became commercially available in 1949.[1-5] In addition, since 1953, the Study Group on Blood Dyscrasias of the Council on Drugs of the American Medical Association has maintained a Blood Dyscrasia Registry and has published semi-annual compilations of voluntarily reported blood dyscrasias associated with drugs and chemical agents. During this period, chloramphenicol was the drug most often associated with pancytopenia. The three nation-wide surveys of the United States Food and Drug Administration between 1952 and 1957 also indicated that chloramphenicol had been used with greater frequency than any other drug in persons who subsequently developed aplastic anemia.[6-8]

In the early years of chloramphenicol use, the evidence of its toxicity was derived entirely from clinical case reports and from the frequency of its association with blood dyscrasias. In recent years, laboratory and clinical studies have contributed a variety of findings supporting the earlier indications of chloramphenicol toxicity for bone marrow.[9-14]

Animal experimentation to detect chloramphenicol toxicity has not been particularly rewarding. However, recent work suggests that chronic bone marrow toxicity can be produced in monkeys by feeding them with chloramphenicol.[15]

The physiological and biochemical mechanisms involved in toxic bone marrow suppression are not known. Also unknown is the relationship of mid reversible changes to the severe changes of aplastic anemia. *In vitro* studies with human bone marrow cultures hold promise of elucidating the nature of chloramphenicol's effect on bone marrow function. Already such studies have shown, by measuring Fe^{59} uptake and incorporation, that chloramphenicol causes a marked decrease in iron uptake by red blood cells thus directly interfering with heme synthesis.[16]

VITAL STATISTICS

Available morbidity data on aplastic anemia are derived from a variety of sources and are not necessarily representative of the occurrence of this disease in the general population. Representative statistical data concerning the occurrence and distribution of aplastic anemia are available only for fatal cases in which the cause of death was recorded as aplastic anemia on the death certificate. Table 1 indicates the numbers and rates of deaths from aplastic anemia in the United States, California and Canada. Approximately 60–80 persons die each year in California from aplastic anemia while about ten times as many die in the United States—that is, about five deaths from aplastic anemia per million population. Table 2 shows that in 1960 the risk of dying from aplastic anemia in California varied from about one person per million at ages 25–34 years to 27 persons per million at ages 65 years and over, with the years of childhood and youth involving greater risk than the years between ages 25–54 year.

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