but the period of disruption seemed to depend on the supplier from which the rats were obtained. This result suggests that a difference in strain or diet may play a role here. Levinson also discussed the difficulties of training rats on avoidance schedules.

Joseph V. Brady (Walter Reed Army Institute of Research) described a different aspect of avoidance behavior. The Walter Reed laboratories have emphasized the chronic features of avoidance behavior and have examined various endocrine and somatic correlates of prolonged exposure. In recent experiments, rhesus monkeys exposed to 72-hour avoidance sessions once per week show, during the first few sessions, high levels of adrenal steroid output and high response rates on the avoidance schedule. With repeated sessions, steroid output falls to or below basal levels and the behavior becomes more efficient. Monkeys subjected to 72-hour avoidance sessions before undergoing ionizing radiation from a source emitting 10,000 r display enhanced radio resistance, and live significantly longer than controls. The elevated steroid levels produced by the avoidance procedure may play a part in this phenomenon.

Roger T. Kelleher (Harvard Medical School) is the new president of the Society and Larry Stein (Wyeth Laboratories) is the new vice president.

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Carbon-14 in Clinical Research

A conference on metabolic studies with carbon-14-labeled substrates and continuous assay of $C^{14}O_2$ in expired air was held at the University of Chicago 25–26 November 1963. These studies are of potential value in clinical research because in man it is seldom feasible to investigate intermediary metabolism in the same detail as in animals where—in addition to blood, excreta, and expired air—organs and tissues are readily available for radiochemical analysis. Continuous assay of expired air yields patterns which give direct information on the rate of respiration of $C^{14}O_2$ formed by the catabolism of substrates labeled in specific positions with carbon-14.

One of the pioneers in this field, Bert Tolbert (Colorado) observed that the basic concept of the method is that catabolic rates are controlled by the dynamics of intermediary metabolism and physiology. If one can measure the rates of respiration of $C^{14}O_2$ from a sufficient variety of labeled substrates it should be possible to define rather clearly and quantitatively the relative importance of the major metabolic pathways in health and disease. In terms of metabolic pathways, the oxidation of most intermediates to carbon dioxide has been well worked out during the past 15 years. In contrast, except in a general way and under quite special conditions, very little is known about the dynamics of intermediary metabolism in the intact subject—the mixing times, pool sizes, turnover rates, and competition between alternative pathways. The development of a body of knowledge on the dynamics of the system and the determination of the dynamics of intermediary metabolism is an essential part of the evolution of the technique that was discussed at the conference.

No formal papers were presented, but there were special discussion periods related to instrumentation, data processing, interpretation of activity-time curves, design of experiments, and radiological safety. A typical instrument system consists of (i) a face mask, helmet, or hood to collect expired air; (ii) a ventilometer; (iii) a radiation detector; and (iv) a carbon dioxide analyzer. For studies of total metabolism an oxygen analyzer is added. A closed system (undiluted expired air collected with a face mask) is suitable for normal subjects and for some patients. An open system with a helmet or a hood is more comfortable for sick or weak subjects, but introduces problems associated with dilution of expired air. Calvin Long (Harvard) reported that air-flow rates of 35 to 40 liters per minute are necessary when working with very sick patients.

The radiation detector in most systems is a flow-through ionization chamber with a vibrating-reed electrometer. A well-calibrated chamber should detect about 0.2 nanocurie (nc) of $C^{14}O_2$ per liter. Don Charleston (Chicago) discussed the Argonne Hospital instrument that uses a 4-π Geiger-Mueller counter which can detect 0.8 nc/liter or 0.5 nc/mmole. Regardless of the type of detector used, all systems are characterized by a large output of information which can only be handled conveniently by machine methods. W. F. Yasdick (Datex Corp.) discussed several methods for analog-digital conversion to make data available for electronic computers. He described in detail the advanced data-logging equipment of the Argonne system. Such installations are costly when they are custom-made, but if investigators could agree on their requirements, less expensive production models would become available.

The curve of radio-activity incorporated into CO_2 recorded during the first several hours after administering a labeled substrate which is oxidizing rapidly (for example, glucose-1-C^{14}), is fairly typical for each intermediate, is quite reproducible in the same subject, and is complex. Its configuration is determined by at least three factors: (i) the behavior of the labeled substrate within its particular metabolic pool, (ii) the rate of intracellular oxidation, and (iii) the kinetics of the carbon dioxide pool through which $C^{14}O_2$ must pass enroute to expired air.

James Robertson (Brookhaven National Laboratory) led off the discussion with a critique of methods that analyze the system as though it consisted of well-mixed, connecting compartments. The explicit solution of this model is a series of exponential terms. Some of the participants considered the results an exercise in curve fitting, and challenged the practice of assigning a physiological or anatomical identification to every or any exponential term. Max Kleiber (Davis) remarked that the final exponential term derived from a curve of decreasing radioactivity is more often a function of the duration of the experiment than of a particular physiological process. In the case of the carbon dioxide pool, LeRoy (Chicago) and Okita (Northwestern) described their application of the theory of indicator-dilution methods advanced by Meier and Zierler [*J. Appl. Physiol.* **6**, 731 (1954)]. The procedure, which has been programmed in Fortran, computes pool size (V), flow (F), and mean transit time ($\bar{t}$). The inputs for this program are digitalized data from continuous assay of expired air obtained during 1 to 2 hours after administration of a dose of $NaHC^{14}O_3$.

The usefulness of information

about the carbon dioxide pool was debated at length. Nome Baker (Veterans Administration, Los Angeles) suggested that $C^{14}O_2$ from a single injection of bicarbonate behaves in the same fashion as that produced by intracellular oxidation. Therefore the results from bicarbonate can be used to predict the behavior of metabolic $C^{14}O_2$. Although some disagreed, Baker's position was supported by LeRoy and Okita who described experiments where $C^{14}O_2$ specific activity was monitored during and after infusion of $NaHC^{14}O_3$ at a constant rate. The incorporation of carbon-14 increased to a maximum and then declined at complementary rates. The curve for the declining rate had the same configuration as that following a single dose.

Uncertainty about interpretation has led most clinical investigators to report results simply as percentage of carbon-14 recovered at various times. Kleiber described his elegant studies of the precursor to product relationship in the constituents of milk from dairy cattle. By integrating curves of specific activity plotted against time for both precursor and products, he calculates a transfer quotient, that is, the amount of carbon arriving in a product from a particular precursor. The transfer quotient does not require information about intervening pools and can be obtained in situations where it is not possible to follow changes in specific activity of the precursor pool so long as information is available on a common pool such as that of carbon dioxide.

A number of clinical applications of the continuous assay method were described by Edgar Gordon (Wisconsin), Walton W. Shreeve (Brookhaven), and others. The application to pharmacological and physiological research with intact small animals was reviewed by George Okita (Northwestern). There are obvious advantages in working with intact, unanesthetized animals. The conferees agreed that it was difficult to evaluate some experimental studies because of variations in the terminology used to report the findings. A number of suggestions were offered to remedy the situation, but no consensus was reached.

A delightful feature of the conference was an after-dinner address by Willard F. Libby (U.C.L.A.) who reviewed the history of the discovery of carbon-14. His presence was particularly appropriate because of his enthusiastic support of efforts to exploit the unique features of radiocarbon in biological and medical research.

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Forthcoming Events

May

11–13. American **Science Film** Assoc., annual, Washington, D.C. (ASFA, 704 17 St. NW, Washington, D.C. 20006)

14–16. American Inst. of **Industrial Engineers**, 15th annual conf., Philadelphia, Pa. (W. J. Jaffe, Dept. of Management Engineering, Newark College of Engineering, Newark, N.J.)

14–16. Society of **Technical Writers and Publishers**, 11th annual convention, San Diego, Calif. (C. M. Johnson, U.S. Navy Electronics Laboratory, San Diego 92132)

16. **Southern California Acad. of Sciences**, annual, Northridge. (R. B. Loomis, Dept. of Biology, Long Beach State College, Long Beach, Calif.)

16–2. European **Energy** Conf., Paris, France. (H. Perdon, Institut Français des Combustibles et de l'Energie, 3, rue Henri-Heine, Paris 16e)

17–20. American Inst. of **Chemical Engineers**, natl. meeting, Pittsburgh, Pa. (F. J. Van Antwerpen, 345 E. 47 St., New York, N.Y. 10017)

18–20. **Radiation Research** Soc., 12th annual, Miami Beach, Fla. (G. D. Adams, Radiological Laboratory, Univ. of California Medical Center, San Francisco 22)

18–20. **Water**, 2nd conf., Technical Assoc. of the Pulp and Paper Industry, Green Bay, Wis. (H. O. Teeple, TAPPI, 360 Lexington Ave., New York, N.Y.)

18–21. Society of **Economic Paleontologists and Mineralogists**, Toronto, Ont., Canada. (R. H. Dott, Box 979, Tulsa 1, Okla.)

18–21. American Assoc. of **Petroleum Geologists**, 49th annual conv., Toronto, Ont., Canada. (R. E. King, American Overseas Petroleum, Ltd., 485 Lexington Ave., New York, N.Y. 10017)

19–20. Council on **Medical Television**, 6th annual, Atlanta, Ga. (S. A. Agnello, Duke Univ. Medical Center, Box 3163, Durham, N.C. 27706)

19–21. **Microwave** Theory and Techniques, intern. symp., New York, N.Y. (H. L. Browman, Airborne Instruments Laboratory, Deer Park, N.Y. 11729)

19–22. **German Metallurgical** Soc., general assembly, Bremen. (Deutsche Gesellschaft für Metallkunde, An der Alteburger Mühle 12, Köln-Marienburg, Germany)

19–22. German Soc. for **Applied Optics**, 65th, Gmunden am Traunsee. (H. Volkmann, Deutsche Gesellschaft für Angewandte Optik, Zeppelinstr. 23, 7920 Heidenheim, Germany)

19–23. **Energy Metabolism**, 3rd symp., Ayr, Scotland. (European Assoc. for Animal Production, Corso Trieste, 67, Rome, Italy)

19–30. International **Electrotechnical** Commission, general meeting, Aix-les-Bains, France. (American Standard Assoc., 10 E. 40 St., New York 16)

20. Memorial Hospital of Long Beach, **medical staff** symp., Long Beach, Calif., (G. X. Trimble, 2801 Atlantic Ave., Long Beach 6)

20–23. Canadian Assoc. of **Geographers**, 14th annual, London, Ont. (CAG, P.O. Box 421, Ottawa, Ont., Canada)

20–28. Modern Methods for **Analysis of Organic Compounds**, symp., Eindhoven, Netherlands. (Gesellschaft Deutscher Chemiker, Postfach 9075, Frankfurt-am-Main, Germany)

21–22. American **Geological** Inst., Toronto, Ont., Canada. (D. M. Kinney, U.S. Geological Survey, Washington, D.C.)

21–22. Southern **Textile Research** Conf., Hilton Head Island, S.C. (American Assoc. of Textile Chemists and Colorists, P.O. Box 886, Durham, N.C.)

21–23. **Minerals**, 9th annual symp., Moab, Utah. (J. C. Fox, Soc. of Mining Engineers, 345 East 47 St., New York, N.Y.)

21–23. California Soc. of **Professional Engineers**, annual, Palm Springs, Calif. (J. C. Huisking, 970 Hillcrest Dr., Pomona, Calif.)

23–24. **Radiosensitizers and Radioprotective Drugs**, 1st intern. symp., Milan, Italy. (R. Paoletti, Pharmacology Inst., Via A. del Sarto, 21, Milan)

24–28. Near and Middle East **Medical** conf., Istanbul, Turkey. (P. Ponthus, Institut de Radiologie et de Lutte Contre le Cancer, Hotel-Dieu de France, Beirut, Lebanon)

24–28. Institute of **Food Technologists**, 24th annual, Washington, D.C. (A. Kramer, Dept. of Horticulture, Univ. of Maryland, College Park)

24–29. International Federation for **Information Processing**, global conf., New York, N.Y. (A. P. Speiser, I.B.M. Research Laboratory, Zurichstr. 108, Adliswil-Zurich, Switzerland)

25. **Organic Solid State**, 2nd symp., Franklin Inst., Philadelphia, Pa. (M. M. Labes, Franklin Inst. Laboratories, 20th and The Parkway, Philadelphia 3)

25–27. American **Gynecological** Soc., Hot Springs, Va. (American Gynecological Soc., 3800 Reservoir Rd., Washington, D.C. 20007)

25–27. **Power Reactors and Radioisotopes**, Canadian Nuclear Assoc., Toronto, Ont. (CNA, 19 Richmond St. West, Toronto 1, Ont.)

25–29. Society of **Physical Chemistry**, 14th annual, Bordeaux, France. (G. Emschwiller, Soc. de Chimie physique, 10, rue Vauquelin, Paris 5e, France)

26–29. **Water Studies**, 17th intern. conf., Liége, Belgium. (Cebedeau—Journees 1964, 2, rue A. Stevart, Liége)

27–29. American **Ophthalmological** Soc., Hot Springs, Va. (AOS, 108 E. 68 St., New York, N.Y. 10021)

27–29. Canadian **High Polymer** Forum, 12th, Ste. Marguerite, Quebec. (H. Daoust,