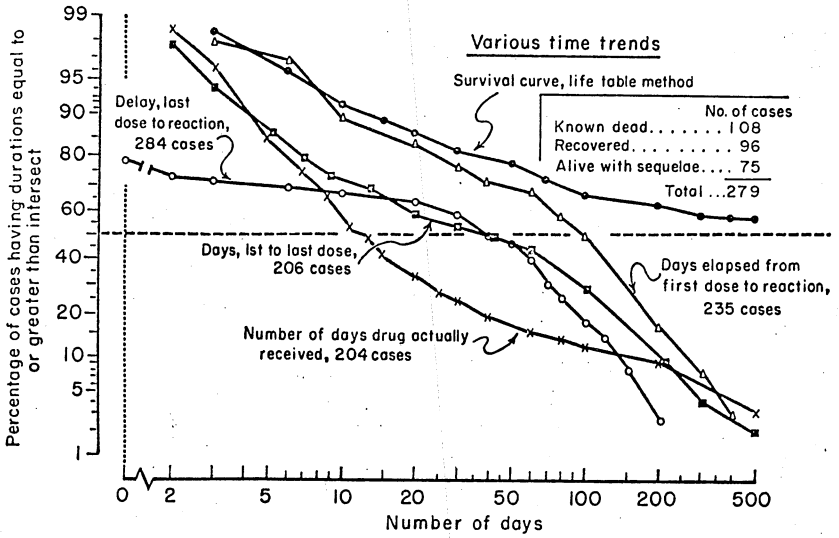
Time of Reaction as Related to Therapy.—One tends to think of adverse reactions as occurring during drug administration or shortly after discontinuation. Such a relationship proves to be the exception for chloramphenicol-associated blood dyscrasias. Among the 284 patients for which such information was available, only 22% showed manifestations of the dyscrasia while the drug was still being given as shown by the appropriate curve of Fig. 4. The median time from discontinuation of the drug until clinical evidence of the dyscrasia appeared was 38 days, and in 10% of cases this time was 130 days or longer. There is a definite downward bending of this curve, and one wonders whether time from first dose to reaction might not more nearly approach a log-normal distribution. This curve has also been charted in Fig. 4, and it shows an incomplete tendency to straightening. The reaction developed 10 days or less following initial dose in 10% of cases, in 95 days or less in 50%, and in 260 days or more in 10%.



4. Number of days chloramphenicol received; elapsed time of chloramphenicol course; time from first dose to reaction; time from last dose to reaction; and survival time. Distribution of values for each curve is indicated cumulatively on log-normal coordinates. The survival curve is based on life-table analysis.

None of the patients in this series are known to have been continued on or rechallenged with the drug after the dyscrasia was diagnosed, and we would not recommend that this be done.

SURVIVAL AND COURSE

Life Table Survival Curve.—Construction of a survival curve for a fatal disease on the basis of a series of patients, all of whom have not yet died at time of analysis, is best performed through the life table method.[8] The present situation differs from that of a uniformly fatal disease in that, in addition to a trend towards mortality, there is also a trend towards recovery. Patients who have recovered are not known to have relapses unless the drug is administered further. In this instance, a satisfactory method of accounting for recoveries in life table analysis is to consider all patients who have recovered to be still alive at a relatively long period following onset of the dyscrasia, regardless of the actual length of follow-up. The top curve of Fig. 4 shows the results of this analysis. Because of recoveries, the curve approaches an asymptote rather than describing a straight line on a log-probability plot. The overall mortality approached is approximately 50%; 10% of the patients in the entire series have died within two weeks of onset of the dyscrasia. The 75% intercept (i.e., median survival for those with fatal outcome) is about 50 days. Rare cases may have a fatal outcome a year or more after diagnosis.

[8] Merrell, M., and Schulman, L. E.: Determination of Prognosis in Chronic Disease, Illustrated by Systemic Lupus Erythematosus, *J. Chronic Dis* 1: 12–32 (Jan.) 1955.