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New Data on the Extraction of B_1 From Natural Material (Yeast)

Investigation was made to determine the most suitable conditions for the extraction of B_1 from yeast.

In a series of assays, using yeast from the same container and using the same enzyme (papain) but a different pH with each assay, it was found that optimum results were obtained at pH 1.0–1.5.

At the same time it was confirmed that synthetic B_1 is best conserved at pH 4.0–4.5.

For the checking of the B_1 the colorimetric method of Melnick and Field was used.

Further work is needed to determine whether the findings apply to the extraction of B_1 from other natural materials; also, on the use of different enzymes or a combination of enzymes.

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The Rh System in the Chimpanzee

The present writer's theory of multiple allelic genes, to account for the hereditary transmission of the Rh-Hr blood types, has received adequate confirmation from family and statistical studies (A. S. Wiener, E. B. Sonn, and H. R. Polivka. *Proc. Soc. exp. Biol. Med.*, 1946, **61**, 382). On the other hand, no substantial evidence has been adduced to support Fisher's theory of gene triplets, which only leads to contradictions and paradoxes (A. S. Wiener. *Brit. med. J.*, 1946, **1**, 982; J. Murray. *Brit. J. exp. Path.*, 1946, **27**, 102). A new argument for Fisher's theory has now been advanced in your columns by Mourant and Race (*Science*, 1946, **104**, 277).

M. Wade and I (*Science*, 1945, **102**, 177) reported that the bloods of every one of 15 chimpanzees tested did not absorb anti-Rh', anti-Rh'', or anti-Rh, agglutinins from human antisera, but did absorb anti-Hr'. This is confirmed by tests on a single additional chimpanzee by Mourant and Race, who also report that the blood of their chimpanzee did not absorb the anti-Hr'' agglutinin. Based on this finding, Mourant and Race conclude that the factors Rh'' and Hr'' are absent from chimpanzee blood and suggest that the hypothetical locus E-e of Fisher is lacking in this species. They consider this apparent separation of one gene pair from Fisher's three

sets of hypothetical genes an argument favoring Fisher's theory of closely linked genes, as against my multiple allele theory.

The reasoning used by Mourant and Race has a number of fallacies which can best be demonstrated by citing analogous observations involving other blood agglutinogens. Rhesus red cells are not clumped by, nor do they absorb, human anti-Rh, agglutinins, which, according to Mourant and Race, would indicate that the Rh, factor is entirely lacking in this species. However, the original antisera for detecting the Rh, factor were prepared by injecting Rhesus blood into rabbits and guinea pigs; in fact, that is how the Rh factor got its name. The correct conclusion is that Rhesus blood does not contain a factor identical with human Rh,—only a related factor, that is, an Rh₀-like factor. Similarly, it seems highly likely that chimpanzee blood actually does contain Rh''-like or Hr''-like factors, or both.

Another obvious fallacy is to assume that every separate agglutination reaction given by an antigen proves the presence of comparable separable components within the antigen. The agglutination test is merely a diagnostic test, and one might just as unreasonably conclude that every time a new qualitative test is devised for a chemical substance this proves the presence of another structure within its molecule. K. Landsteiner (*Specificity of serological reactions*. (Rev. ed.) Cambridge, Mass.: Harvard Univ. Press, 1945. Pp. 114–116) has repeatedly demonstrated how simple chemical compounds can give rise to several distinct but specific immune antibodies, and he has also demonstrated that the number of qualitatively different antibodies is not necessarily correlated with the existence of distinct structures within the antigen molecule. If we were to apply Mourant and Race's arguments in the case of the A-B-O blood groups and the M-N types, we would be faced with a number of queer paradoxes. Studies on the evolution of the M agglutinogen reveal the existence of at least four distinct partial antigens in the human M agglutinin and two partial antigens in the N agglutinin (A. S. Wiener. *Amer. Nat.*, 1943, **77**, 199). According to Fisher, it would therefore be necessary to postulate that agglutinin M of human blood is determined by a gene complex, $M_iM_{ii}M_{iii}M_{iv}$, while agglutinin N is determined by a linked gene complex, N_iN_{ii} . This leads to a situation where corresponding portions of a pair of homologous chromosomes are not homologous, and, if this conclusion were correct, it would be very strange that in millions of tests no evidence of crossing-over, such as a blood $M_iM_{ii}N_{ii}$, has ever been obtained. It seems much more reasonable to conclude that the complicated M and N agglutinogens of human blood are each determined by corresponding genes forming an allelic pair, in accordance with the generally accepted theory of Landsteiner and Levine. The reactions of the bloods of chimpanzees and monkeys with anti-M and anti-N sera can be explained most reasonably and simply by postulating the presence in these species of M-like and N-like agglutinogens rather than portions of a complicated gene complex; that is, the phenomena described are undoubtedly examples of the evolution of complicated chemical

molecules. Otherwise, it would be difficult to explain why the bloods of all chimpanzees tested possessed both M-like and N-like antigens. This must be due to a single agglutinin having properties intermediate between M and N. If the reactions were due to separable antigens, M and N, then all chimpanzees would have to be heterozygous for M and N, which is not possible, because such an unstable distribution would be immediately upset by a single generation of random mating.

When we consider the A-B-O blood groups, the reasoning of Fisher and his co-workers leads to an even more confusing paradox. In place of gene A_1 , we would have to substitute gene complex A_1AF_A ; in place of gene A_2 , the complex A_2OF_A ; in place of gene B , the gene complex $B_1B_{ii}B_{iii}B_{iv}$; and in addition, there is the fourth possibility, gene O . So, instead of a series of four simple allelic genes, Fisher's logic leads us to a series of four nonhomologous chromosome segments of varying lengths. Again it would be difficult to explain why in the course of millions of tests no evidence has ever been obtained indicating crossing-over between these hypothetical gene complexes.

As I have pointed out before (A. S. Wiener and H. Karowe. *J. Immunol.*, 1944, 49, 51), a single letter should be used to designate agglutinogens behaving like units, and separate letters should be used only for agglutinogens that segregate genetically, e.g. group AB, type MN, type Rh₁Rh₂. To use a complicated designation like CDe for the unit agglutinin Rh₁ is just as fallacious as to substitute the name type $M_iM_{ii}M_{iii}M_{iv}$ for the simple name type M. The pertinent question must now be raised as to whether in general, if a substance has several properties or characteristics, one must postulate a separate component to account for each characteristic. A cube has 6 faces, 12 edges, 8 vertices, 24 right angles, and so on, and the number of characteristics rapidly mounts as we amplify the description. Yet the cube, considered as a whole, is a unit. It seems to me that if Fisher's arguments were acceptable and carried to their logical conclusion, it would be necessary to scrap the entire gene theory.

In conclusion I should like to mention that almost everyone who has occasion to write on the Rh-Hr blood types seems to be impelled to propose another nomenclature, so that now more than six are extant. With regard to Fisher's designations, they have the disadvantages of being based upon an incorrect theory, of being unnecessarily complicated, of using symbols like C , E , and e , which have no relation to Rh and which have already been used in the field of blood grouping as symbols for other agglutinogens, and of including the symbol d for an agglutinin the existence of which has not been demonstrated. The other nomenclatures suggested involve the use of numbers and therefore have the same objections as the Moss and Jansky numberings for the blood groups, with the addition that more permutations and combinations are possible, so that even greater confusion would result. Previous experience in the field of blood grouping has proved that progress will be furthered only by the universal use of a single, simple nomenclature. Since the symbolic designations of

the Rh factors as Rh', Rh'', and Rh₀, and of the Hr factors as Hr' and Hr'', have proved to be the most logical, the simplest, and the least ambiguous, they should be universally adopted, also on the basis of priority.

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Consist—A Useful Noun

The language of America's railroad men suggests¹ for English-speaking scientists a new noun—*consist*. The *consist* of a railroad train is more than the sum of the cars involved and is not just the route those cars take. A train may carry produce from Sunburst to Sweetgrass every day, but each time it will almost certainly have a new *consist*. The word includes in the content of its meaning not only the number and kind of cars—refrigerator cars, flat cars, or pullman cars—and all the necessary railroad identification, but also the arrangement of the cars according to destination and content. The cars are arranged so that in a train leaving Chicago the cars for Minneapolis can be dropped without detaching those destined for Grand Forks. Thus, within the meaning of *consist* there is the idea of possible subgroupings.

Biologically, the chromosome is a train of genes, and the *consist* of a given chromosome would be the chain of genes with the arrangement and kind of gene peculiar to a particular chromosome of a particular individual. Thus, every man has a Y-chromosome, and every Y-chromosome has certain features which distinguish it from the X-chromosome with which it is paired in a cell; furthermore, there are differences between the Y-chromosomes of various men. The *consist* of Charles Darwin's Y-chromosome was not the same as that of Jean Baptiste Lamarck's.

In the study of induced mutations where fragmentation of chromosomes occurs, the term *consist* seems to provide new conciseness to the discussion of results, for the *consist* of a chromosome would be altered no matter whether a fragment were altogether removed and destroyed, whether it were removed and attached elsewhere, or whether it were just removed, inverted, and reattached. The conventional language of gene loci relative to other genes becomes cumbersome in any dealing with these matters.

The chromosome, because of its linearity, provides an obvious application of the new noun, but it can also be applied without loss of meaning to three-dimensional bodies. The *consist* of a sodium chloride crystal would be sodium ions and chloride ions arranged alternately at the corners of cubes, eight of which in a large cube constitute the face-centered unit crystal of sodium chloride.

H. L. Mencken, in his *The American language* (Suppl. I), quotes Philip M. Wagner (*Amer. Speech*, 1940, 15, 342), who says that the origin of *consist* as a noun probably lies buried in the history of the papers with which the engineer of a train is provided before each run. These papers describe the cars of which his train consists, their arrangement in his train, and their destination along his route. The term is indeed sometimes applied