





PROCEEDINGS OF A SYMPOSIUM  
SPONSORED BY THE  
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# OXYGEN

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CONNECTIVE TISSUE:  
INTERCELLULAR MACROMOLECULES

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October, 1964, **157**, No. 1

## Preface

THIS VOLUME contains the proceedings of the sixth annual basic science symposium of the New York Heart Association. Our objectives in sponsoring these scientific meetings have been to bring together the most expert, productive workers in a specific area of the life sciences to present new and preferably fundamental knowledge in that area to an audience oriented toward both clinical and basic scientific medicine. In this way the Association hopes to catalyze the generation of new ideas and endeavors which might otherwise lie dormant.

The subjects of these symposia have not directly concerned diseases of the heart, but have dealt with fundamental aspects of the function of the circulatory system, including salt and water metabolism, the plasma membrane, the physics and chemistry of the myocardium, connective tissue, differentiation and development, and, this year, oxygen. It is our conviction that the most important advances in biological and medical science will come from investigations which are not too narrowly conceived in terms of current notions as to the nature of disease.

HERBERT CHASIS, *President*  
*New York Heart Association*

# General Introduction

FEW SUBSTANCES are as familiar as oxygen. Everyone knows that it is essential for life on earth and few are unaware that it is involved in respiration and in a wide variety of chemical and biological reactions.

But, beyond these superficial levels of understanding, mystery appears. For those seeking to learn the basic organization and behavior of matter and to elucidate the laws that govern biological and physicochemical action, each discovery about oxygen immediately poses new problems. Some that are considered in this symposium are the relationships between structure and chemical behavior of oxygen; its transport and utilization within living organisms; the reactions by which oxygen supplies energy for vital processes; the critical balance between oxygen as a useful and as a toxic agent. Because each of these problems originates from some undiscovered fundamental concept, and often requires either a new theoretical or experimental approach for its solution, subspecialties in oxygen have arisen. Each of these subspecialties differs somewhat in its orientation, its basic concepts, its formulations, its techniques, and its language. Therefore, it is not surprising that a scientific isolationism has developed, so that subspecialists in one aspect of oxygen are apt to find difficulty in exchanging ideas with those versed in other aspects. As a corollary, the "generalist" in oxygen has virtually disappeared.

Discontent with this situation prompted the present meeting. The papers and discussions that follow comprise a record of the proceedings of the sixth annual symposium held under the auspices of the New York Heart Association. The topic and program were selected by a special committee of distinguished scientists whose names are listed elsewhere in this volume. This committee provided the engine for this meeting. But, for getting the engine started and keeping it running smoothly, credit goes to Miss Janet Newkirk, Mr. Charles Campbell, and to their staff at the New York Heart Association.

One of the traditional and pleasant responsibilities of the symposium committee is the singling out of one distinguished scientist for special recognition as "Honorary Chairman" of the meeting. For this meeting, the committee chose Dr. Dickinson W. Richards, Professor of Medicine Emeritus, Columbia University College of Physicians and Surgeons, who is well known to all of you for his studies on the interplay of the respiration and circulation in gas exchange.

Finally, all the participants are indebted to the editorial staff of the *Journal of General Physiology* for invaluable help in readying the papers for publication.

ALFRED P. FISHMAN

# Structure and Function of Oxygen

CHAIRMAN: DAVID RITTENBERG

Professor, Department of Biochemistry, College of  
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## Introduction

THE ROLE of a chairman at a scientific session is limited by tradition. It is not expected that he will present new theories or experimental facts, for that is the function of those who will follow him. On the other hand, it is expected that he will say something profound, summarizing the results of years of reflection on the subject of the symposium. Unfortunately, this is a very difficult thing to do, and more especially this morning since I am restricted in that the first speaker will tell us the history of the subject. However, having in my earlier days been a chemist, I cannot refrain from telling you something about the subject, oxygen.

This, as all chemists know, is a quite unusual molecule, especially for one that is so simple. It is highly reactive, and, in view of the suboxidized state of the earth, of the large excess of compounds available for oxygen to oxidize, it is quite extraordinary that any oxygen exists at all.

Further, the composition, from the astronomical point of view, of our immediate vicinity indicates that there is a large excess of hydrogen in the universe. Indeed, over 90 per cent of the atoms in the universe are hydrogen, and one would expect that in the course of periods of time of which the astrophysicists speak, all the oxygen would be combined with the hydrogen or with the carbon or iron. However, this is not the case, at least on the earth. There can be little doubt, however, that when the earth was newly born, there was no oxygen in the atmosphere, and that the atmosphere contained instead methane, ammonium, and other reduced compounds, resembling the atmosphere we now observe on Jupiter.

In this anaerobic environment, organic compounds of greater or lesser complexity were synthesized by the reactions first discovered by Miller (*J. Am. Chem. Soc.*, 1955, **77**, 2351). Electrical discharges and ultra-violet light acting upon methane and ammonium will in the course of time synthesize organic compounds which, dissolved in the oceans, produce a rather dilute solution of a large number of organic compounds. A stationary state, of course, was eventually reached, because in this world things don't all go one way. There were at the same time oxidative reactions which destroyed these compounds, producing carbon dioxide. It is likely, I think, that peroxide formed by the autolysis of water was the oxidizing agent.

This steady-state existed for a long time, until, by pure chance, there must have been formed a compound having catalase-like activity, having the ability to destroy peroxide with the formation of oxygen, and, as a

result of this, the solution in the immediate vicinity of this catalase-like substance was protected from oxidation by peroxide. In its immediate vicinity, the concentration of these organic compounds must have grown and grown, giving an opportunity, again by chance, for producing a second molecule of this catalase-like substance. Eventually, this protected solution must have grown and, in a sense, must have duplicated itself, because it gave the opportunity to form more and more catalase, which permitted the solution to increase in concentration.

Eventually there could have developed, again by chance, a compound with the ability to activate gaseous hydrogen. We know such compounds now, and, in fact, copper uroporphyrin has such properties. It activates gaseous hydrogen. This would provide a mechanism for reducing compounds with hydrogen and gaining energy.

This energy could be used to synthesize energy-rich substances of various forms. It is not to be assumed that these catalysts were the same as those we see today, because their protein portion, if they have one, was undoubtedly very simple compared to what is now available to these substances.

Whatever primitive life forms developed in this medium could obtain an adequate supply of energy from the reduction of carbon dioxide by hydrogen.

However, hydrogen, as we know, is lost from the earth's atmosphere because the gravitational potential is not sufficient to hold it; and so, over a period of time, hydrogen evaporated from the earth's surface, and eventually the time came when there was not enough energy to keep things moving. At that time, photosynthesis either had to be invented or everything would have perished. Since we are all here today, it is clear that some photosynthetic mechanism arose.

Once photosynthesis was developed, simple though the mechanism was at that time, evolution was clearly on its way to produce the more highly evolved forms that we see today. Hydrogen gas became unimportant, and vanished from the surface of the earth.

After this first chance creation of a photosynthetic apparatus, evolution was inevitable, and on that sunny day on which this photosynthetic apparatus first arose, this symposium was predestined.

DAVID RITTENBERG

# The Natural History of Oxygen

MALCOLM DOLE

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**ABSTRACT** The nuclear reactions occurring in the cores of stars which are believed to produce the element oxygen are first described. Evidence for the absence of free oxygen in the early atmosphere of the earth is reviewed. Mechanisms of creation of atmospheric oxygen by photochemical processes are then discussed in detail. Uncertainty regarding the rate of diffusion of water vapor through the cold trap at 70 km altitude in calculating the rate of the photochemical production of oxygen is avoided by using data for the concentration of hydrogen atoms at 90 km obtained from the Meinel OH absorption bands. It is estimated that the present atmospheric oxygen content could have been produced five to ten times during the earth's history. It is shown that the isotopic composition of atmospheric oxygen is not that of photosynthetic oxygen. The fractionation of oxygen isotopes by organic respiration and oxidation occurs in a direction to enhance the  $O^{18}$  content of the atmosphere and compensates for the  $O^{18}$  dilution resulting from photosynthetic oxygen. Thus, an oxygen isotope cycle exists in nature.

## I. INTRODUCTION

Although it is estimated that oxygen is only the third most abundant element cosmically (1) coming behind hydrogen and helium, in that order, it is the most abundant element on the earth's crust, which is important for the living race as oxygen is essential for life.

As we shall see later, oxygen was very probably not present in the early atmosphere of the earth, so it is interesting to consider how oxygen arose in the atmosphere, whether its abundance is now changing, what its isotopic composition is, and how the latter varies between samples of oxygen from different sources. Furthermore, there is probably a close connection between the origin of life on this planet and the growth in the abundance of atmospheric oxygen as recently emphasized by Berkner and Marshall (2). Before considering the interesting factors involved in the development of atmospheric oxygen, however, we shall take up first the history of the formation of the element oxygen in the cosmos. It should be emphasized that many of the conclusions described below must be considered not in the same light in which we view well grounded scientific laws and principles, but rather as the best

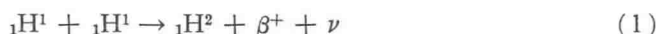


intelligent guesses and deductions that we can now make on the basis of presently available facts and theory.

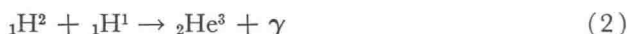
## II. COSMIC FORMATION OF OXYGEN

It is believed that the energy radiated by a star throughout most of its life comes from the so called hydrogen-burning nuclear reaction in which hydrogen is converted to helium (3). If this is true, then at zero time the universe must have consisted largely and probably solely of hydrogen, because there are few nuclear reactions which spontaneously produce hydrogen. In other words, hydrogen is continually being converted to helium and heavier elements and because it is the most abundant element in the universe today it must have been present in overwhelming amount and very possibly completely pure at zero time.

The hydrogen-burning reaction in which helium is produced is the most efficient energy producer, but the actual mechanism probably depends on the temperature of the star. At relatively low temperatures and in the early stages of a star's life before much  $\text{He}^4$  has been produced, the hydrogen-burning chain reaction consists of the following steps:



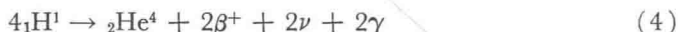
where  $\beta^+$  represents the positron and  $\nu$  the neutrino,



and



where  $\gamma$  represents a gamma ray photon. The total energy yield is 26.2 Mev (equivalent to  $6 \times 10^8$  kcal per mole of  ${}_2\text{He}^4$ ) for the net process which is



(There is a 2 per cent energy loss due to the production of the neutrino.) There are other mechanisms for He formation but the above is believed to be the most important.

As the hydrogen is consumed in the core of the star to form helium, no further nuclear transformations can take place until both the temperature and density have greatly increased. At temperatures of  $10^8^\circ\text{K}$  and densities of  $10^5 \text{ gm cm}^{-3}$   ${}_6\text{C}^{12}$  can be produced by the nuclear reaction



with an energy release of 7.3 Mev per atom of  ${}_6\text{C}^{12}$ . This reaction probably