other than the downstream end of a region dominated by benthic unicells, or in periods of rapidly changing water level, or even from a stream receiving similar pollutants but larger in volume of flow might be expected to show much less marked periodicity.

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Distribution and Heredity of Blood Factor U

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In a previous report (*1*), a new blood factor **U** was described, sensitization to which caused a fatal hemolytic transfusion reaction (*2–4*). The purpose of the present report is to describe further observations on the distribution and heredity of this blood factor.

Tests for factor **U** were carried out on blood specimens from 1100 Caucasoids and 989 Negroids. As is shown in Table 1, all 1100 Caucasoids had the blood factor **U**, and only 12 of the Negroids lacked the factor. The A-B-O groups, M-N-S types, Rh-Hr types, and Kell types of these 12 individuals, as well as the patient who had the hemolytic reaction and from whom the antiserum was obtained, are shown in Table 2. From these results, factor **U** apparently

TABLE 1. Distribution of the blood factor **U**.

Racial group	Number of individuals		
	Positive	Negative	Total
Caucasoids	1100	0	1100
Negroids	977	12	989

TABLE 2. Blood types of individuals with blood lacking factor **U** (type uu).

Blood of	A-B-O group†	M-N-S type	Rh-Hr type	Kell type
Patient 1*	B	MN	$\mathfrak{R}h_1rh$	kk
	O	N	Rh_1rh	kk
2	B	N	Rh_0	kk
3	O	MN.ss	$\mathfrak{R}h_0$	kk
4	B	N	Rh_0	kk
5	O	MN.ss	Rh_0	kk
6	B	MN.ss	Rh_0	kk
7	B	MN.ss	Rh_1rh	kk
8	O	MN.ss	rh	
9	O	N.ss	rh	
10	O	N.ss	Rh_0	
11	O	MN.ss	Rh_2	
12	B	N	Rh_1rh	kk

* The numbers 1–12 represent the 12 individuals referred to in Table 1.
† Only individuals of group B and group O were tested, because the patient's serum contained anti-A agglutinins.

shown later, the low frequency (2.7 percent) of the Henshaw factor found by Chalmers, *et al.* (*6*) among Negroids would tend to exclude that possibility, but the results obtained by them for the Hunter factor (21.7 percent) closely approximate the expected value. However, tests for these factors kindly carried out by William S. Pollitzer, Research Fellow, Institute of Human Variation, Columbia University, on a blood specimen from an individual of type uu were negative for the factors Henshaw and Hunter. This was contrary to expectations were either of the latter an alternate of **U**.

TABLE 3. Family studies on blood factor **U**.

Family number	Father	Mother	Children		
1		O N Rh_1rh kk† uu	O N rh'rh kk ♀ U		
2	O MN.ss $\mathfrak{R}h_0$ kk† uu	O N.ss Rh_1rh kk U	C N.ss Rh_0 kk ♀ uu	O N.ss Rh_0 kk ♀ uu	O N.ss $\mathfrak{R}h_0$ kk ♀ U
3			B MN.ss Rh_0 ♂† uu	O M Rh_0 kk ♂ U	
4	O MN.ss rh† uu	O MN.S Rh_1rh kk U	O MN.ss Rh_1rh kk ♀ U	O MN.ss Rh_1rh kk ♂ U	

† Propositus.

bears no relationship to any of these blood group systems, except possibly the M-N system. Moreover, the distribution of the **U** factor precludes any relationship to Duffy, Kidd, Lutheran, or Lewis systems.

The peculiar racial distribution suggested the possibility that factor **U** might be an alternate of the Hunter factor (*4*) or Henshaw factor (*5*). As will be

With regard to the heredity of the blood factor **U**, the simplest and most plausible theory is that factor

U, like other blood factors, is inherited as a simple Mendelian dominant. An attempt was made to study relatives of the rare individuals of type uu, in order to verify this hypothesis. As is shown in Table 3, we were able to examine two complete families, and in two other cases we tested the daughter and brother of the propositus. In families 1, 3, and 4 of Table 3, the other members of the family all proved to belong to type U. In family 2, the wife belonged to type U, but two of the three children belonged to type uu. The occurrence of two additional individuals of the rare type uu in such a short series of families confirms the hereditary nature of this blood factor. Presumably, the factor is inherited by a pair of allelic genes *U* and *u*, where gene *U* determines the presence of the factor and gene *u* its absence. Thus, type uu individuals are always homozygous (genotype *uu*), while type U individuals may be homozygous (genotype *UU*) or heterozygous (genotype *Uu*). The fact that in family 4, both children belong to type U indicates that gene *U* is dominant to gene *u*. In family 2, the type U parent is evidently heterozygous, accounting for the occurrence of type uu in the children.

From the distribution of the types, the gene frequencies are readily calculated. In Caucasoids, gene *u* is apparently absent, or at least very rare. Since the frequency of type uu in Negroids is 1.21 percent, the frequency of gene $u = \sqrt{\text{type uu}} = \sqrt{0.0121} = 11$ percent. Therefore, the frequency of gene $U = 89$ percent.

From these values, the frequencies of the three genotypes among Negroids can be calculated as follows:

genotype $UU = (U)^2 = 79.2$ percent,
genotype $Uu = 2(U)(u) = 19.6$ percent,
genotype $uu = (u)^2 = 1.2$ percent.

Thus, approximately one-fifth of type U individuals among Negroids are heterozygous, and it is not surprising that we encountered such a family in our short genetic study. Moreover, if there is a blood factor u corresponding to gene *u*, the expected frequency of the factor in Negroids would be 20.8 percent. As has already been pointed out, the results obtained by Chalmers, *et al.*, for the Hunter factor (21.7 percent) are remarkably close to this value. Moreover, the fact that all the type uu individuals found to date belong to type N or type MN also suggests a relationship to the Hunter factor, since one of us had previously found (*7*) that blood specimens containing the Hunter factor belonged to type N or type MN. However, as has already been pointed out, the fact that a type uu blood failed to react with anti-Hu serum is evidence that Hunter is not an alternate of U.

Since factor U proves to be important for the selection of donors for transfusion to Negroids, a source of specific antiserum is desirable. We had available numerous immune rabbit serums prepared by injections of human blood in order to produce anti-M and anti-N serums. Since all the rabbits had almost certainly received blood of type U, the possibility existed that the antiserum might have U antibodies. Accordingly, 11 different serums were absorbed with type uu blood in order to remove the human species-specific antibodies. Tests after absorption failed to reveal the presence of any U antibodies, however. Experiments are now in progress in which one of the type uu individuals is being immunized by injections of type U blood in order to produce typing serum.

Note added in proof: After four monthly injections, there is still no evidence of specific antibody formation.

References and Notes

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Effect of Synthetic Thioctic or Alpha Lipoic Acid on the Voluntary Alcohol Intake of Rats

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It has been shown that a proportion of rats fed a diet containing only 11 pure vitamins as a source of the vitamin-B complex increase their voluntary alcohol intake, and that a large proportion of these rats decrease their intake when they receive a supplement of liver or yeast (*1*). The substance present in liver and yeast responsible for this effect has been called factor N_1 (*2*).

On the other hand, it has been shown that some microorganisms utilize pyruvate only when the medium contains a factor that has been isolated and synthetized and given the names of thioctic acid (*3*) and alpha lipoic acid (*4, 5*).

Since we have assumed, as a working hypothesis, that the increased voluntary alcohol intake observed in the aforementioned experimental conditions could be the consequence of a slight disturbance in the carbohydrate metabolism at a step higher than the C_2 compounds, it seems desirable to study the effect of this synthetic substance on the voluntary alcohol intake of rats depleted of factor N_1 (*6*).

The alpha lipoic or thioctic acid was given to each experimental rat during a period of 4 to 10 days, after at least 90 days of feeding the aforementioned diet and after voluntary alcohol intake was sufficiently stabilized. The alcohol intake was measured daily, and the average for the 11th to 20th days after the first