Meetings

Drugs Affecting Lipid Metabolism

Almost 400 interested scientists convened in Milan, Italy, for the second international symposium on drugs affecting lipid metabolism, on 13–15 September 1965. The first lectures were devoted to orientation in various aspects of lipid metabolism which might be amenable to pharmacologic control.

In the opening talk, F. Lynen, Nobel laureate from the Max-Planck Institute for Zellchemie, Munich, reviewed his group's latest findings on the nature of the enzymes involved in fatty acid synthesis. The purified fatty acid synthetase from yeast, a multienzyme complex, consists of uniform particles having molecular weight of 2.3×10^6. Its individual activities (condensation, acyl transfer, reduction, dehydrogenation) may be assayed separately by the use of model substrates or by isotope exchange methods. The component enzymes are grouped around a central protein containing an exposed sulfhydryl group so constituted that, by free rotation, it can expose the substrate fatty acid to the active center of each member of the complex.

The control of cholesterol biosynthesis was discussed by M. D. Siperstein (University of Texas, Dallas), who reviewed the biological characteristics of the negative feedback system that regulates cholesterol synthesis in the liver of higher animals. Exogenous cholesterol specifically inhibits the reduction of hydroxymethylglutarate to mevalonate. The intracellular site of control of cholesterol genesis is localized in the lipoprotein membranes of the microsomes. Evidence was presented that the cholesterol feedback system in normal liver represents an example of end-product inhibition rather than of enzyme repression. The cholesterol feedback system is absent when hepatomas are present.

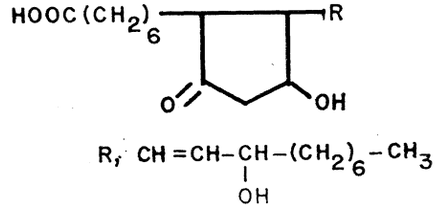
W. L. Holmes (Smith, Kline and French Laboratories, Philadelphia, Pennsylvania) discussed the status of drugs affecting cholesterol biosynthesis. A number of these compounds inhibit the later stages of cholesterol synthesis, and there is a resulting accumulation of sterols (7-dehydrocholesterol, 24-dehydrocholesterol, and others) in liver and plasma. No compounds are known that act at the endogenous site of inhibition of cholesterol genesis, namely, upon hydroxymethylglutaryl reductase. Holmes emphasized the need for a better understanding of the mechanism of action of hypolipemic agents in several animal species and urged examination of drug effects upon all tissue and serum lipid components.

The dynamics and consequences of free fatty acid (FFA) mobilization were discussed by D. Steinberg (National Heart Institute) and L. A. Carlson (Karolinska Hospital, Stockholm). Adipose tissue is now believed to be a major factor in the energy balance of the body by way of the continuous mobilization of FFA from this tissue into the blood. The FFA are transported to various organs where they may be stored or oxidized. The mobilization of FFA is affected by hormones, catecholamines, and the general nutritional state of the organism. The consequences of excessive FFA mobilization are fatty deposition, hyperlipemia, ketonemia, and increased oxygen consumption. Excessive mobilization of FFA may occur in diabetes, thyrotoxicosis, vascular disease, stress, and trauma. Certain drugs such as nicotinic acid or β-pyridylcarbinol, salicylic acid, and 3, 5-dimethylpyrazole (reported by others at the symposium) inhibit triglyceride lipolysis in adipose tissue and hence decrease mobilization of FFA.

Since all serum lipids circulate as components of various lipoprotein complexes several lectures were devoted to lipoprotein metabolism. D. S. Fredrickson (NHI) reported on characteristic lipoprotein patterns (obtained by paper electrophoresis) that may be used for the classification of dislipidemias, and H. A. Eder (Albert Einstein College of Medicine, New York) demonstrated that rat and human plasma contain a lipoprotein-free apoprotein that can combine with lipid in the liver to form lipoprotein.

In all, over 100 papers were presented on topics including the control of the amount of lipid in serum, fatty acid mobilization, and effects upon atherosclerosis of a large variety of hormones and synthetic pharmacologic agents. Two topics are particularly worthy of note.

S. Bergström (Karolinska Institute, Stockholm) and his co-workers (B. Samuelsson, M. Hamberg, K. Gréen, E. Granström, L. Carlson) presented a series of papers on the isolation, structure proof, biosynthesis, and physiology of an extremely potent group of hypotensive agents called prostaglandins. Prostaglandin was first isolated from sheep prostate over 30 years ago; only recently have studies on chemical structure and identification revealed the existence of not one but several closely related prostaglandins. Prostaglandins occur in semen, lung, iris, brain, thymus, pancreas, and kidney. The prostaglandins may be regarded as cyclopentanol-1 derivatives containing two side chains, one, of seven carbon atoms, terminating in a carboxyl group and the other, of ten carbon atoms, containing a hydroxy group and one or more double bonds. The structure of PGE_1 is



and PGE_1 is derived from γ-homolinolenic acid (double bonds at carbons Nos. 8, 11, and 14). Other prostaglandins may be derived from arachidonic acid (C_{20}:double bonds at carbons Nos. 5, 8, 11, 14) or eicosapentenoic acid (C_{20}:double bonds at carbons Nos. 5, 8, 11, 14, 17). D. A. van Dorp (Vlaardingen, Netherlands) discussed the conversion of a variety of unsaturated fatty acids to postaglandin-like compounds by a suitably fortified preparation of sheep vesicular gland. The prostaglandins inhibit release of glycerol (that is, lipolysis) from the epididymal fat pad and counteract the catecholamine-induced mobilization of FFA. At an infusion rate

of 0.1 to 0.2 $\mu g\ min^{-1}\ kg^{-1}$ in man, they cause a drop in blood pressure. The antilipolytic effect of these compounds, their potent muscle-relaxing action, and their relation to the essential fatty acids should make them the focus of much future research activity.

There were several papers on the effect of ethyl *p*-chlorophenoxyisobutyrate (Atromid-S, Clofibrate, CPIB) upon serum lipids in man. M. F Oliver (Royal Infirmary, Edinburgh) reported on a 4-year study of the effect of CPIB; the study showed that this drug lowered serum cholesterol and serum triglycerides in a group of men, reduced platelet adhesiveness, and reduced the extent of appearance of lipid exudates in the eyes of diabetics. The effect of CPIB on serum triglycerides is consistently greater than on serum cholesterol. Oliver feels that CPIB has many features of an ideal hypolipemic agent and is using this drug in an effort to reduce recurrence and mortality in a large group of patients with coronary disease. CPIB was also reported to reduce plasma FFA and to inhibit cholesterol genesis at a stage prior to mevalonate formation. However, CPIB causes liver hyperplasia and a substantial increase in liver lipids in rats, and more needs to be learned concerning its overall mode of action.

A third meeting on this subject is being scheduled for 1968 in Milan. The organizing secretary will again be R. Paoletti, Institute of Pharmacology, University of Milan, via Andrea del Sarto, 21, Milan, Italy.

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Forthcoming Events

March

6–11. American Soc. of **Photogrammetry**, Washington, D.C. (C. E. Palmer, 5917 Brookview Dr., Brookland Estates, Alexandria, Va.)

7–9. Fundamental **Cancer Research**, 20th annual symp., Univ. of Texas, Houston. (M. Mandel, Dept. of Biology, M. D. Anderson Hospital and Tumor Inst., Univ. of Texas, Houston 77025)

7–9. **Electric Propulsion**, 5th conf., American Inst. of Aeronautics and Astronautics, San Diego, Calif. (A. T. Forrester, Electro-Optical Systems, Inc., 300 N. Halstead St., Pasadena, Calif. 91107)

7–9. **Space**, 3rd congr., Cocoa Beach, Fla. (R. M. Barnes, PAA-Guided Missiles Range Div., Bldg. 423, MU 111, Patrick Air Force Base, Fla.)

7–11. American Soc. for **Metals**, western metal and tool exposition and conf., Los Angeles, Calif. (The Society, Metals Park, Ohio)

7–11. Society of **Plastics Engineers**, 22nd annual technical conf., Montreal, P.Q., Canada. (G. L. Bata, Union Carbide Canada, Ltd., P.O. Box 700, Pointe-aux-Trembles, P.Q.)

7–12. Inter-American **Nuclear Energy** Commission, 6th mtg., Washington, D.C. (J. D. Perkinson, Jr., Pan American Union, Washington 20006)

8–3. World **Meteorological** Organization, commission for synoptic meteorology, 4th session, Wiesbaden, Germany. (WMO, 41, avenue Giuseppe Motta, Geneva, Switzerland)

9–11. **Ethics in Medical Progress**, Ciba Foundation symp., London, England. (Ciba Foundation, 41 Portland Pl., London W.1)

9–13. Teaching Machines and **Programmed Instruction**, intern. symp., Nürtingen, Germany. (Arbeitsgemeinschaft Programmierte Instruktion, Inst. für Kybernetik, Pädagogische Hochschule Berlin, Malteserstr. 74-100, 1 Berlin 46)

10–11. **Heat Transfer** to Non-Newtonian Fluids, 12th annual heat transfer conf., Oklahoma State Univ., Stillwater. (J. D. Parker, Dept. of Mechanical Engineering, Oklahoma State Univ., Stillwater 74075)

11–13. National Council of **Teachers of Mathematics**, San Diego, Calif. (J. D. Gates, 1201 16th St., NW, Washington, D.C. 20036)

11–13. National **Wildlife** Federation, annual mtg., Pittsburgh, Pa. (T. L. Kimball, 1412 16th St., NW, Washington, D.C. 20036)

12–13. **Linguistics**, 11th natl. conf., Linguistic Circle of New York, N.Y. (L. Pap, State Univ. College, New Paltz, N.Y. 12561)

14–16. Society of **Toxicology**, annual scientific mtg., Williamsburg, Va. (C. S. Weil, Mellon Inst., 4400 Fifth Ave., Pittsburgh, Pa. 15213)

14–16. **Wildlife and Natural Resources**, 31st North American conf., Pittsburgh, Pa. (C. R. Gutermuth, Wildlife Management Inst., Wire Bldg., Washington, D.C.)

14–20. **Obstetrics and Gynecology**, 8th Australian congr., Hobart. (J. F. Correy, 173 Macquaire St., Hobart)

14–6 May. Extraordinary Administrative **Aeronautical Radio** Conf., 2nd session, Geneva, Switzerland. (Intern. Telecommunication Union, Place des Nations, Geneva)

15–16. **Flame Resistant Polymers**, conf., London, England. (Secretary, Plastics Inst., 6 Mandeville Pl., London, W.1)

15–18. **Optical Soc.** of America, spring mtg., Washington, D.C. (M. E. Warga, 1155 16th St., NW, Washington, D.C. 20006)

17–19. **Isobaric Spin in Nuclear Physics**, intern. conf., Florida State Univ., Tallahassee. (D. Robson, Dept. of Physics, Florida State Univ., Tallahassee)

18–19. **Rural Health**, conf., Colorado Springs, Colo. (B. L. Bible, 535 N. Dearborn St., Chicago, Ill. 60610)

18–20. American **Psychosomatic** Soc. annual mtg., Chicago, Ill. (W. A. Greene, The Society, 265 Nassau Rd., Roosevelt, N.Y. 11575)

20–23. **Solar Energy** Soc., 2nd annual mtg., Boston, Mass. (F. Edlin, Arizona State Univ., Tempe 85281)

21–24. **Aerospace Instrumentation**, 4th intern. symp., College of Aeronautics, Cranfield, England. (E. K. Merewether, ISA Aerospace Industry Div., 4515 Canoga Ave., Woodland Hills, Calif.)

21–25. Institute of **Electrical and Electronics Engineers**, intern. conv., New York, N.Y. (IEEE, 345 E. 47 St., New York)

22–23. **Biomagnetics**, 3rd intern. symp., Univ. of Illinois, Chicago. (M. F. Barnothy, Univ. of Illinois, 833 S. Wood St., Chicago)

22–23. Modern Concepts of **Cardiovascular Diseases**, conf. and workshop, Reno, Nev. (G. T. Smith, Laboratory of Patho-Physiology, Univ. of Nevada, Reno 89507)

22–24. Measurement and Applications of **Neutron Cross Sections**, conf., Washington, D.C. (W. W. Havens, Dept. of Physics, Columbia Univ., 538 W. 120 St., New York 10027)

22–31. American **Chemical** Soc., spring mtg., Pittsburgh, Pa. (ACS, 1155 16th St., NW, Washington, D.C.)

23–25. Institute of **Mathematical Statistics**, Purdue Univ., Lafayette, Ind. (G. E. Nicholson, Jr., Univ. of North Carolina, Chapel Hill)

23–25. Modern Methods of **Weather Forecasting and Analysis**, Chicago, Ill. (J. R. Fulks, U.S. Weather Bureau, 5730 S. Woodlawn Ave., Chicago)

24–26. **Biomathematics and Computer Science** in the Life Sciences, symp., Houston, Tex. (Dean, Div. of Continuing Education, Univ. of Texas Graduate School of Biomedical Sciences, Texas Medical Center, Houston 77025)

24–26. Pediatric and Adolescent **Gynecology**, conf., New York Acad. of Sciences, New York. (W. R. Lang, Jefferson Medical College of Philadelphia, 1025 Walnut St., Philadelphia, Pa.)

24–26. **Pollution and Marine Ecology**, conf., Galveston, Tex. (S. M. Ray, Texas A&M Univ. Marine Laboratory, Galveston 77550)

24–27. International Assoc. for **Dental Research**, 44th general mtg., Miami, Fla. (G. H. Rovelstad, U.S. Navy Dental School, Natl. Naval Medical Center, Bethesda, Md. 20014)

25–26. National Assoc. of **Biology Teachers**, western regional conv., Los Angeles, Calif. (The Association, Professional Building, Great Falls, Mont.)

26–2. **Stress Analysis**, 3rd intern. conf., Berlin, Germany. (H. Kotthaus, Verein Deutscher Ingenieure, Prinz-Georg Str. 77/79, 4 Düsseldorf 10)

26–27. Arizona **Chest Disease** Symp., Tucson. (E. A. Oppenheimer, P.O. Box 6067, Tucson 85716)

27–30. American Assoc. of **Dental Schools**, Miami Beach, Fla. (R. Sullens, 840 N. Lake Shore Dr., Chicago, Ill.)

28–30. **Great Lakes Research**, 9th conf., Chicago, Ill. (B. M. McCormac, IIT Research Inst., 10 W. 35 St., Chicago 60616)

28–31. Collegium Intern. **Neuro-Psychopharmacologicum**, 5th biennial mtg., Washington, D.C. (M. K. Taylor, 3636 16th St., NW, Washington 20010)

29–31. **Airborne Infection**, 2nd intern.