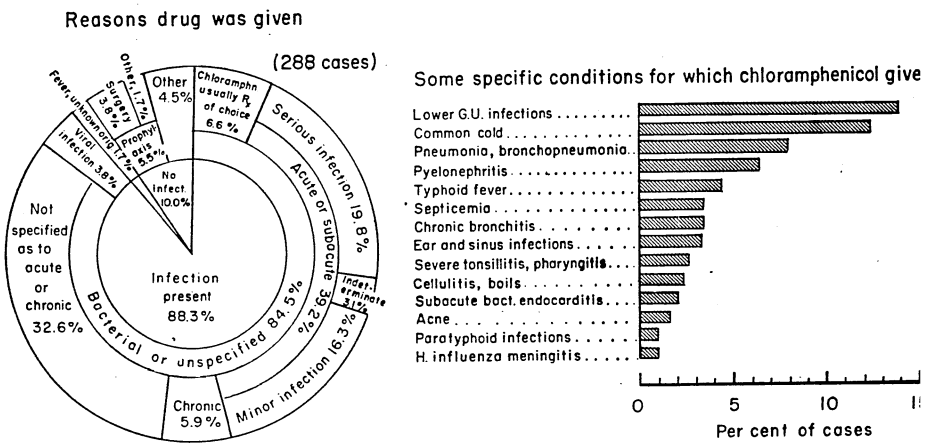
DETAILS OF DRUG ADMINISTRATION

General.—The reason that chloramphenicol had been given (for the most part infection or prophylaxis against infection) was cited in 71% of the 408 cases (Fig 2).



2. Reasons why chloramphenicol given. *Left*, General nature of indications. *Right*, Specific conditions; all those accounting for 3% or more of known indications plus selected conditions with lower percentages.

Chloramphenicol was the only known drug administered during the prior six months to 40% of patients. One other drug was mentioned for 19%, two for 13%, and three or more for 28%. In one case, 17 other drugs were listed. In 9% of all cases, the only other drugs mentioned were members of what the study group considers to be generally "innocent" drugs—aspirin, the barbiturates, chloral hydrate, digitalis glycosides, the penicillins, and the tetracyclines; in 37% of all cases, drugs other than "innocent" ones were administered, but no "toxic" drugs were given; in 9%, another toxic drug was administered, but suspicion was cast most strongly on chloramphenicol; and 4% suspicion was cast most strongly on another toxic drug. Thus, in 96% of cases, there is strong suspicion that chloramphenicol was the causative agent, and in the remaining cases, this possibility cannot be ruled out. Since elimination of those patients receiving another toxic drug had virtually no effect on outcome of the dyscrasia, all cases were included in the analysis.

Duration and Dosage of Chloramphenicol.—It is known that 9% of patients received this drug at least once prior to the course in question.

The dashed line of Fig 3 presents a cumulative plot of average daily dose in milligrams per kilogram per day on a type of graph paper having logarithmic and probability scales. If the log-dose were distributed in gaussian fashion, such a plot should approximate a straight line. Central portions of such curves are generally more accurate than the extremes. In this case there is some deviation from a single straight line, but the fit is not bad. At any rate, interpolation will provide estimates of dosage levels defining selected percentiles. It is seen that 10% of patients received less than 8 mg/kg/day, 50% received less than 23 mg/kg/day, and 10% received greater than 60 mg/kg/day. This is to be contrasted with a manufacturer's recommendation for a starting dose of 50 mg/kg/day in adults and 50 to 100 mg per kilogram per day in children beyond infancy. Either smaller doses tend to be given to susceptible patients, or else the general trend in use of this drug is to administer smaller average amounts than recommended for initial therapy. The latter possibility seems more likely. There appears to be slight differences in patterns of daily dose administration for different age groups. Thus, the median doses were: 33 mg/kg/day for patients 0 to 9 years of age, 24 mg/kg/day for those 10 to 39 years of age; and 18 mg/kg/day for those 40 years of age and older.