will greatly simplify the process of admission, although the University Admissions Officers have still to make their individual decisions. We hope that one effect of the clearing house will be to increase the range of schools from which our students come. At present Churchill College admits students from about 100 schools of widely different types. We are, however, looking for good students wherever we can find them.

Up to now, we have completed our central buildings and rather more than half of our residential accommodation. We are just beginning the construction of our libraries and in the Autumn we expect to begin the construction of a final group of student rooms. This should enable students to have more than two years out of three in College.

NEWS AND COMMENT

Nobel Laureates: Bloch and Lynen Win Prize in Medicine and Physiology

During the past 25 years biochemists have discovered many of the chemical reactions which occur in living cells. Although great gaps remain in our knowledge in this area, at least an outline for the chemistry of life is now plainly visible. This single sentence summarizes one of the great accomplishments of science in the 20th century. Some of the most far-reaching developments in this field, the field of intermediary metabolism, have been achieved by Professor Konrad Bloch of the Chemistry Department at Harvard University and Professor Feodor Lynen at the Max-Planck-Institut für Zellchemie in Munich. On 15 October the Nobel Prize Committee announced that the 1964 prize for medicine and physiology will be awarded jointly to these two men for their contributions to our knowledge of the complex pattern of reactions involved in the biosynthesis of cholesterol and of fatty acids. Their work in both these fields is closely interwoven, but Bloch has been especially concerned with cholesterol, Lynen with fatty acids.

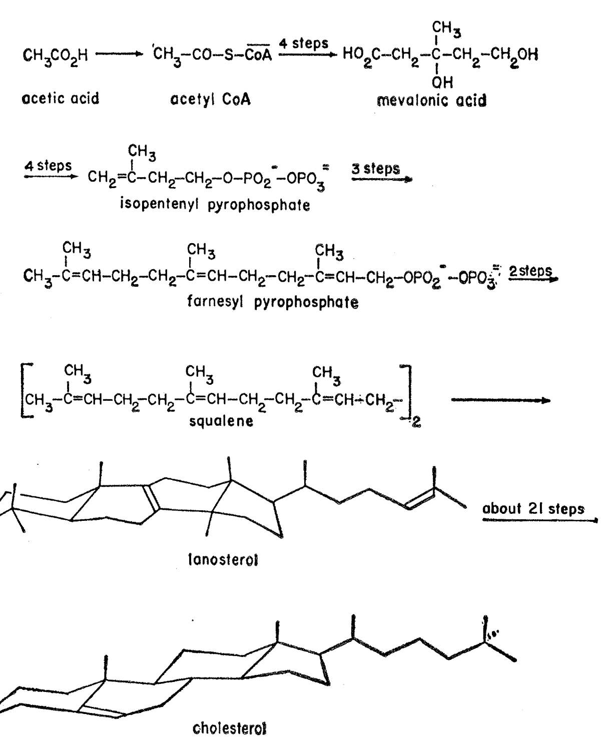
In classical experiments at Columbia in 1937, R. Schoenheimer and D. Rittenberg utilized deuterium as a tracer to show that cholesterol is built up in animal tissues from small molecules. Five years later, Bloch and Rittenberg, using acetic acid labeled with deuterium, proved that this compound is a major precursor of cholesterol in rats. With this work Bloch began the pursuit of a goal—the complete elucidation of the biosynthesis of sterols—to which he has contributed so much during the intervening years.

Although the early work showed that cholesterol must be formed from two-carbon units closely related to acetic acid, and although parallel work demonstrated a similar origin for fatty acids, the chemical nature of the true two-carbon atom intermediate, an "active acetate," remained a baffling problem until F. Lipmann discovered coenzyme A. Subsequently, in 1951, Lynen succeeded in isolating "active acetate" from respiring yeast and showed that it is the acetyl thiol ester of coenzyme A. This discovery has proved fundamental to an understanding of the mechanism of the biosynthesis of both sterols and fatty acids.

The transformation of acetic acid through acetyl coenzyme A to cholesterol involves about 36 steps. The pathway is sketched in the adjacent diagram.

The hydrocarbon squalene proved a landmark in unraveling the biosynthetic pathway shown above. This hydrocarbon is abundant in the livers of sharks, and therefore Bloch planned to inject radioactive acetic acid into dogfish (the dogfish is a member of the shark family), isolate squalene from their livers, and test whether it is an intermediate in the overall synthesis of cholestrol. But even the best research plans sometimes strike unusual snags. Bloch set out for Bermuda, where marine biologists hunted dogfish. But the dogfish proved refractory and promptly died in captivity before they could metabolize acetic acid. So, after a few days on the Bermuda beaches, Bloch returned to the University of Chicago and there, with R. G. Langdon, succeeded in isolating labeled squalene from the livers of rats injected with radioactive acetate. With this material in hand, Bloch and Langdon proved that squalene is biologically converted to cholesterol. Shortly thereafter R. B. Woodward and Bloch proposed a mechanism for the cyclization of squalene to form lanosterol. Their hypothesis received strong support

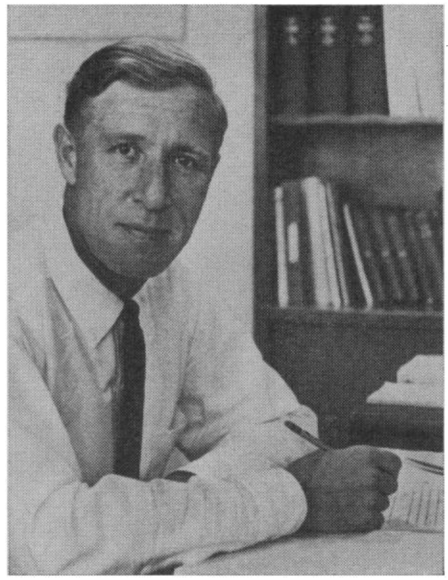
Pathway of the transformation of acetic acid to cholesterol.



from the experiments of J. W. Cornforth and G. Popjàk, whose chemical degradations of the sterol nucleus revealed the pattern of labeling from radioactive acetate which was predicted by the Woodward-Block formulation.

Not all the steps between lanosterol and cholesterol are known in detail even today, but Block and his coworkers have found many of the intermediates, purified many of the individual enzymes, and fitted them into a unified and satisfying mechanistic scheme.

An important link in the pathway from acetate to squalene was supplied by Karl Folkers and his collaborators at Merck, Sharp and Dohme. They isolated mevalonic acid as a bacterial growth factor and demonstrated that it can be converted to cholesterol in high yield. This lead was vigorously exploited with cell-free enzyme systems. The conversion of mevalonic acid to squalene through isopentenyl pyrophosphate was almost simultaneously discovered in the laboratories of both Bloch and Lynen.



Konrad Bloch

Wide World Photos

Feodor Lynen

Isopentenyl pyrophosphate is closely related to the hydrocarbon isoprene. Not only cholesterol and the other steroids but terpenes, sesquiterpenes, triterpenes, and rubber are members of the large class known as "isoprenoid" compounds. In a series of papers in the early 1920's, L. Ruzicka had pointed out the structural similarities among these compounds and formulated his "isoprene rule," stating that all these compounds can be formally regarded as derivatives of isoprene. The "active isoprene" of Bloch and Lynen (isopentenyl pyrophosphate), together with the detailed mechanism for the enzymic condensation of isopentenyl pyrophosphate to farnesyl pyrophosphate, which Lynen established, provides a solid biochemical foundation for the isoprene rule and builds yet another bridge between chemistry and biochemistry. Undoubtedly the knowledge gained on the biosynthesis of cholesterol will have widespread application to other substances with structures which follow the rule.

As for the significance for medicine of the new knowledge gained by research on cholesterol itself, it is widely held that atherosclerosis involves a derangement of lipid metabolism associated with high levels of cholesterol in the blood. Although the exact role of cholesterol in the pathogenesis of atherosclerosis is by no means understood, a knowledge of the biosynthesis of the sterol contributes to continuing efforts to understand mechanisms which control the level of cholesterol in blood and tissues.

While his work on the biogenesis of cholesterol was especially cited in the award of the Nobel prize, Bloch has made outstanding contributions to other fields of biochemistry; those on the biosynthesis of glutathione and on the metabolism of fatty acids have proved especially significant. His researches on glutathione provide a model for one mode of activation of amino acids to form peptide bonds. His current interest in the biological formation of unsaturated fatty acids complements the work of Lynen and others (discussed below) on the biosynthesis of fatty acids.

Feodor Lynen has also made distinguished contributions to many aspects of biochemistry other than the biosynthesis of cholesterol. In particular, he and his group have played an essential role in explaining the metabolism of the fatty acids. These acids are degraded by Beta-oxidation, and many of the intermediate stages in the process were found in Lynen's laboratory by the skillful application of the art of enzymology and the imaginative use of analogs of coenzyme A. His recent studies on the mechanism of fatty acid synthesis are of basic importance.

The biosynthesis of fatty acids, like that of cholesterol, begins with acetyl coenzyme A. But the condensation of many molecules of this compound to form the backbone for long-chain fatty acids requires that the acetate be further activated. After the requirement of carbon dioxide for this activation was discovered by a team headed by S. J. Wakil in the laboratory of D. E. Green, several investigators capitalized upon this finding to show that carbon dioxide combines with acetyl coenzyme A to produce malonyl coenzyme A. Now Lynen's group has isolated a multienzyme complex from yeast which catalyzes the formation of long-chain fatty acids from acetyl coenzyme A and malonyl coenzyme A. The overall stoichiometry of the multistep process (the reduced triphosphopyridine nucleotide needed as reducing agent is omitted) is shown below.

$$\underset{\text{acetyl CoA}}{CH_3CO{-}S{-}\overline{CoA}} + 7\,\underset{\text{malonyl CoA}}{HO_2C{-}CH_2{-}CO{-}S{-}\overline{CoA}} \longrightarrow$$

$$\underset{\text{palmitic acid}}{CH_3{-}(CH_2)_{14}{-}CO_2H} + 8\,CoA + 7\,CO_2$$

This equation emphasizes the catalytic role of carbon dioxide; carbon dioxide is required to convert acetyl coenzyme A to malonyl coenzyme A but is then ejected in the subsequent condensation process. The stoichiometric equation is a highly oversimplified summary not only because the many intermediate steps are omitted but also because (as Lynen and his collaborators have shown) the intermediates involved in the condensation reactions are bound to the enzymes throughout—that is, the fatty acid residues are linked covalently to the enzyme complex. The group at Munich has clarified most of the intermediate stages in this reaction sequence.

The fixation of carbon dioxide to form malonyl coenzyme A is an essential step in the synthesis of fatty acids. In another major contribution Lynen and his associates have discovered the role which the vitamin biotin plays in this and many other such carboxylations. The problem was complicated by the fact that biotin does not function as a free molecule but is enzyme-bound. Nevertheless, Lynen found an enzymic system which will cause carbon dioxide to react with free biotin and has identified 1′-*N*-carboxybiotin as the essential intermediate which transfers carbon dioxide from solution to organic compounds such as acetyl coenzyme A. With this work Lynen added "active carbon dioxide" to his discovery of "active acetate" and his contribution to the discovery of "active isoprene."

Bloch has recently turned his attention to the biosynthesis of olefinic fatty acids. His investigations have revealed that these compounds are formed by two different pathways. One of these, present only in aerobic organisms, requires molecular oxygen to effect the desaturation of preformed acids, while the other, utilized by anaerobes, provides for the introduction of the double bond during the condensation process which forms the aliphatic chains. These studies have led Bloch to a consideration of comparative and evolutionary biochemistry, and his thinking in this area has provided a new sense of unity in lipid metabolism.

These synthetic pathways to fatty acids and cholesterol are complex and are interesting in detail largely to the expert. But they are of general scientific interest because their elucidation provides almost a new dimension to the description of living organisms. Admittedly, our knowledge is still fragmentary. But the work of Bloch and of Lynen goes far to justify the claim made in the opening paragraph that a rough scheme for the chemistry of life is visible. To be sure, intermediary metabolism extends far beyond the work of Bloch and Lynen, far beyond steroids and fatty acids. Much brilliant work has been done in tracing the pathways for the formation of purines and pyrimidines, of amino acids and carbohydrates, and of many other important metabolites. The achievements of Konrad Bloch and Feodor Lynen are thus significant not only in and of themselves but because they illuminate by example the spectacular recent developments of intermediary metabolism.

Feodor Lynen was born in Munich on 6 April 1911, the son of Wilhelm L. Lynen, a distinguished professor in the Technische Hochschule. He received his training in chemistry at the University of Munich, where he studied under Heinrich Wieland, himself a Nobel laureate, whose daughter Eva, Lynen married in 1937. Lynen was appointed lecturer at the University of Munich in 1942 and was made professor in 1947. He is, at present, director of the Max-Planck-Institut für Zellchemie at Munich. His laboratory has become a center of training for young American biochemists as well as for Europeans. An enthusiastic mountaineer, Lynen has made an avocation of climbing and shares with Bloch a love of skiing. He is the father of five children.

Konrad Bloch was born in Neisse, Germany, on 21 January 1912, and attended the Technische Hochschule in Munich from 1930 to 1934. After Hitler came to power in Germany he escaped to America via Switzerland, where he stayed long enough to carry out his first published biochemical researches. He obtained his doctorate with Hans Clarke at Columbia in 1938 and subsequently served as instructor and as research associate with R. Schoenheimer at Columbia's College of Physicians and Surgeons. In 1941 he married Lore Teutsch, whom he had first met many years earlier in Munich, and in 1946 the Blochs went to the University of Chicago, where he was made professor in 1952. In 1954 he was named Higgins Professor of Biochemistry at Harvard University. The father of two children, Konrad Bloch is an enthusiastic skier and tennis player. He retains from childhood days his strong love of music.

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REPORT FROM EUROPE

Great Britain: Science and Labor's Squeak-in

17 October. Despite advance billing, the need for a more vigorous government stimulation of science played neither a starring nor a featured role in the British election campaign that ended 15 October in the narrowest of victories for Harold Wilson's Labor party and its activist ideas. Ever since Wilson proposed, at the annual party conference in Scarborough in 1963, that Labor take as its new campaign theme the harnessing of science to socialism, many have said that the 1964 British election would be the first political campaign, in a major country, in which science was a central issue. The grouping of British government scientific activities and the effect of scientific policy on Britain's economic future were much argued in the year that led up to the overturn of the Conservative party after 13 years in office. But in the last month of campaigning it seemed that, however vital an explicit policy about science and technology may be to a country's economic future, such complex questions have little to do with a politician's intense last-minute serenading of the wavering voter.

Despite the increasing interest in scientific policy among intellectuals and informed officials, immediate or traditional themes dominated British campaign manifestos and speeches: Should Britain continue to develop an independent nuclear force? What was the quality of the Labor and Conservative Front Benches? What were the prospects for continued prosperity? The Conservatives said the British had never had it so good, and the Laborites said the British will have to fight to improve their lot. It is possible that not even these "gut" issues were paramount, and that the outcome depended on the simple judgments that it was or was not