Reports and Letters

Notation for Hemoglobin Types and Genes Controlling Their Synthesis

For the sake of precision in discussions of genetics, such as that held recently at Cold Spring Harbor (*1*), it is important that genes and gene products be given separate symbols. A belated and much needed attempt to systematize blood-group notation along these lines has recently been made (*2*). A great deal of information on the biochemistry and genetics of abnormal human hemoglobins is now available. The nomeclature of the hemoglobin types was standardized at a meeting held in January 1953 by the Hematology Study Section of the Division of Research Grants of the National Institutes of Health, Bethesda, Maryland (*3*).

It was proposed that fetal hemoglobin should be referred to as type F, normal adult hemoglobin as type A, and sickle cell hemoglobin as type S. Two other variants were termed type C and type D. Another genetically determined abnormality of hemoglobin previously described by Hörlein and Weber (*4*) was overlooked. The defective globin formed in this disease is responsible for a distinctive variety of methemoglobinemia, and this hemoglobin can conveniently be termed type M(*5*). Since 1953 descriptions of six other hemoglobin types—E(*6*), G(*7*), H(*8*), I(*9*), J(*10*), and K(*11*)—have been published.

I have recently obtained evidence, a detailed report of which is in preparation, that the hemoglobin in the primitive generation of red blood cells in early fetal life is different from the fetal and adult hemoglobin types. This third normal hemoglobin will be termed primitive-type P. It seems that the processes leading to the formation of the three normal hemoglobin types (P, F, and A) are under independent genetic control. In the mouse, there is a gene *f* which, when present in double dose, severely retards the synthesis of fetal hemoglobin but has no influence on the synthesis of primitive and adult hemoglobins. In this way, a severe hypochromic anemia is produced in late fetal life which spontaneously recovers after birth (*12*). The thalassemia gene in human beings has the converse effect: It retards synthesis of adult hemoglobin, but seems to have no effect on fetal hemoglobin synthesis (*13*). The various genes that are responsible for the formation of abnormal human hemoglobins, such as the sickle cell gene, also have no detectable influence on fetal hemoglobin formation.

The relationship of the genes affecting hemoglobin synthesis in human beings is not completely clear, but some generalizations can be made. The formation of hemoglobin types S, C, and G is controlled by genes that appear to be allelomorphs of a gene controlling one stage of adult hemoglobin formation (*14*), and the same may prove to be true of the genes controlling formation of hemoglobins D, H, I, J, and K. There is some evidence, however, that the thalassemia gene is not an allelomorph of the other genes affecting hemoglobin formation (*10, 11*).

No uniform or widely accepted notation for these genes is available. Usually the same symbol is used indiscriminately for a gene and for the hemoglobin type that is produced in its presence. Neel has used the symbol *Sk* for the sickle cell gene and *sk* for the normal allele (*15*) and *Th'* and *Th* for the thalassemia gene and its normal allele, respectively (*16*). Silvestroni and others (*17*) have used the symbols *M* (for microcythemia) and *m*. These symbols, which imply that the sickle cell and thalassemia genes are dominant to the normal alleles, fail to draw attention to one of the most remarkable features of the abnormal hemoglobin genes: The occurrence of contrasting allelomorphs, each of which has dominant effects. In all the cases analyzed so far, heterozygotes are distinguishable from homozygotes by biochemical and other tests.

A new notation for the genes that is uniform and in accordance with that adopted elsewhere in genetics is therefore proposed. Genes should be consistently placed in italics and letters for the hemoglobin types themselves should not be italicized. Each locus should be indicated by a single capital letter or a capital and a small letter, and the allelomorph should be indicated by an appropriate suffix attached to the locus symbol. A capital in the suffix is dominant to a small letter in the suffix. When allelomorphs, each with a capital in the suffix, are brought together they both exercise their effects. Thus, a capital in the suffix represents a gene that exercises its effect whenever present, the effect of one dose not necessarily being the same as that of two doses.

In this case, the locus for the gene controlling normal adult hemoglobin synthesis, which is allelomorphic to the genes controlling the formation of sickle cell hemoglobin, and so forth, should be termed *Hb* (for hemoglobin). The normal allelomorph is then indicated by the suffix A, the sickle cell allelomorph by the suffix S, and the allelomorphs controlling the formation of hemoglobin types C, D, and G by the suffixes C, D, and G, respectively. Thus, the normal individual is of genotype Hb^A/Hb^A, the carrier of the sickle cell trait is of genotype Hb^A/Hb^S, and the patient with homozygous sickle cell anemia is of genotype Hb^S/Hb^S; those with sickle cell:hemoglobin-C disease are of genotype Hb^S/Hb^C, and correspondingly for other genotypes and phenotypes.

Since the thalassemia locus appears to be different from the sickle cell locus, it is indicated by a different symbol, *Th*. The normal allelomorph is indicated by the suffix N, and the thalassemia allelomorph by the suffix T. Thus, the normal individual is of genotype Hb^A/Hb^A; Th^N/Th^N, the heterozygote for thalassemia is of genotype Hb^A/Hb^A; Th^N/Th^T, and the patient with sickle cell:thalassemia [who is heterozygous for both the sickle cell and the thalassemia gene (*10*)] is of genotype Hb^A/Hb^S: Th^N/Th^T. The locus for Hörlein and Weber's methemoglobinemia is unknown.

If any allelic gene controlling hemoglobin formation is discovered that is not recognizable at all in the heterozygous condition, the corresponding suffix should be a small letter. Genes affecting primitive or fetal hemoglobin would not be placed at loci *Hb* or *Th* (*19*).

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References and Notes

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3 June 1955

Natural Redistributon of a Quahog Population

It has been characteristic of intertidal quahog (*Venus mercenaria*) sets in Maine that they are of commercial importance only at infrequent intervals and that survivors that reach market size are generally poorly distributed over the available flats. Approximately 95 percent of the fishery is intertidal, and whenever there are sets of commercial importance —as there were in 1938, 1939, 1947, and 1952—they usually occur in limited areas and in very dense concentrations. Although mortality rates are high and invariably exceed 90 percent by the end of the second season, it has been assumed by shellfish biologists working in Maine that the concentrations—sometimes as high as 25,000 quahogs per square foot—take place shortly after setting, probably as the result of involuntary redistribution (*1*).

The actual process of redistribution has not been observed, nor, heretofore, has its extent been measured. Since concentrations made up of individuals as small, on the average, as 3 mm in diameter have been observed, it has also been assumed that redistribution takes place only among the smaller sizes and does not occur on an involuntary basis among adults.

In November 1949 the residue of two widely separated concentrations from the 1947 year-class was discovered in Maquoit Bay, Maine. Because it has been customary during the past decade to transplant overcrowded quahogs to adjacent barren flats to resupply the commercial fishery, salvage operations were carried on from May to December 1950, using quahogs from the more unfavorably located of these two concentrations.

Similar operations for the other area had to be postponed until the spring of 1951. It was decided, in the meantime, to use this remaining concentration as a study area, to survey its geographic limits, to estimate its population and the volume of that population, to measure winter survival, and to make other related observations and determinations during the cold-weather period.

A plane table survey using a telescopic alidade was made during daylight low-water on 17 and 18 Oct. 1950. A flat ledge outcrop within the concentration served as an excellent station for setting up the instrument. The purpose of using a plane table (*2*) for the survey was to insure a high order of accuracy in determining the limits of the occupied area (a reconnaissance of this concentration had indicated that it was surrounded by barren flats several hundred feet in width) and to locate as accurately as possible the sample plots that had been selected for measurement of density and size distribution.

Horizontal stadia to 11 critical points on the perimeter of the concentration were measured. These points were selected wherever a marked change in direction occurred. The remainder of the perimeter was interpolated between these established points. Within the perimeter, 35 sampling stations were surveyed and plotted. The lateral error did not exceed 0.1 ft, and it was estimated that horizontal error, since the longest stadia measurement was only 478 ft, did not exceed 1.0 ft. The population density of the concentration averaged 79.5 per square foot, with a size range from 27 to 56 mm and a median diameter of 43 mm. After the survey had been completed, the area of the concentration was determined by planimeter to be 3.28 acres, more or less.

The concentration remained under periodic observation during the winter and, following the discovery of mass mortalities that took place between 24 Dec. 1950 and 4 Feb. 1951—apparently as the result of gales that removed the sediment (*3*) cover and that were followed by alternate freezing and thawing air temperatures, during low-tide periods—a resurvey to assess the damage was made (*4*). Reconnaissance of the concentration before resurvey indicated considerable displacement and dispersal of the population during the winter. This observation was confirmed by the resurvey made on 29 Mar. and 20 Apr. 1951 in which the procedure of the initial survey was duplicated, except that the sampling fraction was increased from 1/4080 to 1/2895 for greater accuracy.

The redistribution of the population, in general, followed the expected pattern. The storms that had the highest wind velocities, one of a recorded 76 mi/hr, were from the southeast, and the greatest displacement was toward the northwest for a maximum distance of 387 feet, although some redistribution had taken place all around the old perimeter of the concentration, except at the southwestern end. In a small tip at the southwestern end, which had previously had an average density of 23 per square foot, the quahogs had been completely displaced. On the other hand, one previously barren area, the center of which was 182 ft northwest of the old perimeter, had acquired a living population density of 36 per square foot.

The plane table and alidade provided precise means for defining the limits of the geographic redistribution, and sampling within the area supplied detailed information on the extent of this redistribution. Since all sample plots had been surveyed, it was possible to compare changes in population density within a relatively small subarea before and after redistribution.

One 10,300-ft² subarea with its long axis running north and south had in October contained an average population of 116 per square foot, but by spring it had been further subdivided into smaller subareas having average densities from north to south of 19, 40, 21, and 40 per square foot.

The most densely occupied portion of the concentration in October had been one of 38,800 ft² that contained an average population of 125 per square foot. By the time of the resurvey, this average had been reduced to 40 per square foot, and in some sections to concentrations as low as 23 per square foot. Even the most densely populated section, one of less than 1000 ft², had a population of only 63 per square foot.

Several small colony-like concentrations of 30, 36, and 65 per square foot were discovered during the resurvey northwest of the old perimeter in flats that had been barren the preceding October. These colonies occupied areas from slightly more than 2000 ft² to nearly 17,000 ft².

Although the concentration at the time of the initial survey occupied an area of 3.28 acres, more or less, the surviving redistributed population, which had been reduced 40.3 percent by winter mortalities, occupied an area of 6.81 acres, more or less, and the physical center of the redistributed population had been displaced northwesterly an average distance of 100 ft. While the resurvey accounted for all animals, living and dead, that had occupied the area at the time of the initial survey, the density per square foot of 79.5 in October had been changed to an average combined living and dead density of 41.7 by the time of the resurvey.

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