Summary. A method is described for measuring fibrinolytic activity on fibrin plates. Staining of the plates facilitates the manual measurement of lysed areas and also permits a rapid and more accurate quantitation of fibrinolytic activity by a photometric technique. The procedures employed minimize the effect of a number of variables and require a relatively short incubation period.

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Toxicity of Cephalothin for McCoy Cell Cultures.* (32324)

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Sodium cephalothin was introduced for general clinical use in 1964 as a broad spectrum antibiotic with "the almost negligible toxicity of penicillin" for humans and experimental animals(1). Except for bone marrow depression with neutropenia in 4 patients (2,3) clinical reports so far have indicated a low toxicity for the drug. That it may possess considerable toxicity under some circumstances is suggested by reports from one laboratory which described marked morphologic changes in human amnion and mouse embryo cell cultures on exposure to cephalothin(4,5).

The present report describes the marked inhibitory action of cephalothin on the growth of a strain of cultured human cells at concentrations commonly in the sera of patients under treatment with the drug.

Materials and methods. Methods of propagating and counting the fibroblast-like McCoy strain(6) of human cells were identical with those previously described(7). Sterile vials of sodium cephalothin and sodium benzylpenicillin G were diluted and incorporated in the medium to give the final concentrations noted. Morphologic observations of the living cells were made directly and also by examination of Wright stained cover slips on which the cells were grown in a replicate series of culture tubes. Each experiment was repeated 3-4 times.

Results. The results shown in Fig. 1 indicate a progressive inhibition of cell growth by sodium cephalothin at concentrations of 10^{-5} M (4.18 μg/ml), 3×10^{-5} M (12.54 μg/ml), 6×10^{-5} M (25.08 μg/ml) and 10^{-4} M (41.8 μg/ml). Morphologic evidence of toxic effects was observed at the higher concentrations and consisted of rounding up of cells, increased granularity of cytoplasm, and at a concentration of 6×10^{-5} M a considerable number of large rounded cells. The same molar concentrations of sodium benzylpenicillin did not inhibit growth or produce morphologic changes indicating toxicity.

Discussion. Cephalothin and benzylpenicillin G are structurally related(8) and produce a similar biochemical injury to the staphylococcus by selectively inhibiting cell wall synthesis(9). Thus the finding of a significantly greater toxicity of cephalothin for the McCoy strain of human cells and other mammalian cultured cells(4,5) is surprising. Cephalothin possesses, however, a broad spectrum of antibacterial activity compared with penicillin. Broad spectrum antimicrobial activity implies injury to a biochemical process present in a wide variety of living cells. Since mammalian and bacterial cells have in common a number of similar metabolic pathways it would seem reasonable to anticipate that broad-spectrum anti-

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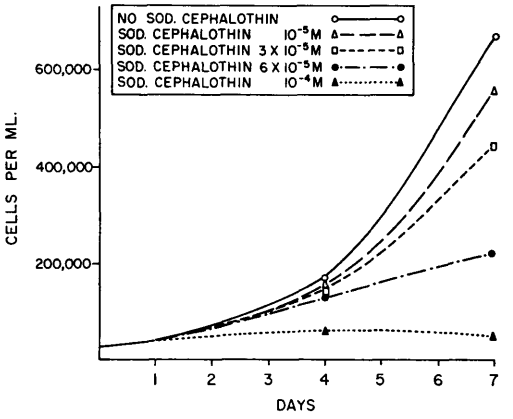

FIG. 1. Effect of sodium cephalothin on growth of McCoy cells in culture.

microbial drugs might be more injurious to mammalian cells than narrow-spectrum antimicrobial agents. The biochemical lesion produced in cultured mammalian cells by cephalothin is unknown though the toxic effects are produced by concentrations suitable for bacterial inhibition.

The demonstration of marked toxicity of cephalothin for McCoy cells in the present study and the findings of significant toxicity of the drug for human amnion and mouse embryo cell cultures(4,5) indicate a need for further studies on the potential toxicity of cephalothin. Caution would seem indicated in the use of this agent in patients with impaired renal and hepatic function in whom very high blood levels of the drug might accrue, in pregnant women because of its unknown teratogenic possibilities, in patients where tissue repair is important, etc.

Summary. Cephalothin, in concentrations present in patients on treatment with the drug, produced a marked inhibition of growth of the McCoy strain of cultured human cells and morphologic evidence of toxicity.

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Disappearance of DL-Lactate-2-C^{14} from Blood in Normal and Diabetic Rats.* (32325)

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Recent recognition of the syndrome of lactic acidosis, which may develop in diabetes, has engendered interest in lactic acid and pyruvic acid metabolism in this disease. The possibility that there is an abnormal metabolism of lactate and pyruvate in diabetes was demonstrated by *in vitro* experiments with diaphragm(1) and cardiac muscle(2). However, the question whether lactate can be metabolized in a normal manner by diabetic animals or humans has not yet been extensively studied.

Shreeve *et al*(3) and Anderson *et al*(4) reported that the blood lactate was slightly elevated in diabetic subjects. The rise in this product of glycolysis represents either increased production or diminished disposal, or a combination of these two factors, and such imbalance might be a contributory cause

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