changes in propionibacterial numbers were minimal with only three of 11 patients showing a ≥1 log10 reduction in mean count expressed as cfu/mg comedonal material after at least 8 weeks oral therapy with either minocycline (Fig 1) or tetracycline (Fig 2). Changes in staphylococcal numbers varied from individual to individual but surprisingly six of 11 patients showed an increase of >0.5 log10 (Figs 1 and 2). Overall, there was no change in the mean counts of staphylococci or propionibacteria following treatment with either antibiotic (Table II). Pre-treatment, 37% of comedones were not colonized (i.e., <102 cfu/mg) by staphylococci and 34% were not colonized by propionibacteria. Following treatment, there was no alteration in the proportion of uncolonized follicles; 39% were not colonized by staphylococci, and 36% were not colonized by propionibacteria.

**Effect of Therapy on Cytokine Levels** Bioactive IL-1 alpha-like material was detected in 76.9% of open comedones before treatment and in 75.8% after treatment. However, the mean concentration of IL-1 alpha-like bioactivity per mg comedonal weight was significantly increased post-treatment in minocycline-treated patients (p <0.01, Fig 1) and when data from both treatment groups were combined before analysis (p <0.05, Wilcoxon matched pairs [Table III]). In eight patients (three of six on minocycline and five of five on tetracycline), the increase in IL-1 alpha-like bioactivity corresponded with an increase or decrease in numbers of staphylococci (Figs 1 and 2). Bioactive IL-1 beta was not detected before or after therapy with either antibiotic. Following treatment, the incidence of immunochromatographically detectable IL-1 alpha rose from 12.1% to 28.8% of comedones and the mean concentration/mg comedonal material was significantly raised (p <0.05, Wilcoxon [Table IV]). Both the incidence (p <0.001, χ2) and mean concentration/mg comedonal material (p <0.05, Wilcoxon) of immunochromatographic IL-1 beta rose significantly post-treatment when data from both treatment groups were combined (Table V). The greatest increases were recorded in tetracycline-treated patients. This difference between treatment groups was due to the significantly higher baseline incidence of immunochromatographic IL-1 beta-containing comedones in the group assigned to minocycline therapy (p <0.001, χ2). In this group, all six comedones from two patients contained immunochromatographic IL-1 beta before therapy was initiated. However, the incidence and mean concentration of immunochromatographic IL-1 beta post-treatment was similar in both treatment groups (Table V).

TNFalpha-like bioactivity was detected in 4.5% of comedones

**Table I. Changes in Comedonal Weight Following Treatment**

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Pre-Treatment</th>
<th>Post-Treatment</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minocycline (n = 36)</td>
<td>0.86 ± 0.43</td>
<td>0.93 ± 0.77</td>
<td>NS</td>
</tr>
<tr>
<td>Tetracycline (n = 30)</td>
<td>0.90 ± 0.49</td>
<td>0.63 ± 0.29</td>
<td>NS</td>
</tr>
<tr>
<td>All patients (n = 66)</td>
<td>0.88 ± 0.30</td>
<td>0.79 ± 0.42</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Calculated from student t × SEM.

**Table V. Changes in Mean Cytokine Levels Following Treatment**

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1 alpha</td>
<td>32 pg</td>
<td>35 pg</td>
<td>NS</td>
</tr>
<tr>
<td>TNFalpha</td>
<td>12 pg</td>
<td>15 pg</td>
<td>NS</td>
</tr>
<tr>
<td>IL-1 beta</td>
<td>8 pg</td>
<td>10 pg</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Calculated from student t × SEM.
Figure 1. Effect of minocycline therapy on IL-1alpha-like bioactivity (A) and on viable counts of staphylococci (B) and propionibacteria (C) per mg comedonal material. Each pair of bars shows the mean ± 95% confidence limits (Student t X SEM) for six open comedones collected from each patient before (■) and after (□) treatment.

Figure 2. Effect of tetracycline therapy on IL-1alpha-like bioactivity (A) and on viable counts of staphylococci (B) and propionibacteria (C) per mg comedonal material. Each pair of bars shows the mean ± 95% confidence limits (Student t X SEM) for six open comedones collected from each patient before (■) and after (□) treatment.
pre-treatment and in 6.1% of comedones following treatment. Immunochemo
tical TNFalpha was present in 9.1% of comedones before treatment but was not detected following treatment. Immunochemo-
ical IL-6 and IL-6 bioactivity were undetectable both before and after treatment.

**DISCUSSION**

The tetracycline antibiotics are used extensively in the therapy of acne vulgaris. Although they inhibit the growth of Propionibacteri-
ium acne both in vitro and in vivo, it is unlikely that antibacterial activity alone is responsible for their therapeutic efficacy because better antimicrobial agents such as benzoyl peroxide are less clinically effective [19,20]. Both tetracycline and erythromycin have been shown to reduce potassium iodide–induced cutaneous inflammation in human skin [12]. In vitro, the tetracyclines exert a number of effects on host defense mechanisms such as the down regulation of cell-mediated immune responses and the inhibition of neutrophil functions [21–25]. More recently, we have shown that minocycline and, to a lesser extent, tetracycline enhanced IL-1beta secretion by LPS-stimulated mononuclear cells from five different donors [14]. Therefore, it appears that there are a number of possible mechanisms whereby the tetracyclines could modulate immune responses and hence inflammation in vivo. However, evidence to show that the tetracyclines interfere with any of these physiologic processes during therapeutic use has been lacking.

We have previously demonstrated the presence of bioactive IL-1alpha–like material in the majority (76%) of open comedones from untreated acne patients [6]. The identity of the comedonal mediator with monocyte-derived IL-1alpha has not been confirmed; we have followed the recommendation of Camp et al [26] and referred to the activity as IL-1alpha–like. We have now shown that treatment with tetracycline antibiotics upregulates the produc-
tion of bioactive IL-1alpha–like material and immunochemoical IL-
1beta. As in our earlier study, we found no correlation between bioassay and immunoassay data for IL-1alpha, suggesting possible differences in the epitopes expressed by the skin-associated and the monocyte-derived cytokine. However, the activity in the IL-1 bioassay was completely neutralized by anti–IL-1alpha antibody. The observed increase in comedonal IL-1 is difficult to reconcile with the anti-inflammatory effects of the tetracyclines because IL-1 is usually considered to be a pro-inflammatory cytokine. Camp et al have already demonstrated that the injection of 100 pg of IL-
1alpha–like material from human skin promotes dose-related visible erythema lasting up to 48 h [26]. Using this criterion, 58.5% of comedones removed pre-treatment and 65.2% removed post-treatment contained sufficient IL-1alpha–like material (>100 pg/mg) to promote visible inflammation if released into the dermis following spongiosis or rupture of the follicle wall. Furthermore, the mean concentration of IL-1alpha–like material was four times higher following therapy. In follicles in which the initial stimulus (still unidentified but possibly bacterial) has set the inflammatory cascade in motion, the normal chain of events leading to eventual resolution of the lesions will occur irrespective of whether treatment intervenes. The enhancement of IL-1 production within such follicles by tetracycline therapy may accelerate resolution by decreasing both the extent and duration of the inevitable inflammatory stage of the disease. In normal follicles, in which there is no breach in the follicle wall, increased levels of IL-1 resulting from antibiotic therapy will be sequestered within the duct and thus unable to promote inflammatory changes. IL-1 is also recognized to play a role in wound healing following thermal or traumatic damage to the epidermal barrier [27,28] and may thus facilitate repair of the damaged follicular epithelium. On the other hand, modulation of IL-1 levels may not be related to the anti-inflammatory action of the tetracy-

**Table II. Microbial Numbers Before and After Antibiotic Therapy**

<table>
<thead>
<tr>
<th>Micro-Organism</th>
<th>Therapy</th>
<th>Number of Comedones</th>
<th>% Positive</th>
<th>log10 cfu/mg Comedonal Material</th>
<th>Range</th>
<th>Mean ± 95% Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococci</td>
<td>Pre-treatment</td>
<td>35</td>
<td>80</td>
<td>1.00 – 6.36</td>
<td>3.82 ± 0.78</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-treatment</td>
<td>36</td>
<td>83.3</td>
<td>1.12 – 6.61</td>
<td>3.37 ± 0.75</td>
<td></td>
</tr>
<tr>
<td>Propionibacteria</td>
<td>Pre-treatment</td>
<td>35</td>
<td>80</td>
<td>1.30 – 6.77</td>
<td>4.20 ± 0.88</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-treatment</td>
<td>36</td>
<td>83.3</td>
<td>0.70 – 7.21</td>
<td>4.11 ± 0.84</td>
<td></td>
</tr>
<tr>
<td>Staphylococci</td>
<td>Pre-treatment</td>
<td>30</td>
<td>76.7</td>
<td>0.32 – 5.84</td>
<td>2.40 ± 0.77</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-treatment</td>
<td>30</td>
<td>80</td>
<td>0.90 – 6.33</td>
<td>2.56 ± 0.72</td>
<td></td>
</tr>
<tr>
<td>Propionibacteria</td>
<td>Pre-treatment</td>
<td>30</td>
<td>83.3</td>
<td>0.90 – 6.79</td>
<td>2.67 ± 0.82</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-treatment</td>
<td>30</td>
<td>70</td>
<td>1.06 – 6.53</td>
<td>2.68 ± 0.92</td>
<td></td>
</tr>
</tbody>
</table>

* Range of positive values.
* Mean for all comedones.
* Calculated from Student t × SEM.

**Table III. Levels of Bioactive IL-1alpha–like Material before and After Treatment**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Number of Comedones</th>
<th>% Positive</th>
<th>pg IL-1alpha/mg Comedonal Material</th>
<th>Range</th>
<th>Mean ± 95% Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment</td>
<td>Minocycline (n = 6)*</td>
<td>36</td>
<td>91.7</td>
<td>31 – 1170</td>
<td>308.2 ± 101.8</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>Tetracycline (n = 5)</td>
<td>29</td>
<td>58.6</td>
<td>23 – 1750</td>
<td>227.0 ± 158.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>73.3</td>
<td>51 – 1127</td>
<td>336.9 ± 137.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>65</td>
<td>76.9</td>
<td>23 – 1750</td>
<td>272.0 ± 88.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>66</td>
<td>75.8</td>
<td>41 – 11050</td>
<td>844.3 ± 196.7</td>
</tr>
</tbody>
</table>

* Range of positive values.
* Mean for all comedones.
* Calculated from Student t × SEM.
* Number of patients in each group. IL-1alpha–like bioactivity was measured in six open comedones extracted from each patient.
* Post-treatment means were significantly higher than pre-treatment means for minocycline-treated patients (p < 0.01) and when an analysis (p < 0.05, Wilcoxon matched pairs).
Table IV. Levels of Immunochemical IL-1alpha Before and After Treatment

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Number of Comedones</th>
<th>% Positive</th>
<th>Range&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Mean±95% Confidence Limits&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment</td>
<td>Minocycline (n = 6)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>36</td>
<td>16.7</td>
<td>119 - 427</td>
</tr>
<tr>
<td></td>
<td>Tetracycline (n = 5)</td>
<td>36</td>
<td>36.1</td>
<td>78 - 2040</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>All patients (n = 11)</td>
<td>66</td>
<td>28.8</td>
<td>78 - 2040</td>
</tr>
</tbody>
</table>

<sup>a</sup>Range of positive values.
<sup>b</sup>Mean for all comedones. Comedones in which the level of IL-1alpha was below the detection limit were considered not to contain the cytokine.
<sup>c</sup>Calculated from Student t X SEM.
<sup>d</sup>Number of patients.

The concentration of IL-1alpha was significantly higher post-treatment when data from both groups were combined before analysis (p < 0.05, Wilcoxon matched pairs).

clines, which could instead be mediated by one or several other well documented effects on cellular immunity (vide supra) or could be a secondary consequence of changes in microbial numbers (vide infra).

In a previous study, we found an association between the lower limit of microbial density and comedonal levels of IL-1alpha–like bioactivity although there was no evident correlation between numbers of individual microbial species and concentrations of this cytokine [6]. In addition, three comedones that contained no microorganisms contained no detectable IL-1alpha–like bioactivity. We believe that any real relationship that may exist between microbial numbers and cytokine content of open comedones might be revealed by concomitantly measuring changes in both variables as a result of antibiotic therapy. We confidently expected numbers of propionibacteria to fall based on our own previous data [9] and those of others [8]. Leyden et al [8] measured decreases of > 2 log<sub>10</sub> in propionibacterial numbers in follicular casts following 6 weeks of oral therapy with either 1000 mg of tetracycline or 200 mg of minocycline. In the present study, we found no overall decrease in numbers of propionibacteria/mg comedonal material following ≥ 8 weeks of oral therapy with an equivalent dose of tetracycline or 100 mg minocycline. The reasons for this difference are unclear. It is possible that bacteria in acne lesions respond more slowly to antibiotic therapy than surface organisms or those in normal follicles due to interference with antibiotic penetration by hypercornification and blockage of the follicular opening. Paradoxically, staphylococcal numbers increased during therapy in six of 11 patients and in eight patients the increase or decrease in staphylococcal numbers correlated with a corresponding increase or decrease in the concentration of IL-1alpha–like bioactivity. Therefore, comedonal levels of IL-1alpha–like bioactivity may, at least in part, be determined by staphylococcal and not propionibacterial population densities.

This possibility is supported by the demonstration that as few as 10 cells per monocyte of "Staphylococcus albus" (now Staphylococcus epidermidis) stimulated production of high levels of IL-1 in culture [29]. We must be careful not to overinterpret our preliminary observations, which are based on the measurement of bacterial densities and cytokine levels at one time point only. It would be pertinent now to follow the changes in IL-1 concentration and microbial numbers at several time points during a standard 6-month course of therapy. In this way we should obtain a much clearer picture of how the changes resulting from treatment with the tetracyclines relate to each other, to the therapeutic outcome, and to the anti-inflammatory effects of the antibiotics.

The cellular origin of the IL-1 detected in acne comedones was not investigated in the present study. The major species of IL-1 found in normal human epidermis appears to be IL-1alpha [30,31]. Cultured human keratinocytes secrete bioactive IL-1alpha but not beta, whereas monocytes secrete both cytokines in a bioactive form [32]. Keratinocytes secrete inactive IL-1beta because they lack the necessary proteinase to convert it into the active form [32]. Therefore, the increase in bioactive IL-1alpha and immunodetectable but biologically inactive IL-1beta following treatment with tetracyclines is consistent with their production by ductal keratinocytes.

As far as we are aware, this is the first report to demonstrate an effect of antibiotic therapy on cytokine levels in vivo. Whether or not modulation of IL-1 production contributes to the therapeutic efficacy of the tetracyclines in acne cannot be predicted from the results of this study. The demonstration of a wide range of effects of so-called "antibacterial" antibiotics in physiologic concentrations on a variety of functions in eukaryotic cells should at least lead to a

Table V. Levels of Immunochemical IL-1beta Before and After Treatment

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Number of Comedones</th>
<th>% Positive</th>
<th>Range&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Mean±95% Confidence Limits&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment</td>
<td>Minocycline (n = 6)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>36</td>
<td>52.8&lt;sup&gt;b&lt;/sup&gt;</td>
<td>14 - 104</td>
</tr>
<tr>
<td></td>
<td>Tetracycline (n = 5)</td>
<td>36</td>
<td>83.3</td>
<td>4.3 - 540</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>All patients (n = 11)</td>
<td>66</td>
<td>93.3&lt;sup&gt;c&lt;/sup&gt;</td>
<td>18 - 270</td>
</tr>
<tr>
<td></td>
<td></td>
<td>66</td>
<td>28.8</td>
<td>14 - 104</td>
</tr>
</tbody>
</table>

<sup>a</sup>Range of positive values.
<sup>b</sup>Mean for all comedones. Comedones in which the level of IL-1beta was below the detection limit were considered not to contain the cytokine.
<sup>c</sup>Calculated from Student t X SEM.
<sup>d</sup>Number of patients.
<sup>e</sup>The number of comedones containing IL-1beta pre-treatment was higher in the group assigned to minocycline therapy (p < 0.001, χ²).

<sup>f</sup>The number of comedones containing IL-1beta was significantly higher post-treatment in tetracycline-treated patients and when data from both groups were combined before analysis (p < 0.001, χ²).

<sup>g</sup>The concentration of IL-1beta was significantly higher post-treatment when data from both groups were combined before analysis (p < 0.01, Wilcoxon matched pairs).
reappraisal of their mode of action in the therapy of acne and other inflammatory dermatoses.

This work was supported by Cyanamid (Lederle Laboratories, Hampshire, U.K.).

REFERENCES


CALL FOR PAPERS

Tokyo Symposium: New Frontiers in Hair Research will be held October 25–26, 1993 in Tokyo, Japan. The meeting will be immediately before the Second Tricontinental Meeting of the Japanese Society for Investigative Dermatology (JSID), the Society for Investigative Dermatology (SID), and the European Society for Dermatological Research (ESDR), Kyoto, Japan. President: Hideoki Ogawa, M.D., Department of Dermatology, Juntendo University School of Medicine.

For further information please contact: Symposium Secretariat Ryusuke Imai, M.D. Fax, 81-3-3813-2205.