rearrangements in retarded children may indicate the presence of a similar effect in humans [6].

YVES LACASSIE,[1] THEODORE F. THURMON,[2]
MARGARET C. TRACY,[2] AND MARY Z. PELIAS[2]

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[1] Institute of Nutrition and Food Technology, University of Chile, Santiago, Chile.

[2] Louisiana Heritable Disease Center, Department of Pediatrics, Louisiana State University Medical Center, 1542 Tulane Avenue, New Orleans, Louisiana 70112.

ADENOSINE DEAMINASE DEFICIENCY: ANOTHER FAMILY WITH A "SILENT" ADA ALLELE AND NORMAL ADA ACTIVITY IN TWO HETEROZYGOTES

To the Editor: In a previous paper [1], we reported the existence of an adenosine deaminase "silent" allele (designated as ADA^0) in a family with a child who died of severe immunodeficiency disease (SCID). The assignment of the ADA^0 allele was determined by the unusual transmission of the ADA phenotypes and quantitative assays of the enzyme in family members. Since then, a total of four families with a similar transmission of ADA phenotypes have been found [2, 3]; one was found in a normal family and the other in families with SCID. We would like to document another SCID family in which the silent allele could be traced through 3 generations and to reemphasize that heterozygotes for the silent allele may, on occasion, have normal ADA activity in their red cells.

In accordance with the previous report [1], the pedigree (fig. 1) shows the ADA phenotype, the presumed genotype, and ADA activity in each of the family members. The ADA phenotypes of the parents of the proband (II-1 and II-2) were ADA 1 and ADA 2; however, their children had four different phenotypes—ADA 2 (III-1), ADA 2-1 (III-2), ADA 1 (III-3), and no detectable ADA (III-4). It seems apparent that each parent carries a "silent" gene which was transmitted as allelic to the normal ADA^1 or ADA^2 in the family. Therefore, the genotypes of their children should be ADA^2/ADA^0, ADA^2/ADA^1, ADA^1/ADA^0 and ADA^0/ADA^0, respectively.

An important observation from this pedigree is that two of six heterozygotes

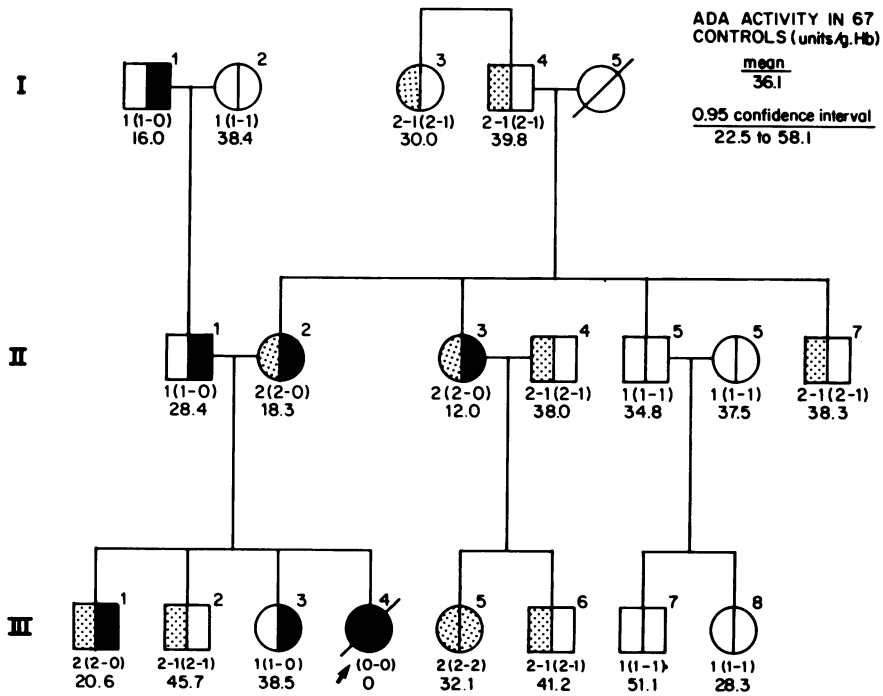

FIG. 1.—The inheritance of *ADA*[1] (○), *ADA*[2] (○) and *ADA*[0] (●) in a family with a child affected with severe combined immune deficiency. The presumed genotype is in brackets, and the phenotype and specific activity of ADA in the red cells (U/g Hb) are indicated for each individual.

(*ADA*[1]/*ADA*[0] and *ADA*[2]/*ADA*[0]) did not have reduced enzyme activity in their red cell hemolysates; they were the father and sister of the proband (II-1 and III-3). They had ADA activity of 28.4 and 38.5 U/g hemoglobin (Hb), respectively, which are well within our range for normal persons of 22–58 U/g Hb. This observation is consistent with reports [4] that some obligate heterozygotes for the ADA deficiency may have enzyme activity within the normal range. Demonstration of normal ADA activity in two heterozygotes who were clearly shown to be carriers of a "silent" ADA allele again emphasizes the skewed distribution of the activities towards the high range in the normal population and also makes the proposed concept of an "inherited inhibitor" [5] as a mechanism for ADA deficiency difficult to explain.

S.-H. CHEN,[1] C. R. SCOTT,[1] E. R. GIBLETT, [2] AND A. S. LEVIN[3]

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[1] Division of Genetics, Department of Pediatrics, University of Washington, School of Medicine, Seattle, Washington 98195.

[2] Puget Sound Blood Center, Terry at Madison, Seattle, Washington 98104.

[3] MML/Solano Laboratories, Berkeley, California 94705.

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Postgraduate Course in Medical Genetics

A postgraduate course, entitled "Diagnosis, Treatment and Prevention of Genetic Disease" and sponsored by the Harbor General Hospital Campus of the UCLA School of Medicine, the American College of Physicians, and the National Foundation–March of Dimes, will be held at the Riviera Hotel, Palm Springs, California from March 6–8, 1978. This course is designed to familiarize the clinician with the principles of medical genetics and their relevance to clinical practice. For further information write to Dr. D. L. Rimoin, Harbor General Hospital, 1000 W. Carson, Torrance, California 90509.