SIR VICTOR NEGUS

BIOLOGY OF RESPIRATION

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by

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FOREWORD

THE basic interest of John Hunter was the study of life. Respiration, the ability to breathe, is the first essential of life. When respiration ceases, life gives way to death. All else is, therefore, subordinate to this one function. Respiration and life are indivisible. The only other characteristic of life is the ability to reproduce. If reproduction fails the species comes to an end. Hunter studied both these features of life and his museum contained much material on respiration.

Sir Victor Negus has devoted a life-time of study to this subject and on essentially Hunterian lines. Since 1921, a period of 44 years, he has worked on it in the Royal College of Surgeons. He has also worked in the London Zoo, in the Department of Physiology at King's College London, and at the Ferens Institute of the Middlesex Hospital Medical School, but his main workplace has been in the laboratories of the College. He acknowledges his debt to the inspiration and guidance of those two great men, Sir Arthur Keith and Professor Wood Jones, but it is clear that to only one man is due the credit of this monumental work, namely Sir Victor.

The presentation of the material that forms the substance of his "Biology of Respiration" now forms an integral part of the Hunterian museum. Hunter would have rejoiced to see this splendid display of material drawn from nearly 500 specimens collected, dissected and presented by Sir Victor himself. It is a monument to his life's work and this book is essentially both a catalogue and a guide to the sections of the museum dealing with Respiration in its many phases.

The book, in addition to being fully descriptive and illustrated, goes beyond what a museum display can achieve in that it carries the description of the biology of respiration to the ultimate biochemical activity of the cells. In this Sir Victor is enabled to use knowledge and learning that was not available to Hunter, but how Hunter would have rejoiced to know about it!

In addition to almost half a century of work on this Hunterian subject, Sir Victor has given much more to the Hunterian Museum through his tireless and selfless devotion. His service on the Board of Hunterian Trustees culminated fittingly in his election as Chairman of that important body. It is the hope of everyone in the College that he will be able to continue in this important post for many years.

The specimens on which his book is based rest in the newly built and re-organised Hunterian Museum; a renovation necessary after the holocaust of 1941. The rehousing of the Museum was the work of many, but to no one is more credit due than to Sir Victor Negus who has provided enthusiasm, sound counsel, inspiration, persistence, perseverance and example over the many years needed for this great task. His specific contribution of his collection of specimens illustrating the biology of respiration and their presentation within such important sections of the Museum will give pleasure and profit to many generations. So also will his book. The College is grateful and will be for ever in his debt.

January 1965. RUSSELL BROCK

PREFACE

THIS is not intended to be a text book, but rather a monograph recording my personal interpretation of a complex subject As a rhinologist and laryngologist it has been my desire through many years of clinical practice to learn something of fundamental principles, without which the interpretation of disordered states is difficult and often impossible; with this as a basis I have found the greatest interest in studying the respiratory mechanisms of all species, whether vegetable or animal.

I have had the privilege and great advantage of working for forty-three years in the Royal College of Surgeons, by the courtesy of successive Presidents and Council; there one feels the inspiration of the great collection built up originally with almost incredible effort by the great master of the scientific approach to medicine and surgery. I firmly believe that the right approach is that taken by John Hunter, by whom nothing in the world of nature was overlooked in his search for information.

In these surroundings, working under the patronage of such great successors to Hunter as Sir Arthur Keith, Professor Frederic Wood Janes and Mr. R. H. Burne, I have been given unrivalled facilities and encouragement, supplemented by studies in the laboratories of the Zoological Society of London and in the Ferens Institute of the Middlesex Hospital Medical School. During a busy life in clinical work these opportunities have afforded great interest, which continues even when clinical practice has been given up as old age advances.

Not only from Conservators of the past, but also from the present holder of the post, Professor Causey, I have received very considerable support, not only in being enabled to rearrange the collection of specimens I have built up since 1921 but also in practical help and advice.

Professor Causey has been kind enough to help me by putting the subject matter for this monograph into orderly sequence and he has also gone to the trouble of reading the text, not only once but even a second time, with great advantage to clarity of expression and the elimination of inaccuracies.

Miss Dobson, Curator of Anatomy, has given me much help in the arrangement of specimens and in the provision of information from her wide store of knowledge; like many others I am most grateful to her. I have also been provided with all the necessary facilities for physiological research, first in Professor McDowall's department at King's College and later in the Ferens Institute and in Professor Slome's laboratories; Professor Slome has been kind enough to read the manuscript and to keep the opinions expressed within the bounds of physiological truth.

In this department I have derived much benefit from the expert neurophysiological knowledge of Doctor Barry Wyke, who has written the section on the central control of respiration and also that on the important subject of carbonic anhydrase; he has also read and commented on the text of the book.

The expansion of the Royal College of Surgeons with its many departments has allowed me to consult authorities on various aspects of respiration. Doctor Sloane Stanley gave me help on tissue respiration and Doctor Long, head of the Department of Biochemistry, read and corrected what I had compiled on this subject; he assured me that the interpretation is accurate as far as it goes.

Doctor Nunn, with an intimate knowledge of respiratory exchanges, has made many additions and alterations to that section.

Doctor Eastoe, of the Department of Dental Science, gave me valuable information regarding the physical properties of mucus, a subject of much interest and considerable importance.

It is obvious that I have taken advantage of the expert knowledge available in the Royal College of Surgeons and I give my sincere thanks to all who have helped in bringing intelligibility and as little inaccuracy as possible to this monograph.

At the same time I would emphasise that none of these authorities are answerable for inaccurate statements, since the arrangement and writing of the text are my own responsibility.

Many years study in the Hunterian Museum has, I trust, imbued me with an appreciation of the approach followed by the great master; if it is thought that the results are in any way worthy of his example I shall be more than satisfied.

VICTOR NEGUS

London, 1964

ACQUISITION OF ANATOMICAL MATERIAL AND FACILITIES FOR RESEARCH

THROUGH the courtesy of various Presidents and Council and Conservators of the Royal College of Surgeons of England, I have acquired a considerable number of specimens from the stores and have included these in certain sections of the Museums, particularly in that section of the Hunterian Museum devoted to Respiration, of which most of Hunter's specimens had been destroyed. I have also had facilities for research at the College, with skilled assistance from Mr. S. Steward, Mr. Bartlett and more recently from Mr. Drewell and Mr. Edwards.

Work in the laboratories of the Zoological Society of London provided many specimens, more recently added to by Doctor Osman Hill.

For four years I was Curator of the Ferens Institute of the Middlesex Hospital Medical School and am greatly indebted to the Directors for the facitilies provided, which allowed me to carry out various researches and also to make Reconstruction models of the nose of animals, most of the work on which was carried out by Mr. D. Bishop, the Chief Technician.

Professor Cunningham has given me help and Doctor Walter of the Department of Pathology took part with me in investigations of the cutaneous permeability of eels, an important line of approach to interpretation of the function of mucus and the passage of fluid through mucous membranes. Doctor Walter has also made various constructive criticisms of value.

Various specimens were presented by the late Sir Frank Colyer from his unrivalled odontological collection and others by the British Museum, *Natural History*, The Marine Biological Laboratory, Plymouth, The Haslemere Educational Museum, The Freshwater Biological Association, Ambleside, by Doctor Underwood of the Faculty of Agriculture, University of the West Indies, Professor Goldby of St. Mary's Hospital, Doctor Chesterman, Mr. Donald Leney, Mr. T. G. Wilson and the Director of the Peter Redpath Museum, Montreal. Acknowledgements are made for the gift of specimens in the appropriate places.

Doctor Tompsett, of the Royal College of Surgeons, has provided casts of the tracheo-bronchial tree of various species, and also of the air sacs of birds.

During the course of the last year I have had the co-operation in certain aspects of research of Doctor John Kirchner, Professor of Otolaryngology at Yale University; he also read and usefully criticised the whole book, for all of which I am grateful.

In the glossary the numbers of specimens in the Hunterian Museum are given; it was to describe the collection in Series M (Respiration) that this monograph was written.

CONTENTS

INTRODUCTION

A VITAL necessity of all living tissues is oxidative metabolism to release energy by chemical change, an end product of which is carbon dioxide; this process can only take place in watery solution.

There are differences in the details of this mechanism dependent on or adapted to the environment of the individual, whether aquatic or terrestrial, with many and varied modifications, especially in species with lungs; the various methods adopted will be considered on the similarity of the functional plan and will therefore transgress the boundaries of classification by species.

It is desirable, at the commencement, to outline some general principles governing the transfer of oxygen from the environment, whether aquatic or terrestrial, to the cells of the individual plant or animal; oxygen can only reach the tissues after it has passed through the surface covering of the animal.

There are four main types of respiratory mechanism which must be mentioned at the outset, with the object of clarifying the general principles of evolutionary adaptation.

The first method is by diffusion of oxygen through the surface membrane, with no specialization for respiration; the second is the use of gills with increased surface; the third is the formation of pits in the surface of the body later extended to form tubules or tracheae carrying oxygen to all parts of the body; and the fourth is the development of a pulmonary system, with tubes or bronchi dividing repeatedly into a multitude of fine air passages terminating in minute air sacs, the loculated subdivisions of which are lined by a specialized thin membrane, through which oxygen can pass.

The surface of the body is thus extended and enlarged by invagination of the superficial layer to form complex organs such as tracheae and lungs. The respiratory membranes are usually looked upon as within the organism, but consideration of the lungs, as an example, shows that in the stages of development the early embryo, with its covering layer of cells, is folded on itself in such a way that the cephalic end encloses the foregut, a region previously placed on the surface. The walls of this enclosure are lined by a layer of cells continuous with the more obvious surface layer of the skin. In the floor of the foregut, now differentiated to form the pharynx, the pulmonary outgrowth appears, to extend downwards as the trachea and bronchi, eventually branching into bronchioles with their acini and air sacs as the terminal subdivisions. It is easy to trace the invagination of the surface in this way and to understand the means by which increased area has been afforded for respiration.

By various additions it is possible to modify the environment, with its content of oxygen, before the latter comes into contact with the now highly specialized surface membrane through which the basic function of gaseous exchange takes place. The evolution of tracheae follows the same general lines but with less complication.

The usual concepts of ectoderm and endoderm are misleading, because they appear to indicate some basic difference which, in fact, does not exist. Mesoderm is of course another matter, but even though there are definite distinctions in function, the differences are less than was at one time accepted.

In small organisms, transfer through the surface, or minor modifications of the surface such as tracheae, can be adequate. In trees and plants with a very large surface provided by leaves it is also possible to have successful transfer. But in large bodies with a relatively small surface such as man, even the increase in useful respiratory surface such as that provided by the lungs is too far removed from the tissues to enable oxygen to diffuse directly to the cells; a blood vascular system is therefore interposed, allowing transfer first of oxygen from the environment to the blood through the diffusing membrane and then a transfer by the blood to the tissue cells.

Carbon dioxide follows a reverse course.

The factors to be considered are: the supply of water or air, whether passive or active; the regulation of entry and exit; conveyance of water or air from the surface of the body; diffusion of oxygen and CO_2 through a membrane; transport of oxygen to tissues and removal of CO_2 by coelomic fluid or by a cardiovascular system; tissue respiration. Diffusion and tissue respiration must occur in all cases.

CHAPTER I

RESPIRATION IN WATER

FIRST to be considered is the respiration of *aquatic species*, in which a variety of methods are adopted.

RESPIRATION THROUGH THE SURFACE

The simplest method is exchange of oxygen and CO_2 through *the surface of the plant or animal, as occurs in submerged plants such as Canadian pond Weed* (Fig. 1); the epidermis has no cuticle and is permeable to dissolved gases and salts. Hornwort is similar (Fig. 1). Some species living in water have a very primitive type of existence and can be sustained by the simplest respiratory arrangements; diffusion of oxygen in water is very much slower than in air, and is similarly greatly inferior in speed of exchange in the tissues of an animal or plant as compared with diffusion in air.

Most aquatic bacteria require oxygen, which in aerobic types is absorbed through the cell membrane; anaerobes, however, are destroyed by free oxygen and obtain their supply of energy from plant and animal remains decomposed as a result of their activity. In an aquatic Protozoon, such as Amoeba, there is free exchange of gases between the body surface and the surrounding watery medium by diffusion (Fig. 2). Oxygen concentration in Amoeba is always lower than in the outside water, while CO_2 diffuses out because it is at a higher concentration than in water. The animalcule is minute and its exposed surface is large in proportion to its bulk; furthermore, it has no thick protective layer.

The surface of a sphere has the smallest possible area in relation to a given volume; conditions improve with any deviation from a spherical form and are better in thread-like animals. Diffusion alone can provide sufficient oxygen for unicellular organisms of 1 mm. diameter or less, even if their metabolism is fairly high, as it is in some protozoa.

Diffusion raises the question whether there is an actual cell membrane with a specialized composition and structure or whether the surface of a cell is composed of cytoplasm in the gel state; observation of a time-lapse film speeded up very considerably shows macrophages passing through mast and other cells with no damage, the surface appearing to separate and re-unite behind the motile corpuscle.

CIRCULATION OF WATER

The submerged plant and amoeba do not make purposive movements to attract currents of water, but when other organisms are examined it is found that in some, such as a two-layered Coelenterate—Hydra—flagella cause circulation

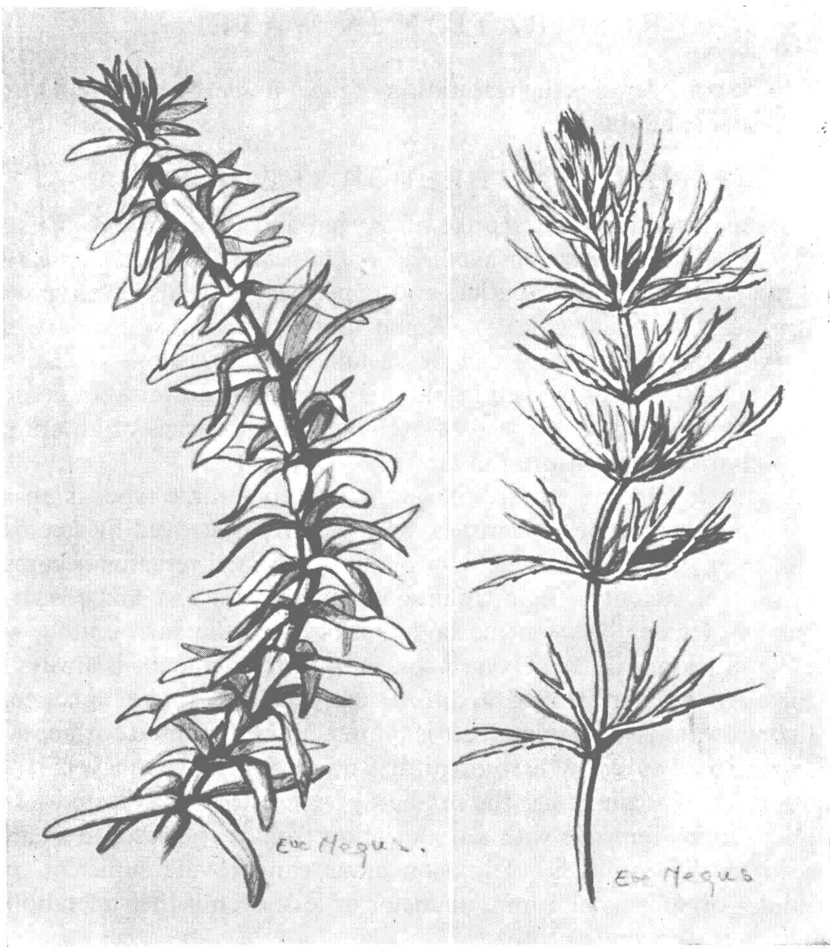

FIG. 1

Aquatic Plants

On the left is Canadian water or Pond Weed (*Elodea densa*) which is completely immersed and breathes entirely by surface respiration.

On the right Hornwort is shown (*Ceratophyllum demersum*); it lives a completely aquatic life below the surface of the water.

It flowers under water, pollen being conveyed to the stigmas through the water. There are no true roots, the plants floating freely erect. (*From Mr. A. L. Jewell, Curator Haslemere Educational Museum.*) (M2000) of a current through the gastro-vascular cavity (Fig. 3). Exchange of oxygen and CO_2 is by diffusion into and out of the cells of the endoderm, most of which, and also those of the ectoderm, are surface cells exposed to water; there is no internal transport system. Sponges also have a mechanism of water circulation, there being flagella as in hydra; water enters the cavity of the colony of the many-

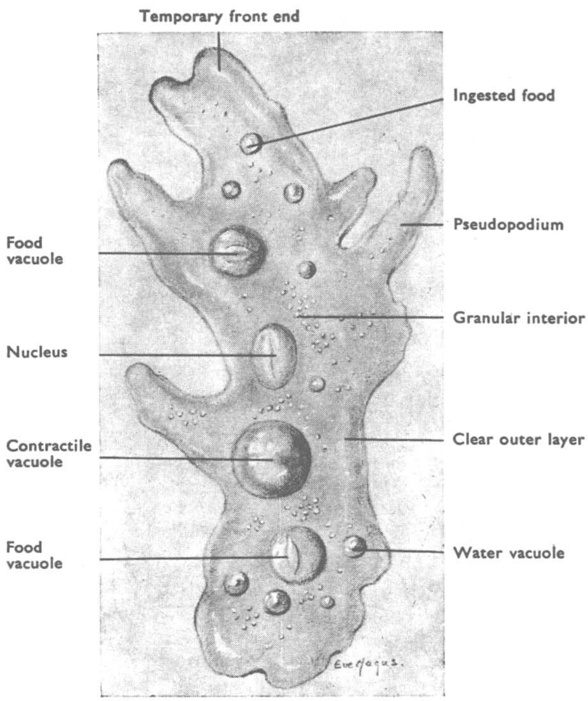

FIG. 2

Amoeba mira

(From a model constructed from a diagram in "Animals without backbones", by R. Buchsbaum.)
(M2001)

celled organism through pores, and leaves by a large opening; in its passage it furnishes a supply of oxygen for all the cells and carries away CO_2 and waste products (Fig. 4). There is no specialized respiratory mechanism, exchanges being effected by surface diffusion (Buchsbaum, 1948).

In Sea Cucumbers or Holothuria there are branched, thin-walled tubes stretching throughout the length of the body, emptied and refilled with seawater and acting as water lungs by a process of diffusion; they are not very efficient.

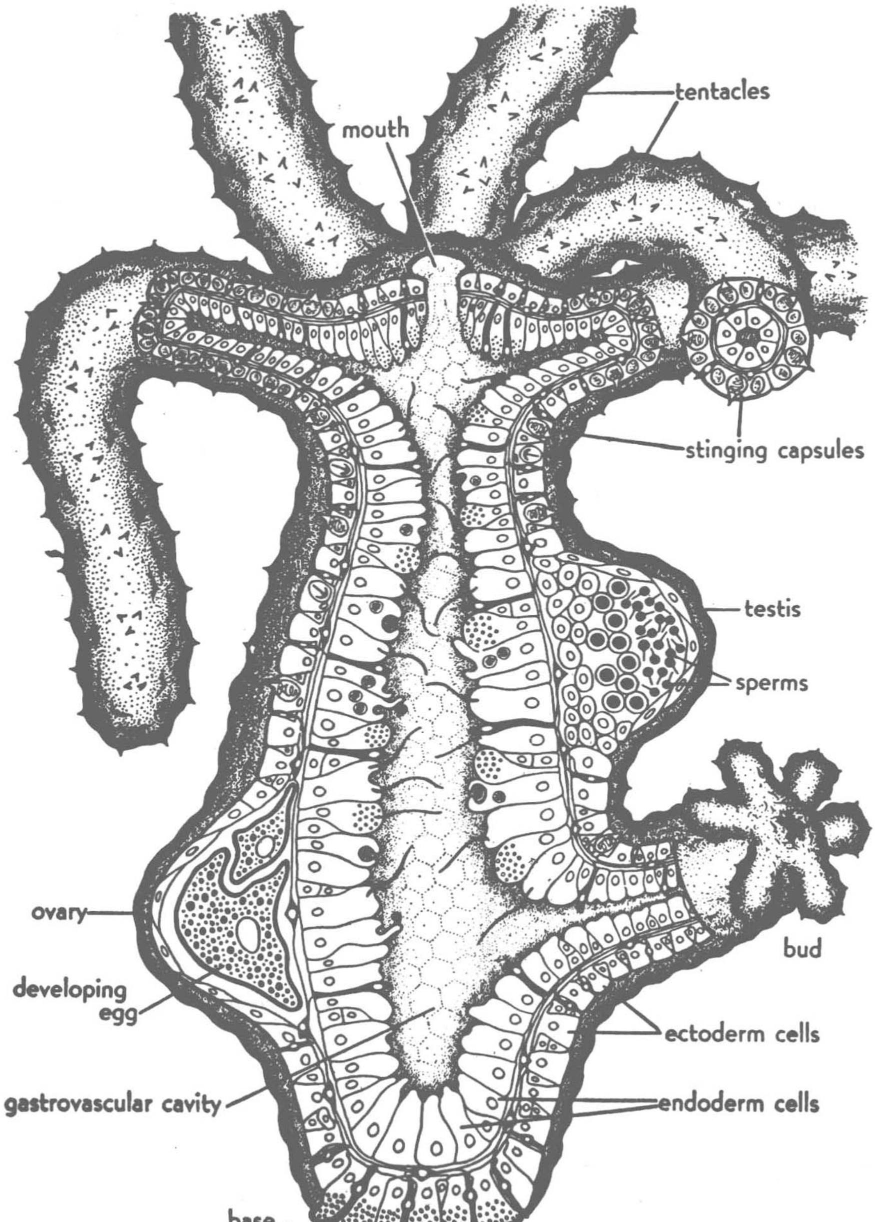

FIG. 3

A hydra cut away to show structure

(*Reproduced from* "*Animals without backbones*", 1948, *2nd Ed. Ralph Buchsbaum. University of Chicago Press.*)

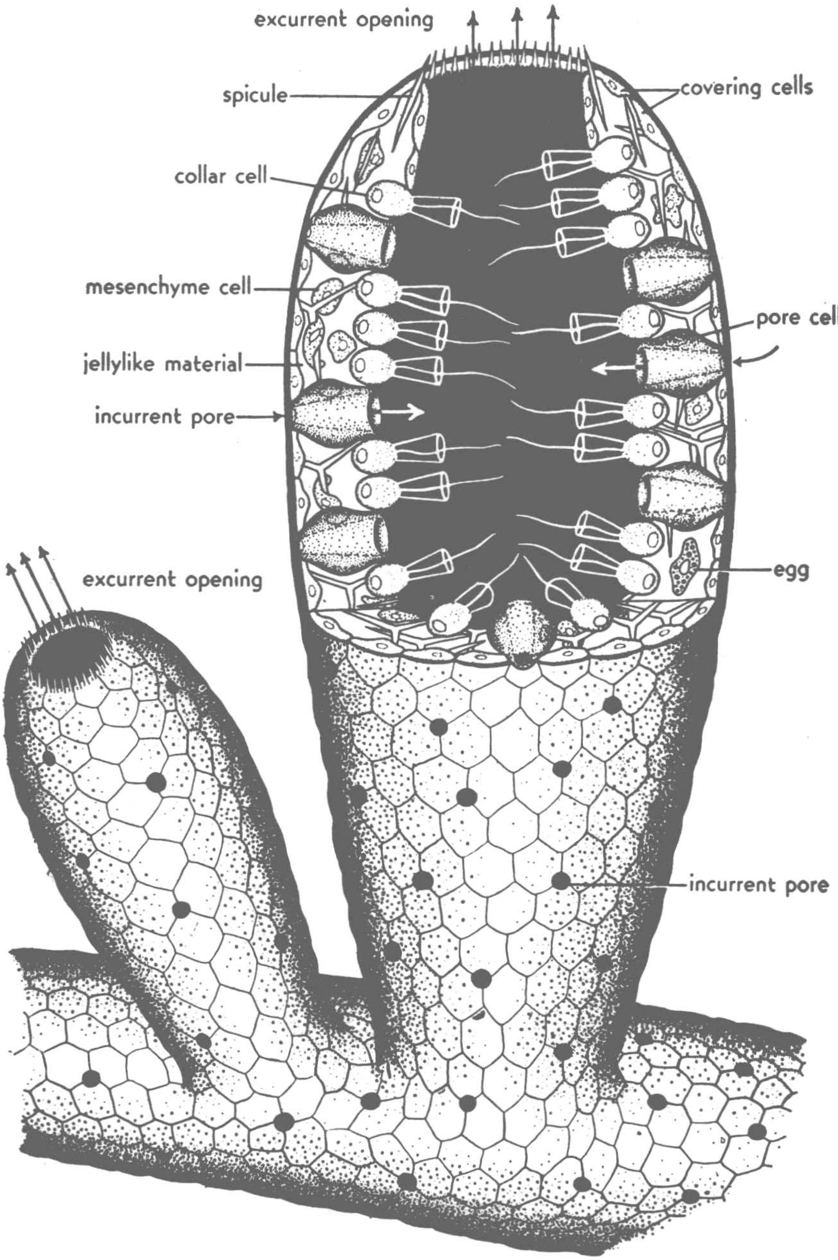

FIG. 4

Part of a colony of a simple Sponge. The upper part is cut away to show structure. (*Reproduced from "Animals without backbones"*, 1948, *2nd Ed. Ralph Buchsbaum. University of Chicago Press.*)