never be treated with chloramphenicol. Excepting only the situations noted under indications, above, this interdiction includes all infections caused by bacteria, rickettsia, bedsonia, and mycoplasma.

Undefined illnesses that might be infectious in cause should never be treated with chloramphenicol.

Similarly, chloramphenicol should never be used as a prophylactic agent.

Senator NELSON. Is it commonly used as a prophylactic agent?

Dr. HOEPRICH. I do not think it is. Again, this is a function of time. There was a period in the history of the development of antimicrobial therapy when this drug was used. At least as I observe it, as other agents have become available, and as the toxic hazards of chloramphenicol have been recognized, this kind of usage is quite uncommon.

Senator NELSON. In the study that Dr. Best compiled, of the 408 aplastic anemia cases submitted, 5.5 percent were ones in which the drug had been given for prophylaxis. Now, that was from 1953 to 1964. Has that statistic changed since then?

Dr. HOEPRICH. Well, I think so. There was, for example, a period of time when urologists would use this drug as prophylaxis against infection complicating prostatic surgery. I think that this use has largely disappeared. I may be mistaken about this. I see just a limited segment of practice, and use may vary from area to area, I am sure.

### SIDE EFFECTS

In order of increasing seriousness, there are four major side effects to administration of chloramphenicol. These are: (1) ecologic disruptions; (2) irritative phenomena; (3) direct toxicity; and (4) hypersensitivity. All except hypersensitivity are dose related—the higher the dose and the longer the period of administration, the more likely become the adverse reactions (1), (2), and (3). Withdrawal of chloramphenicol, quite reasonably, is the first step toward reversing such adverse effects. On the other hand, hypersensitivity reactions are not clearly dose related and do not predictably abate on withdrawal of the drug.

1. Ecologic disruption is consequent to the selective elimination or suppression of those micro-organisms normally resident on and in persons that are susceptible to the antimicrobial action of chloramphenicol. Elements of this resident microbiota that are resistant to chloramphenicol are freed of competition and can attain to abnormally high population densities. Also, micro-organisms resistant to chloramphenicol may be acquired from the environment external to the person—drawn in, as it were, by the shelter of chloramphenicol suppression of microbial competition. Termed superinfections when the overgrowing or invading micro-organisms cause disease, this side effect is not unique to chloramphenicol but is, to a greater or lesser extent, a liability of any antimicrobic used in therapy.

2. Irritation is most common in the gastro-intestinal tract, taking the form of nausea, vomiting, diarrhea that is often associated with a brassy, unpleasant taste in the mouth. There may be irritation in the crotch region.