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Quantitative Bacteriological Analysis of Sputum as a Test of Antibiotic Efficacy

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After 5 days of treatment, sputa were analyzed from 40 patients treated with sodium fusidate and 20 patients treated with naficillin. There was a significant decrease in the number of staphylococci, but no significant change in the other flora. The quantitative bacteriological analysis of sputum specimens proved to be a useful laboratory procedure for providing information on the in vivo effectiveness of specific antibacterial therapy in respiratory infections.

Sputum specimens from patients with tuberculosis frequently contain other bacterial species. Most of these bacteria apparently have little effect on the clinical course of the disease or on its treatment. This secondary bacterial flora was used in the present investigation to determine the in vivo effectiveness of specific antistaphylococcal therapy, as reflected in the quantitative bacteriological analysis of sputum specimens obtained before, during, and after antibiotic therapy.

The value of quantitative analysis of bacterial populations in sputum as a guide to antibiotic treatment of patients has previously been reported by Louria (2).

MATERIALS AND METHODS

Patients with pulmonary tuberculosis included in the study were first tested for 3 consecutive days and were shown to have relatively stable populations of staphylococci, the majority of which were coagulase-negative strains. Pretreatment sputum specimens from many of these patients also contained variable numbers of other bacteria, primarily α-hemolytic streptococci, *Neisseria* species, pneumococci, *Haemophilus* species, and smaller numbers of gram-negative bactera.

The 60 selected patients were divided into two groups (group I, 40 patients; group II, 20 patients). Group I received 0.5 g of sodium fusidate (Fucidine, Squibb Institute for Medical Research, New Brunswick, N.J.) orally every 6 hr for 4 days. Group II received 1 g of nafcillin (Unipen, Wyeth Laboratories, Philadelphia, Pa.) orally every 6 hr for 5 days.

Sputum specimens were obtained from all patients at the end of the first 48 hr, and again at the end of the treatment period. Final specimens were obtained on the 3rd post-treatment day.

The sputum specimens were homogenized with beads, and diluted with water to 1:10, 1:1,000, and 1:20,000; 0.5 ml of each dilution was plated on blood-agar, eosin-methylene blue agar, and brain-heart-agar (BBL) with 5% Fildes enrichment. After incubation at 37 C for 24 to 30 hr, the species were identified and the colonies were counted (1). Antibiotic sensitivity was determined by use of discs. All strains of staphylococci were susceptible to both drugs used.

RESULTS

The frequency with which staphylococci were cleared from the sputum specimens with either antibiotic is shown in Table 1, and the detailed figures for each patient are shown in Fig. 1.

The frequency with which staphylococci were cultured from the sputum decreased within 48 hr of the start of therapy in 52.5% of the group receiving sodium fusidate, and in 25% of the nafcillin group. The greatest number of negative cultures were obtained immediately after the end of therapy in both treatment groups.

The percentage of sputum specimens that contained staphylococci at the time of post-treatment culture was greater in the group treated with nafcillin (70% positive) than in the sodium fusidate group (27.5% positive).

Results obtained with counts of bacteria other than staphylococci in the sputum specimens showed that α-hemolytic streptococci were found in all specimens before treatment (40,000 to 30 million cells per ml) and that neither sodium fusidate nor nafcillin had an effect on these bacteria.

Pneumococci were found in 14 patients before treatment and ranged in number from 20 to 80 cells per ml, except in 2 patients where only 300,000 and 3 million cells were found. Sodium fusidate was not effective, but nafcillin eradicated the pneumococci in five of seven patients. *Neisseria* cells ranged in number from 20,000 to 20

TABLE 1. *Effect of orally administered sodium fusidate and nafcillin on counts of staphylococci in sputum*

Time sputum specimens were obtained	No. of patients with negative counts/no. tested	
	Sodium fusidate[a]	Nafcillin[b]
Pretreatment	0/40	0/20
After 48 hr of therapy	21/40	5/20
At end of therapy	28/40	13/20
Third post-treatment day	29/40	6/20

[a] Dosage of sodium fusidate was 0.5 g every 6 hr for 4 days.

[b] Dosage of nafcillin was 1 g every 6 hr for 5 days.

million per ml. *Haemophilus influenzae*, between 600 and 1,300,000 per ml and *Pseudomonas*, between 300,000 and 10,200,000 per ml.

Neither of the two drugs significantly affected these microorganisms. There appeared to be no correlation between the rate of change in sputum counts of staphylococci and the counts of other bacteria.

Four patients treated with sodium fusidate complained of mild nausea or heartburn, or both. No adverse effects were recorded for the patients treated with nafcillin.

Although these results were obtained in a relatively small number of patients, and were concerned mainly with staphylococci, an analysis of them indicated that quantitative determination of bacterial populations in the sputum is a useful laboratory procedure for evaluation of the in vivo effectiveness of an antibiotic therapy.

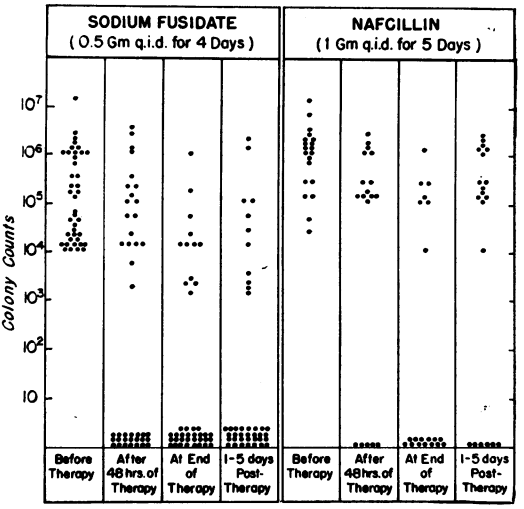

FIG. 1. *Effect of orally administered sodium fusidate and nafcillin on counts of staphylococci in sputum. Each dot represents a specimen from a single patient. The dots at the bottom represent "zero" or no colonies.*

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