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The Effects of Chloramphenicol on the Synthesis of Bacterial Ribonucleic Acids

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It has been known for some time that amino acids play an important role in regulating the rate of biosynthesis of bacterial RNA (Pardee & Prestidge, 1956; Gros & Gros, 1958; Aronson & Spiegelman, 1961a,b). High concentrations of chloramphenicol (up to 0.2 g/l) inhibit protein synthesis severely and spare the requirement for amino acids as stimulants of RNA synthesis (Aronson & Spiegelman, 1961a; Kurland & Maaløe, 1962). Further, when bacteria are grown in an enriched medium containing amino acids the overall rate of RNA synthesis is virtually unaffected by adding chloramphenicol, whereas it is almost doubled when the antibiotic is added to cultures growing in glucose-salts medium (Fraenkel & Neidhardt, 1961; Kurland & Maaløe, 1962).

Using the technique of DNA-RNA hybridization (Gillespie & Spiegelman, 1965; Pigott & Midgley, 1968), I have studied the antibiotic-induced changes in the rate of mRNA synthesis in *Escherichia coli* M.R.E. 600 growing in broth, glucose-salts or sodium lactate-salts media at 37°C. On comparing the kinetics and relative rates of incorporation of [5-³H]uracil into mRNA, rRNA and tRNA, after addition of chloramphenicol, with those holding for all states of steady exponential growth (Gray & Midgley, 1969), I found the following.

(1) mRNA is stabilized in the presence of chloramphenicol and accumulates as about 6% of the total cellular RNA (Midgley, 1963; Friesen, 1966). Though also RNA turnover can be demonstrated in antibiotic-inhibited cells, and the pools of nucleotides are of normal size, the kinetics of labelling all RNA fractions gives incorporation curves that extrapolate to the origin.

(2) Whereas in exponentially growing cells in any medium and at all temperatures exogenous uracil enters mRNA and stable RNA pools in a 1:2 (weight/unit time) ratio, only 14% of the RNA formed in the presence of chloramphenicol has the hybridization characteristics of mRNA. Thus the synthesis of mRNA in bacteria is not rigidly coordinated with that of rRNA + tRNA.

(3) The kinetics of labelling mRNA in broth cultures suggests that, when chloramphenicol is

added, about half the mRNA present eventually decays, and the remainder persists throughout chloramphenicol inhibition.

(4) It appears that, in antibiotic-inhibited cultures, new steady states of synthesis of the various RNA fractions are set up that are unlike those found in normally growing cultures. The question whether these changes are brought about by alterations in the rate of RNA transcription by DNA-dependent RNA polymerase or in the rates of initiation of new chains is considered by Midgley (1970).

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The Rate of Transcription of 23S Ribosomal Ribonucleic Acid in Normal and Chloramphenicol-Inhibited Bacteria

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Gray (1970) has shown that, when exponentially growing and dividing cultures of *Escherichia coli* M.R.E. 600 are inhibited by the addition of chloramphenicol, a rapid change takes place in the relative rates of production of various RNA species. Further, when cultures growing in simple defined media such as lactate-salts or glucose-salts are incubated with the antibiotic, the overall rate of RNA synthesis is rapidly increased (Fraenkel & Neidhardt, 1961; Kurland & Maaløe, 1962). In broth media, where amino acids are in plentiful supply, there is virtually no change in the rate of RNA synthesis in the presence of chloramphenicol, although mRNA is stabilized and accumulates (Friesen, 1966).

I have studied the kinetics of synthesis of the 23S rRNA of *E. coli* at 37°C in each of three media, in the presence or the absence of 0.2 g of chloramphenicol/l. My object was to discover if the alterations in