Cell Division in Erwinia: Inhibition of Nuclear Body Division in Filaments Grown in Penicillin or Mitomycin C

Abstract. *Low concentrations of penicillin or mitomycin C in cultures of* Erwinia *sp. inhibit cell division. Electron-microscopic analysis of serial sections of these nondividing cells reveals that division of the nuclear body is also inhibited.*

D-Serine, penicillin, and mitomycin C inhibit cell division in a species of *Erwinia*; they also cause a decrease (30 to 40 percent) in the deposition of cell-wall mucopeptide, and induce leakiness through the cell membrane (*1*). Furthermore, D-serine inhibits division of the nuclear body in such filamentous cells (*2*). Therefore, we initiated experiments to determine if penicillin and mitomycin C also inhibit nuclear body division.

Penicillin was studied because the primary and sole site of its action appears to involve the terminal cross-linking reaction in the synthesis of bacterial cell-wall mucopeptide (*3*). Thus, if division of the nuclear body is inhibited in filaments produced by growth in the presence of penicillin, it would indicate that such inhibition is a secondary effect due to a weakened cell wall. The primary effect of mitomycin C is less clear, but this may be due in part to large variations in the amounts employed (*4*).

Serial sectioning of cells followed by observation with the electron microscope is almost essential for demonstrating inhibition in division of the nuclear body in filamentous cells (*2*). Filaments grown in the presence of penicillin and mitomycin C possess nuclear bodies which traverse great lengths of these cells and are therefore inhibited from dividing (Figs. 1 and 2).

Constrictive cell division occurs in these cells (*5*); that is, no evidence can be obtained to demonstrate formation of a completed membranous septum prior to laying down of cell wall in the division area as shown in some bacteria by Chapman (*6*). Further, constrictive cell division can be initiated prior to separation of the nuclear body (Fig. 2b).

We believe that the cell membrane is the key structural component involved in the initiation of cell division (*5*); therefore, continued consideration should be given to whether any changes relative to the cell membrane can be considered primary effects of the division-inhibiting compound or whether such changes occur only as secondary effects of inhibition in cell-wall mucopeptide deposition. The following information appears to be germane. (i) Cell division in preformed filamentous cells can be initiated and completed simply by making the growth medium hypertonic with either organic or inorganic compounds (*1*). (ii) Triggering and division within filaments under hypertonic conditions or in the presence of pantoyl lactone does not bring about repair of the lesion (or lesions) that results in a decreased mucopeptide content in the cell wall, whereas leakage through the cell membrane can be drastically reduced (*1*). (iii) Hypertonic conditions or compounds such as pantoyl lactone or spermine, which trigger constrictive cell division in preformed filaments, must be present throughout the period during which the cell is dividing, otherwise division activity is minimized. The latter observation, in particular, strongly indicates that these types of reversing compounds exert a physical effect on a membrane "complex" of some type which is necessary for cell division. The effect cannot be osmotic because relatively low concentrations are used (0.001*M* spermine; 0.042*M* pantoyl lactone) (*1*). Further, we have observed that although spermine will stabilize *Erwinia* spheroplasts produced with D-serine, pantoyl lactone cannot bring about such stabilization.

Precise definition of a primary chemical interaction or structural involvement in cell division is difficult particularly because our data now reveal that deposition of cell-wall mucopeptide, membrane function, and division of the nuclear body are somehow related.

Reports that the action of penicillin is primarily and solely directed toward the cross-linking enzyme in cell-wall mucopeptide fabrication mitigates against any interpretation of penicillin action which has as its basis primary damage to the cell membrane. In support of the requirement for cell-wall involvement, all chemicals or conditions that we have studied which inhibit cell division (D-serine, penicillin, vancomycin, D-cycloserine, mitomycin C, and ultraviolet light) inhibit deposition of cell-wall mucopeptide (*1*). Still, some agents which inhibit cell division may not inhibit cell-wall synthesis. Also, some compounds such as penicillin and vancomycin, which can effectively inhibit cell-wall synthesis, may have more than one site of action (*7*).

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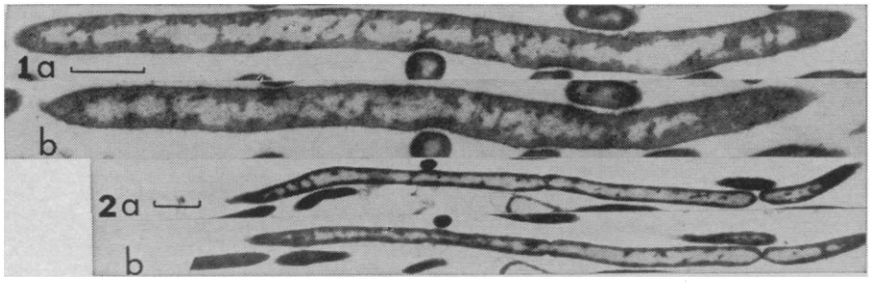

Fig. 1. (a and b) Sections through a portion of a filamentous cell grown 16 hours in the presence of pencillin (40 units/ml). Fig. 2. (a and b) Sections through a portion of a filamentous cell grown 16 hours in the presence of mitomycin C (0.14 μg/ml).

References and Notes

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