others showed individualized timing in peak activity. The "36-hour-fasting adapted" animal may be useful, Potter concluded, in studies on mechanisms of regulating enzyme synthesis or activation and may suggest how human subjects might initiate a program of stress-conditioning.

In the session on behavior of enzymes in vitro, D. B. Villee (Harvard Medical School) discussed the effects of progesterone on enzyme activity of adrenals in organ culture, and J. P. Changeux (Institut Pasteur, Paris, France) discussed allosteric interactions in quaternary structure.

D. B. Villee reported that human fetal and mouse adrenal glands can be maintained for 24 hours in a histologically and enzymatically differentiated state in organ culture. Adrenal glands cultured in the presence of progesterone showed enhanced utilization of progesterone and decreased activity of the 3-β-hydroxysteroid dehydrogenase-isomerase enzyme systems after being homogenized and incubated with progesterone-4-^{14}C and pregnenolone-7-α-^{3}H, respectively. Since these findings may represent examples of control of enzyme activity by substrate and product in mammalian cells in organ culture, such a system is of great experimental interest.

Changeux analyzed the implications of the model proposed by Monod, Wyman, and Changeux which assumes that allosteric proteins able to mediate homotropic interactions are oligomers made up of a small number of identical subunits. These subunits are associated in such a way as to confer at least one axis of rotational symmetry to the molecule. The two most significant implications of this model are (i) that interactions between ligands binding at distinct sites on the same protein molecule may be accounted for even though the binding of one ligand may have no direct effect on the inherent dissociation constant of another, and (ii) that globular proteins involving several identical subunits may possess an element of symmetry and should tend to conserve such symmetry in the event that they undergo a conformational alteration. Various examples of this interesting regulatory process in mammalian enzyme systems were discussed.

Regulation and Isozymes

W. E. Knox (Harvard Medical School) chaired the session on regulation and isozymes. M. K. Schwartz (Sloan-Kettering Institute for Cancer Research) reported on isozymes of aspartate aminotransferase in tissues and blood of man. The values for the Michaelis constant—K_m (L-aspartate)—were the same for the anionic isozyme of heart or liver and were distinctly higher than those for the cationic components. Values for K_m (α-ketoglutarate) were the same for the anionic isozyme of heart or liver and were distinctly lower than those for the cationic components. The relationship of the electrophoretic pattern of aspartate transaminase in human tissues to that in the serum was examined. The appearance of a cationic component in the serum of patients with neoplastic disease was associated with an acute phase of the disease and its disappearance with the subsidence of this phase.

N. Katunuma (Tokushima University, Tokushima, Japan) described the regulation of the urea cycle and tricarboxylic acid cycle by ammonia. A new metabolic pathway of reduced nicotinamide adenine dinucleotide (NAD) and reduced NAD phosphate to nicotinamide, including reduced pyridine nucleotide pyrophosphatase and nicotinamide mononucleotide oxidase, was first proved to occur in mitochondria of rat liver. The new pathway was accelerated by addition of ammonia. High-protein diet, administration of cortisone, or diabetes markedly increased the hepatic supernatant aspartate and alanine transaminase isozymes, but did not affect the mitochondrial transaminase isozymes.

The special symposium lecture was given again this year by Sir Hans Krebs (Oxford University). Krebs discussed the regulation of the release of ketone bodies by the liver, bringing evidence to reconcile the previously contradictory findings. He distinguished between the mild ketosis of starvation of low-carbohydrate diets, which is a useful process, and the severe ketosis of the diabetic coma and the lactating cow, which is uncontrolled ketone-body formation and is harmful. By the recognition of the association of severe ketosis with excessive rates of gluconeogenesis which, in turn, drains off oxaloacetate into gluconeogenesis, an advance was made in the understanding of the mechanisms involved. The gluconeogenic drain results in a decline of oxaloacetate level which, in turn, decreases the energy supply through the tricarboxylic acid cycle when the concentration of oxaloacetate decreases below the K_m value of the condensing enzyme. In consequence, the liver must perform an excessive oxidation of fatty acids to acetyl-CoA, which is then formed in excess of the capacity of the condensing enzyme and therefore results in ketone-body formation. Krebs concluded that the abnormal formation of ketone bodies is a type of respiration forced upon the liver when excessive gluconeogenesis, namely, excessive conversion of oxaloacetate to phosphoenolpyruvate, limits the rate of the tricarboxylic acid cycle. Since the severe ketosis arises from high rates of gluconeogenesis, clinical treatment must aim at a reduction of the need for gluconeogenesis. In diabetics the administration of insulin or glucose plus insulin will achieve this result. In bovine ketosis this aim is most readily obtained by the parenteral administration of appropriately large quantities of glucose.

Krebs's lecture was a beautiful example of problem-solving at the highest level of penetrating biochemical analysis in both the molecular and the clinical spheres. Thus it was a fitting and satisfying conclusion to a stimulating and useful meeting.

The symposium was sponsored by Damon Runyon Memorial Fund, Inc., Indiana University School of Medicine, the American Cancer Society, the Burroughs Wellcome Co., Hoffman-LaRoche Inc., and Merck Sharp and Dohme. The full text of the papers, edited by George Weber, will be published as volume 4 of *Advances in Enzyme Regulation* (Pergamon Press, New York and Oxford).

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Catecholamine Symposium

The first Catecholamine Symposium which was held in 1958 played an important role in stimulating the many advances which were subsequently made in this field. The developments since that first symposium have been so many and of such importance that a second symposium was organized and held at the Istituto Di Ricerche Farmacologiche Mario Negri in Milan, Italy, 4–9 July 1965.

U. S. von Euler (Sweden) gave the opening address entitled "Twenty years of noradrenaline," commemorating his

identification of noradrenaline as the sympathetic neurotransmitter substance. The subsequent sessions attest to the remarkable advances which have taken place in the short period of time since the last symposium. Most of the details concerning the enzymology of catecholamine biosynthesis were not known in 1958, and the presentations of H. Blaschko, S. Udenfriend, T. Sourkes, S. Kaufman, O. Hayaishi, M. Goldstein, and C. E. Sekeris summarized clearly the advances made. These advances include isolation and characterization of tyrosine hydroxylase and dopamine-β-hydroxylase and studies on the enzyme mechanisms. Direct evidence was also presented that tyrosine hydroxylase limits the rate of norepinephrine production. Details of the enzymes monoamine oxidase and catechol *O*-methyl-transferase, which are responsible for the metabolism of the catecholamines, were elegantly summarized by P. Holtz, J. Axelrod, V. Gorkin, A. Pletscher, and B. Belleau.

Mechanisms related to the interaction of catecholamine with the enzymes and cofactors involved in carbohydrate metabolism (cyclase, cyclic adenylic acid, phosphorylase, and phosphofructokinase) were presented by those who have pioneered in this field, including E. Sutherland, E. Krebs, T. Mansour, C. R. Park, E. Helmreich, N. Haugaard, and J. R. Williamson.

The implications of catecholamines in lipid metabolism (activation of lipase in adipose tissue) are most recent; presentations by M. Vaughan, D. Steinberg, R. W. Butcher, L. Carlson, and S. Garattini brought up to date the exciting developments in this area. L. Lundholm, B. B. Brodie, L. D. Carlson, and A. Goldfien discussed the regulative function of catecholamines in vivo and their interaction with other hormones.

Much of the explosive growth of interest in catecholamines stems from the development of analytical methods for the neurohormones themselves and for their metabolites. The most interesting development in this area has been the introduction of fluorescence microscopy for detecting catecholamines *in situ*. O. Eranko, who first applied this procedure to adrenal medulla, discussed his work, and C. Owman and B. Falck discussed their applications of the method to visualization of the sympathetic nervous system in tissues.

Studies on the intracellular distribution of catecholamines within adrenergic tissues have shown them to be associated with specific subcellular particles. The role of catecholamines in adrenergic transmission has also received intensive study, as was apparent from the reports of J. H. Burn, W. W. Douglas, G. Burnstock, H. O. Schild, N. C. Moran, I. J. Kopin, and E. O. Titus. Douglas' report on the relationship of calcium to catecholamine release was received with great interest.

A most important session was the one on modification of sympathetic function, which summarized advances in the pharmacologic, immunologic, and surgical procedures which have been recently introduced to inhibit or enhance sympathetic nervous activity.

A number of reports dealt with the implications of catecholamines in man, including catechol-secreting tumors, hypertension, heart failure, and the central nervous system and behavioral aspects of catecholamines. A highlight of the final session was the report by N. A. Hillarp and K. Fuxe on elucidation of the sympathetic innervation in the central nervous system by use of fluorescence microscopy. Hillarp, who had pioneered this work, died shortly before the symposium and the paper was given by his colleague, K. Fuxe.

The symposium, which ranged from enzymology to electrophysiology and clinical medicine, covered essentially all aspects of catecholamines and is therefore of interest to scientists in many divergent disciplines. The American Society for Pharmacology and Experimental Therapeutics, which sponsored the symposium, has arranged for publication of the proceedings as a supplement to *Pharmacological Reviews*. The symposium proceedings (about 600 pages) will also be published by Williams and Wilkins.

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Forthcoming Events

February

8–9. **Cost Aspects of Water Supply**, 8th sanitary engineering conf., Urbana, Ill. (J. H. Austin, 203 Civil Engineering Hall, Univ. of Illinois, Urbana 61803)

9–11. **Solid State Circuits**, 13th annual conf., Philadelphia, Pa. (K. H. Fischer, U.S. Army Electronics Command, Attn: AMSEL-KL-I, Fort Monmouth, N.J.)

10–11. **Snow**, eastern conf., Hartford, Conn. (G. Ayer, P.O. Box 948, Albany 1, N.Y.)

10–12. **Intermediate Energy Physics**, conf., College of William and Mary, Williamsburg, Va. (R. T. Siegel, Physics Dept., College of William and Mary, Williamsburg 23185)

13–16. **Radiation Research** Soc., 14th annual mtg., Coronado, Calif. (F. Smith, Biology Dept., American Univ., Washington, D.C.)

14–16. **Transplantation**, 7th intern. conf., New York Acad. of Sciences, New York, N.Y. (F. T. Rapaport, New York Univ. Medical Center, 550 First Ave., New York 10016)

14–18. Society of **Economic Geologists**, New York, N.Y. (J. O. Kalliokoski, Dept. of Geology, Princeton Univ., Princeton, N.J. 08540)

15–17. **Radioisotope Applications in Aerospace**, symp., Dayton, Ohio. (P. Polishuk, Flight Dynamics Laboratory, Wright-Patterson AFB, Ohio)

15–18. Treatment and Storage of Highly **Radioactive Waste**, symp., Richland, Wash. (W. H. Regan, Jr., U.S. Atomic Energy Commission, Washington, D.C. 20545)

16–17. **Voluntary Health**, 2nd natl. conf., Chicago, Ill. (Dept. of Community Health and Health Education, American Medical Assoc., 535 N. Dearborn St., Chicago)

16–18. Practical **Space Applications**, symp., San Diego, Calif. (C. Tross, Box 931, Rancho Santa Fe, Calif.)

16–19. National Soc. of **College Teachers of Education**, Chicago, Ill. (E. H. Goldenstein, Administration Bldg., 413, Univ. of Nebraska, Lincoln 68508)

16–19. Institute of **Management Sciences**, annual mtg., Dallas, Tex. (W. M. Campbell, Atlantic Refining Co., P.O. Box 2819, Dallas 75221)

17–19. American **Educational Research** Assoc., Chicago, Ill. (R. A. Dershimer, The Association, 1201 16th St., NW, Washington, D.C. 20036)

18–20. American **Psychopathological** Assoc., symp., New York, N.Y. (F. A. Freyhan, The Association, Natl. Inst. of Mental Health, c/o St. Elizabeths Hospital, Washington, D.C. 20032)

19. **Pleistocene of Ohio**, interdisciplinary conf., Ohio Acad. of Science, Columbus. (J. L. Forsyth, Dept. of Geology, Bowling Green State Univ., Bowling Green, Ohio)

21–25. **Analytical Chemistry and Applied Spectroscopy**, Pittsburgh, Pa. (R. E. Hein, Mellon Inst., 4400 Fifth Ave., Pittsburgh 15213)

21–25. Society for **Nondestructive Testing**, spring natl. conv., Los Angeles, Calif. (E. L. Criscuolo, U.S. Naval Ordnance Laboratory, White Oak, Silver Spring, Md. 20910)

21–25. **Non-Elastic Processes in the Upper Mantle**, symp., Upper Mantle Committee, Intern. Union of Geodesy and Geophysics, Newcastle, England. (D. C. Tozer, School of Physics, The University, Newcastle-upon-Tyne, 1, England)

22–24. **Offshore Exploration**, 1st conf., Long Beach, Calif. (P.O. Box 88, 2550 Via Tejon, Palos Verdes Estates, Calif. 90275)

22–26. Canadian Assoc. of **Radiologists**, 29th annual, Montreal, Quebec. (The Association, 1555 Summerhill Ave., Montreal 25)