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Wall degradation of antibiotic-pretreated staphylococci within macrophages

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In previous studies it was described that one important factor of wall degradation resistance of untreated staphylococci was the large amount of O-acetyl groups in their peptidoglycan [4]. The degree of O-acetylation increased after application of the bacteriostatic antibiotic chloramphenicol (2). This increased number of O-acetyl groups of the peptidoglycan under chloramphenicol may enhance the degradation resistance of staphylococcal walls [5]. Comparable results were obtained after application of erythromycin [5]. Beside increasing the number of O-acetyl groups, this antibiotic was able to induce the formation of huge amounts of wall material [5]. In contrast to such antibiotics that are blocking the ribosomal protein synthesis, trimethoprim as a bacteriostatic, but non-antibiotic, chemotherapeutic agent failed to induce such thickened bacterial walls [3]. Therefore, it was of special interest to compare trimethoprim with chloramphenicol or erythromycin as to their influence on the degradability of staphylococcal walls.

Results and Discussion

Phagocytosis experiments were performed with bone marrow derived macrophages of mice. Opsonized staphylococci were added to the adherent macrophages. After 30 min ingestion the macrophages were carefully washed. The following digestion period lasted for 1, 2, 3 and 4 days, respectively.

The electron microscopical data showed that staphylococci after trimethoprim treatment were highly resistant to the lytic capacity of the macrophage (Fig. 1). In a quantitative assay the degradability of staphylococcal walls after trimethoprim (TMP) treatment was determined by introducing a specific wall label and measuring its release from the cultivated macrophages after different digestion times. For a more detailed information about the degradation process within macrophages the staphylococcal wall was either labelled before (so-called primary wall) or during TMP treatment (so-called secondary wall). As it can be

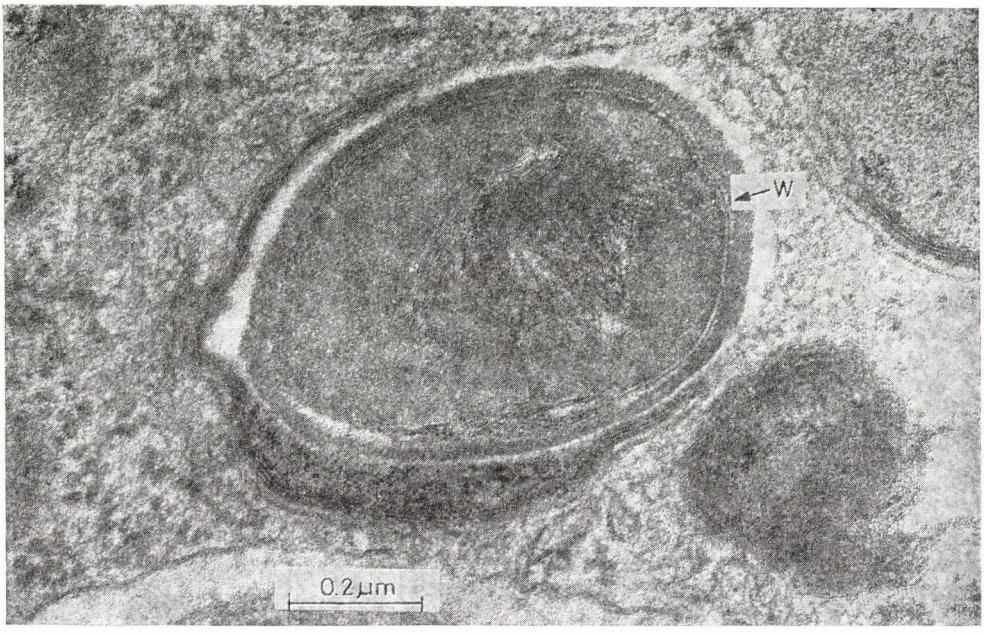

FIG. 1. Thin section of a trimethoprim-pretreated staphylococcal cell within a macrophages after 2 days of digestion; no indication of wall degradation can be detected (W = staphylococcal wall)

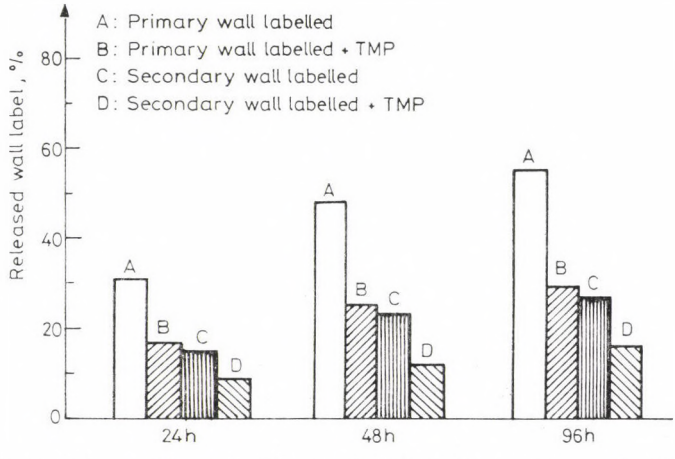

FIG. 2. Wall degradation with and without trimethoprim pretreatment of staphylococci within bone marrow-derived macrophages in terms of release of specific wall label

clearly seen from the diagram summarizing the release measurements (Fig. 2), the cell wall built under TMP treatment (secondary wall) revealed a higher degradation resistance than did untreated bacteria (compare D with C). Astonishingly, treatment with TMP reduced the degrada-

bility of the primary wall, too. With regard to our findings that bacterial autolytic enzymes do not play an important role in the degradation process within phagocytes [1], this finding suggests that the primary wall became structurally changed under TMP treatment. In fact, TMP-treated staphylococci proved to contain more O-acetyl groups in their peptidoglycan than did untreated bacteria. Other bacteriostatic antibiotics such as chloramphenicol or erythromycin also induced a higher degree of O-acetylation connected with a remarkably increased degradatin resistance to the lytic attack of macrophages [5]. Moreover, these antibiotics produced huge amounts of cell wall material, while trimethoprim, due to its different mode of action, did not.

Altogether, if the risk of chronic inflammatory processes, induced by undegraded bacterial wall material, is indicated, trimethoprim should be preferably applied rather than inhibitors of ribosomal protein synthesis. However, penicillin represents a better alternative in curing infections caused by certain bacteria, since the loose wall material produced under this antibiotic is degraded much faster than that of untreated staphylococci [1].

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