

CASE REPORTS OF LEUKEMIA FOLLOWING USE OF CHLORAMPHENICOL OR PHENYL-
BUTAZONE

During the course of this study reports were received of six additional cases of leukemia in the United States following bone marrow depression attributed to chloramphenicol or phenylbutazone. Toxic reaction to the drug, however, had not previously been registered at the AMA or FDA, so these cases are summarized separately in Table 6. Although lacking a reference population, the characteristics of these cases were generally more suggestive of a causal relation between drug intake and leukemia than the leukemia cases detected by the follow-up survey. All patients had myelocytic leukemia; in three it occurred subsequent to the use of chloramphenicol and in three others, following phenylbutazone therapy. All had evidence of bone marrow deficiency preceding the diagnosis of leukemia, which was termed "aleukemic" leukemia in four instances. There was no history of exposure to radiation therapy. All patients were females, from 43 to 77 years of age. In the three patients treated with chloramphenicol, the infection antedated by many years the manifestation of hematological disorder. The estimated chloramphenicol dose varied between 7 and 200 gm, with leukemia developing from 2 to 12 years after start of treatment. In three patients with leukemia following phenylbutazone treatment, the underlying rheumatic conditions were chronic and unlikely to be early manifestations of leukemia. The estimated doses of phenylbutazone exceeded 15 gm. and leukemia was diagnosed from 1 to 12 years after the start of treatment.

It is noteworthy that all previously reported cases of leukemia following the use of chloramphenicol or phenylbutazone occurred in countries other than the United States. Chloramphenicol has been implicated much less frequently than phenylbutazone in the etiology of leukemia. Mukherji⁸ described a 63-year-old man in whom aplastic anemia developed following administration of 12 gm of chloramphenicol; the aplastic process persisted until seven months after drug exposure when a diagnosis was made of acute myelogenous leukemia. Lebon and Messerschmitt⁹ reported the case of a 5-year-old boy who died of acute myelogenous leukemia following a one-year history of aplastic anemia, which may have been due to chloramphenicol therapy. In an epidemiologic study of leukemia in Israel, Davies and associates¹⁰ noted that 20 of 150 leukemia patients received drugs a "short time" before the diagnosis of leukemia and in 11 cases the drug was chloramphenicol.