

General Conclusions

The trends of the three processes can be mapped throughout the heavy-element region, and there is reason to believe that the abundance curves will be amenable to quantitative treatment in terms of beta decay rates and of the cross-sections for the neutron- and proton-capture processes. In the past, this has not been possible, for it was not realized that the abundance curve represented a superposition of contributions from several processes. The magic number peaks in the *s*-process and their shifted counterparts in the *r*-process are not as pronounced in the over-all abundance curve as they are in the contributing curves. It is already clear that both the slow and rapid neutron-capture processes operated under conditions of "steady streaming." For instance, in the case of the *s*-process, it appears that the products obtained by multiplying the abundances built through the *s*-process by the appropriate (*n*, γ) cross sections of the stable nuclei are remarkably constant from isotope to isotope, as would be expected on the basis of steady streaming. There is one notable discrepancy, in the case of the element lead. Neutron-capture processes should terminate in a cycling among the lead isotopes at the onset of alpha activity. If steady streaming has occurred, there should be a consequent building up of the abundance of lead, and we find that the abundance as given by Suess and Urey (*11*) is too low, by a factor of approximately 10 to 10², to be consistent with this.

A consideration of the building of the transuranic elements by the *r*-process has enabled us to estimate the numbers of progenitors of U²³⁵ and of U²³⁸. Ura-

nium-235 results from the alpha decay which follows the beta decay of the neutron-rich nuclei produced with *A* = 235, 239, 243, 247, 251, and 255. Beyond *A* = 259, the ultimate decay is probably by spontaneous fission rather than by alpha emission. Uranium-235 results from production at *A* = 238, 242, 246, and 250. Thus U²³⁵ has six odd *A* progenitors while U²³⁸ has four even *A* progenitors. Odd-even pairing energy effects become progressively less important throughout the heavy stable nuclei, and we would expect neutron-capture cross sections to be very nearly equal for odd-*A* and even-*A* elements in the heaviest nuclei. This must indeed be the case in the rapid neutron-capture peak near *A* = 194 (similar to the peak at *A* = 130 in Fig. 1), where the abundances of odd *A*-even *A* are nearly equal—for example, Pt¹⁹⁵/Pt¹⁹⁴ = 1.03. Thus, it appears that the production ratio U²³⁵/U²³⁸ was probably about 1.5 and, in any case, was unlikely to be less than unity. If we suppose that the elements of which the earth is composed were not all built at one moment of time but were built at a uniform rate, starting at the time of origin of the galaxy and extending almost up to the formation of the solar system some 5 × 10⁹ years ago, then, using the ratio of the uranium isotopes found at present in the earth, the age of the galaxy can be calculated. For the case of a production ratio of U²³⁵/U²³⁸ equal to unity, the age is 7.5 × 10⁹ years, while a still greater age is obtained if a production ratio of 1.5 is used for U²³⁵ relative to U²³⁸. The argument for this high value can be restated as follows. At the time of the formation of the solar system, we can calculate that the ratio U²³⁸/U²³⁵ = 3.5. On the basis of production, either in a single

event or continuously, an additional time interval is required to reach the time at which U²³⁸/U²³⁵ ≈ 1.

Finally, it may be remarked that, since the production of the heavy elements (*A* > 60) is a by-product of ordinary thermal cooking that depends on the adulteration of the hydrogen out of which a star forms, it is to be expected that these elements will be synthesized in abundances that are very low compared with the ordinary products of thermal cooking (for example, O¹⁶, Si²⁸, and Fe⁵⁶). This is precisely the case.

References and Notes

1. W. A. Fowler *et al.*, *Bull. Am. Phys. Soc. Ser. 2* 1, 191 (1956).
- 1a. C. L. Cowan, Jr., *et al.*, *Science* 124, 103 (1956).
2. P. W. Merrill, *Science* 115, 484 (1952).
3. J. L. Greenstein, *Mém. soc. roy. sci. Liège* 14, 307 (1954); E. M. Burbidge and G. R. Burbidge, *Astrophys. J.* 124 (1956).
4. J. P. Wild, J. D. Murray, W. C. Rowe, *Nature* 173, 532 (1954).
5. G. R. Burbidge *et al.*, *Phys. Rev.* 103, 1145 (1956).
6. P. R. Fields *et al.*, *ibid.* 102, 180 (1956).
7. F. Hoyle, *Monthly Notices Roy. Astron. Soc.* 106, 366 (1946); *Astrophys. J. Suppl.* 1, 121 (1954).
8. E. E. Salpeter, *Astrophys. J.* 115, 326 (1952); A. G. W. Cameron, *Astrophys. J.* 121, 144 (1955).
9. W. A. Fowler, G. R. Burbidge, E. M. Burbidge, *ibid.* 122, 271 (1955); *Astrophys. J. Suppl.* 2, 167 (1955).
10. W. A. Fowler and J. L. Greenstein, *Proc. Natl. Acad. Sci. U.S.A.* 42, 173 (1956).
11. H. E. Suess and H. C. Urey, *Revs. Mod. Phys.* 28, 53 (1956).
12. A detailed quantitative account of this work is in preparation. This work was supported in part by the joint program of the Office of Naval Research and the U.S. Atomic Energy Commission. We wish to take this opportunity to thank Stanley Thompson and Rosemary Barrett of the University of California, Berkeley, for helpful discussions of material to be published on the properties of the transuranium nuclei including Cf²⁵⁴.
13. C. D. Coryell, *Lab. for Nuclear Sci. Ann. Rept.* (1956).

Nomenclature of Enzymes of Fatty-Acid Metabolism

H. Beinert, D. E. Green, Priscilla Hele,
O. Hoffman-Ostenhof, F. Lynen,
S. Ochoa, G. Popják, R. Ruysen

Spectacular developments during the last few years have led to the isolation in a soluble form of a number of enzymes of fatty-acid metabolism in several independently working laboratories. This circumstance resulted in the denoting of enzymes that catalyze similar reactions

by different names, either according to the substrate attacked or according to the favored equilibrium of the particular reaction. This could lead to confusion among those not working in the field.

The second International Conference on Biochemical Problems of Lipids, at-

tended by representatives of 20 nations and held between 27 and 30 July 1955 at the University of Ghent, Belgium, under the presidency of R. Ruysen, gave an opportunity to iron out these difficulties. A special meeting to discuss problems of nomenclature was convened at the conference. A memorandum by Priscilla Hele and G. Popják, London, was presented and formed the basis of the discussions. There was unanimous agreement, and the conclusions reached are presented here.

Suggested Principles

Before we considered individual enzymes, an agreement was reached concerning the broad principles that should govern the nomenclature.

It is recommended that enzymes be called by a systematic name that should

denote the substrate or substrates acted on and the over-all reaction catalyzed (1). However, the mechanism of the reaction should not be implicit in the name of the enzyme, for further discoveries may change present-day concepts of reaction mechanisms.

Since the systematic names may be unwieldy in everyday use and even when referred to several times in a publication, it appears highly desirable to have trivial names also. For the trivial name, a shortened version of the systematic name is generally recommended.

While it appears desirable to denote the enzymes according to the favored equilibrium of the reactions, this aim cannot be fully realized where an unwritten convention already exists—for example, in the case of enzymes that catalyze oxidations and reductions. These are usually called “dehydrogenases,” irrespective of whether the equilibrium of the reaction favors reduction (reductase) or oxidation (dehydrogenase). A further difficulty may arise in this connection with reactions that have equilibria lying in opposite directions at different pH values. For these reasons, the use of the term *reductase* is not recommended, at least not until the present convention is altered by some future international agreement.

Since it is now well known that, in general, fatty acids are not metabolized unless they are in combination with coenzyme A or other thiols, it is considered unnecessary to include coenzyme A in the terminology. However, in order to indicate that the substrate is not the free acid, it is recommended that the name of the acid radical be used to denote the substrate. For example, *butyryl-dehydrogenase* indicates an enzyme acting on butyryl-coenzyme A; *butyric-dehydrogenase*, on the other hand, would describe an enzyme whose substrate was free butyric acid.

Most of the enzymes of fatty-acid metabolism act on substrates derived from fatty acids of differing (although approximately the same) chain length. It is recommended that in such instances the enzyme be called after that chain length for which it shows the highest

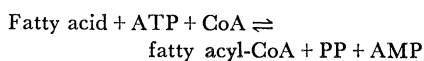
affinity, or, if one optimum chain length cannot be defined, after the range of chain lengths involved.

In all instances where “free” coenzyme A may be considered to be a substrate of the reaction (either explicitly or implicitly), the term denoting the function of the enzyme should be preceded by the prefix *thio*—for example, *thiokinase*, *thiolase*, *thiophorase*.

Individual Enzymes of Fatty-Acid Metabolism

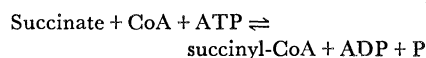
Individually the enzymes concerned in fatty-acid metabolism were considered under five headings according to the reactions they catalyze. These are (i) activation, (ii) condensation and cleavage, (iii) reduction and oxidation, (iv) hydration and dehydration, and (v) transfer reactions.

Activating enzymes. The reaction catalyzed (2) is



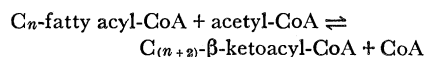
It is recommended that this group of enzymes be called *thiokinases*, with a prefix denoting the main substrate attacked. Thus, the first enzyme in the coenzyme A field, that discovered by Lipmann in 1945 (3), would be called *acetic-thiokinase* (not *acetyl-thiokinase*). The other two enzymes known in this group, one with a chain-length optimum at C₇–C₈ (4) and one with an optimum at C₁₂ (5) are called accordingly *octanoic (caprylic)-thiokinase* and *dodecanoic (lauric)-thiokinase*, respectively. These enzymes at present are generally referred to as “acetate-activating enzyme” (AAE) and “fatty-acid-activating enzymes” (FAAE).

In the construction of the term *thiokinase*, it was considered that, although fatty acyl-coenzyme A may be formed by a number of reactions, the primary activation usually involves a high-energy phosphate group (that of ATP in the case of enzymes of animal origin); thus, the usage of the term *kinase* here is in accord with that current in biochemistry today. It was further agreed that these activating enzymes should be called thiokinases regardless of whether the split of ATP resulted in the production of AMP + pyrophosphate (PP) or in ADP + orthophosphate. Thus the enzyme, discovered by Kaufmann (6), which activates succinic acid according to the reaction



is called *succinic-thiokinase*.

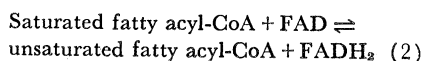
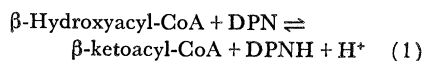
Condensation and cleavage enzymes. The reaction catalyzed is



Lynen *et al.* (7) proposed the name “ β -ketothiolase” for the enzyme(s) that catalyze(s) this reaction, and Green’s group (4) proposed “ β -ketoacyl CoA cleavage enzyme.”

It has been agreed that, although this group of enzymes might also be considered to be transacylating enzymes, the term *thiolase* is the most appropriate name for this class, for it expresses the essentially thiolytic nature of the reaction, the equilibrium of the reaction lying far in the direction of cleavage. The recommended systematic name is β -ketoacyl-thiolase; examples are as follows: *acetoacetyl-thiolase*, β -ketoheptanoyl-thiolase (or β -oxoheptanoyl-thiolase), and so forth. The recommended trivial name is *thiolase*.

Enzymes catalyzing oxidations and reductions. It has been recommended (see the foregoing discussion) that all these enzymes should be called dehydrogenases generically, irrespective of the equilibrium of the reactions. There are two reactions considered in this class:



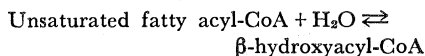
Enzymes that catalyze reaction 1 have been described by both Green’s and Lynen’s groups. Green (4) proposed the name “ β -hydroxyacyl-CoA dehydrogenase”; Lynen’s terminology has been varied: “ β -ketohydrase” (7), “ β -ketohydrogenase” (8), and “ β -ketoreductase” (9).

The recommended systematic and trivial name for enzymes that catalyze reaction 1 is β -hydroxyacyl-dehydrogenase; an example is β -hydroxybutyryl-dehydrogenase.

Enzymes that catalyze reaction 2 have been described by Seubert and Lynen (10) under the name “ethylene reductase,” and three enzymes have been described by the Madison group (4) under the names “butyryl-coenzyme A dehydrogenase” (green enzyme) and “fatty acyl coenzyme A dehydrogenase” (yellow enzymes, Y₁ and Y₂).

The recommended systematic and trivial name for enzymes that catalyze reaction 2 is *acyl-dehydrogenase*; examples are *butyryl-dehydrogenase*, *hexanoyl (caproyl)-dehydrogenase*, and *hexadecanoyl (palmityl)-dehydrogenase*.

Enzymes catalyzing hydration and dehydration. The reaction catalyzed is



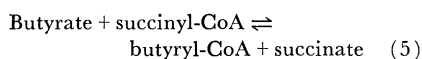
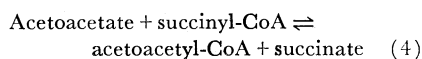
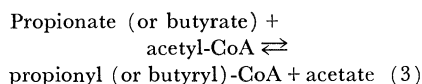
An enzyme that catalyzes this type of reaction has been described by Green (4) and by Ochoa’s group (11, 12). Green’s terminology has been “unsaturated fatty acyl coenzyme A hydrase.” Ochoa’s group called their enzyme “crotonase” in analogy with fumarase.

Dr. Beinert and Dr. Green are on the staff of the Institute for Enzyme Research, University of Wisconsin. Dr. Hele is with the Medical Research Council, Experimental Radiopathology Research Unit, Hammersmith Hospital, London, England. Dr. Hoffman-Ostenhof is with the First Chemical Laboratory, University of Vienna, Austria. Dr. Lynen is with the Institute for Cell Chemistry, German Psychiatric Research Institute (Max Planck Institute), Munich, Germany. Dr. Ochoa is with the department of biochemistry, New York University College of Medicine. Dr. Popják, who was chairman of the special meeting, is with the Medical Research Council, Experimental Radiopathology Research Unit, Hammersmith Hospital, London, England. Dr. Ruyssen, who was president of the conference, is with the Laboratory of Pharmaceutical and Medical Chemistry, University of Ghent, Belgium. The authors plan to publish their proposals in the scientific journals of various nations.

Enoyl-hydrase (or *Enoyl-Hydratase* in German) is recommended as the systematic and trivial name for this group of enzymes; examples are *crotonyl-hydrase* (*but-2-enoyl-hydrase*), *hex-2-enoyl-hydrase*, *oct-2-enoyl-hydrase*, and so forth.

Since crotonyl-hydrase has been obtained in crystalline form (13) and, although of broad specificity, is most active on crotonyl-CoA (14), it has been agreed that the term *crotonase* be retained as the trivial name for this enzyme.

Transferring enzymes. Three reactions are known in this group:



The first of these reactions (reaction 3) was discovered by Stadtman in extracts of *Clostridium kluyveri* (15). Since the reaction involved the transfer of CoA from acetyl-CoA to an acceptor fatty acid, the name "CoA-transphorase" was proposed for the enzyme(s) responsible (16). Stern, Coon, and del Campillo (17, see also 11) have described enzyme

preparations that catalyze reaction 4, and Green's group (4) has reported on preparations responsible for both reactions 4 and 5.

These enzymes may be considered coenzyme A-transferring enzymes, and accordingly *thiophorase* is recommended as a systematic and trivial name for them. The systematic names for the enzymes that catalyze the three reactions (reactions 3, 4, and 5) listed in this group are: (i) *propionyl-acetic-thiophorase* (or generically, *fatty acyl-acetic-thiophorase*), (ii) *acetoacetyl-succinic thiophorase*, and (iii) *butyryl-succinic-thiophorase*.

The differentiation in denoting the acid substrates with the suffix *-yl* or *-ic* in this instance has been dictated by the equilibrium of the reactions.

We believe that these suggestions represent the beginning of an effort to introduce uniformity into the present, somewhat confused, terminology of enzymes of fatty acid metabolism and hope that this subject will be reconsidered in due course by the Commission on Enzymes of the International Union of Biochemistry.

References and Notes

1. O. Hoffman-Ostenhof, *Advances in Enzymol.* 13, 219 (1953).

2. The following abbreviations are used: ATP, adenosine triphosphate; ADP, adenosine diphosphate; AMP, adenosine-5'-monophosphate; CoA, coenzyme A; PP, inorganic pyrophosphate; DPN and DPNH, oxidized and reduced diphosphopyridine nucleotide; FAD and FADH₂, oxidized and reduced flavine-adenine dinucleotide.
3. F. Lipmann, *J. Biol. Chem.* 160, 173 (1945).
4. D. E. Green, *Biol. Revs. Cambridge Phil. Soc.* 29, 330 (1954).
5. A. Kornberg and W. E. Pricer, *J. Biol. Chem.* 204, 329 (1953).
6. S. Kaufmann, in *Phosphorus Metabolism*, W. D. McElroy and B. Glass, Eds. (Johns Hopkins Press, Baltimore, 1951), vol. 1, p. 370.
7. F. Lynen, *et al.*, *Angew. Chem.* 24, 687 (1952).
8. F. Lynen, *Bull. soc. chim. biol.* 35, 1061 (1953); O. Wieland, *Klin. Wochschr.* 32, 385 (1954).
9. F. Lynen, *Federation Proc.* 12, 683 (1953); ———, *Nature* 174, 962 (1954).
10. W. Seubert and F. Lynen, *J. Am. Chem. Soc.* 75, 2717 (1953).
11. F. Lynen and S. Ochoa, *Biochim. et Biophys. Acta* 12, 299 (1953).
12. J. R. Stern and A. del Campillo, *J. Am. Chem. Soc.* 75, 2277 (1953).
13. J. R. Stern, A. del Campillo, I. Raw, *J. Biol. Chem.* 218, 971 (1956).
14. J. R. Stern and A. del Campillo, *ibid.* 218, 985 (1956).
15. E. R. Stadtman, *J. Cellular Comp. Physiol.* 41, suppl. 1, 89 (1953); E. R. Stadtman and T. C. Stadtman, *Ann. Rev. Microbiol.* 7, 143 (1953).
16. H. A. Barker, in *Phosphorus Metabolism*, W. D. McElroy and B. Glass, Eds. (Johns Hopkins Press, Baltimore, 1951), vol. 1, p. 204.
17. J. R. Stern, M. J. Coon, A. del Campillo, *Nature*, 171, 28 (1953).

André Mayer, Scientist, Soldier, Statesman

André Mayer, who died in Paris on 27 May 1956, was born in that city on 9 November 1875, the son of one of the many Alsatians who had left their native province in 1871 after the German annexation. After distinguished studies at the Lycée Condorcet, he entered the Medical School of the University of Paris at the age of 16, then interned with Charcot. After a few years spent as the senior assistant of Dastre, himself the closest assistant and successor of Claude Bernard, Mayer undertook to equip and staff at his own expense a laboratory in an old house next to the Collège de France, which he maintained until World War I as an active research center.

His first major contribution consisted of several classic papers (1901–05) on

thirst. He demonstrated that this sensation arises when osmotic pressure increases, affecting both the mucous membranes of the throat and, more importantly, central structures, or "osmoreceptive centers." This first correlation between a sensation and a physical measurement elicited vivid interest, not only among physiologists and psychologists, but also among philosophers.

In collaboration with Victor Henri, André Mayer established many of the now classic colloidal properties of living matter, including the concept that the structure of protoplasm is that of a gel. With Schaeffer and Terroine, he established the concept of "cellular constants," characterizing the interrelation between various components of each tis-

sue. For example, he demonstrated the relationship between the "lipocytic ratio" (cholesterol: fatty acids) and the degree of hydration of cells. He demonstrated that "physical" properties—for example, osmosis, capillarity, and diffusion—are not adequate to interpret urinary excretion but that tubular reabsorption must involve specific chemical transport and active secretion. His personal friendship with Pierre Curie led Mayer to the first observations of the effects of radioactivity on biological materials. Curie had come to consult him on a skin sore just above the waist, which Mayer correctly surmised to be due to Curie's habit of carrying a small radioactive sample in his right vest pocket. This led him to the first demonstration of the destructive effect of radiation on colloids, cells, and small mammals. With Armand Delile, Mayer devised in 1913 the first "synthetic" medium for the culture of microorganisms. His field of investigation during that period extended to many other topics, in particular to the study of diabetes: for example, he was the first to examine the effect of superimposing the removal of other endocrines, in particular the adrenals, on pancreatectomy.

Came World War I. André Mayer volunteered immediately and served as regimental surgeon on the Verdun front.