PENICILLINASE AND PENICILLIN THERAPY OF MIXED STAPHYLOCOCCAL AND PNEUMOCOCCAL INFECTION

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The lifespan of mice infected with a mixed culture of staphylococci and pneumococci was reduced by treatment with benzylpenicillin.

Previous investigations have shown that penicillinase isolated from staphylococci during treatment of staphylococcal infections with benzylpenicillin is transformed from a factor of natural metabolism [4] into a factor of protection of the agent against the antibiotic.

The object of the investigation described below was to study the action of benzylpenicillin on the outcome of mixed staphylococcal and pneumococcal infection, the staphylococcal component of which was a penicillinase producer, while the pneumococcal component was highly virulent to mice and sensitive to benzylpenicillin.

EXPERIMENTAL METHOD

Two series of experiments were carried out: series I on 120 noninbred albino mice weighing 16-18 g, and series II on 60 albino mice of line BALB/c of the same body weight. Mixed infection was produced by inoculating the animals with a clinical strain of staphylococcus (No. 160), actively producing penicillinase (250 units/10^{10} bacterial cells), and resistant to benzylpenicillin (300 units/ml), intraperitoneally in a dose of 5×10^8 (series I) or intravenously in a dose of 1×10^8 (series II) bacterial cells and with a strain of type 1 pneumococcus highly sensitive to benzylpenicillin (M.I.D. 0.005 unit/ml), penicillinase-negative, intraperitoneally in a dose of 50×10^6 (series I) or 5×10^6 bacterial cells (series II). In control tests (inoculation with each microorganism separately), the same doses were used as in the experimental series.

The experimental animals inoculated with one of the microorganisms or with pneumococci and staphylococci simultaneously received benzylpenicillin daily for 4 days, starting 24 h after infection, in a relatively small dose (5000 units/kg) compared with previous experiments [1] using the same strain of penumococcus. Death of the animals was noted after 12-120 h. The mean lifespan of the control and experimental animals was determined and compared, the criterion of significance being $P < 0.05$.

EXPERIMENTAL RESULTS

Analysis of the data given in Table 1 shows a regular increase in the mean lifespan of the mice infected with pneumococci and treated with benzylpenicillin ($P < 0.01$ in both series). Administration of the antibiotic in staphylococcal infection was ineffective. Treatment of the mixed staphylococcal and pneumococcal infection with benzylpenicillin shortened the mean lifespan of the experimental animals compared with the control (from 54.6 to 38.9 days in series I and from 88.8 to 78.8 days in series II, although in series II the difference was not statistically significant).

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TABLE 1. Lifespan of Infected Animals Receiving Benzylpenicillin (M ± m)

Agent administered	Series	Survival rate of mice	Lifespan (in h)	P
Pneumococcus	I	20/20	54,0±5,02	—
	II	10/10	33,6±5,50	—
Pneumococcus + benzylpenicillin	I	13/20	73,2±4,33	0,01
	II	2/10	102,0±5,60	0,01
Staphylococcus	I	17/20	69,6±4,33	—
	II	0/10	120,0±0	—
Staphylococcus + benzylpenicillin	I	17/20	70,2±4,33	0,9
	II	0/10	120,0±0	—
Pneumococcus + staphylococcus	I	16/20	54,6±5,02	—
	II	7/10	88,8±5,60	—
Pneumococcus + staphylococcus + benzylpenicillin	I	20/20	38,9±3,58	0,002
	II	6/10	78,8±5,60	>0,1

Numerator gives number of mice dying; denominator number of animals in group.

A previous investigation [2] showed that the outcome of mixed infection depends on a number of factors, including the biological properties of one of the infective agents – the staphylococcus. Comparison of the mean lifespans shows conclusively that pneumococcal infection is the predominant cause of death of the mice with the mixed infection. Staphylococcal infection evidently had (especially in series II) an interfering effect on death of the mice from pneumococcal infection (untreated animals). Shortening of the lifespan of the animals with mixed infection by administration of benzylpenicillin can be attributed conjecturally to the catalytic hydrolysis of the antibiotic by staphylococcal penicillinase, the quantity of which was increased through induction of synthesis of the enzyme by the penicillin [3]. In the presence of benzylpenicillin, a penicillin-producing strain of staphylococcus [5] gave improved growth, fermented glucose, galactose, and lactose more actively, and coagulated plasma more strongly. An increase in the level of enzymes determining the potential pathogenicity of the microorganism could eliminate the slight interfering effect of staphylococcal infection on the development of the pneumococcal component of the mixed infection observed in the absence of antibiotic therapy.

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