

that the American Medical Association established the Registry of Blood Dyscrasias, hoping, among other things, to recognize such effects early when they occurred for other new drugs. The Registry and its study group have since accumulated data on a large number of drugs, have issued periodic tabulations and resumes of cases submitted, and have authored commentaries on various associated problems.¹⁻⁵ During this period, chloramphenicol has been implicated in more reports to the Registry than has any other single drug. It appeared that useful information could be obtained through a more thorough review of Registry reports.

Included in this study were 408 cases, reported to the Registry from 1953 through 1964, who were known to have received chloramphenicol during the year preceding a non-neoplastic depression of blood cell formation.

Generalizations from this experience would be most valuable if cases reported to the Registry represented an unbiased sample of the condition as it occurred throughout the world. However, there are unavoidable and, no doubt, unidentifiable biases in this collection of cases. For example, most cases have been voluntarily reported from selected sources, and the composition and attitudes of these sources have changed from year to year.

Some cases were abstracted from the medical literature. Nonetheless, this appears to be the best data available for study.

The Registry contains a total of 298 US reports, 25 known to be published, 273 not; plus 110 foreign reports, 70 known to be published, 40 not.

Yunis and Bloomberg reviewed much of the literature on this disorder, summarizing data on 94 cases.⁶ Twenty-one US and eight foreign literature cases are common to their review and to the Registry; their other cases are not in the Registry. The Registry contains 1 US and 65 foreign literature cases which were not covered in their review. There have been additional published case reports which appear neither in the review by Yunis and Bloomberg nor in the Registry.

METHODS OF ANALYSIS

During the years of existence of the Registry, the report form has gone through several different versions, more recent ones tending to call for more complete information. In general, no systematic attempt has been made to obtain more detailed clinical information or late follow-up of cases.

Reports were coded and punched on 80-column computer programming cards, using from 4 to 36 cards per patient, under the direction of Norman De Nosaquo, MD, and Mrs. Helene Weston of the AMA staff. Data transformation, reduction, tabulation, and analysis were performed by the author using computers and over 30 special computer programs.

GENERAL CHARACTERISTICS OF CASES

Age and Sex.—Females accounted for 62% of 407 cases. There was a wide distribution of cases by age with a rate of 0.5% to 1.5% of total cases per year of age from the teens through the 70's, occasional cases in older age groups, and a striking peak occurrence of about 5% per year of age in the 3- to 7-year age group. There was some difference in sex distribution at different ages: females accounted for 69% of 113 patients 0 to 9 years of age, 69 (73%) of 94 patients 10 to 39 years of age, but only 47% of 150 patients 40 years of age or older.

The percentage of females was essentially the same for cases reported from the United States as compared to reports from elsewhere; however, there is a much less striking peak of occurrence for the 3- to 7-year age group in the latter series (Fig 1).

¹ Motulsky, A. G.: Drug Reactions, Enzymes, and Biochemical Genetics, *JAMA* 165: 835-837 (Oct. 19), 1957.

² De Nosaquo, N.: Development and Purpose of the Registry on Blood Dyscrasias, *JAMA* 170: 1925-1926 (Aug. 15), 1959.

³ Huguley, C. M., Jr., Erslev, A. J.; and Bergsagel, D. E.: Drug-Related Blood Dyscrasias, *JAMA* 177: 23-26 (July 8), 1961.

⁴ Erslev, A. J., and Wintrobe, M. M.: Detection and Prevention of Drug-Induced Blood Dyscrasias, *JAMA* 181: 114-119 (July 14), 1962.

⁵ Best, W. R.: Drug-Associated Blood Dyscrasias: Recent Additions to the Registry, *JAMA* 185: 286-290 (July 27), 1963.

⁶ Yunis, A. A. and Bloomberg, G. R.: Chloramphenicol Toxicity: Clinical Features and Pathogenesis, *Prog Hemat* 4: 138-159, 1964.