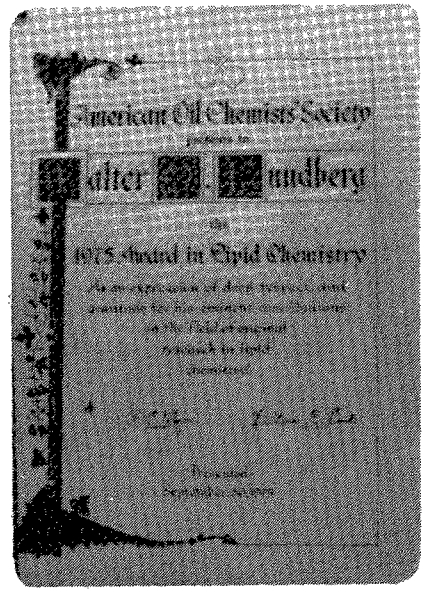
Walter O. Lundberg

1975 Award in Lipid Chemistry

Dr. Arthur Rose presents Dr. W.O. Lundberg with the honorarium that accompanies the AOCS Award in Lipid Chemistry



Yesterday and Today in Lipid Science and Technology

The following presentation was made by Dr. Walter O. Lundberg in accepting the 1975 Award in Lipid Chemistry at the opening plenary session of the Fall Meeting of the American Oil Chemists' Society in Cincinnati on September 29, 1975. Dr. Lundberg, a former president of the Society and editor of Lipids, *recently retired as Professor of Biochemistry at the University of Minnesota and Executive Director of The Hormel Institute.*

President Link, Dr. Rose, AOCS Officers and all members and guests of this distinguished Society:

We are deeply honored to receive this prestigious award. When President Link called to notify me, my initial surprise turned to humble gratitude and warm pleasure, because I know quite well the history and significance of the award. Again, my thanks to the Society and to Dr. Rose of Applied Science Labs, whom I have known as a good friend through think and thin for many years.

I have been asked to give a brief technical talk. Actually, I retired reluctantly on the advice of physicians last year and, therefore, have not been very actively engaged in lipid research since that time, although still maintaining an active interest in an advisory capacity with The Hormel Institute. Therefore, my remarks will consist of two parts: first, some general observations concerning the fantastic changes that have taken place in lipid science and technology during my association with them and, second, a brief summary of some of the recent researches at The Hormel Institute. Dr. Ralph T. Holman and senior staff members of The Hormel Institute furnished me with copious materials which necessarily had to be condensed, since time will not permit critical analysis of a single specific research topic, let alone 30 or more.

General Observations

When my 30 years of association with The Hormel Institute began, I was already teaching a course in lipid chemistry at the University of Minnesota, but had difficulty in defining lipids, one of the three recognized major classes of biological substances. The chemistry of carbohydrates, proteins, and closely related substances had become somewhat sophisticated compared with the chemistry of lipids, which embraced a heterogeneous collection of supposedly inert biological materials whose structures and functions were largely unknown. The main substances in quantity, triglycerides, were regarded mainly as sources of energy or as materials for use in the production of inedible products such as protective coatings and soaps. Our one journal in the field at that time bore the title *Oil and Soap.*

The problem of defining lipids has not simplified. Originally we used the late Prof. Bloor's classical definition—materials related chemically or biologically to fatty acids. Analytical methodology consisted mostly of measuring iodine numbers, saponification values, and thiocyanogin numbers, plus a few methods for fringe lipids such as phospholipids, cholesterol, and a few others. Glycolipids and sulfolipids were mentioned but poorly understood.

How things have changed! To mention only a few milestones, it was discovered by an AOCS member that certain fatty acids were essential in the diet of rats. Two earlier past presidents of AOCS published monumental works on the chemistry and technology of fats, fatty acids, and other lipids which contributed greatly to science and to the prestige of AOCS. Another past president, who is still active, has contributed much as editor of *JAOCS* and was primarily responsible for initiating the Society's second journal, *Lipids.* I am deliberately avoiding mentioning names because many others have made momentous contributions to the Society and the science and technology of lipid substances and it would be impossible to name all of them. Our members have been responsible for a host of new lipid researches, new lipid compounds, new preparative and analytical techniques, new lipid sources, new applications, and the increasing biological importance of lipids that have developed in recent years. These are described in our journals and others.

AOCS has become international, having members in many other countries. This has broadened its interests greatly, although I presume that America will always remain the home base of the Society. There have been suggestions for modifying our name, but if any changes are eventually considered, the name The International Oil Chemists' Society might well be brought into the discussions.

Current Hormel Institute Activities

Like my primary devotion to AOCS among the various scientific societies of which I am or have been a member, my affections also belong in a somewhat different way to The Hormel Institute. This unit of the Graduate School of the University of Minnesota has developed a broad spectrum of researches in the chemistry, biochemistry, and clinical chemistry of lipids. Because time is limited, only representative researches in this spectrum will be mentioned. Although postdoctorate fellows, technicians, and collaborators in other institutions contribute much of the effort in these researches, we shall name only the 10 group leaders. We invite you to write for recent annual lists of publications to The Hormel Institute, Austin, MN 55912 or write directly to group leaders for further information.

Dr. R.T. Holman, The Director of the Institute, and his colleagues are continuing his long time studies of essential fatty acids. Recently they have observed deficiency symptoms in humans maintained by fat free intravenous nutrient solutions. The symptoms are similar in several respects to those previously found in experimental animals. The elevated content of eicosatrienoic acid and decreased content of arachidonic acid were most drastic in the phospholipids of tissue lipids. Both the clinical and biochemical symptoms of EFA deficiency are reversible. The mass spectrometry of lipids has been under study at the Institute for a decade. The fragmentation mechanisms have been delineated for methyl esters, partial glycerides, triglycerides, diol lipids, and wax esters. Most recent studies have concentrated on the use of pyrrolidides of fatty acids as a means of emphasizing the fragmentation diagnostic for double bond position, methyl branches and other structural features. The mass spectra of pyrrolidides have been found especially useful for locating double bonds in monounsaturated fatty acids and polyunsaturated acids. Recently a comparison has been made between the metabolic capacities of liver microsomes from normal rats and rats fed chronic dose levels of DDT and Kelthane. Both of these chlorinated pesticides were found to inhibit the microsomal activities for chain elongation and desaturation of fatty acids.

One of several current projects of **Dr. Hermann Schlenk's** group is the study of mosses, in particular, of their highly unsaturated lipids which have been recognized as "essential" for higher animals. Mosses are plants that survive extreme environmental conditions such as heat, cold, or dryness. Adaptation to such conditions affects lipid composition and subcellular structure. Arachidonic and 20:5ω3 acids are bound in lipids of all mosses and 22:5ω3 was found in some of them. Acetylenic acids that resemble linoleic and linolenic acids more closely than any other polyunsaturated acetylenic acid have been identified. The ultrastructures of moss tissues grown under different conditions are now under investigation by electron microscopy. Several other novel features were found in the wax ester fractions from several moss species. Notably, they contain phytanic acid as the major acyl component and phytol as predominant alkyl component. In another project, interesting findings concerning the furanoid acids of fish have been made.

When triparanol, a cholesterol depressant, is fed to white rats, most of the animals develop cataracts. If triparanol feeding is discontinued, many of the cataracts clear within three to five months. **Dr. J.R. Chipault** and associates have found that feeding triparanol resulted in a lower level of sterols in the lens prior to cataract formation, but a sharp increase in sterols accompanied the appearance of cataracts. In addition, cholesterol accounted for only 72% of the four sterols found in the newly formed cataracts, whereas in normal control animals cholesterol constitutes 98% of the total sterols. Other chemical changes were found, especially in the phospholipids. Another study in this group is concerned with the effect of diet on fecal bile acids and sterols in relation to cancer of the colon but is not sufficiently advanced to report any results.

Dr. O.S. Privett and colleagues have four main projects under way. First is a study of biological effects of air pollutants. Studies of the toxicity of ozone and related pollutants demonstrated the importance of vitamin E and the mode of its protective action in blood, particularly on red blood cells. A second project is concerned with developing a variety of soybeans from the standpoint of oil quality in collaboration with Prof. J.W. Lambert of the Department of Plant Genetics of the University of Minnesota. Following four years of selection of varieties of low linolenic acid soybeans, several varieties having an approximate 50% reduction in linolenic acid have been obtained. Thirdly, a search is being made for a method for the early detection of cancer based on determination of lipid profiles of liver and breast cancer in rats and humans. The fourth project is concerned with the metabolic effects of "trans" unsaturated fatty acids. The results indicate some influence on normal secretion of liver lipids, but the clinical importance, if any, of these observations has not been determined.

Dr. H.H.O. Schmid and his coworkers have been studying the structure and metabolism of ether lipids for several years. Recently they observed that the biosynthesis of the *O*-alkyl glycerol backbone of ether phospholipids is a process which is not very specific in regard to the structure of the long chain primary alcohol serving as the donor of the alkyl moiety. It is thereby possible to produce in vivo phospholipid analogs having unusual structures such as extremely high unsaturation or additional functional groups such as hydroxy and keto groups. Currently, the physical and biological effects of such phospholipid analogs as constituents of biomembranes and as substrates for various phospholipases are being studied. Such work also led to investigations on the metabolism and physiological effects of highly branched fatty acids, especially as constituents of membrane phospholipids and of the wax esters of skin. In this laboratory, work on the structure and biosynthesis of skin lipids includes studies of long chain primary alcohols, 1,2-alkanediols, α-hydroxy fatty acids and their esters.

In the microbiology laboratory of **Dr. H.M. Jenkin** and his associates, one study has concerned the lipid control of the growth of normal and tumorigenic cells. The effects of theophylline, insulin, and fatty acids on the growth and lipid metabolism of rat Novikoff hepatoma cells in vitro were studied. Theophylline inhibited both growth and lipid metabolism of the cells when ^{14}C sodium acetate and ^{14}C sodium oleate were employed as tracers, and both effects of theophylline were antagonized by a physiological concentration of insulin. Oleic acid inhibited de novo lipid synthesis from acetate at concentrations which did not affect cell growth. A redistribution of the label from triglyceride to phospholipid was observed in cellular lipids labeled from acetate. The redistribution was inhibited by unlabeled sodium oleate but was not affected by insulin or theophylline. The results in this study indicate regulation of lipid metabolism by exogenous lipid and suggest a role for cyclic AMP regulation of growth and lipid metabolism in rat Novikoff hepatoma cells. This group is conducting four other projects. Attempts to cultivate *Treponema pallidum*, the cause of syphilis, appear to be successful. Wound

healing is being studied using a presumed lipid substance that appears to heal third degree burns rapidly without scar formation. Lipid metabolism of normal and infected cells cultivated in vitro are being compared. Lastly, studies of lipid metabolism of Chlamydia agents are being made. These agents are important because they cause trachoma–the major cause of blindness in the world, arthritis in man and sheep, and possible cervical carcinoma when a second organism, herpes virus, is present in the vagina.

Major research efforts of **Dr. W.J. Baumann** and his coworkers have been concentrated on the structure, metabolism, and function of unusual lipid components which contain a short chain diol instead of glycerol. These diol lipids occur widely in nature but are usually found at low levels. Higher levels of diol lipids accumulate, for example, during phases of rapid proliferation, such as in regenerating rat liver or in fast-growing tumors. It is of interest that diol-derived lecithin analogs show lytic activity which exceeds that of lysolecithins, and that diol-derived phosphatidyl serine analogs posses anticoagulant activity. Diol lipids are being widely used in this and other laboratories as model compounds to study substrate requirements of enzymes that are normally involved in glycero-lipid metabolism. The low level of diol lipids commonly found in biological materials has required development of new methodologies for their reliable identification and accurate quantitation, which involve the use of internal deuterated diol lipid standards and gas chromatography-mass spectrometry. The biosynthesis of diol lipids is under investigation, and it appears that diol monoesters play a central role in the formation of neutral diol lipids as well as diol phospholipids. The enzymes catalyzing these reactions are subjects of some of the current studies. Other activities in this group involve studies on membrane structures and membrane functions, using nuclear magnetic resonance as a tool to elucidate the role of unusual phospholipids in biological membrane assemblies.

Studies by **Dr. Eldon Hill** and coworkers with miniature pigs fed atherogenic diets for 24 weeks showed that the pigs developed a severe hyperbetalipoproteinemia of the "broad beta" type, which differed from the human type III LP profile by having a significantly increased amount of high density lipoprotein in the serum, and by having a broader LP spectrum. These atherosclerotic pigs also had severely elevated serum cholesterol values, but only minor elevations in serum triglycerides. Studies with chickens fed similar atherogenic diets showed 100% incidence of aortic lesions in 12 to 20 weeks. Dietary supplements of massive doses of vitamin C did not reduce or prevent atheromatous lesions of the aorta, and actually induced higher levels of serum cholesterol, serum triglycerides, and liver and aortic cholesteryl esters and free cholesterol.

Research conducted under the direction of **Dr. E.M. Stearns** has dealt with the control of synthesis of unsaturated fatty acids in higher plants and plant cell cultures. Studies performed under aerobic and anaerobic conditions in developing soybeans have shown a close interrelationship between newly synthesized individual fatty acids and their appearance in specific phospholipids. Current studies are concerned with differentiating between substrate or transport functions for the phospholipids. A modified treatment of plant tissues developed in this laboratory has enabled generation of a number of lines of soybean callus. Administration of plant hormones to suspension cultures of these cells at the 1 ppm level for 24 weeks has been shown to alter the pattern of fatty acids synthesized. For example, a mixture of cytokinin and gibberellin has effected an elevation of linoleic and depression of linolenic acids synthesized. Cultured soybean cells used in synthetic studies of lipids show the same reactions observed in cells from developing plants and at approximately the same relative rates. This makes possible assays and manipulations of cells that could be important to development of new strains with altered characteristics.

Dr. Howard L. Brochman's group is working on the relationships between the physical behavior of lipids and proteins at interfaces and on the regulation of lipid metabolism. They are currently measuring the kinetic and thermodynamic parameters which govern cholesteryl ester hydrolysis and the properties of the enzyme, aortic cholesteryl esterase, which catalyzes it. The experimental system used monolayers of substrates at either an air-water or oil-water interface with cholesteryl esterase in an aqueous phase. The specificities and magnitudes of the interactions being studied will provide a basis for understanding the relationship between the intrinsic physicochemical properties of aortic lipids and the accumulation of cholesteryl esters in the aorta. Another study in this group concerns the role of bile salts and colipase in the hydrolysis of glycerides by pancreatic lipase in defined monolayer systems. ■

CALL FOR NOMINATIONS:

North Central Section

Alton E. Bailey Award

The North Central Section of AOCS is requesting of the society members written nominations for the 1975-76 Alton E. Bailey Award. The purpose of the Bailey Award is to recognize research and/or service in the field of fats and oils. The nomination should contain at least 5 pertinent references or contributions in the field of oils, fats, waxes, et cetera. Some of the past Bailey Award winners are: V.C. Mehlenbacher (1959), R.H. Potts (1960), J.C. Cowan (1961), A.R. Baldwin (1963), T.P. Hilditch (1965), D. Swern (1966), W.O. Lundberg (1967), H.J. Dutton (1968), H.S. Olcott (1969), H.E. Carter (1970), J.F. Mead (1971), R.T. Holman (1972), C.M. Gooding (1973), S.S. Chang (1974), and W.M. Cochran (1975).

Please send nominations to the Alton E. Bailey Award Chairman, Dr. B.F. Szuhaj, Central Soya Company, 1825 N. Laramie Avenue, Chicago, IL 60639. The deadline for nominations in January 1, 1976, and notification of selection will appear in this journal. The presentation of the Bailey Award is scheduled for March 17, 1976. ■