

director of the Radiation Laboratory of the National Research Committee. Dr. I. I. Rabi, of the department of physics, officiated as chairman.

DR. WILLIAM H. ADOLPH, acting professor of biochemistry and nutrition at Cornell University, addressed on October 17 the University of Cincinnati Section of the Society of the Sigma Xi. He spoke on "Chemistry in China."

DR. ALFRED BLALOCK, professor of surgery and director of surgery at the Johns Hopkins University and surgeon-in-chief, the Johns Hopkins Hospital, will deliver the second Harvey Society Lecture of the current series at the New York Academy of Medicine on November 15. The title of the lecture will be "Physiopathology and Surgical Treatment of Congenital Cardiovascular Defects."

A SERIES of three lectures will be given by Dr. Torbjörn Oskar Caspersson, director of the department for cell research of the Medical Nobel Institute, Stockholm, under the Edward K. Dunham Lecture-ship for the promotion of the medical sciences at the Harvard Medical School, on November 13, 14 and 16. The title of the series is "Cytochemical Studies of Nucleic Acid and Protein Metabolism."

THE first meeting of the Society for the Study of Blood was held at the New York Academy of Medicine on the evening of November 8. The scientific program included papers by Dr. John T. Edsall, associate professor of biological chemistry, and by Dr. Louis K. Diamond, assistant professor of pediatrics, both of the Harvard Medical School; by Dr. Randolph West, associate professor of medicine, and by Dr. Erwin Chargaff, assistant professor of biochemistry, both of the College of Physicians and Surgeons, Columbia University.

THE American Fern Society has received as a bequest from Miss Amey Lillibridge, of Providence, R. I., the sum of \$1,000 in addition to her library and herbarium of ferns.

THE fifty-second annual meeting and twenty-seventh colloquium of the American Mathematical Society will be held at the Museum of Science and Industry, Chicago, on Friday and Saturday, November 23 and 24, in conjunction with meetings of the Mathematical Association of America. The sessions

of the society will begin on Friday at 9:30 and will continue through Saturday afternoon. The sessions of the association will be held on Saturday evening and Sunday morning. The colloquium will consist of four lectures on "Length and Area" by Professor Tibor Radó, of the Ohio State University, on Friday at 9:30 A.M. and 2 P.M. and on Saturday at 10 A.M. and 2 P.M. The nineteenth Josiah Willard Gibbs Lecture will be delivered by Professor J. C. Slater, of the Massachusetts Institute of Technology, on Friday evening at 7:30 P.M. The title of this address is "Physics and the Wave Equation." The annual business meeting and election of officers will be held on Saturday morning at 9:30 A.M. At 11 A.M., by invitation of the Committee to Select Hour Speakers for Western Sectional Meetings, Professor S. M. Ulam, of the University of Southern California, will deliver an address entitled "On the Stability of Solutions of Functional Equations."

THE centenary of the Imperial College of Science and Technology was celebrated in London in October. The college was constituted by Royal Charter in 1907; it is a federation of the Royal College of Science, the Royal School of Mines and the City and Guilds College. They are related to earlier institutions, the earliest of all being the Royal College of Chemistry, which was founded in 1845.

THE *British Medical Journal* reports that the Government of India established on September 1 a Department of Agriculture, a Department of Health and a Department of Education, in place of the existing single Department of Education, Health and Lands. Sir Sardar Jogendra Singh, minister in charge of the conjoint department in the Viceroy's Executive Council, will for the time being take charge of all three departments.

ERRATUM: In the review by Professor Noble P. Sherwood of Dr. Landsteiner's book entitled "Specificity of Serological Reactions" which appeared in *SCIENCE*, 102: 360-361, 1945, the word "neutralize," from before the word "strychnine" in the last sentence of the first paragraph discussing Chapter 5, was accidentally omitted. The sentence should read, "In connection with this, the author discusses the attempts and failures to produce antibodies to neutralize strychnine and the success achieved in producing antibodies to thyroxine."

SPECIAL ARTICLES

A CHEMICAL-MECHANICAL THEORY OF MUSCULAR CONTRACTION¹

THE obvious problem of muscular contraction is

¹ The Bureau of Medicine and Surgery of the Navy

to determine the mechanism by which the energy developed as adenosine triphosphate in carbohydrate

does not necessarily endorse views or opinions expressed in this paper.

metabolism is transferred to myosin and converted into mechanical energy. The contributions of Engelhardt and co-workers² need not be detailed here except to acknowledge that their finding that the transfer of energy of adenosine triphosphate is apparently associated with the relaxation of the myosin has provided the stimulus for a theory to be presented at this time.

This theory does not account for all the phenomena involved in muscle contraction, but it does provide a chemical-mechanical basis of that contraction which should be subject to experimental proof or disproof. It is unique in that it employs the only known system of energy transfer involving side chains of amino acids known to be present in the myosin molecule.

The theory may be stated briefly as follows: The contraction phase of myosin activity is visualized as a result of the condensation of the sulfhydryl and the phosphorylated hydroxyamino acid side-chains of the myosin molecule with the consequent release of inorganic phosphate and formation of a thio-ether linkage. Such reactions could bring about a considerable shortening of the myosin molecule if the sulfhydryl and hydroxyamino acid side-chains were strategically placed in the polypeptide chain. The relaxation of myosin would involve the phosphorylytic cleavage of the thio-ether linkage by adenosine triphosphate to produce free sulfhydryl and phosphorylated hydroxyamino acid side-chains.

The evidence for such reactions is, at best, of an indirect nature and rests largely upon observations made on the mechanism of the conversion of homocysteine to cysteine by liver tissue of rats. It has been found that the thio-ether containing amino acid cystathionine is cleaved to cysteine and probably a phosphorylated hydroxyamino acid by a phosphorylytic mechanism involving adenosine triphosphate.³ As in the adenosine triphosphate activity of muscle only the terminal phosphate is utilized. The cleavage of cystathionine would correspond to the relaxation phase of myosin activity.

The contraction phase, or the condensation of sulfhydryl and phosphorylated hydroxyamino acid side-chains, finds an analogy in the condensation of homocysteine with serine to bring about the formation of cysteine with the probable intermediate formation of cystathionine.⁴ A further analysis of this reaction⁵ has revealed that in the presence of homocysteine the

phosphate of phosphoserine is transferred to adenosine diphosphate with the formation of adenosine triphosphate. The condensation of homocysteine with the serine must take place, for some cysteine is formed and a considerable portion of the homocysteine disappears, coincident with the formation of adenosine triphosphate. It has been suggested above that the condensation of sulfhydryl with phosphorylated hydroxyamino acid side-chains of the myosin molecule would result in the release of inorganic phosphate. The condensation of homocysteine with phosphoserine, on the other hand, brings about the formation of a phosphate grouping of high energy. The apparent contradiction in the theory proposed for myosin activity and the observed behavior of the homocysteine-phosphoserine system is resolved when it is considered that the energy normally residing in the sulfhydryl-phosphorylated hydroxyamino acid system would be utilized in the mechanical process of shortening the myosin molecule or lost as heat in isometric contraction.

The reactions suggested as being involved in the myosin molecules may be presented schematically as in Fig. 1.

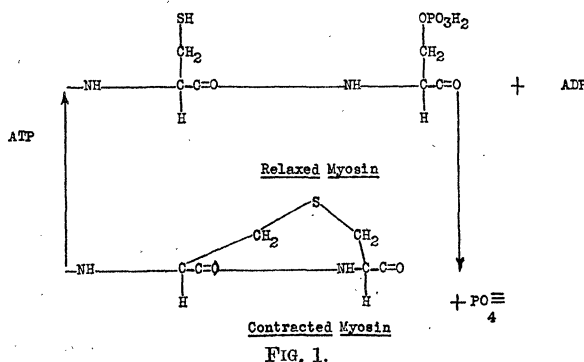


FIG. 1.

The concept of transfer of phosphate of high energy by a protein molecule by the sulfhydryl-phosphorylated hydroxyamino acid side-chains system may be of importance to an understanding of enzyme action in other phosphate transfer systems for, if the enzyme molecule is constructed so that little energy is involved in the condensation phase, the reaction between the protein and such compounds as adenosine triphosphate and creatine phosphate should be reversible.

The theory as presented is consistent with the evidence for the participation of sulfhydryl groups in the adenosine triphosphatase activity of myosin but a discussion of that evidence need not be made at this time. An interpretation of the x-ray data and the temporal relationships of muscular activity as related to the theory will be postponed, inasmuch as there

² W. A. Engelhardt and M. N. Ljubimova, *Nature*, 144: 668, 1939. W. A. Engelhardt, "Advances in Contemporary Biology," 14 (1941), as translated in *Yale Jour. Biol. Med.*, 15: 21, 1942.

³ F. Binkley, *Jour. Biol. Chem.*, 155: 39, 1944.

⁴ F. Binkley and V. du Vigneaud, *Jour. Biol. Chem.*, 144: 507, 1942.

⁵ F. Binkley, unpublished observations.

appears to be no *a priori* inconsistency and the predictions which may be made are, in the most part, subject to experimental attack.

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THEORY AND NOMENCLATURE OF THE Hr BLOOD FACTORS¹

THE hypothesis proposed by Fisher² that there are three different varieties of antisera capable of agglutinating Rh-negative blood, corresponding to the three varieties of anti-Rh sera^{3,4} appears to be gaining ground. Therefore, there is need for a clear statement of the status of the Hr factors and an acceptable method of designating the sera and factors postulated under the theory, such as has been devised for the Rh blood factors.^{5,6}

Since the three varieties of antisera reacting with Rh-positive bloods are collectively known as Rh antisera, the three varieties postulated by Fisher as acting on Rh-negative bloods may be designated collectively as Hr antisera. The great majority, if not all, Hr antisera found until recently have given reactions resembling those described by Levine and Javert⁷ for the original Hr antiserum in that the sera regularly agglutinated bloods not reacting with anti-Rh' serum. That Levine obtained only 30 per cent. positive reactions with his Hr antiserum, while Race and Taylor⁸ obtained 80 per cent. positive reactions with their Hr antiserum (designated by them St after the first two letters of the name of the patient from whom the serum was obtained) has been explained by Wiener⁹ as due to the low potency of Levine's serum so that only bloods homozygous for the Hr factor reacted with it. Sera of this specificity will henceforth be designated standard anti-Hr sera, just as Rh antisera giving reactions parallel with the original anti-rhesus serum of Landsteiner and Wiener are known as standard anti-Rh sera.

According to the theory of Race and Taylor, which is now firmly established, standard anti-Hr sera react with the agglutinogens determined by genes Rh_z , Rh'' , Rh_0 and rh , but not with the agglutinogens determined by genes, Rh_1 , Rh' , Rh_y and Rh_z . Therefore, standard anti-Hr serum and anti-Rh' serum are related serolog-

ically and genetically like anti-M and anti-N.^{9,10} To indicate this, standard anti-Hr serum may also be designated simply as anti-Hr'. Since the other two Hr antisera postulated by Fisher are related to anti-Rh'' and anti-Rh₀, in the same way that anti-Hr' (or standard anti-Hr) is related to anti-Rh', these two antisera may now be designated as anti-Hr'' and anti-Hr₀, respectively.

The reactions of the three sorts of anti-Hr sera with the agglutinogens determined by the six standard Rh allelic genes of Wiener^{3,4} and the genes Rh_y and Rh_z of Race and Taylor^{11,12} can now be summarized as shown in Table 1.

TABLE 1
THE RH SERIES OF ALLELIC GENES*

Designation of genes†				Reactions with Rh antisera		Reactions with Hr antisera	
1 Pre-ferred	2	3	4	Rh'	Rh''	Rh ₀ (stand-ard Rh)	Hr' (stand-ard Hr)
rh	rh	rh	rh	-	-	-	+
Rh_0	Rh_0	Rh_0	Rh_0	-	-	+	+
Rh'	Rh'	Rh'	Rh'	+	-	-	+
Rh_1	Rh_1	Rh_1	Rh_1	+	-	+	+
Rh''	Rh''	Rh''	Rh''	-	+	-	-
Rh_y	Rh_y	Rh_y	Rh_y	-	+	+	-
(Rh_y)	(Rh_y)	(Rh_y)	(Rh_y)	(+)	(+)	(-)	(-)
Rh_z	Rh_z	Rh_z	Rh_z	+	+	+	+
		or Rh_0''					

* Does not include the intermediate genes. Reactions, genes and antisera enclosed in parentheses have been predicted but not yet encountered.

† These do not represent different nomenclatures but merely variations of a single method of designating the genes.

It will be seen that in Table 1, four slightly different methods of designating the genes of the Rh allelic series are given. The reason for this is that certain minor objections have been raised to the first and simplest method of designating the genes—the one preferred by the present writer. According to the convention adopted by American geneticists, genes belonging to the same allelic series are assigned the same basic symbol and are differentiated by superscripts, while subscripts are reserved for genes at different loci having similar effects. Since very few allelic series are known for man in contrast to the situation in *Drosophila*, there is hardly any danger of confusion from the use of subscripts instead of superscripts in man, but if a change in nomenclature becomes essential in order to satisfy the geneticists, the second set of designations could be adopted. With regard to the third and fourth sets of designations, these are preferred by many workers because the names of the genes more clearly indicate with which Rh antisera the corresponding agglutinogens react. There is no

¹⁰ P. Levine, *SCIENCE*, 102: 1, 1945.

¹¹ R. R. Race and G. L. Taylor, *Nature*, 153: 560, 1944.

¹² J. Murray, R. R. Race and G. L. Taylor, *Nature*, 155: 112, 1945.

¹ Aided by a grant from the United Hospital Fund of New York City.

² Cited after R. R. Race, *Nature*, 153: 771, 1944.

³ A. S. Wiener, *SCIENCE*, 98: 182, 1943.

⁴ A. S. Wiener, *Proc. Soc. Exp. Biol. and Med.*, 54: 316, 1943.

⁵ A. S. Wiener, *SCIENCE*, 99: 532, 1944.

⁶ A. S. Wiener, *Jour. Amer. Med. Assn.*, 127: 294, 1945.

⁷ Cited by P. Levine, *Jour. Ped.*, 23: 656, 1943.

⁸ R. R. Race and G. L. Taylor, *Nature*, 152: 300, 1943.

⁹ A. S. Wiener, I. Davidsohn and E. L. Potter, *Jour. Exp. Med.*, 81: 63, 1945.