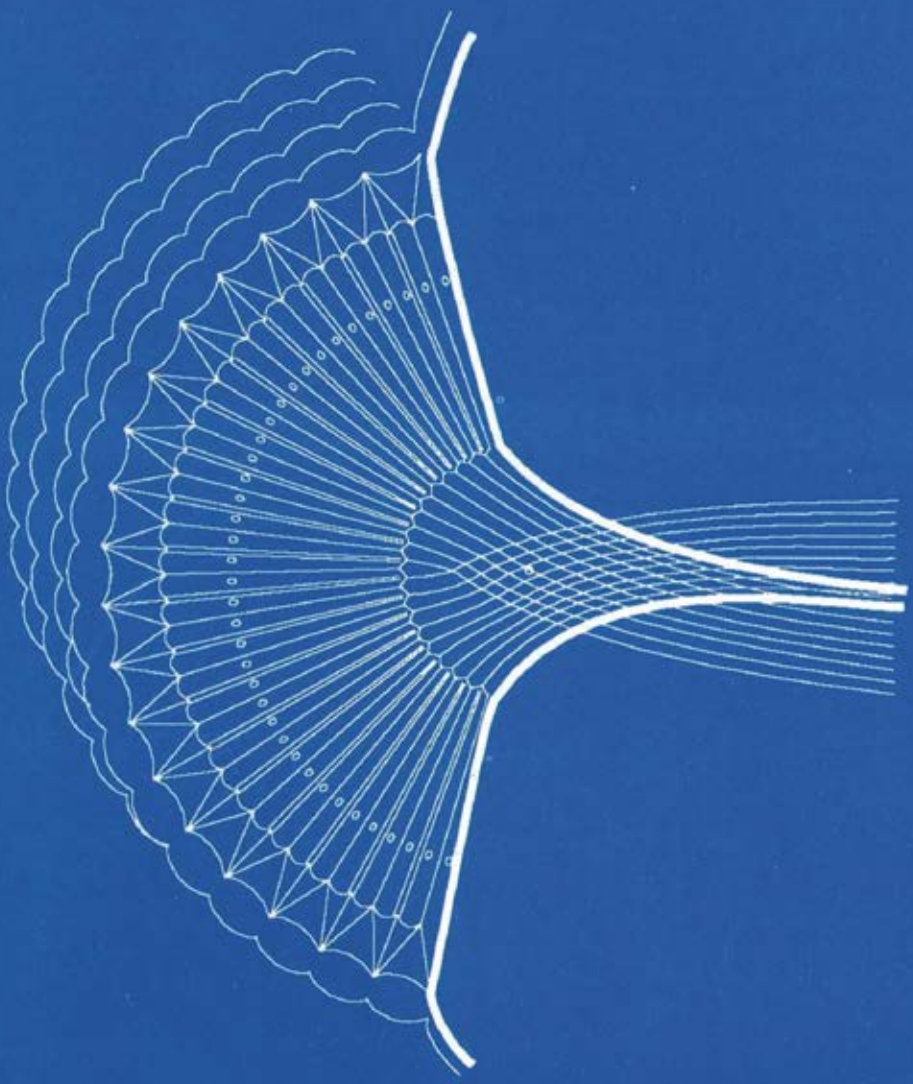
Ontogeny and Phylogeny of the Functions

Verónica Guarner



ONTOGENY AND PHYLOGENY OF THE FUNCTIONS
Verónica Guarner

Ontogeny and Phylogeny of the Functions

ONTOGENY AND PHYLOGENY OF THE FUNCTIONS

Verónica Guarner

Illustrations by
Patricia Ringenbach

Información Profesional Especializada, S.A. de C.V.

Ontogeny and Phylogeny of the Functions

ISBN: 968-6779-13-2

© 1996
All Rights Reserved/Derechos reservados por:
Información Profesional Especializada, S.A. de C.V.
Francisco Márquez 127, 06140 México, D. F.

Miembro de la Cámara Nacional de la Industria Editorial
Registro No. 2394

Printed in Mexico/Impreso en México

No parts of this book may be reproduced in any form or by any means without written permission from the publisher.

Prohibida la reproducción total o parcial de este libro por cualquier medio visual, gráfico o sonoro, sin permiso escrito del editor.

Contents

Preface

The idea of a parallel existing between ontogeny and phylogeny surges from Aristotle and draws enormous prosperity through to the end of the 19th Century with Haeckel's contribution of the "Theory of Recapitulation." This theory later witnessed a disastrous fall as an experimental approach, as it was against the 'norm' of that era, and speaking of a parallel between ontogeny and phylogeny became a shameful topic. Nevertheless, having felt certain that a relationship existed between the two processes, many researchers have recently taken back this proposal in order to reevaluate the mechanisms that may be able to create the parallel, and to analyze the significance of those events from the historical and epistemological points of view. Besides that, there does not currently exist any work where, one by one, the ontogeny and phylogeny of each function of the animal organism is analyzed, constituting the present objective of this book.

The information contained in this work began its formation as a series of notes for the teacher in a postgraduate program of the University. These notes were later elaborated to serve as a guide to students. The notes' good reception served as an inspiration to attempt to complete the work and present it now to you in the form of this book. As this version of the book progresses, all terms employed are attempted to be defined, so it may be of interest for biologists, doctors, veterinarians, and medical surgeons interested in physiology, embryology and that are concerned in knowing the evolution of the functions, and other people who are interested in the chemical and biological fields.

A large quantity of fascinating and interesting aspects of physiology are included in this work, dispersed throughout numerous sources of information. It analyzes the distinct physiological solutions that the organisms have encountered in order to survive in different, current terrestrial environments, in those in which they have evolved over a large period of time and in the manner in which their ontogenic development occurs.

Currently, physiology in an adult mammalian is too vast a field for any one person to completely know, understand and manage adequately.

Furthermore, trying to also contain the ontogeny and phylogeny of each is a never-ending chore. The information on which we count over these aspects is fragmentary; one author describes a small field of physiology in a certain species and in a moment of its development, while another chooses another aspect, different species and stages. In trying to join the information together, it seems that what we have is the description of each one of the isolated points of a punctilious picture; nevertheless, no one is able to form a clear concept of if the picture illustrates a landscape or a vase. While the book presents this concept, it is certainly not complete nor free of errors. It only attempts to provide a global vision of what we currently know about the ontogeny and phylogeny of the functions. Besides, the investigation is limited to the development of superior mammalians and does not cover the embryology of different species. The work attempts to advance with a perfectible investigation, hoping to reach a definitive and final explanation in time, which is very difficult to obtain for the moment. We hope that the critics of students in other professional fields will help us further and better our research.

I wish to express my deepest appreciation to many people who have contributed in the preparation of this book. I am particularly grateful to Enrique Guarner for careful revision of the manuscript and to Patricia Ringenbach for the drawings and illustrations.

Introduction

THE HISTORICAL POINTS OF VIEW

ONTOGENY

Ontogeny can be defined as the development of an individual from its fertilization to its death. Aristotle understood ontogeny as a growth in the level of perfection of the organism through the successive invasion of the body by various souls: a nutritive, sensory and finally a rational soul. He postulated that the ovule was the most important structure in the development, that in it was found all the substance to construct an organism and that the sperm only induced the process. The followers of Aristotle were later known as "Ovists."

The preformist theory about ontogeny is historically the oldest and some of its followers were Epicure, Seneca and Harvey. They understood the adult to be contain entirely in the germ, meaning, in the ovule or in the sperm, and the development not being more than the progressive growth of an initial miniature. Through religion, this notion arrived at absurd, proposing that all humanity is found in the ovaries of Eve or in the testicles of Adam.

The preformist theory was later changed, each part of the future organism being represented by a region of the egg. The germ is then presented as a mosaic of territories or organ-forming plasmas. In 1760 Charles Bonnet simplified the preformist point of view, stating that the information is found stored in a form of code.

The epigenetic theory understood by Thinkers such as Diderot arose later, proposing that the structure of the embryo surges little by little, through a successive series of stages, from a simple, initial phase. It would appear that there exists a force that carries development. This surges from God in agreement with the mystics or existed within the human organism in agreement with the vitalists.

Later, the German philosophers of the 19th Century proposed that nature imposes restrictions, conditioning the development to a large

extent. At the end of the said Century, Ernst Haeckel postulated that ontogeny guards the historical origin of the ancestors of the individual. He proposed his "Biogenetic Law or of Recapitulation," in which the embryo surges, in the course of its development, repeating the evolutionary history of its ancestors in an abbreviated lapse. Haeckel (1834–1916) studied medicine in Berlin and later became interested in natural history, dedicating himself mainly to zoology. After learning of the work of Charles Darwin, he supported his thoughts in conferences and publications, converting himself into a fervent evolutionist. Through his theory of recapitulation, he sought to study the evolution of organisms through their embryonic development.

Later researchers considered ontogeny as a series of current events susceptible of being causally analyzed, and here experimental embryology was born at the end of the 19th Century.

The first experiments of this type were conducted by Chabry, Conklin and Dalcq, separating the blastomeres of embryos of ascidias and observing the formation of complete embryos in early stages and of hemi-embryos in somewhat later stages. Driesch repeated these experiments in the globefish.

Wilhelm Roux (1850–1924), who is considered to be the Father of experimental embryology, made attempts to discover how the organs and tissues acquire their structure and function from the moment of fertilization. This German author heated blastomeres of frog eggs and produced hemi-embryos. His observations were misinterpreted by other scientists, attributing the harmful action of destroyed blastomeres over the development of healthy ones. Spemann separated the two first blastomeres using a tourniquet made with fine hair. He observed that if it corresponded to the bilateral plane of symmetry, two complete embryos developed while if the plane was perpendicular to the bilateral plane, only one of the blastomeres originated a normal embryo, while the other detained its development in the blastula stage. The birth of experimental embryology with this type of manipulations permitted a better understanding of ontogeny and contributed to the eventual disuse and fall of the "Biogenetic Law" by Haeckel.

EVOLUTION AND PHYLOGENY

Phylogeny is the evolution of different types of organisms, from the single-cell to complex beings such as humans, during the history of our planet. From the Greek Thinkers, such as Empedocles and Anaximandro, exists the idea that the different types of organisms can transform from one to another. In fact, it was a very widespread belief during the Middle Ages that animals could surge from inorganic material, and this belief did not disappear until the experiments of Louis Pasteur or of Francesco Redi and Lazaro Spallanzani who demonstrated that spontaneous generation does not occur.

However, the idea that the species remained, together with the Judeo-Christian culture penetrated the understanding, and already Linneo in his natural history considered organisms as separate and independent entities, discarding the possibility that some evolve from others.

The idea of the transformation of organisms again appears in some of the explanations of the French naturalists in the 17th Century, such as George Buffon, describing that the modification of the organism into another is a degradation of the original being.

The first complete theory of evolution was that of the French naturalist Jean Baptiste Pierre Antoine de Monet Chevalier de Lamarck (1744–1829). In this theory he proposed that the organisms alter themselves in specific response to the changes of the environment. This transformation was described as an essential capacity of the live organisms and held the belief that the characteristics altered by the environment resulted as hereditary. Therefore, Lamarck thought that there existed an inherent tendency in material to return each time more complex. His work, however, was based on subjective speculations.

One contribution of Charles Darwin (1809–1882) was the affirmation that the transformation of the organisms from one to another occurred as a fact and that therefore, we all originate from a few ancestors. Another important contribution of Darwin was the application of natural selection from a large unadaptable variability, as a mechanism of the rise of one species from another. The genetics of Darwin was originally that of Lamark, and his theory only rejected the existence of an internal impulse towards the complexity in the development of the physical structure of

living beings. The work of Darwin is based on his observations made in the Galapagos Islands, projecting through its enormous capacity of synthesis and the originality of the mechanisms that he applied.

The modern theory of evolution has been modified by the contributions of a large quantity of scientists through the ideas of the era of Darwin. Alfred Russel Wallace, Darwin's contemporary, arrived at similar conclusions, amplifying his observations with information obtained in the Amazon and in the Molucca Islands. Friedrich Leopold Weismann established the independence of the germinal line in relationship with the somatic. The laws of Gregor Mendel, which remained forgotten for many years, were rediscovered at the beginning of the 20th Century, and permitted in part the understanding of the nature of the phenomenon of variation between the individuals of a species. Fisher, Haldane and Wright explained the continuous modifications of the species by alternate forms of the genes on many points of the chromosomes (loci) and described that small differences in the adaptation of the individuals are sufficient for determining the evolutionary direction. Dobzhansky and Ford described methods for measuring genetic variability and natural selection. Mayr and Rensch in the animals and Stebbins in the plants, explained the variation of the populations through geographic factors and the rise of new species, known as "speciation." Simpson explained the registry of the fossils in Darwinian terms, as an illustration of evolution.

The development of molecular biology also supports the theory. The principle of Weismann about the independence of the somatic and germinal lines is explained by the central dogma of molecular biology and some techniques, such as electrophoresis, allow for the measurement of genetic variability. On the other hand, the sequences of the proteins and of DNA provide valuable information about the phylogenetic relationships between the organisms.

Despite its current force, the theory of evolution had to face, for its acceptance, a large quantity of problems and to refute poorly founded theories. It needed to surpass the immobility of living beings accepted by Linneo, refuse the theories of spontaneous generation and of preformism. It also had to substitute the typological thoughts for the reasoning in terms of populations, postulating that not only commonness within the diversity is important but also that diversity within itself is primordial.

THE PARALLEL BETWEEN ONTOGENY AND PHYLOGENY

The idea that a parallel exists between ontogeny and phylogeny stems from Aristotle. This thinker saw a growth in the level of perfection in evolution as well as in ontogeny. He proposed that they were the same souls that invaded the embryo and distinct organisms during evolution.

In the 19th Century the movement of the philosophers and writers of nature surged, such as Meckel, Serres, Hertwig, Goethe and Zola, who attempted to explain the parallel between ontogeny and phylogeny through similar external restrictions during both processes, without there existing any relationship between the two. They proposed the existence of a single tendency of universal development, or that there are little paths present to develop the complexity from a simple being.

In the middle of the 19th Century, Ernst Haeckel appeared postulating that ontogeny recapitulates phylogeny. According to this author, the branchia in the embryos of mammalians are characteristic of those in ancestral adult fish, which were pushed toward embryonic life during their development. He affirmed that the phylogeny of an organism could be traced by studying its ontogeny. His postulates became a system of work, and in order to explain recapitulation, he proposed an active mechanism consisting of the terminal addition of traits to advance the development and the acceleration or condensation of the process of acquisition of these new traits. Haeckel never tried to experimentally test the mechanisms that produced recapitulation, but simply utilized his idea as dogma, and from it, he designed phylogenetic trees. Haeckel was correct in proposing a temporal change, but was wrong in that the process always consisted in the addition and in that it was the adults' states that were repeated during ontogeny. It is possible to mention that Haeckel's idea of terminal addition was in agreement with the very popular Lamark positions of that era.

In the middle of the Century the ideas of Karl Ernst von Baer (1792–1876) appeared. He was an embryologist interested in compared anatomy, and established a series of fundamental concepts about animal development. This author understood the existence of common embryonic states in the ontogeny of vertebrates. Embryology was a process of differentiation toward distinct specializations and not a ladder to arrive at perfection. The organs adapted to the functions. According to this author, the parallel between ontogeny and phylogeny is owed to

a conservative process in which heredity preserves early states of the development of our ancestors. Although his ideas are, in a certain sense, very close to those of Haeckel, this author denies the acceleration and the changes in temporality. Below is a paragraph by von Baer, making fun of Haeckel. The published paragraph is of how recapitulation would be seen from the point of view of birds. It reads:

"We imagine birds studying their own development from the research of the structure of the adult mammalian and of Man. By chance would their physiology text books not teach the following?: Those animals of two and four feet present many similarities to our embryos: their cranial bones are found separated and do not include a beak; equal to us, during the first five or six days of incubation, their extremities are very similar to ours before the formation of the wings; they do not have one true feather over their entire body but only possess the principal shaft of the feather, in a manner which we as chicks in the nest find ourselves more advanced than they will ever be... And these mammalians are not able to obtain their own food for some time after their birth and are not ever able to rise from the surface of the ground. Are they able to consider themselves as more highly organized that us?"

Apart from these comments, Haeckel eclipsed von Baer and the philosophers of nature and obtained great prestige. Darwin favored the ideas of von Baer and although the theory of this author was each time more accepted, the practice of utilizing ontogeny for creating phylogenetic trees as Haeckel had instituted, was not changed.

Little by little others began to accumulate a large quantity of evidence against the proposed mechanisms of Haeckel in order to explain the theory of recapitulation or biogenetics, but the hypothesis did not fall, it instead was quickly accommodated and modified to continue being compatible with its censors. As example of this type of accommodation we have the following critiques of the theory and their answers:

1. Ancestral adult forms do not always appear in ontogeny and not all organs suffer acceleration in the same proportion.
   Answer: There exist fixed traits defining which type of animal the embryo is in each stage of its ontogeny. These are the ones that should be kept in mind instead of total morphology. The disappearance of certain characteristics of the adult organism in the embryonic stage is due to adaptation of the body to the conditions in which it develops.

2. Many organisms present a delay and not an acceleration.
   Answer: The juvenile traits are not the product of the delay, but of the acceleration, in reality being senile traits or of the second infancy. We do not see the previous accelerated states to those seeming delayed, because the velocity is so rapid that they disappear. However, the acceleration predominates during the development and is most important.

The defensors of recapitulation even arrived to adopt the mechanisms of evolution. They utilized natural selection to explain the acceleration in the ontogeny, saying that it is adaptive for the individual to grow rapidly in order to be able to defend itself, and it also is adequate to acquire reproduction capacity from an early age. In this manner the acceleration and the condensation are justified as processes that produce recapitulation.

This theory did not fall because of the empirical critics, nor was its fall due to the accumulation of a large quantity of exceptions stating that not all of the organs accelerate in equal measure, that the addition of many new characteristics is not only terminal and that development also is characterized by delay in the appearance of characters. Recapitulation fell when it became old fashioned as experimental approach. Descriptive embryology surged with a structuralist focus and experimental embryology developed as well. The results of these disciplines and the rediscovery of the laws of Mendel invalidated the mechanisms of the biogenetic law.

Little by little evidence was accumulated against the mechanisms of recapitulation resulting in the destruction of the theory. It was demonstrated that the terminal addition was not given through the heredity of acquired traits. It became clear that the genes that produce the addition are always in the genome of the organism and can be activated in any moment of development. It was also observed that the explanation for the acceleration and the delay were the same and that the traits delayed were not exceptions, having the same probability of appearing as the accelerated ones. Recapitulation was considered as a mechanism like many others that are capable of producing similarities between ontogeny and phylogeny. Models began to be postulated to explain the parallels. The panorama became each time more confusing and ended up losing its popularity totally.

In parallel form with the fall of the theory of recapitulation, the term 'evolution' changed its significance. At first, this term referred to the unfolding of parts that previously existed in compact form. Aside from Darwin and from the discussions about the recapitulation of phylogeny during ontogeny, there appeared the modern significance of evolution, which is a change in the organization or whatever type of connected events in a series.

The study of the rise and the fall of the theory of Haeckel's's recapitulation reminds us that the mechanism that makes science advance is not the accumulation of evidence in favor or against a paradigm, but the rise of a new mark of reference.

THE INFLUENCE OF THE THEORY OF RECAPITULATION IN OTHER AREAS

As a consequence of the Haeckel's law of biogenetics, other areas of knowledge were modified:

1. The field of teratology. The explanation of abnormal formations as a part of phylogeny was attempted.
2. Infantile education and development. Influence of the theory of recapitulation can be found in the work of Jean Piaget. This author stated that the development of thought in children recapitulates the evolution of the conscience of the species. He proposed that the mechanism which provokes this recapitulation is the same one that the philosophers of nature postulated: similar external restrictions in both cases and little possibilities of development of thought by other means.
3. Racism. It was proposed that behavior of White children was similar to that of Black adults or of the wrongly called inferior races. The behavior of White women was found in an intermediate state between White children and White adult males, and that the men in adolescence and youth have feminine attitudes (they cry, seek protection in other people, have heroes, etc.).
4. Criminal Anthropology. Caesar Lombroso affirmed that criminals correspond to organisms of inferior species and that children are natural criminals.

5. Psychoanalysis. Sigmund Freud proposed that individuals repeat the history of humanity in their development and that some pathologies result from the altered development of this process. In the recapitulation of structures, a form substitutes another, but in the evolution of thought, the ideas are not substituted, but are able to coexist. Freud titled his 1913 work as "Totem and Taboo: Correspondences Between the Social Life of the Savages and of the Neurotics."

These examples show the enormous impact and importance that the theory of recapitulation collected. It was also observed that the influences of the law of biogenetics had some positive effects as was the growth of tolerance towards children during their education, they had to recapitulate the history and were not able to avoid it. However, the theory also obtained many harmful effects as was racism and the loss of liberties for many individuals, which contributed to its final fall and loss of prestige.

CHAPTER 1

Mechanisms of Differentiation in Ontogeny and Phylogeny

ONTOGENY

This term can be defined as the development of an individual from its fertilization until its death. During ontogeny the following processes are carried out: 1) decoding of information, 2) cellular maturation, 3) cellular division, 4) migration and 5) cellular death.

Decoding of information

The instructions for differentiation during ontogeny are found in the nucleus and in the cytoplasm. In the nucleus, the information is coded within the deoxyribonucleic acid (DNA) sequences that constitutes the structural and regulatory genes. Despite that in an organism there exists hundreds of different types of cells, all of them possess the same genome. Their differences appear because, during development and differentiation, the expression of genes is regulated by what we know as transcription complexes that are combinations of signals that arise from the surrounding medium and/or are synthesized by the cell. These complexes unite with the DNA near to the gene that is going to be transcribed or repressed. In order for a gene of a eukaryote organism (with a well-defined nucleus) to transcribe, besides the transcription factors, other proteins are needed which permit the complex to put itself in contact with the DNA. These proteins are coded by regions of the gene, whose expression depends upon other transcription complexes. In this manner, the turning on or off of the genes in a cell depends upon a chain of successive reactions, being regulated by the environment and by the cell itself (fig. 1).

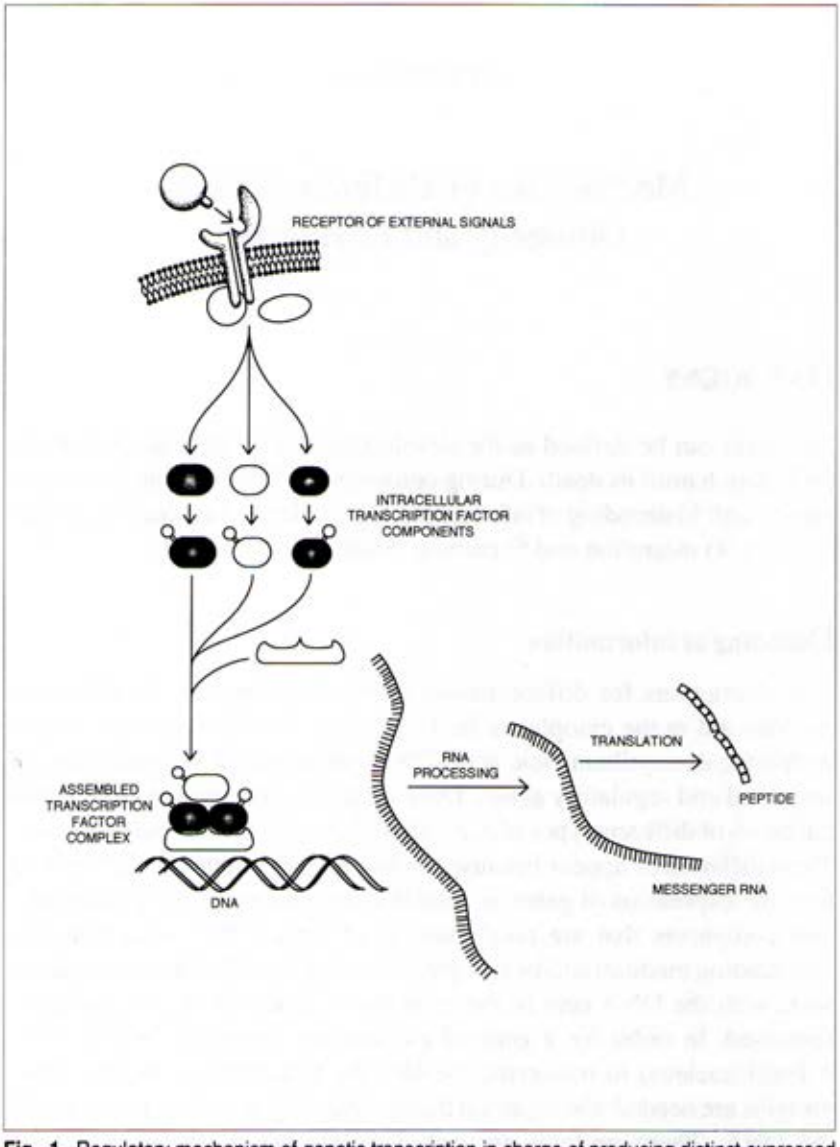


Fig. 1. Regulatory mechanism of genetic transcription in charge of producing distinct expressed characteristics despite the fact that all the cells contain the same genetic material. The exterior signals are used in the construction of a transcription factor that regulates the reading of a part of the DNA. This process generates a molecule of messenger RNA, which is processed and finally generates a specific protein. This new protein can again form part of another transcription factor or constitute part of the cellular structure.

The cytoplasm guards the information in form of concentration of ions, quantity of nutritious material and type of proteins in each region of the membrane. These factors differ between the distinct cells from early phases of development since before the division of the fertilized egg, there is no duplication of the cytoplasmic components and therefore, the daughter cells inherit distinct cytoplasm and membranes. These components can form part of the transcription complexes that regulate the turning on and off of the genes. As an example of the large quantity of information found stored in the cytoplasm, remember that in the globefish the meridian section of the blastomeres results in the formation of two complete offspring organisms, because each blastomere product of this division contains all the information to complete the process; while the equatorial section separating the blastomere in the animal pole from that of the vegetal does not produce viable offspring since certain blastomeres lack information to continue the development. If after the equatorial section of the blastomeres of the globefish there is an interchange of the animal micromeres to the vegetal middle, and of the vegetal to the animal middle, the organisms develop into complete larvas, since together with the micromeres the information that was required to complete the development is transferred.

Another example of the influence of the signals of the cytoplasm over the differentiation is that from the stage of formation of the first somite there exists cells determined to constitute a heart. It has been observed that if these cells are left to grow *in vitro* in a medium which contains an enriched fraction in ribonucleic acid (RNA) from the adult heart, it induces the early differentiation of the cardiac cells because they are provided with the necessary information to advance their development.

Cellular maturation

In the formation of an organism, the cells pass at first through a process of cellular determination in which, although no morphological change is observed, they are obligated in a specific pathway of differentiation. When these determined cells are transplanted to another position in the embryo, they will differentiate themselves towards the cellular type with which they were bound. Determination is carried out by inducing molecules. As an example of the inducing molecules, a factor may be

remembered which is secreted through the dorsal lip of the blastopore during gastrulation. At this stage, the embryo is formed by two layers and a cavity known as a blastocoel, which opens to the exterior by the blastopore. This factor sensitizes and pre-differentiates the cells that will constitute the nervous system.

Once determined, the cells enter into the stage of differentiation, where they may already be recognized in relation to others. Finally they acquire their adult characteristics.

Cellular division

From the beginning of development the cells multiply, but they do it in an organized manner, carrying each component of the new organism to its corresponding form and size. Some consequences of the distinct rate of division of the cells in differentiation may serve as examples, such as the appearance of the folds and the partitions of the cardiac tube and of the neural groove as well as the ramifications of the bronchial tubes and the pulmonary bronchioles.

The separations within the cardiac tube and the ramifications of the pulmonary tree may be formed by passive mechanisms in which a ring of conduct divides and grows more slowly than the lateral regions. The divisions between the atria and the interventricular septum are examples of separations that form through this mechanism (fig. 2).

By contrast, the foldings of the cardiac tube can be the result of the pressure that is exercised by the cells and the conjunctive tissue which forms the matrix of the duct against the more superficial tissue constituting its wall. This substance modifies its volume by cellular division depending on the intercellular concentration of ions in distinct portions of the tube. In turn, the layer of cells of the wall possesses distinct grades of compliance or capacity of stretching as a consequence of a certain pressure in the different regions. This is found regulated by the quantity of myofibrils that the cells contain and by the rugosity of the cellular membrane.

In the regions of the cardiac tube in which the wall has an elevated compliance, a growth in the volume of the matrix will manifest as a

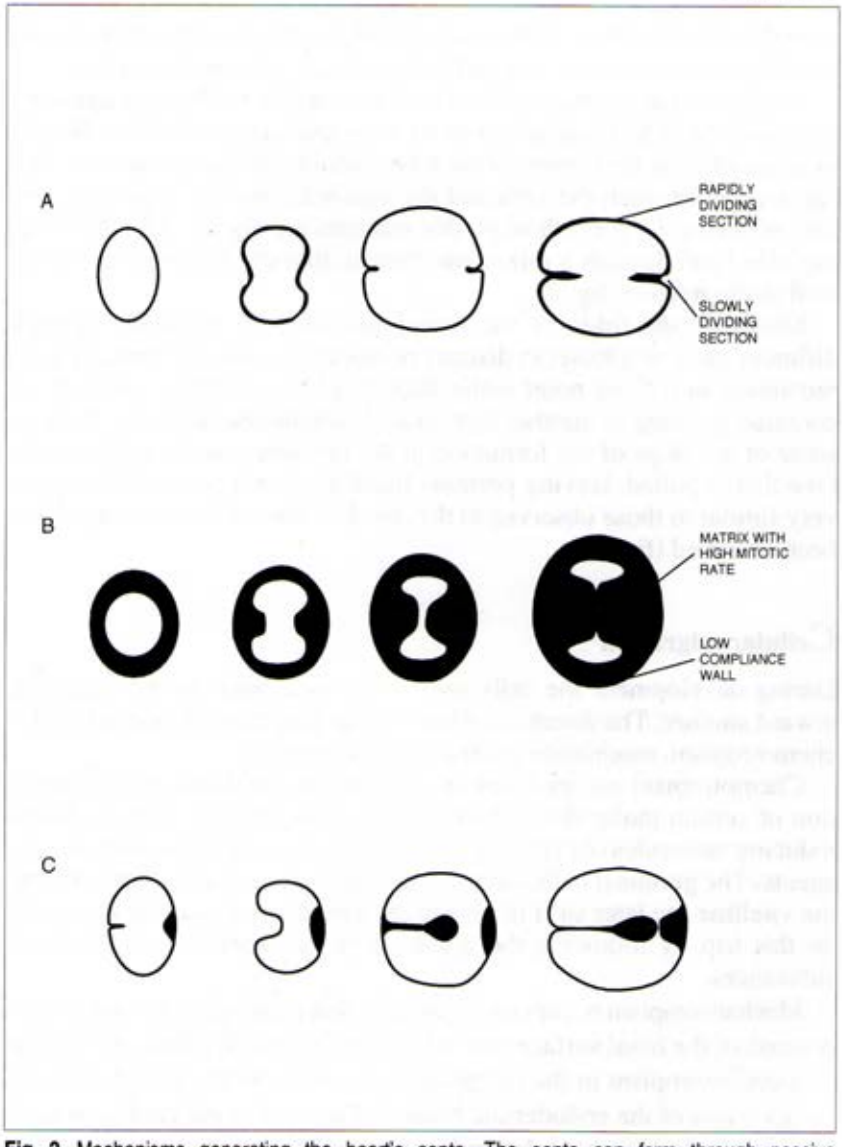


Fig. 2. Mechanisms generating the heart's septa. The septa can form through passive mechanisms; meaning, some sections of the tube multiply more slowly than others, resulting in a constriction (A). The second mechanism is active, in which a part of the interior cells of the tube reproduce more rapidly and as the exterior of the tube presents little compliance (capacity to stretch when pressure is applied), the cells accumulate towards the interior. The third example is the combination of the active and passive mechanisms.

growth in the longitude of the canal. If this growth only occurs on one of the sides of the tube in a longitudinal section, it will produce a bent.

On the contrary, when the matrix of the cardiac wall grows against a portion of the superficial layer with little compliance, the matrix will tend to accumulate in the interior of the tube, forming divisions within it. The separations between the atria and the ventricles and the separations of the bulbus cordis form through this mechanism (fig. 2). The divisions can also form through a mixed mechanism that combines the active as well as the passive (fig. 2).

Similarly, the folds of the neural tube can be produced through different rates of mitosis in distinct points of the tube, or through cells remaining in a fixed point while their neighbors migrate, multiply or continue growing in another direction. A simulation has been made of some of the steps of the formation in the nervous system using a latex tube that is pulled, leaving portions fixed in certain points and images very similar to those observed in the development of living beings have been observed (fig. 3).

Cellular migration

During development the cells move from one point in the organism toward another. The direction of the cellular migration is determined by chemotropism, mechanotropism or galvanotropism.

Chemotropism occurs when the cells follow gradients of concentration of certain molecules and migrate towards or away from it. Many inducing molecules of differentiation act simultaneously as chemotropic agents. The germinal cells located at the beginning of development near the vitelline sac later shift to invade the gonad; encountering their path on this trip by following the gradients of concentration of chemical substances.

Mechanotropism occurs when the cells that migrate recognizing components of the basal surface over which they move. We find an example of mechanotropism in the morphogenesis of the heart. The changes in composition of the endodermic basal surface and of the cardiac gelatin secreted by the myocytes determine the migration of the pre-myocardial and pre-endocardiac cells. The composition of the cardiac gelatin is modified during development. At first it consists of hyaluronic acid, chondroitin and chondroitin sulfate low in sulfur, and little by little in chondroitin sulfate, becomes its principal component. Similarly, the

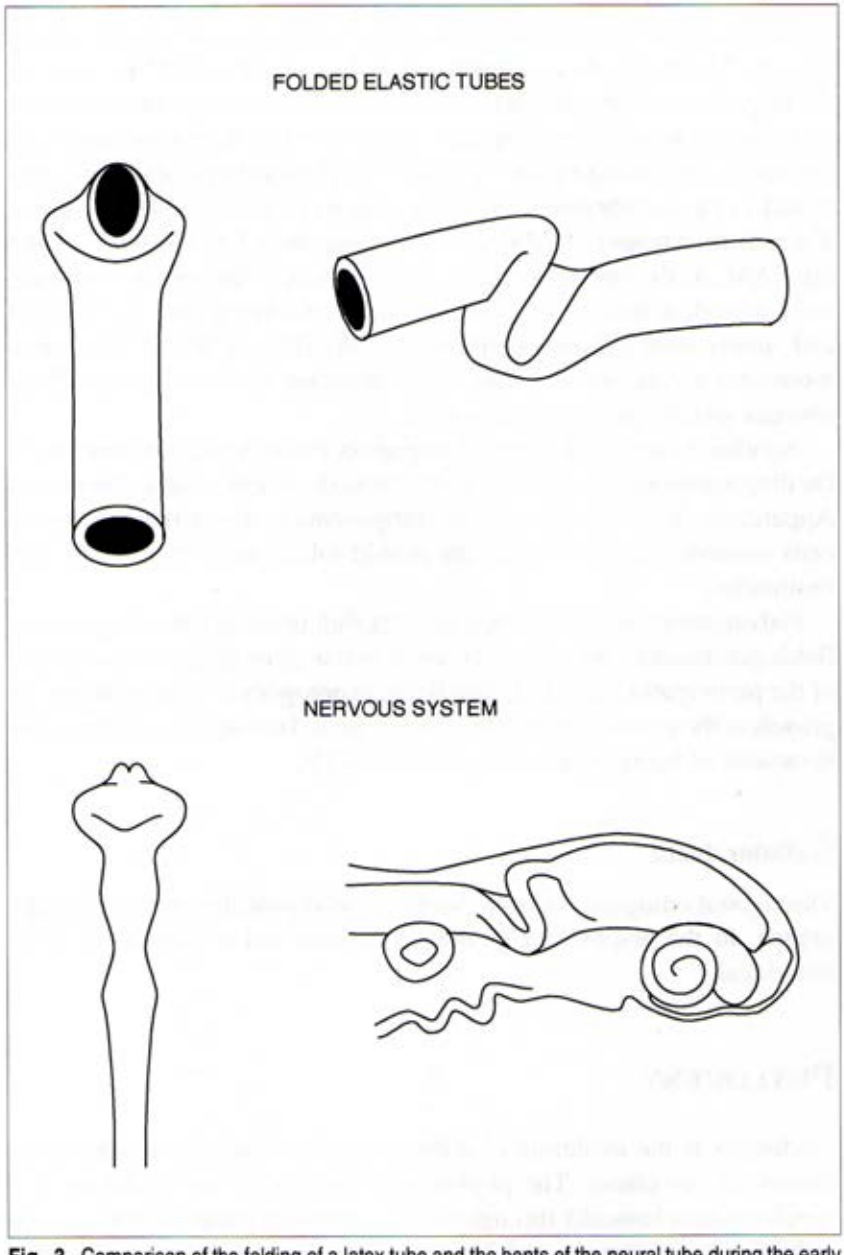


Fig. 3. Comparison of the folding of a latex tube and the bents of the neural tube during the early development of the nervous system.

concentration of fibronectin and the type of collagen in the cardiac gelatin change. These signals are altered when the cells that form the base for the migration modify their pattern of secretion, but many times the cells that migrate modify these signals. Another example of mechanotropic signals is constituted by the "CAMs" (cell adhesion molecules), contained in the membranes of nervous cells in process of differentiation. Three distinct types of CAMs have been described: L CAM, N CAM and Ng CAM. At the beginning of the development of the nervous systems, the L as well as the N CAM manifest, later exhibiting only the N CAM and finally only expressing the Ng CAM. The expression of distinct molecules of adhesion determines the direction of the migration of the neurons and the growth of the axons.

Another example of directed migration through mechanotropism is the displacement of the germinal cells from the vitelline sac to the gonad. Apparently, these cells search for components in the membranes of the cells covering the route that they should follow until they reach their destination.

Galvanotropism occurs when the cells shift or move following electric fields generated by the accumulation of ions in other cells. As an example of the participation of the electric fields in ontogeny, it is known that the growth of the axonal cone of the neurons toward the determined direction is capable of being regulated by electric fields.

Cellular death

Throughout ontogeny, cellular death occurs during the formation of the organs, in the acquisition of their functions and at the death of an individual.

PHYLOGENY

Phylogeny is the evolution of different types of organisms during the history of our planet. The phylogenetic history or the evolution of a species occurs basically through two processes: 1) variation between the individuals of a species, and 2) natural selection. Each one is described below.

Variation

There exist numerous factors that produce diversity between individuals in a population, which at long term can conduce to the generation of new species. Inclusive are mutations, recombination, genetic transference and genetic drift.

Mutation may be punctual, involving a sole pair of bases of genetic material or may include long segments of chromosomes. These alterations are inversions, additions or suppressions of genetic material. Mutations can occur in structural genes modifying the characteristics and function of a specific organ or in regulating genes causing changes in chronology of the appearance of traits. Normally, mutations occur by chance and are only conserved in the offspring if the information is altered in the germinal cells. Directed mutations are also spoken of when the adaptive change passes to the germinal cells through a virus of RNA. Mutations may be expressed immediately in individuals or remain silent for a long time.

Genetic transference is the passage of material from one organism to another horizontally in time; meaning, within the same generation of individuals, modifying its characteristics. It occurs through two mechanisms: plasmids that are parts of the genes that reproduce independently from the rest of the genome and can pass from one species to another, and transposones or jumping genes that can accommodate on distinct points of the genetic material. Plasmids as well as transposones require for their expression in the individual that acquires them of a reverse transcriptase or of the presence of retro-viruses in order to carry out the horizontal transference.

Recombination occurs during the passage of information from parents to offspring; meaning, vertically between distinct generations of individuals. It acts as a source of variation when reproduction is sexual and the offspring conserve half of the genetic information of each one of its progenitors, having therefore a different genome of whichever of its parents. There exists an "imprinting" of the genes by which some of the genes have a higher probability of expressing than others.

Genetic drift is the combination of variations in the genetic compositions of different populations of individuals in the same species. Genetic

drift gives rise to speciation or generation of new species, which can be either allopatric or sympatric. The process is called allopatric when it occurs through geographic isolation or migration of a population of the species, which results in a population that can no longer reproduce with the rest of the species. Sympatric processes result through genetic isolation of a population of a certain species by physical impediments, making impossible the copulation between individuals, the fusion of the sexual gametes, or when offspring are not viable.

Natural selection

Through this process, some of the individuals produced by the variation, are preserved and reproduce in higher proportion than the others. The factor of selection can be the environment or the same individuals of the population through sexual selection. The selection is prezygotic when individuals are chosen in the moment of reproduction, or post-zygotic when the offspring die. At the same time that the environment selects the individuals, they also select the medium they inhabit and modify it, changing the favoring or impairing factors.

MECHANISMS PRODUCING A PARALLEL BETWEEN ONTOGENY AND PHYLOGENY

Evolution is the control of the development and maturation of the organisms of a species imposed by ecological factors. It occurs through the expression or appearance of new codes of information during ontogeny, which is the result of a change in environment.

The alterations in ontogeny can occur through:

1. Introduction of new traits. This aspect generally occurs as a result of mutations in the structural genes, which may be inversions, additions or suppressions of genetic material. They originate a parallel between ontogeny and phylogeny, and possibly constitute the basis for the terminal addition proposed by Haeckel. Nevertheless, its effect can also be suppression or simply modification.

2. Temporal changes in the events of development, known as heterochrony. They are the consequence of alterations in the regulating genes and occur in different forms, its result being variable. There exist four important possibilities:
   A. Delay in the somatic development with normal temporality of the reproductive development. This heterochronic process is known as neoteny, and result in paedomorphosis; meaning, a kind of escape of specialization. An example would be of a larva that very early acquired the capacity to reproduce and detains its corporal development.
   B. Delay of sexual maturation. This process is known as hypermorphism, and results in a growth in the level of specialization or the appearance of new structures, as recapitulation proposed.
   C. Acceleration of somatic development. This also results in over-specialization and the appearance of new corporal features. This process is classic recapitulation as proposed by Haeckel.
   D. Acceleration of sexual maturation. This process is known as progenesis, and its results are again paedomorphosis or the escape of specialization.

The type of heterochrony favors the appearance of certain ecological strategies. The processes of progenesis increase the adaptability of the species with reproductive strategy "r" meaning, many offspring are generated to whom they dedicate little time for their care. On the other hand, the mechanisms of neoteny increases the adaptability of the species with reproductive strategy "k" in which few offspring are generated dedicating much time for their care. This shows us how the subject of a parallel between ontogeny and phylogeny plays very closely with the evolution of ecological strategies and the biology of regulation. We can conclude that despite the success and the fall of the theory of recapitulation, it cannot be denied that evolution impacts embryonic development.

CHAPTER 2

The Early Stages of Ontogenetic and Phylogenetic Development

THE EARLY STAGES OF ONTOGENETIC DEVELOPMENT IN MAMMALIANS

Development begins with fertilization, stimulating the zygote for the initiation of a series of rapid cellular divisions, known as segmentation. These divisions form a solid sphere of 16 cells known as a "morula" (fig. 4 A and B). The cells of the morula organize to form the "blastocyst," which consists of an external cellular mass known as a trophoblast, the embryoblast being a group of cells with no communication with the periphery, and a space filled with liquid between these structures, known as the cavity of the blastocyst (fig. 4 C). Cells from the trophoblast invade the endometrial epithelium during implantation and form the placenta.

A space is created between the internal cellular mass and the trophoblast, where the amniotic cavity will originate (fig. 2.1 D). The internal cellular mass morphologically molds, making way for an embryonic disc consisting of two layers: the endoderm, adjacent to the cavity of the blastocyst. .nd the ectoderm and mesoblast related to the amniotic cavity. The ceiis of these layers migrate, circling the amniotic cavity and the cavity of the blastocyst, which now converts into the primitive vitelline s .c. The unions between the cells of the intermediate layers of the vitelline sac and the wall of the amnios proliferate and comprise the extra-embryonic mesoderm (fig. 4 E). There appear spaces in the extra-embryonic mesoderm that fuse together to comprise the extra-embryonic coelom, which is continuous except at the site where the amnios is inserted into the trophoblast, known as the body stalk that will form the umbilical cord (fig. 4 F). The coelom divides the extra-

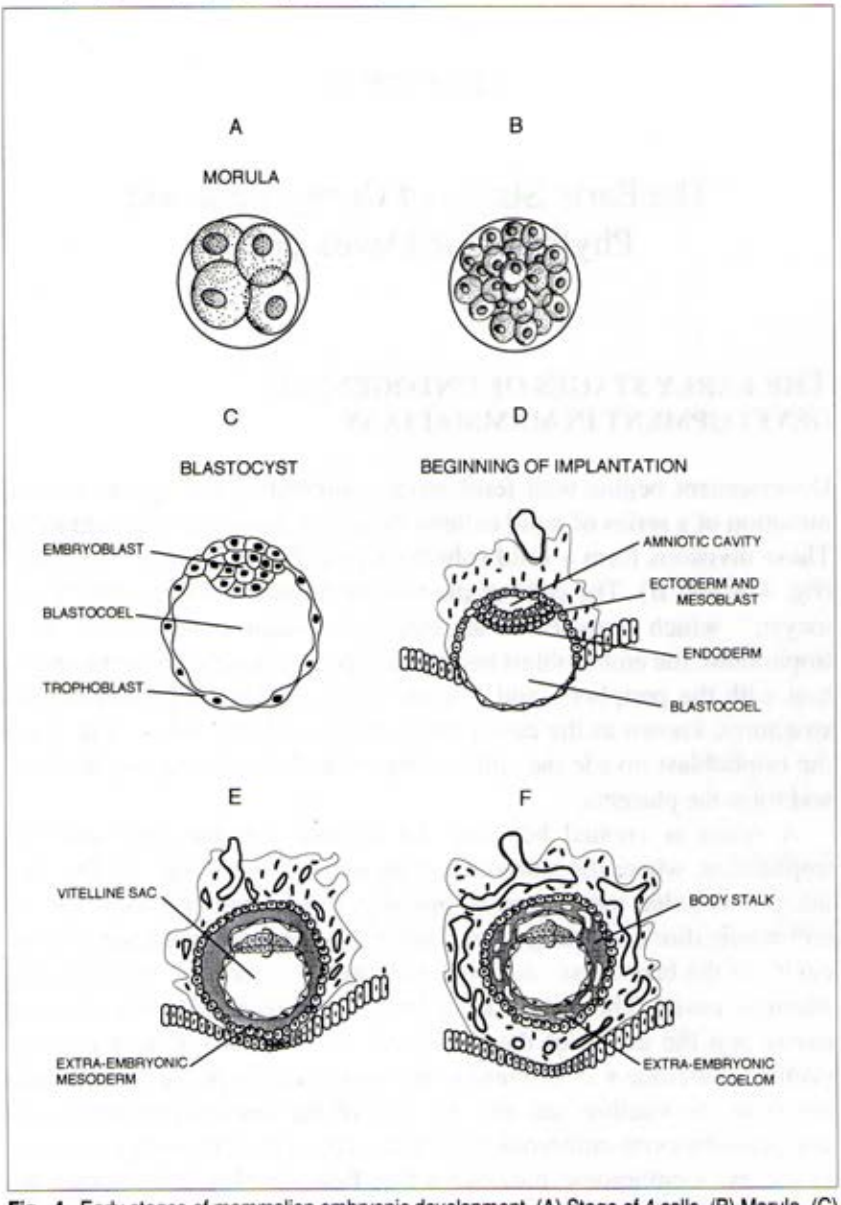


Fig. 4. Early stages of mammalian embryonic development. (A) Stage of 4 cells. (B) Morula. (C) Blastocyst. (D) Blastocyst during implantation, assessing the formation of the amniotic cavity. (E) Formation of the amniotic sac and of the extra-embryonic mesoderm. (F) Formation of the extra-embryonic coelom and of the body stalk.

embryonic mesoderm into somatopleura, which together with the trophoblast forms the chorion and the splanchnopleura.

Within the bi-laminar disc produced in the embryoblast, there appears a region of enlarged ectoderm known as the primitive groove with a node or blastopore. The cells of the mesoblast migrate toward the primitive groove and penetrate the disc through the node, placing themselves between the ectoderm and the endoderm, constituting the intra-embryonic mesoderm. This process is known as ''gastrulation'' (fig. 5 A). Later, the notochord is formed from the mesoderm and the creation of the neural tube or ''neurulation'' begins by the ectoderm. The mesoderm constructs, besides the notochord, bands or columns on both sides of it, distinguishing various portions: the paraxial mesoderm, the intermediate mesoderm and two lateral mesodermic laminas or plates which become slim toward the sides (fig. 5 B). The columns divide into pairs of parallel cuboid bodies to the notochord, named ''somites,'' beginning from the cephalic and extending toward the caudal regions. Spaces appear in the mesodermic lamina, fusing to form the intra-embryonic coelom. The two layers of mesodermic tissue will form the somatopleura, covering the corporal wall, and the splanchnopleura that will line the primitive intestine (fig. 5 C). Later, the intra-embryonic coelom divides into three corporal cavities: the pericardial containing the heart, the pleuras covering the lungs, and the peritoneal that envelops the visceral organs.

The superficial ectoderm will form the epidermis, hair, nails, skin and mammary glands, tooth enamel, inner ear and the crystalline lens. The neuroectoderm will form the neural tube from which configures the spinal cord and the central nervous system, retina, pineal gland and the posterior hypophysis. The neuroectoderm also will form the neural crests, from which will originate the nerves, sensitive cranial ganglia and the suprarenal medulla.

The endoderm forms the parts of the pharyngial epithelia, thyroids, tympanic cavity, Eustachian tube, tonsils, salivation glands, tracheal epithelia, bronchia and the lungs, the epithelia of the gastrointestinal tube, the liver, pancreas and the urinary bladder.

The vertebral column will form from the notochord. From the paraxial mesoderm the following will originate: muscles of the trunk, all parts of

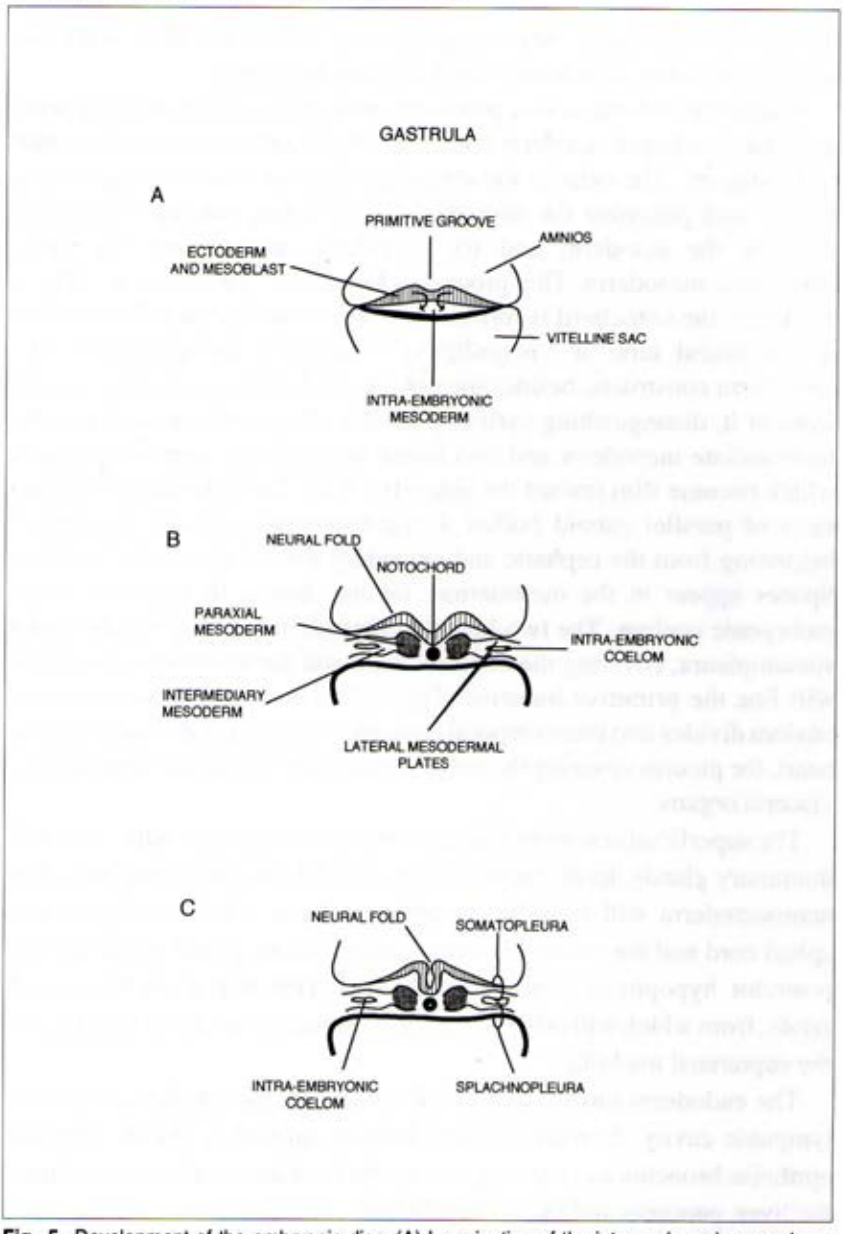


Fig. 5. Development of the embryonic disc. (A) Invagination of the intra-embryonic mesoderm. (B) Formation of the notochord, the neural folds and of the somites. (C) Development of the intra-embryonic coelom.

the skeleton except the cranium, the dermis, and the conjunctive tissue. The intermediate mesoderm will form the urinary system, the gonads, their canals and accessory glands. From the lateral mesoderm originates the cranium, the muscles and connective tissues of the head, the ivory of the teeth, the connective tissue and visceral musculature, the pleura, the pericardium and peritoneum, the blood and lymph cells, the cardiovascular and lymphatic system, spleen and the suprarenal cortex.

THE OUTLINE OF PHYLOGENY

Although evolution remains undoubted, it has provoked an enormous amount of speculation about the course of events that created the distinct animal phyla as we know them. The evolutionary origin of the majority of these phyla, including the beings of soft body, is still unknown, since the fossil archives of the Archeozoic era are fragmented and difficult to interpret. Because of this, the relationships between these groups have been established on a basis of morphological and embryological evidences. However, some of these are convincing, for example, the presence of trochophore larva similar in mollusks and annelids, which suggests an affinity between these two groups and the fact that many aspects of arthropods indicate the existence of an annelid ancestor for this group, or at least a common ancestor for the two conglomerates. The establishment of the phylogeny of the invertebrates continues being to date a fascinating field, because of the enormous quantity of controversy it creates.

Evolution of multicellular organisms

One of the controversial points about the evolution of invertebrates is the manner in which the multicellular organisms originated from the unicellular. There are two theories about this evolutionary step: The colonial and the syncytial.

The first hypothesis suggests that multicellular organisms originated from flagellated organisms, which organized into colonies through inter-

dependence and developed cellular specialization. The most primitive multicellular organism was possibly composed of a spherical and empty colony, which could very well have been the precursor of the hydra and the sponge. In accordance with this explanation, the organisms containing a body cavity, coelomated, would be more primitive than those that lack one, acoelomated. This hypothesis is supported by the presence of flagellated spermatozoids in a large number of organisms, possibly being the cells of a primitive colony specialized in reproduction.

The second theory proposes that the most primitive multicellular organism was a ciliated multinuclear organism that partitioned off, forming an acoelomated organism with bilateral symmetry similar to a platyhelminth, the group to which the current planarian belongs. The term syncytial alludes to the histological organization characterized by the absence of cellular membranes between nuclear neighbors. The coelomated organisms with radial symmetry would have appeared later. This theory is supported by the tendency of the ciliated organisms to display bilateral symmetry. The hypothesis, however, does not explain the presence of flagellated spermatozoids, nor does it explain the derivation of radial symmetry from the bilateral.

It has also been proposed that the multicellular beings had a polyphyletic origin from distinct unicellular groups, combining the flagellated colony and syncytial theories.

The coelom

Another controversial point in the evolution of the metazoa is the appearance of the coelom. The coelom is the corporal cavity of an organism that makes the wall of the body independent of the internal organs, facilitates interior transport, and can serve as a hydraulic skeleton. Although there exist some invertebrate which lack coeloms, called acoelomated, most invertebrates have some type of cavity. When there is a single cavity, organisms are called "ameria." If the organism contains three pairs of cavities (protosome, mesosome and metasome), the organisms are called "oligomeres," such as the echinoderm and hemichordates. Finally, when this coelom consists of many associated compartments, each accompanying a metamere or corporal subdivision

as in the case of the annelids, the organisms are called "poligomeres." There are three hypotheses explaining the origin of the cavity: the theory of enterocoelom, schizocoelom and that of gonocoelom.

The first theory implies that the cavity originates from the evaginations of the intestine. These sacs form in the oligomere organisms (three pairs of cavities) which are the most primitive and the loss of all the coelomic sacs, except the last, generated the americ organisms. Later, through the segmentation of the only coelom or the proliferation of it, poligomere organisms surged (coelom with many compartments) (fig. 6). According to this theory, the medusa, polyp and the hydra would be the progenitors of the coelomated organisms, forming acoelomated organisms such as the platyhelminths. This hypothesis is supported by the fact that in the hemichordates and the echinoderms, the coelom is formed by the evagination of the primitive intestine.

The schizocoelom theory proposes that the corporal cavity was generated from spaces in the form of clefts in the interior of the mesoderm. The acoelomated organisms would be the most primitive, preceding the appearance of the coelomated organisms. The cavity with many compartments, such as in mollusks and annelids, would be more primitive than that of the oligomere organisms with three pairs of cavities. The last organisms to evolve were those with one cavity that resulted from the fusion of the multiple hollow cavities. This theory is supported by the appearance of concavities in the mesoderm of acoelomated organisms, such as the platyhelminths, which form the tubules of the reproductive organs, circulatory and lymphatic systems.

The theory of the gonocoelom suggests that it is a persistent gonadal cavity. The annelids provide the principal support, because in the members of this group known as polychaete, the epithelial coelom forms the gametocytes that mature inside the coelom. This hypothesis proposes that the first cavity that appeared, was segmented, and then later lost its divisions in order to create oligomere and americ organisms. In opposition, it has been argued that it is very improbable that organisms with metameres appeared before unsegmented organisms. Other evidence against the theory states that during embryonic development, the gonads never appear prior to the coelom. Besides, the primitive organisms should

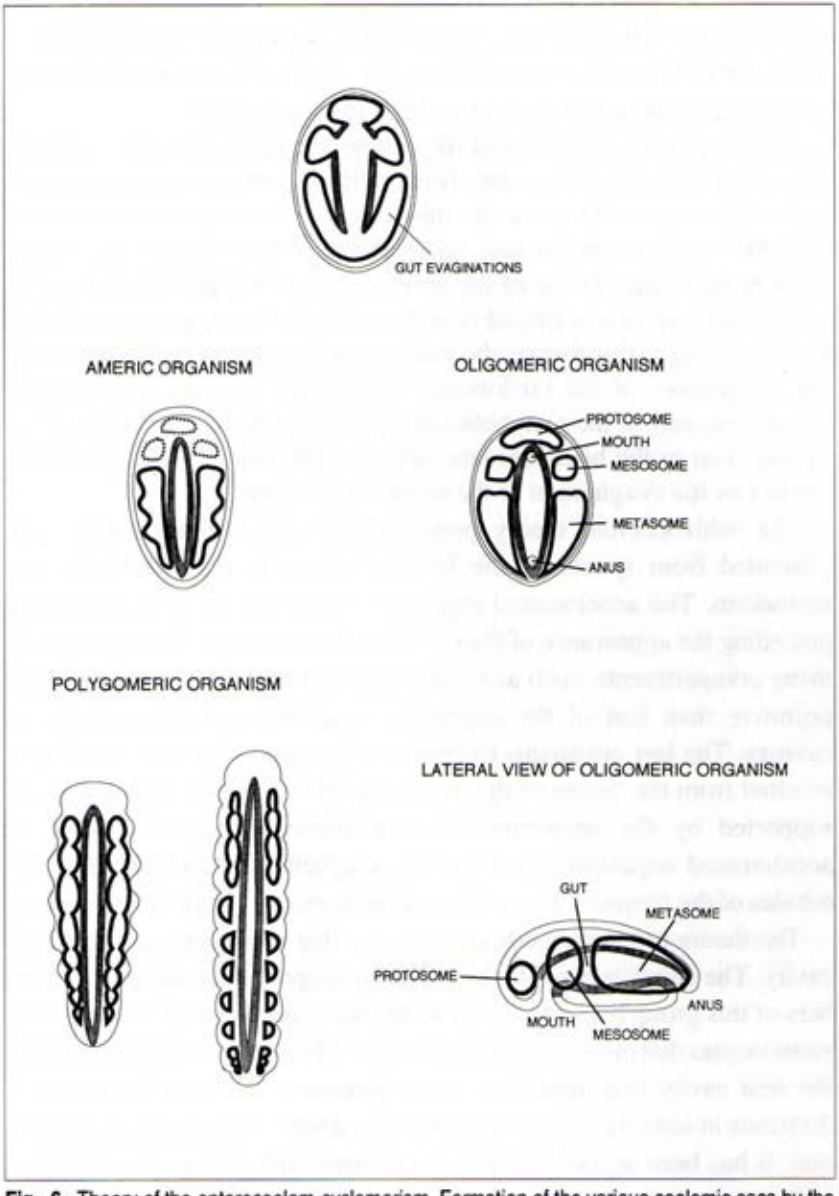


Fig. 6. Theory of the enterocoelom-cyclomerism. Formation of the various coelomic sacs by the evagination of the intestine. Formation of a single coelom through the loss of the protosome and mesosome. Posterior subdivision of the metasome associated with the evolution of the metamerism.

have had at least two stages of breeding in their vital cycle, when the more simple organisms customarily only present one of these cycles.

Finally, it has been proposed that coeloms may have had diverse origins, forming a good number of radial lines in phylogeny.

Metamerism

The third point of controversy regarding the evolution of the metazoa is the appearance of metamerism, or the subdivision of the corporal wall. Two theories have been proposed for the appearance of metamerism: the hypothesis of the fission of the bulb and also that of cyclomerism.

The bulb fission theory explains metamerism as the incomplete separation of chains of organisms that divide by fission or bi-partition, and maintain their dependence from each other. In opposition to this hypothesis, it has been seen that a gradation is not present in the ages of the distinct metameres.

The theory of cyclomerism includes the idea of the enterocoelom hypothesis and postulates that the metameres form through the proliferation of the posterior pair of coelomic sacs. It has the same evidence supporting it and against it as the enterocoelom theory has.

Protostome and deuterostome organisms

Practically all the phylogenetic trees separate the evolutionary lines of the protostomes and deuterostomes (fig. 7). The protostome organisms are those in which during the embryonic stage, the mouth develops from the blastopore or from a region in close proximity to it. The blastopore is the opening of the blastocoel to the exterior in the embryonic state known as gastrula. Classified within this group are the mollusks, annelids and insects, which are ameria (only one corporal cavity) or poligomeres (many cavities).

The deuterostome organisms are those in which the anal opening forms from the blastopore and the mouth forms in a distant region. Corresponding to this classification are the echinoderms, hemichordates and the chordates, which are oligomeres (having three pairs of corporal cavities).

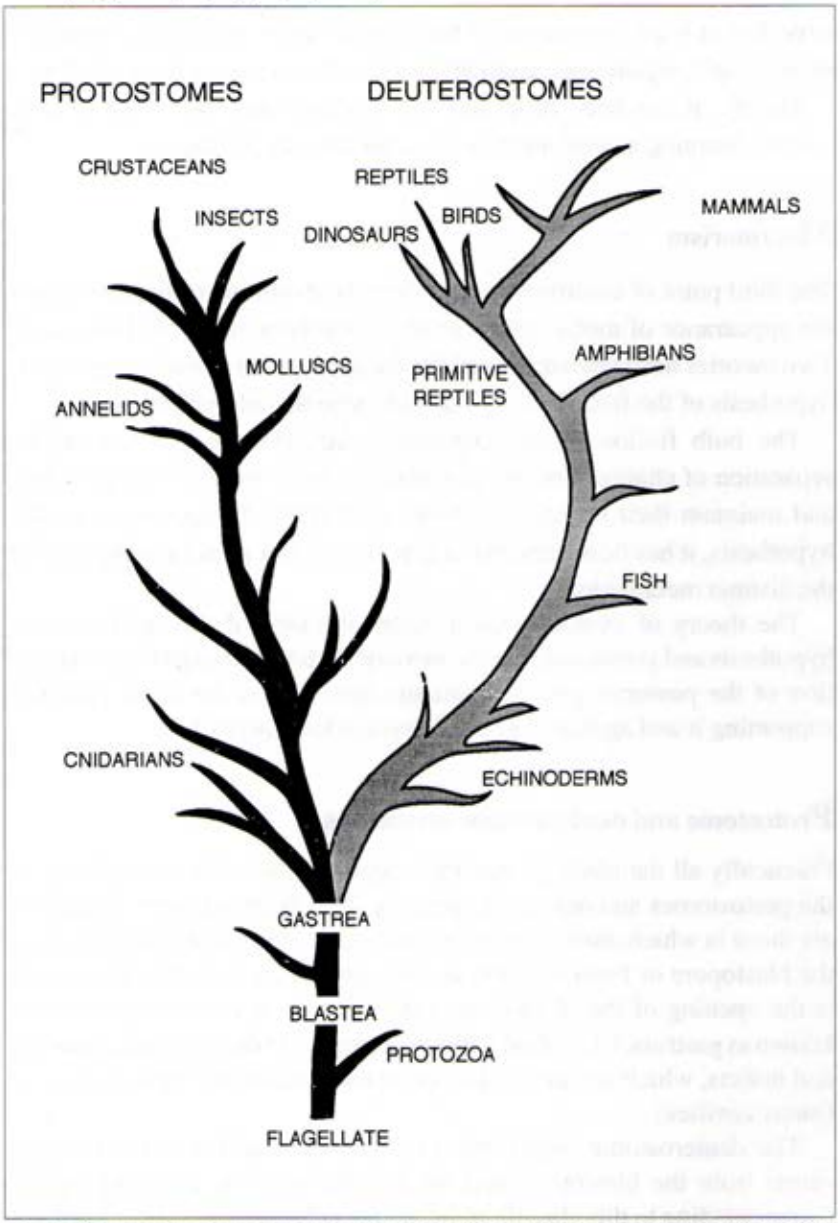


Fig. 7. Scheme of a phylogenetic tree exemplifying the evolutionary relationships in the animal kingdom. In this tree, the flagellated colony parts as a precursor of the multicellular organisms. The grey field corresponds to the deuterostomes and the black field to the protostomes.

If the coelom of the protostomes formed in accordance with the enterocelom theory through the loss of two of the cavities of an oligomere organism (with three pairs of cavities), and through the posterior division of the metacoelom or remaining cavity; then the deuterostome organisms would form an evolutionary standpoint, preceding the protostome organisms. On the other hand, if the segmented coelom was the most primitive and the oligomere organisms and the ameria originated from the fusion of the cavities, as the schizocoelom theory proposes, then the protostomes preceded the deuterostomes. Finally, it has been proposed that the protostomes and the deuterostomes appeared as divergent lines from acoelomated organisms such as the platyhelminths.

The origin of chordates

The hemichordates derived from a common ancestor along with the echinoderms. Some hemichordates generated mobile forms, at least in the larval stage, from which derived the chordates by neoteny, meaning, acquisition of the reproductive capacity before the onset of the adult stage (fig. 8). The most important evidence for this supposition is the enormous similarity that exists between some larvae of the hemichordates and the Amphioxus, one of the most primitive chordates. Within the chordate group, from fish formed amphibians, the amphibians in turn formed reptiles, and from the reptiles derived birds, as well as mammalians, as divergent lines.

Some considerations about human evolution

Chimpanzees and humans are almost identical in their structural genes. The basic mechanism of evolution was the modification of the regulating genes (moments of gene activity and inactivity). The predominant process during the evolution of monkeys to man was neoteny, since this process supports a complex social development, the establishment of rank in the hierarchy, and the increase of participation by the brain in the functions maintaining individual independence from the parents during infancy. It can be affirmed that in the human, the social and cerebral consequences of neoteny are more important than their morphological consequences, however, the process of neoteny also delays overspecialization.

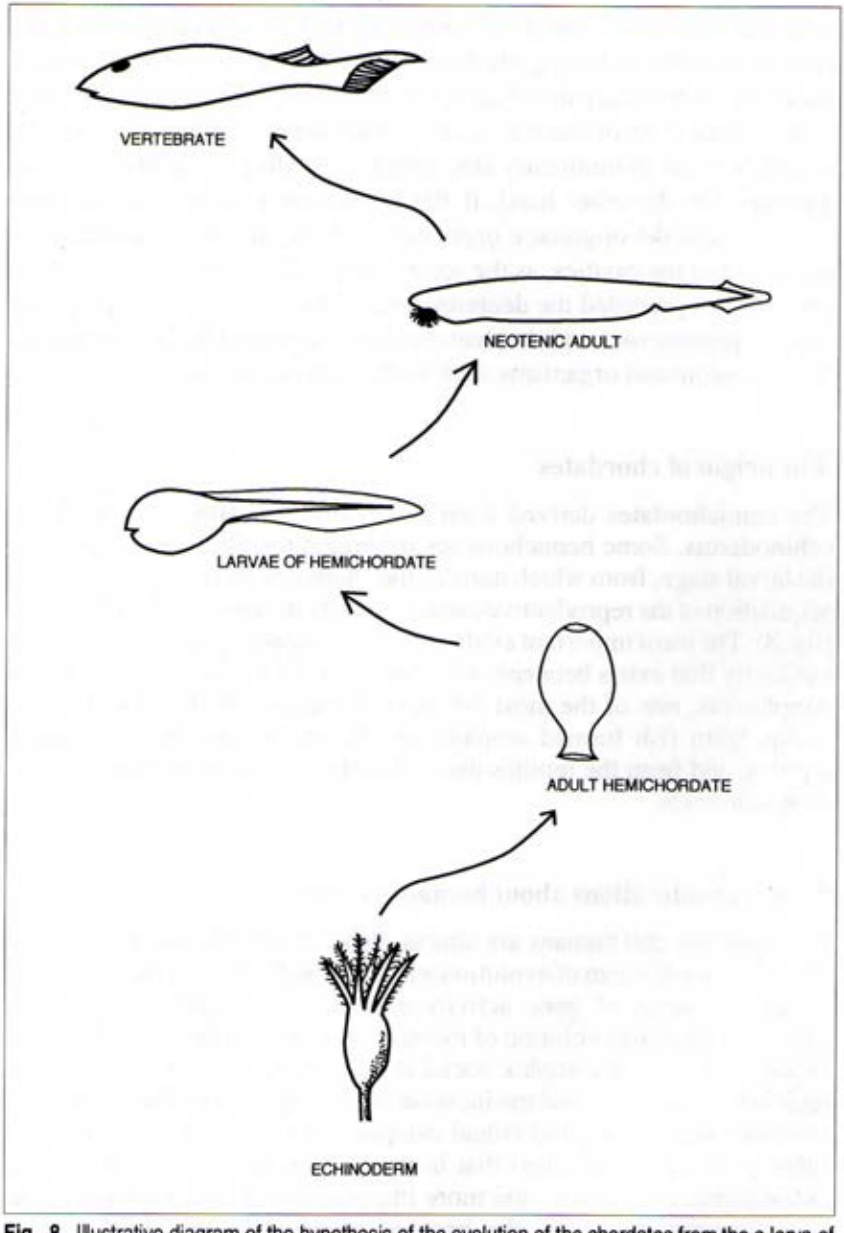


Fig. 8. Illustrative diagram of the hypothesis of the evolution of the chordates from the a larva of echinoderm that, through neoteny, acquires reproductive capacity and detains its somatic development, thus retaining larval characteristics.

THE PARALLEL BETWEEN THE FIRST STAGES OF ONTOGENETIC DEVELOPMENT AND THE FIRST PHASES IN PHYLOGENY

The intent to outline the parallel between ontogeny and phylogeny in their first stages is not totally valid, since the major part of the theories explaining the first periods in phylogeny are based solely upon evidence derived from embryology, with which we are attempting to establish the parallel and not by any other type of independent tests. However, the following similarities may be signaled:

1. The theory of the flagellated colony, proposing that empty and spherical organisms are the most primitive multicellular that later invaginate to form two layers of cells, shows a parallel in the first stages of embryonic development, particularly with the periods of the blastula and the gastrula.
2. The theory of the multinuclear ciliated organism mimics the ontogeny of some invertebrate because, for example, the development of the Drosophila (fruit fly) parts from a fertilized ovule in which the nuclei multiply and later fragment the cytoplasm.
3. The theory of the enterocoelom shows a parallel with the formation of a large quantity of digestive glands from the evagination of the gastrointestinal tube.
4. The theory of schizocoelom presents similarities with the formation of the amniotic cavity through the appearance of a cavity between the embryoblast and the trophoblast, and through the rise of hollow areas in the extra-embryonic mesoderm of the amniotic sac.

CHAPTER 3

The Ontogeny and Phylogeny of the Nervous System

THE NERVOUS SYSTEM IN SUPERIOR ADULT MAMMALIANS

Possibly the most important characteristic of the nervous system is that it is formed by excitable cells. The excitability fundamentally occurs due to an important difference in the composition and charges between the cell interior and external medium. There is a negative internal potential resulting from a high concentration of proteins, which in the intracellular pH environment are negatively charged. Furthermore, there are important differences in the distribution of ions between the interior and the exterior of the cell. Potassium accumulates inside, while sodium is found in higher concentrations outside. These ionic concentrations tend to balance, but the cell inverts energy to maintain the differences through the action of a pump known as the sodium- potassium ATPase. This introduces two potassium ions for every three sodium ions that are extracted from the cell interior. The facts that the quantity of potassium escaping from the cell is higher than the amount of sodium penetrating it as a result of a tendency of ions to seek balance and due to the pump extracting a higher number of sodium ions than the number of potassium it moves, also contribute to the intracellular negative overcharge. The polarization between both sides of the cellular membrane is known as resting or membrane potential.

When a neuron is excited, within it are produced a series of ionic movements following electrochemical gradients that, altogether, are known as action potential. When the cell is excited, sodium channels are opened and through them, positive charges enter and it becomes depolarized. This depolarization opens the potassium channels, allowing

potassium to exit the cell and it repolarizes. During the exchange, the concentration of sodium and potassium on both sides of the membrane activate the sodium potassium ATPase pump, returning the concentration of ions to their original level. As these processes allow less sodium than potassium to escape, the cell hyperpolarizes transitorily. The action potential propagates through the nervous fiber causing the opening of calcium channels in the synaptic knob. The increase of calcium induces the fusion of the synaptic vesicles containing neurotransmitters. Upon the fusion of these, the neurotransmitter is liberated and the information is transmitted to other nervous cells or to the effectors, which are mainly the muscles and the glands.

Afferent system

The afferent neurons carry information from the receptors of the periphery to the central nervous system. Their cellular bodies are outside, but adjacent to the brain and the spinal cord. From the cellular body parts, a large prolongation that innervates the receptors. A second projection parts from the soma toward the central nervous system where it ramifies and ends in synaptic unions with other neurons.

Efferent system

The efferent division is more complicated than the afferent, subdividing into the somatic nervous system and the autonomous nervous system.

The somatic nervous system is composed of all the fibers coming from the superior cell centers to the muscular skeleton. The cellular bodies of these neurons are found in groups within the brain and the spinal cord; their myelinic and thick axons leave the central nervous system and arrive directly at the cells of the muscular skeleton.

The autonomous nervous system innervates the cells of the cardiac and smooth muscles or of the glands. This system divides in the sympathetic nervous system, which exits from the thoracic and lumbar regions of the spinal cord and in the parasympathetic nervous system, forming from the brain stem, and from the sacral portion of the spinal cord. The majority of the organs receive innervations from the two systems, although some structures are found to only be regulated by the

sympathetic. The fibers of the autonomous nervous system form two synapses; the first at the exiting of the central nervous system in cellular groupings called ganglia, and the second at the level of the neuroeffector unions. The fibers passing between the superior centers and the ganglia are the autonomous preganglionic fibers, and those fibers which pass between the ganglia and the effector organ constitute the postganglionic fibers. The sympathetic ganglia are found adjacent to the spinal cord in a well-defined chain called the sympathetic, found halfway between the spinal cord and the innervated organ. Therefore, the sympathetic preganglionic fiber is short and the postganglionic is long. On the contrary, the parasympathetic ganglia are found within the walls of the effector organ, and the preganglionic fiber is much longer than the postganglionic.

Central nervous system

Spinal cord

The spinal cord is an elongated cylinder located within the vertebrate column. Its central area is formed by grey matter, which contains cellular bodies and dendrites, interneurons, efferent neurons and entering fibers of afferent cells. The peripheral region of the spinal cord is composed of white matter and contains nervous axons that conduct action potentials between different levels of the spinal cord, or between it and the brain. The fibers divide into tracts organized according to their function, and consist of prolongations of neurons conducting the same type of information. The afferent fibers entering the spinal cord through the dorsal region constitute the dorsal roots. From the spinal cord leave afferent fibers through the opposite side, constituting the ventral branches. Shortly after emerging from the cord, the ventral and dorsal roots from the same level fuse and combine to form a spinal nerve.

The brain

The three main divisions of the brain are the brain stem, the cerebellum and the anterior brain. The brain stem is composed of the protuberance, the bulb and the mesencephalon. Through it passes all the nervous fibers

carrying afferent and efferent signals between the spinal cord and the superior cerebral centers. The brain stem contains the cellular bodies of the motor neurons that control the skeletal muscles of the head and many of the cranial pairs. Throughout the brain stem the reticular formation is found, composed of a diffuse cluster of small and ramified neurons. The reticular formation receives and integrates information proceeding from numerous afferent routes and also from other regions of the brain. Some neurons within the reticular formation are grouped, forming nuclei and centers of the brain stem as in the case of the centers of deglutition, cardiovascular, respiratory, of vomiting, etc.

Functionally, the exit of the reticular formation is divided into the ascendant and descendant system. The descendant components influence the function of the efferent neurons and the ascendant components affect aspects such as sleeping and wakefulness, as well as the direction of the attention toward specific events.

The cerebellum participates in the unconscious coordination of voluntary muscular movements and coordinates a large part of the equilibrium.

The part of the brain excluding the brain stem and the cerebellum is called the anterior brain. Its external part, the cortex, is in charge of integrating the afferent information in complex perceptual images and of the control over the efferent systems, both autonomous and somatic. This part of the brain is also in charge of the intellectual functions. The cortex, an area of grey matter containing numerous neuronal bodies and limited myelinic nervous fibers, divides into the frontal, parietal, occipital and temporal lobes. The subcortical nuclei form an area of grey matter found, as the name indicates, underneath the cortex. Some of them as the caudal and putamen nucleus contribute to the coordination of the muscular movements. The thalamus is a relay station and an important integrating center for all sensory entrances (except smell). It also contains an important part of the reticular system. The hypothalamus is located underneath the thalamus, and is responsible for the integration of autonomous endocrine and somatic functions, resulting in the area of control for the regulation of the internal environment. In the anterior brain there exists a circuit that interconnects various structures, such as the tonsils, hypothalamus, parts of the thalamus and the cortex that we know as the limbic system, which intervenes in the generation of the emotions.

THE ONTOGENY OF THE NERVOUS SYSTEM

The formation of the nervous system begins in the late gastrula stage. In this stage, it has been observed that the mesoderm in the dorsal lip of the blastopore secretes a peptidic substance, known as an inducing factor, acting over part of the ectoderm to sensitize and pre-differentiate it in what will be the nervous system. For its formation, its posterior part needs a shorter period of time in contact with the inducer than does the anterior part, which indicates differences in sensitivity of the distinct portions of the nervous system. It has been reported that the portions of the posterior nervous system develop in mixed cultures of neuroblasts and mesodermic cells when there exists a higher proportion of the second than of the first. In contrast, when there is a predominance of neuroblasts, structures of the anterior brain develop in the culture media.

The nervous system originates from an enlarged zone of the ectoderm known as the neural plate. This invaginates towards its central axis to form a groove with neural folds on each side. The folds fuse to form the neural tube. The first part to unite is that which will become the brain stem, where some of the most important centers are found for survival, such as the respiratory, vasomotor and cardioinhibitory. Some ectodermic cells remain outside the tube and constitute the neural crests (fig. 9). From the tube develops the central nervous system, and from the neural crests form the ganglia and cranial nerves, as well as the rachidian and autonomic nerves.

Formation of the neural tube

The lateral walls of the neural tube thicken until a minimal central canal forms, known as the ependyma. Around it is found the layer of cells known as proliferative. More towards the periphery is found the intermediate zone, while on top of it the marginal layer is encountered. The neurons are generated in the proliferative strait and migrate among the three mantels during their maturation, where there exist cells in delay in the periventricular part, cells in ascendant and descendant division in the

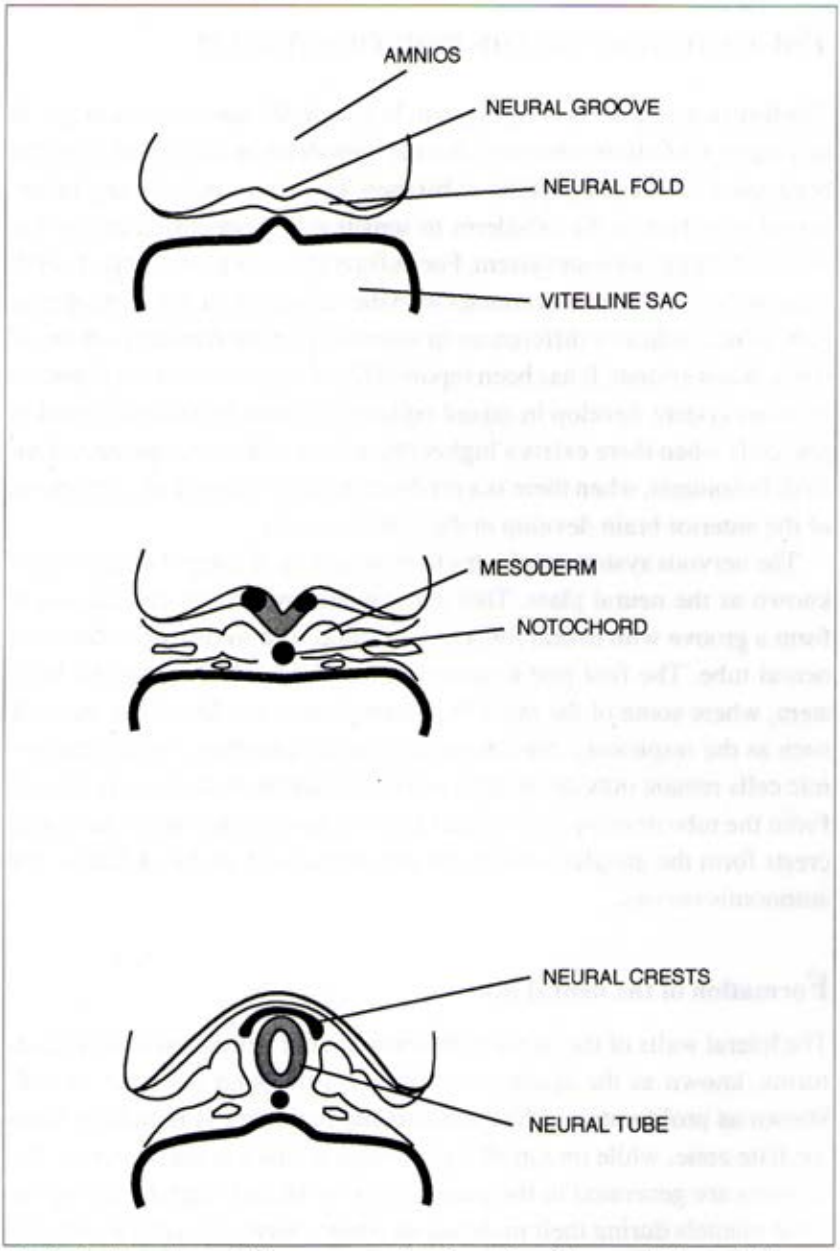


Fig. 9. Early development of the nervous system. Formation of the neural fold, neural tube and the neural crests in the embryonic disc.

intermediate zone, and differentiated cells in the marginal layer. This migration among the three layers of the neural tube will be guided by the cells of the glia, known as radial cells. The radial cells are located near the central canal and present long prolongation extending to the external border of the neural tube. They act as mechanical and chemical guides thanks to their form and to the proteins that over look their walls. At the end of the migration, the neurons take on clearly determined positions; those which shift or move early, occupy the most profound layers and those shifting later are located more towards the surface. During development, the tube continues to thicken and the distance between the layers of neurons grows progressively. Once differentiated, the cells establish themselves in the marginal layer, from which they will migrate to their definitive position in the nervous system. From the neuroepithelial, cylindrical and stratified cells form the neurons, and from the intermediate zone originate the glial cells (astrocytes and oligodendrocytes). The mesenchymatous cells surrounding the central nervous system will originate the microglia.

Cellular maturation

Cellular maturation can be divided into four phases:

A. The first stage is that of neuronal proliferation through prenatal mitosis.

B. The second is a period of growth and differentiation of neurons and glia, characterized by the formation and the growth of the axons and dendrites. The construction of the neural circuits occurs during this phase. Their formation takes place prior to the cells having occupied their places. The growth cone develops within them, tending to extend to form the axon and establish connections with other neurons. The axons in growth group together. To date, the factors determining the direction of their growth remain unknown. The aleatory theory suggests that the development is random, and that later there occurs a selection and reinforcement of the axons located well in relationships with the experience. The growth of neuron fibers is guided by chemoaffinity, implying the

existence of surface molecules acting as guides that the cells recognize. Molecules currently known as CAMs or "cell adhesion molecules" are able to act as surface guides. Three have been isolated: the L-CAM, separated from the liver; the N-CAM, of neural origin; and the Ng-CAM, found in neurons as well as in the glia. At the beginning of brain development, the L and N-CAM are expressed. Besides, the quantity of adhesion molecules varies in the distinct stages of brain formation. It is low during the period of migration and increases when the cells reach their positions. It is possible that the adhesion molecules also guide the growth of the axons. On the other hand, the elongation of the axons may be determined by the tendency of the growth cone to search for a preestablished track, in such a way that the already formed tracks serve as guides for other axons in growth. According to this hypothesis, the cone will search for the direction with less resistance. Also, axon growth would be able to be guided through gradients of concentration of certain substances, such as the NGF or "nerve growth factor." In the beginning, large quantities of interneuronal connections are established, and many of them are later eliminated through cellular death and degeneration of the axons. This process allows for the refining of circuit connections. Experience is necessary for neuronal circuits to function correctly and a critical period exists for the interconnections to fix and adjust themselves in agreement with experience.

C. The third is the stage of synaptogenesis and the appearance of electric activity in the neurons. The first action potentials are spikes due to calcium entry to the cell, later the depolarizations through the entrance of sodium appear. It has been postulated that possibly the mitotic rate of cells depends upon the intracellular concentrations of ions, and it is because of this that the stages of proliferation never occur simultaneously with the phases in which the electric activity appears.

D. The fourth and last period in cellular maturation is that of axonal myelinization, during which substances accumulate, such as: cholesterol, triglycerides, phospholipids, sphingomyelin, gangliosides and cerebrosides. Myelinization of the cord begins in fetal life.

Formation of the brain

Three vesicles are constructed in the anterior part of the neural tube due to changes in the rate of cellular proliferation in their different parts: These vesicles are:

1. The prosencephalon, which later divides into the telencephalon and the diencephalon. The first one will form the cerebral hemispheres and the lateral ventricles, while the diencephalon will form the thalamus and the third ventricle.
2. The mesencephalon will form the structures related to the medial portion of the brain and its peduncles.
3. The rhombencephalon divides into the metencephalon and the myelencephalon. The first will form the protuberance, the cerebellum and the fourth ventricle, while the myelencephalon will generate the medulla oblongata, also known as the brain stem.

The anterior part of the tube, besides forming the vesicles, bends constituting a fold at the level of the myelencephalon, a cervical crease between the medulla and the caudal brain, and a fold in the opposite direction (fig. 10).

General tendencies in the development of the nervous system

A. Of the prolongations of the neurons, the axon appears first and then the dendrites.
B. Initially, the motor routes develop and the sensorial routes appear afterwards.
C. Originally, the unspecific systems develop (reticular activator system, diffuse nucleus of the thalamus) and later the specific systems develop.
D. The systems primordial for survival mature in the moment of birth, and later other less necessary systems mature.

Evolution of the metabolism of the nervous system

It has been observed that the fetal and neonatal brain is resistant to hypoxia. During the perinatal period, the brain oxidizes limited glucose and has little mitochondrial activity. This contrasts with the adult brain, which is the principal consumer of glucose. The encephalon of the fetus and of the newborn is capable of oxidizing fatty acids and ketone bodies. The synthesis of proteins is increased in the fetal brain.

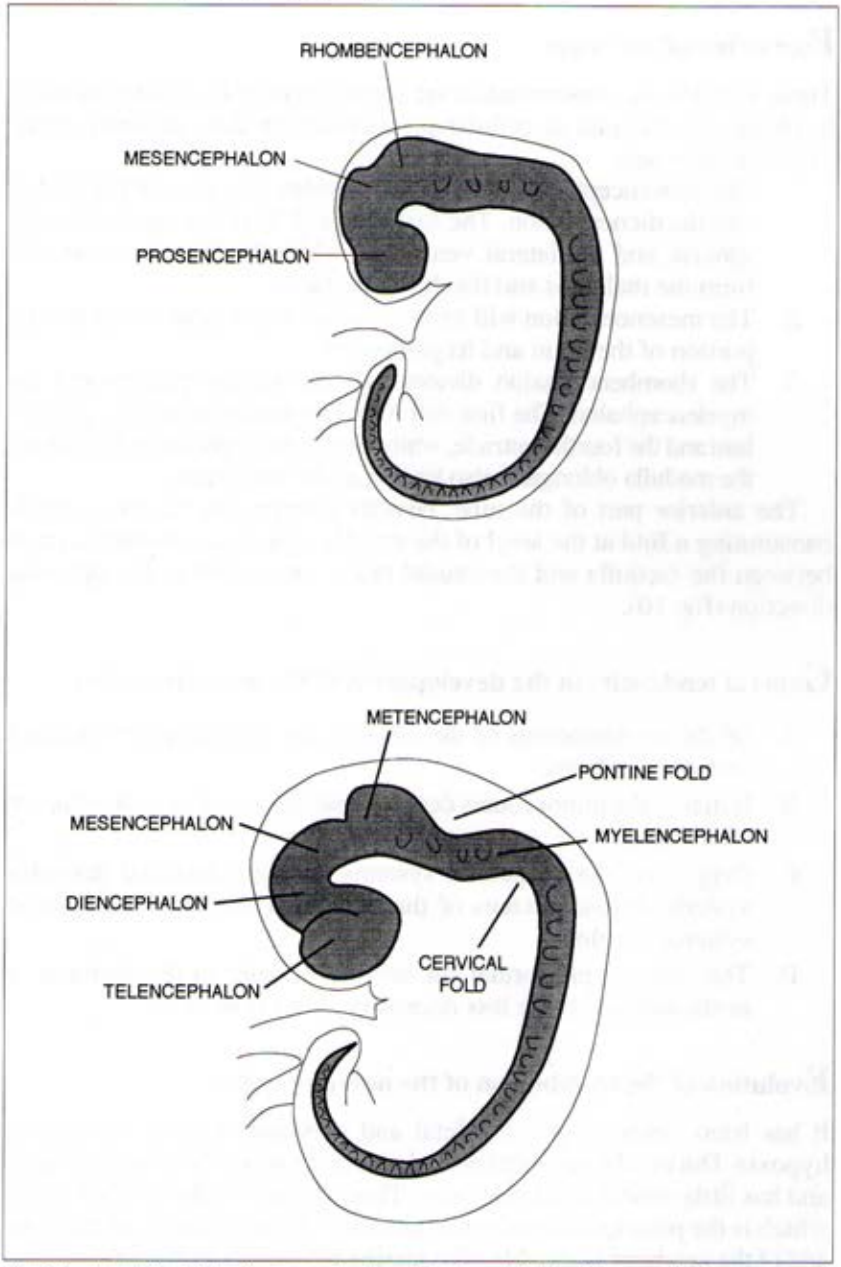


Fig. 10. Formation of the primary cerebral vesicles through folds of the neural tube.

Ontogeny of sensory organs

The ocular globe forms from two evaginations of the neuroectoderm of the anterior brain, known as optical vesicles. When these vesicles reach the surface of the ectoderm, they induce the conformation of the crystalline primordia. The optical vesicle divides to form an internal and an external layer. The external layer converts into the pigmented epithelia, ciliary body and iris, while the internal differentiates into the neural layer, unpigmented ciliar epithelia and the posterior epithelia of the iris (fig. 11).

The ear forms from an enlargement of the epidermis at the sides of the rhombencephalon, known as the otic placoid that, upon invagination, produces the vesicle known as the ear and the otocyst, which eventually separates from the epidermis. In order for the sound waves to arrive at the vesicle, accessory structures develop. These structures are formed from the branchial clefts. The first cleft converts into the external auditory meatus, the first and second branchial arcs transform into the small bones of the middle ear, and the first visceral sac forms the auditory canal, the tympanic cavity and the air spaces of the middle ear.

Ontogeny of sleeping

Two stages are distinguished during the sleep of adult mammalians: the stage of profound sleep that manifests on the electroencephalogram through large amplitude and low frequency waves, and is the stage during which the organism rests. On the other hand, the REM or "rapid eye movement", paradoxical or unsynchronized sleep, is characterized by the movement of the eyes and by the appearance of high frequency waves and low amplitude in the registry of electric activity of the cortex. This stage is where active dreaming is presented. The two phases of sleep are more abundant in the fetus and in the newborn than in the adult. In a newborn human, the sleeping cycle lasts approximately 16 hours per day, and of these 16 hours, 8 hours correspond to REM. The adult sleeps 8 hours and of those 8 hours, only 20% corresponds to REM sleep. It has been described that this type of activity helps the differentiation and maturation of the brain.

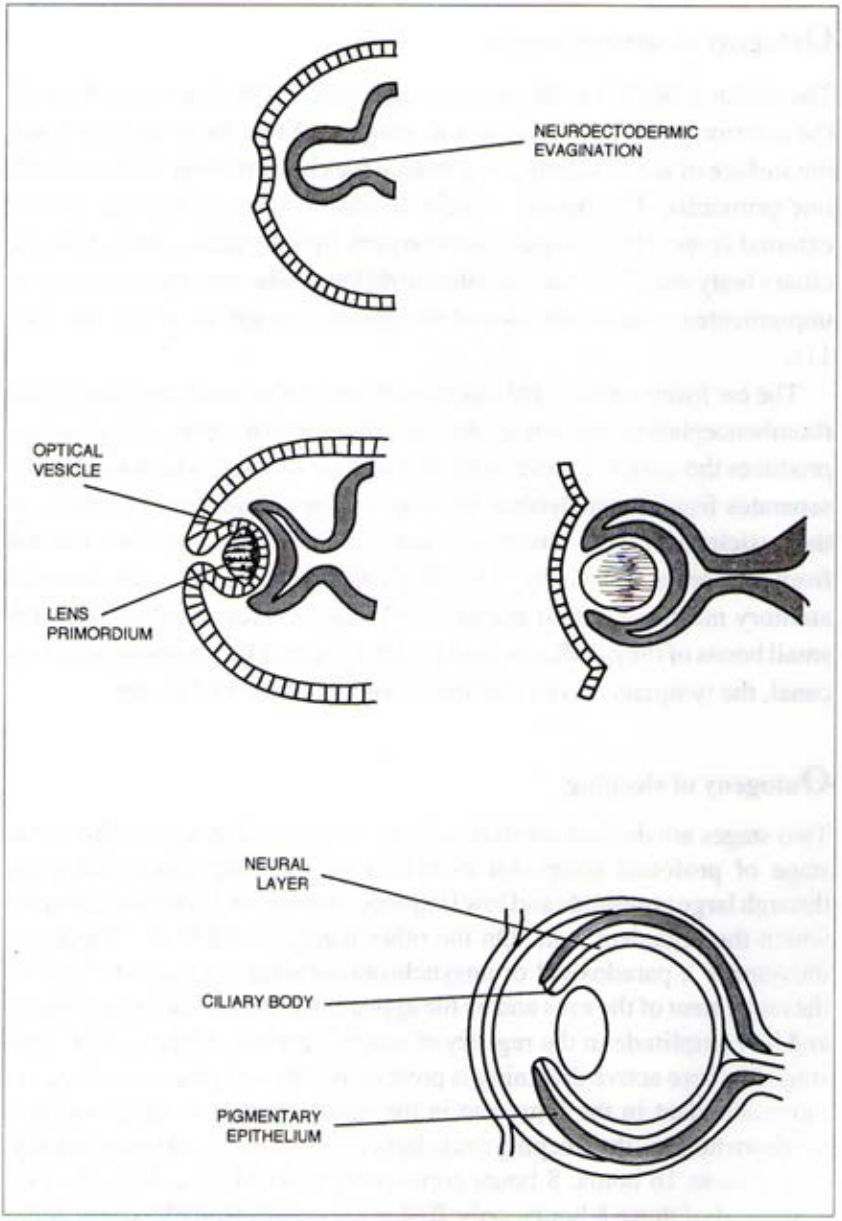


Fig. 11. Embryonic development of the eyes of vertebrates. The optic vesicles are evaginations of the encephalon, which make contact with the crystalline plate. This invaginates and pushes the optic vesicle to form the optic cup.

Ontogeny of the associative prefrontal areas

The prefrontal cortex is the last of the cortical regions in reaching morphological and functional maturity. Until puberty arrives, cellular volume, dendritic arborization, the number of synaptic contacts and complete myelinization are obtained. On the other hand, degenerative alterations manifest in these regions first.

THE PHYLOGENY OF THE NERVOUS SYSTEM

The polarity of the membranes and therefore the excitability appears simultaneously with the surge of living beings. In fact, in some subcellular components and organelles, such as the mitochondria, differences of potential are created through extracting hydrogenions, and this potential is used for the synthesis of ATP (adenosine triphosphate). Therefore, it is possible that the first potential differences between the interior and exterior of the living cells appeared since prokaryotic organisms that lacked a nucleus surrounded by a membrane, such as bacteria. In all eukaryotes, beings in which cells present a nucleus surrounded by a membrane, potential gradients are created between the cellular interior and exterior; therefore apparently the ionic channels permitting the flow of current through the membrane and the pumps that move ions must have appeared very early in evolution. In unicellular organisms, such as the paramecium, there exist potassium and calcium channels. These protozoans swim forward when their membrane potential is negative and when colliding with an object in their path, their membrane depolarizes by opening calcium channels and their swimming direction changes. The depolarization opens the potassium channels, making the membrane potential return to its original state and the forward swimming movement resumes.

An important step in evolution was the substitution of the calcium for sodium channels. This ion does not have such a broad range of actions as an intracellular messenger and allows a more rapid conduction of current. In the hydras and the medusa there are sodium channels, that are different from those of the superior mammalians in that they are not sensitive to medications as tetrodotoxin. Sodium channels similar to ours

are found all the way from platyhelminths, a group including the planarian.

Another important event in the evolution of the nervous system is the appearance of the synapses. The first synapses were observed in the coelenterates. In them the unions are bi-directional and have vesicles containing a neurotransmitter in both extremes of the connection. Cholinergic synapses are found on the platyhelminths.

Nervous system in distinct organisms

In unicellular organisms we are unable to speak of a nervous system, since no neurons exist, as the being is formed by a single cell. However, as we previously described, they are capable of responding in an integrated form to the diverse stimuli as would be the collision against an obstacle during swimming. In the paramecium there exist neuromotor fibers that extend from the anterior extreme of the animal to all of its cilia. The first specialized neurons are found in the hydra and other coelenterates. In these organisms there exist synapses and neuronal unions that are surprisingly similar to those observed in more evolved beings. Despite this, in these organisms a central nervous system is not observed, but the neurons are found regularly distributed throughout their body, forming a type of network. On the other hand, sensorial and motor neurons are not distinguished, since they are all interconnected and function as a unit. Nevertheless, certain neurons are connected to receptors and others to contractile cells.

In the medusas and the anemones the neural cords begin to be distinguished, characterizing the nervous systems of the majority of invertebrate and that are found very developed in arthropods. In invertebrates, a brain and a longitudinal ventral nervous cord are observed, but still the sensorial and motor fibers cannot be differentiated, although the impulses already preferentially transmit in one direction. In the annelids exist a solid central nervous cord (not a tube), which extends the entire longitude of the body and allows the coordinated movement of separate segments. Each segment also has a pair of ganglia. The anterior

part of the cord is an extended ganglion known as a brain, which sends impulses to the entire cord (fig. 12). If the brain is eradicated, the animal is capable of moving, but when encountering an obstacle it continues advancing instead of going around it. In other invertebrates the nervous system is similar to that of the annelids, with a ventral neural cord to the digestive apparatus, although the ganglia tend to fuse (fig. 12).

In the vertebrates, a dorsal neural tube is present, in which distinct segments develop little by little. The brain of reptiles almost exclusively has a brain stem, hypothalamus and a thalamus. In birds and inferior mammalians, the limbic system is added, and in mammals, the cortex is added, which tends to increase its surface in more evolved organisms. The size of the brain in relation to the spinal cord tends to increase (fig. 13).

Evolutionary tendencies

In general, it can be affirmed that the following inclinations can be observed in the evolution of the nervous system:

1. Multiplication of neurons
2. Diversification of their form and function. The neurons specialize in sensorial, motor and integratory.
3. Increase in the speed of conduction. This is obtained through an increase in the longitude of the nervous processes decreasing the number of synapses or through the growth in diameter of the fibers, which occurs by the fusion of various axons, forming a thicker prolongation and through the acquisition of myelin.
4. Complication of the interneuronal connections making so that an impulse can be worth more or less than one. This is attained by the creation of connections that converge or diverge making the information arrive to distinct effectors with multiple significances, using exciting or inhibiting chemical mediators.
5. Reunion of neurons with common functions that carry to centralization or cephalization.
6. Cephalic dominance. Superposition over the brain stem of the limbic system and posteriorly of the neocortex and progressive growth in surfaced covered by it.

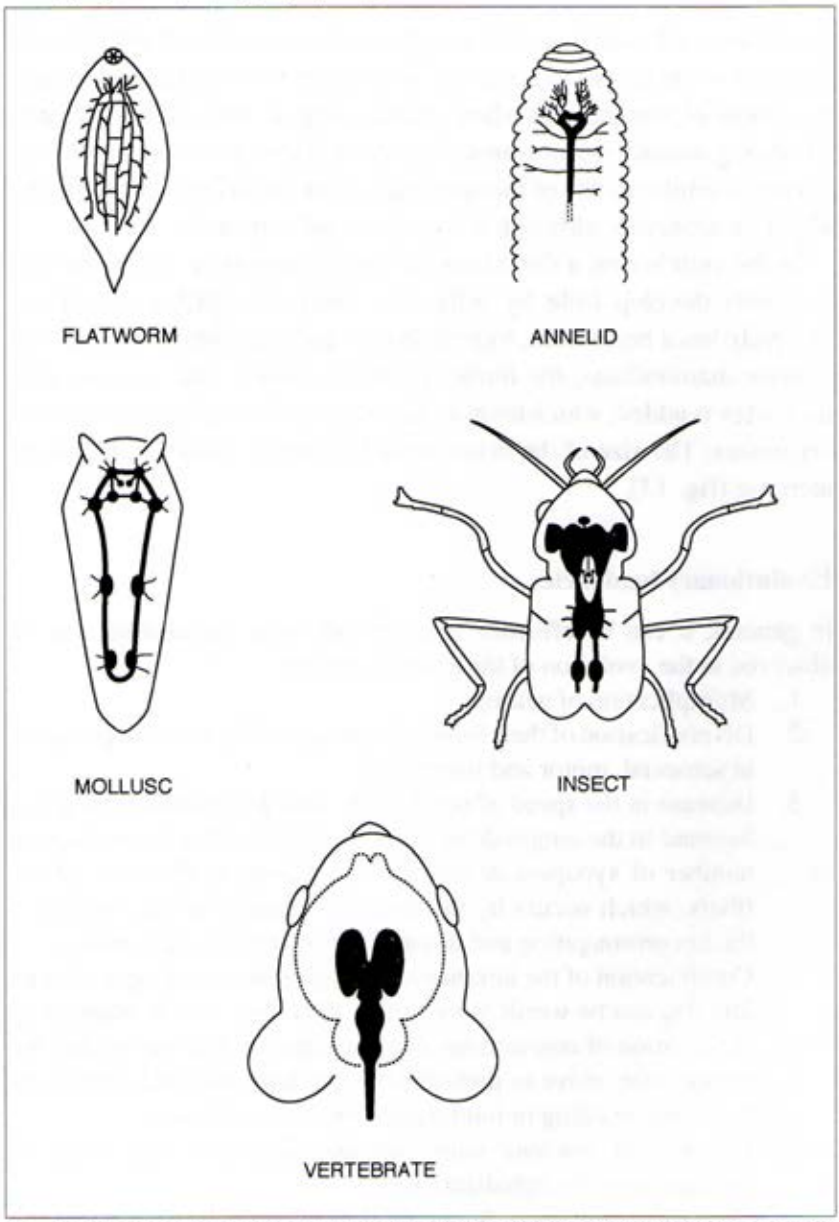


Fig. 12. Scheme of phylogenetic development of the central nervous system. Nervous system of a platyhelminth, an annelid, a mollusk, an insect and a vertebrate. The centralization and cephalization are considered.

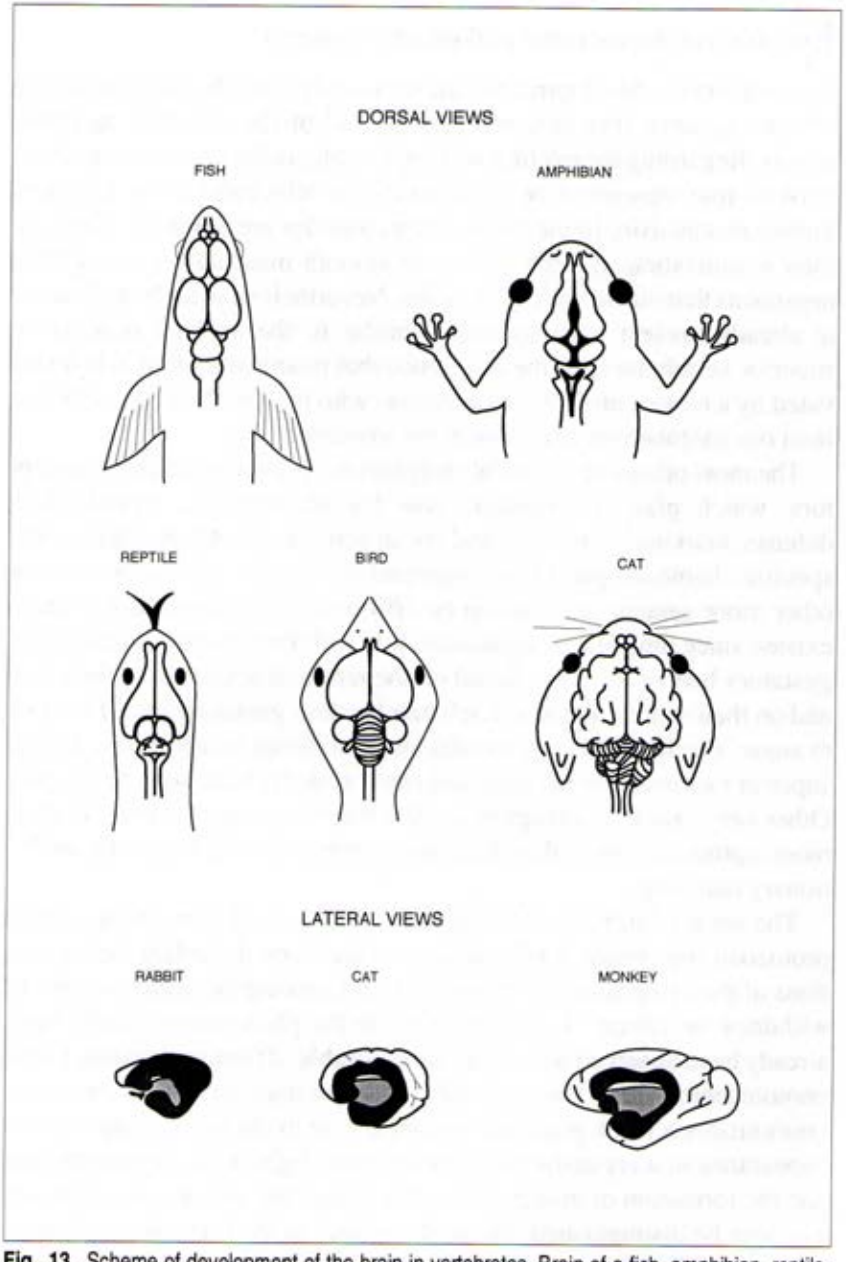


Fig. 13. Scheme of development of the brain in vertebrates. Brain of a fish, amphibian, reptile, bird and a mammalian. Increase in the cerebral cortex area in mammalians.

Evolution of the receptor and effector systems

In parallel to the development of the nervous system, the evolution of the effector systems (muscles and glands) and of the sensorial receptors occurs. Regarding the evolution of the muscle, in the coelenterates there exist no true muscular fibers; however, the cells contract by a no well known mechanism. In the invertebrate, muscles are observed which, in their organization, resemble more to smooth musculature of superior organisms than to the skeletal muscles. Nevertheless, in arthropods there is already present a musculature similar to the skeletal muscles of superior vertebrate with the difference that practically all of it is innervated by a motoneuron, which contrasts with the vertebrates in which at least one motoneuron exists for every muscular fiber.

The most primitive sensorial receptors are probably the chemoreceptors, which play an important role for alimentation, reproduction, defense, marking of territory and social activities. In the evolution very specific chemoreceptors have appeared for certain substances and for other more general ones. It can be affirmed that chemoreceptors have existed since unicellular organisms. It is well known that in insects the gustatory hair of the fly is found on the terminal segments of their legs and on their searching parts. Each hair has four gustatory receptors; one to sugar, one to water, two to salts and one tactile receptor (fig. 14). In superior mammalians the taste and smell systems have been developed. Other very primitive receptors are the mechanoreceptors and the thermoreceptors, however, they have not suffered such an important evolutionary radiation.

The sense of sight also has appeared early in evolution. In fact, in the protozoan the existence of ocular spots has been described, being portions of the cytoplasm that respond to light making the organism tend to withdraw or retreat. In the platyhelminths photoreceptor cells have already been observed which still are incapable of forming images. These photoreceptors have the form of half an orange on whose concavity concentrates a black pigment. The following evolutionary step was the appearance of a crystalline that concentrates light in the photoreceptors and the formation of images. Once the crystalline appears, two types of eyes can be distinguished: the ocular globes in the form of a camera as those found in polyps, squid and vertebrates, and the eyes composed in

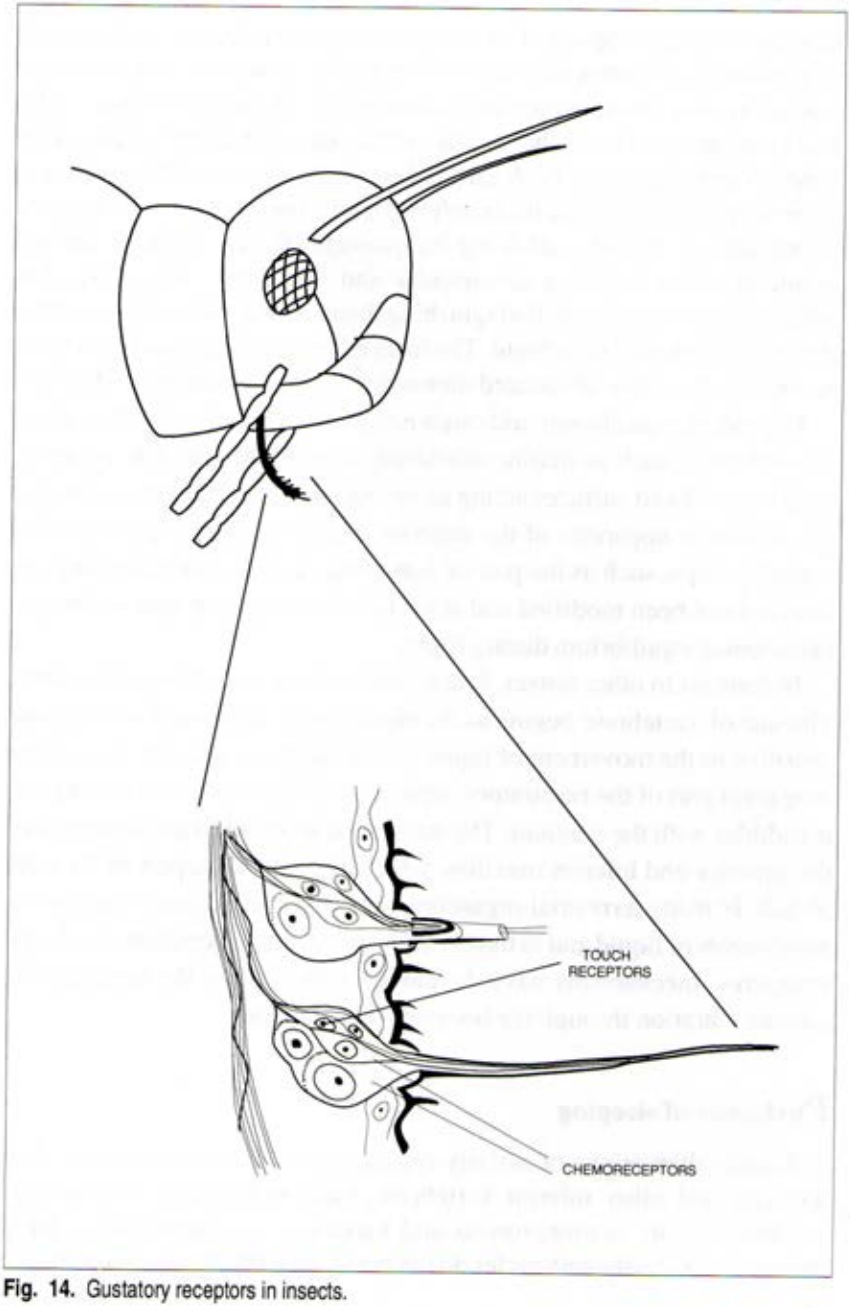


Fig. 14. Gustatory receptors in insects.

mosaic of the arthropods. The composed eyes are formed by hundreds of thousands of monopolar neurons united in groups of seven or eight and each group has its cornea and its crystalline. The cornea is an enlarged and transparent area of the cuticle, while the crystalline is formed by special epithelial cells. Each unit is known as an ommatidia and has a layer of pigmented cells in its inferior part. The pigment can migrate proximally or distally, allowing the passage of light through various ommatidia that facilitate crepuscular and nocturnal vision. Besides, arthropods are capable of distinguishing distinct longitudes of waves than the eyes of superior vertebrate. The images that the composed eyes form are not precise, but can succeed themselves in high frequencies (fig. 15).

Regarding equilibrium, although less primitive, it is present in some invertebrates, such as marine crustaceans, which accumulate grains of sand over ciliated surfaces acting as otoliths. From these organs develop the vestibular apparatus of the superior vertebrate, and organs in other animal groups, such as the pair of rear wings in flies. The rear wings of insects have been modified and stimulate mechanoreceptors helping in maintaining equilibrium during flight.

In contrast to other senses, few animals perceive auditory sensations. The ear of vertebrate begins as an equilibrium organ and its cells are sensitive to the movement of liquid. The middle ear and the Eustachian tube form part of the respiratory apparatus of fish, the stapes uniting the mandibles with the cranium. The hammer and the anvil are remnants of the superior and inferior maxillas, which also act as support of the gills of fish. In many terrestrial organisms not possessing organs sensitive to movements of liquid and in those which do not have specialized auditory structures, mechanisms have developed which allow the detection of ground vibration through the bones of the inner ear.

Phylogeny of sleeping

Although alternations of activity-repose cycles have been observed in annelids and other inferior vertebrate, such as fish and amphibians, cerebral activity is monotonous and variations corresponding to each phase of the activity-rest cycles do not occur. In reptiles, two sleep phases

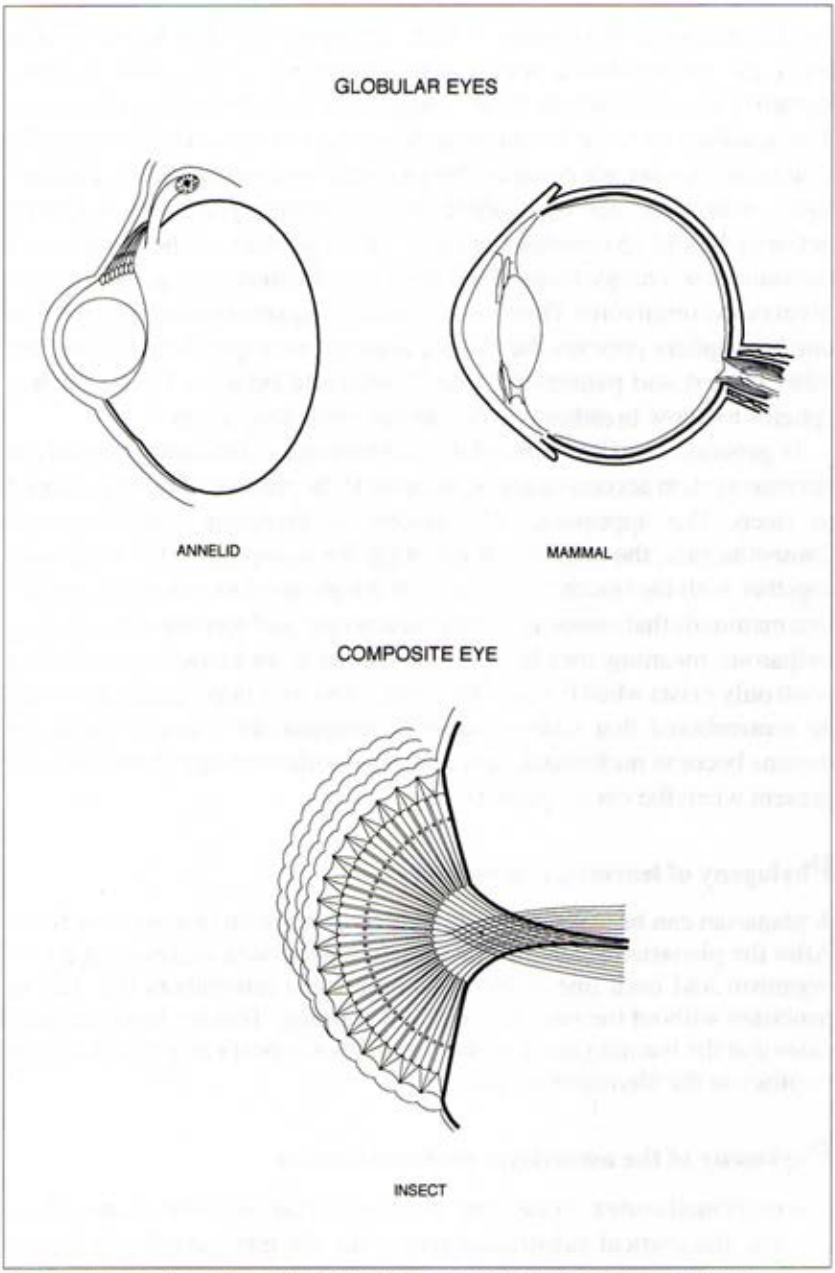


Fig. 15. Comparative scheme of the eyes of an annelid, an insect and of a mammalian.

are distinguished: the passive, which corresponds to slow wave sleep of birds and mammalians; and an active precursor of the oniric activity known in mammalians as REM. Despite that these two sleep phases are distinguished in these chordate groups; their electroencephalographic characteristics are not equal to those of birds and mammalians. Furthermore, within the mammals, there are less dreaming animals that sleep between 10 and 15 minutes each day. These animals are herbivores and consume low-energy food, while the large dreamers are generally carnivores and omnivores. On the other hand, in aquatic mammalians, while one hemisphere presents the electric activity corresponding to sleep, the other is alert and patterns of activity alternate between the two hemispheres to allow breathing at the surface while they sleep.

In general, it can be affirmed that the increase in the complexity of the nervous system accompanies an increase in the amount of time dedicated to sleep. The appearance of paradoxical dreaming coincides with homeothermia, the echidna constituting the exception. This organism, together with the ornithorhyncus form the group of monotremes, primitive mammals that conserve some characteristics of reptiles such as being oviparous, meaning, they lay eggs. Dreaming as we know it in the human adult only exists when the cerebral cortex develops importantly. It should be remembered that when a superior mammalian is decorticated, its dreams become multiphasic and contrasts with the monophasic activity present when the cortex persists.

Phylogeny of learning and memory

A planarian can be trained so that it enters a recipient in search for food. After the planarian is cut, each fragment regenerates to construct a new organism and each one of the new organisms remembers the way to penetrate without the necesity of a new training. This information indicates that the learning and memory capacities appear early (the platyhelminths) on the phylogenetic scale.

Phylogeny of the associative prefrontal areas

The prefrontal cortex is one of the last areas of the neocortex that evolves because the cortical substratum serves for the intellectual and mental functions. This grows unproportionately in the human.

SIMILARITIES AND DIFFERENCES BETWEEN ONTOGENY AND PHYLOGENY

Similarities

1. The step of cords to longitudinal nervous tubes, the appearance of ganglia at the sides of the cord or tube and the cephalization occur in ontogeny as well as in phylogeny.
2. The step of a smooth brain to a pleated or folded one with grooves and convolutions is observed in ontogeny as well as phylogeny.
3. The formation process of the ear and eye are similar during ontogeny and phylogeny.

CHAPTER 4

The Ontogeny and Phylogeny of the Circulation of the Internal Medium

THE CARDIOVASCULAR SYSTEM IN THE ADULT MAMMALIAN

The cardiovascular system consists of a cluster of canals, blood vessels through which blood flows, and of a pump, the heart, which produces the flow. In Man, as in all mammalians, there exist two circuits whose beginning and ending is in the heart, dividing it longitudinally into two functional halves. Through one circuit, blood is pumped from the right half of the cardiac viscera to the lungs, arriving at the left heart. Through the second circuit, the systemic, blood is pumped from the left heart to the tissues of the body, the lungs are naturally an exception, and from there returns to the right half of the heart.

In both circuits the vessels through which blood leaves are called arteries, and those carrying blood to the heart are called veins. In the systemic circuit, blood parts from the left half of the cardiac viscera through a single large artery, the aorta, whose ramifications conduct the blood to diverse organs and tissues. These vessels divide into branches each time smaller, known as arterioles, which ramify into very small vias called capillaries, where the exchange of gases between the tissues and plasma occurs. The capillaries then unite to form venules that join with the objective of comprising veins. Finally, two large veins are formed: the superior and inferior cavas, both of which flow into the heart. In the pulmonary circulation, the blood leaves from the right heart through the pulmonary artery, which divides to form the pulmonary capillaries, and the liquid returns to the left heart through the pulmonary veins. This circulation pattern differs only in the hepatic organ where part of the blood supply is venous as it proceeds from the spleen and gastrointestinal

tract. The systemic and pulmonary circulations differ only in that the pressures with which they pulse liquid are distinct. In the systemic circuit, pressure is elevated for the blood to leave through the capillaries, while in the pulmonary circuit, it is pulsed at low pressures to circulate through the lungs and become oxygenated, but the plasma does not escape through the pulmonary capillaries.

The cardiac muscular cells are capable of spontaneous and rhythmic auto-excitation. This is because the units forming the sino-atrial (SA) node do not have a stable membrane potential and they depolarize through a permeability decrease of potassium. The impulses generated in this zone of the heart propagate to the rest of the tissue and the rhythm of depolarization of the zone is imposed to the rest of the viscera. The cells of the sino-atrial node make contact with the surrounding atrial fibers of the myocardia. From the SA node, the wave of excitation spreads through to the right atrium. There also exists a specialized bundle of fibers that conducts the impulse directly from the SA node to the left atrium, securing the almost simultaneous contraction of both. In the base of the right ventriculum, very close to the interventricular wall, the wave of excitation encounters a second mass of specialized cells known as the atrio-ventricular (AV) node. The transmission of the impulse within this nodule is very slow, assuring that the atria contract before the ventricles do. After exiting the AV node, the impulse travels quickly through the longest of the specialized fibers of the myocardia, those descending through the interventricular wall in the form of bundles, later dispersing the right and left ventricular myocardia. Finally, these fibers make contact with the muscles, and the impulse spreads from cell to cell, assuring a coordinated contraction of the ventricles from the apex of the heart to its base. The action potentials produced in the atrial and ventricular tissues are different from that of the nerves presenting, after depolarization, a phase of plateau where calcium enters the cell. Because of it, the duration of the action potentials is almost the same of that of the contraction.

The rhythmic discharge of the SA node occurs spontaneously in total absence of whatever nervous or hormonal influence. However, it is regulated by the constant influx of nervous impulses and through internal secretions. A large quantity sympathetic and parasympathetic fibers end in the SA node, as well as in areas of the conducting system. The

parasympathetic fibers belong to the vagus nerve and its stimulation, or the application of acetylcholine, the neurotransmitter secreted in these nerve endings, decreases cardiac frequency. The stimulation of the sympathetic, or the application of noradrenaline, produces the contrary effect. Adrenaline, a hormone released by the suprarenal medulla, accelerates the heart.

Another regulating factor is the stroke volume. This, multiplied by the number of contractions per minute is what is known as cardiac output and is constantly regulated in the organism. The stroke volume is determined by the distension of the ventricular fibers, which depends upon the intraventricular blood pressure. This is determined by the quantity of blood returning to the heart, which is conditioned by the level of arterial constriction or dilation. The arterial tone depends upon local controls that assist the metabolic necessities of specific tissues, such as the partial pressure of oxygen and carbon dioxide, determining the tone of the precapillary sphincters. It is also regulated by the reflexes and hormonal controls that integrate and coordinate the necessities of the entire body, also including the vascular tone adjusted by the sympathetic nervous system and the action of hormones, such as angiotensin which increases arterial pressure.

The primary cardiovascular control centers are found in the brain stem. The cardioinhibitory and vasomotor centers are located in this region. These centers receive peripheral baroreceptor and chemoreceptor information from the carotid sinus and from the wall of the aortic arch. They also receive information from sensitive peripheral receptors of all classes (pain, cold, etc.) and from many superior cerebral centers, particularly the hypothalamus. An increase in arterial pressure increases the flow of impulses from the baroreceptors; these impulses ascend through the afferent nerves to the brain stem and arrive at the centers in charge of cardiovascular control, inducing a decrease in cardiac frequency, a decrease in its contractility, and in the level of arterial and venous dilation. The overall result is a decrease of the cardiac output and of the peripheral resistances, with the return of normal blood pressure.

On the other hand, the intra-thoracic pressure fixes the quantity of blood arriving to the heart. The nervous and hormonal influences also establish the force with which the cardiac viscera contracts. At last, the emotions too alter the cardiovascular function, as in the cases of anguish, where palpitations surge.

THE ONTOGENY OF THE CARDIOVASCULAR SYSTEM

Angiogenesis

Formation of the blood vessels begins in the extra-embryonic mesoderm of the vitelline sac. Mesenchymatous cells, known as angioblasts, cluster together to form isolated masses known as blood islets, within which appear spaces and form cords. The angioblasts shift or move around the cavity, constituting the primitive endothelium. The vessels, isolated at the beginning, fuse to form canal networks (fig. 16), and the mesenchymatous cells surround the vessels, forming muscular and connective tissue. The primitive plasma and blood cells form from the endothelial cells at the same time that the vessels develop, first in the vitelline sac, immediately in the allantoides and later in the liver, spleen, and lymphatic ganglia.

Morphogenesis of the heart

During the embryonic period, the cardiac viscera forms from the ventral splanchnic mesenchyma, which forms two cardiac cords. These acquire light in their interior to compose the endocardiac tubes, which fuse together beginning at the cranial part to form a single medial endocardial canal. This canal develops dilations and constrictions that will constitute: the aortic sac, the truncus arteriosus, the bulbus cordis, ventricle, atrium and the sinus venosus. The bulbus cordis and the ventricle grow, making the cardiac tube fold over itself, and constitutes the bulboventricular vault that has a "U" shape. The atrium and sinus venosus situate in the position dorsal to the bulbus cordis, truncus arteriosus and ventricle (fig. 17 A and B).

At the height of the constriction, separating the atrium from the ventricle, enlargements of subendocardial tissue form, growing and fusing to develop the endocardiac cushions (fig. 4.2 b). The separation of the atria originates from a primary membrane or septum, which grows from the dorso-cranial wall toward the endocardiac cushions. This membrane does not completely close, leaving an opening between its inferior border and the cushions, known as the primary foramen. Soon,

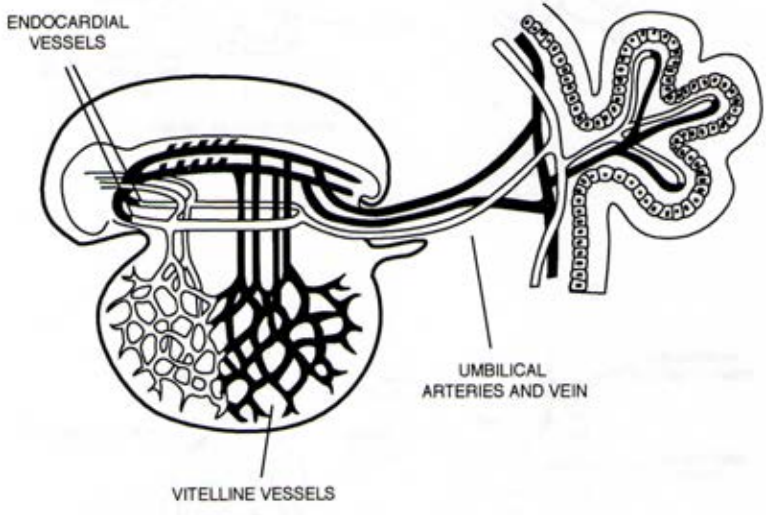


Fig. 16. Scheme of the primitive cardiovascular system, in which the localization of the endocardiac tubes is shown. Each cardiac canal gives rise to a dorsal aorta that ramifies into de vitelline vessels. The blood returns to the heart through anterior cardinal veins, the vitelline veins and the umbilical vein.

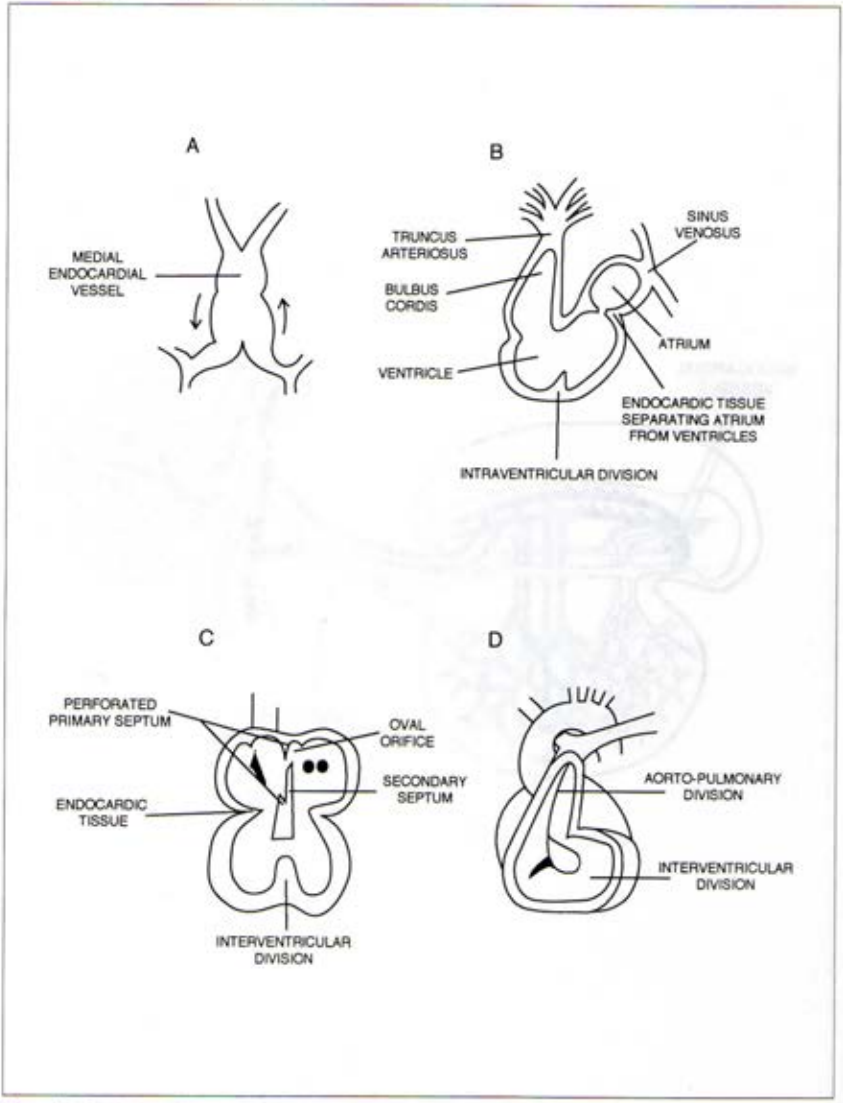


Fig. 17. Early development of the heart. The cardiac tubes fuse together and form a single medial endocardial vessel in which the atrium, ventricle, bulbus cordis and truncus arteriosus are distinguished. The tube folds, the endocardiac cushions appear separating the atrium from the ventricle and the interventricular septum begins to form. The primary and secondary septa form and separate the atria. The aorto-pulmonary wall is formed and fuses with the interventricular septum and the endocardiac cushions, keeping the aorta in the left ventricle and the pulmonary artery in the right.

perforations appear in the central and superior part of the septum, constituting the secondary foramen or oval orifice. Simultaneously, a second membrane or septum forms, growing from the endocardiac cushions toward the dorso-cranial wall and covering the secondary foramen. This septum constitutes an incomplete wall partially covering the oval orifice (fig. 17 C). In the beginning, the sinus venosus opens in the center of the right atrium and gradually becomes incorporated into it. Its left horn will form the coronary sinus. The major part of the left atrium is formed from the primitive pulmonary vein, which reabsorbs and comprises the pulmonary vessels.

The interventricular wall develops simultaneously with the interatrial, and with the division of the bulbus cordis when the aorto-pulmonary wall molds. The interventricular partition originates as a muscular fold, growing from the apex in the floor of the primitive ventricle to the endocardiac cushions (fig. 17 B and C). The separation of the bulbus cordis is produced through enlargements of the subendocardial tissue that form bulbar borders. These take a spiral orientation and upon fusing, configure the aorto-pulmonary wall, separating the aorta from the pulmonary artery (fig. 17 D). Initially, an orifice exists between the free border of the interventricular wall and the endocardiac cushions. This orifice closes by the fusion of the bulbar borders, the endocardiac cushions and the interventricular wall. After the closure of the orifice, the pulmonary trunk communicates with the right ventricle, as does the aorta with the left ventricle. The bulbus cordis incorporates gradually into the walls of the ventricle.

The semilunar and atrio-ventricular valves develop from the borders of the subendocardial tissues at the level of the aorta, the pulmonary trunk and of the tissue surrounding the atrio-ventricular canals. These borders perforate and form again to develop three thin walled valves.

Between the important mechanisms intervening in the morphogenesis of the heart, we can signal the changes in volume of the matrix of distinct portions of the cardiac tube, which exercise pressure against the wall, which varies in its level of compliance (capacity to stretch under pressure). The volume of the matrix modifies by altering any one of the following factors: the mitotic rate of the cells, the different adhesion of these units while they migrate to distinct portions of the cardiac viscera,

cellular death, variations in the temporal and geographic rate, and by distribution of the secreting activity and of the level of hydration of conjunctive material.

On the other hand, the hemodynamic pressures also participate in the process of the morphogenesis of the heart. It has been postulated that the spiral form taken on by the division of the bulbus cordis is the result of blood turbulence.

Cellularity and ultrastructural aspects of cardiac development

In contrast to skeletal muscle, cardiac muscle conserves its mitotic activity after birth, although it decreases to a very low value. During the initial phases of the development of the heart, growth is the product of this mitotic activity (hyperplasia), and the cells are of a reduced size. When the heart begins to grow through cellular hypertrophy, the division rate gradually decreases and the cells increase in dimension. It would be useful to know the factor that induces the myocytes to divide and/or to increase in size, then allowing the lesioned tissue, by an infarction, to be replaced by new cells. The increase in the size of the cells decreases the density of the nuclei as well as the amount of the cytoplasmic membrane. At the same time, the fluidity of the membrane increases, elevating the cholesterol/phospholipid rate. The quantity of sarcoplasmic reticulum and the transverse intercalated discs increases, while the number of lateral contacts between cells decreases. Meanwhile, the number of mitochondria increases during development as well as the number of mitochondrial crests. The number of mitochondria varies from one species to another and depends upon a large number of conditions, such as the level of maturity reached at the moment of birth.

The contractile mass of the heart increases throughout development. It comprises only 30% of the weight of the heart in a fetus while it comprises 60% of its weight in an adult viscera. Not only does the quantity of myofibrils increase, but they modify their distribution and type of subunits by which they are formed. In effect, a change in the expression of the subunits of the contractile proteins occurs, particularly in the heavy and light chains of myosin. This is found in distinct forms known as the varieties V1, V2 and V3. The V1 and V2 myosin possess a chain with high ATPase activity, while the V3 myosin is formed by a

chain with less activity, slower and more efficient. The embryonic ventricle exclusively expresses V3 myosin, while only myosin V1 is found in the ventricle of a newborn and of an adult. The three types of myosin are expressed in the atria during development and in adult life.

Histological development

The ventricular wall of the heart is comprised of cells of mesodermic origin. Some of the cells form the endocardium, which organizes as if it were an epithelial layer, while others migrate towards the exterior of this stratum, secreting a collagenous matrix that comprises the myoepicardial layer, matrix or cardiac gelatin. Therefore, this structure is formed by an epicardial and a pericardial plate composed of mesothelial cells and a spongy layer of myoblasts. The endocardium grows toward the spongy layer of the cardiac gelatin, forming chords of myocardia lined by endocardia, which are isolated and adopt a radial orientation. The ventricle compacts, but some of these trabeculas subsist, constituting the papillary muscles. Later, the heart is invaded by other heterogeneous cellular groups, finally being composed of: the myocytes, fibroblasts, endothelial and nervous cells and phagocytes. Complex interactions exist between the distinct groups of cardiac cells in tissue cultures. The fibroblasts induce the formation of a functional syncytia from the isolated myocytes and provoke metabolic changes within them.

As the chambers of the heart form, a layer of conjunctive tissue grows from the epicardia, separating the atria from the ventricles, except in the case of some fibers that form the nodes and bundles of the conduction system. These fibers constitute the sino-atrial and atrio-ventricular nodes and the ventricular fibers are innervated by them in abundance immediately. The sino-atrial node is originally found in the sinus venosus and incorporates to the wall of the right atrium, situating at the point where the vena cava enters the atrium. The elements of conduction are separated by the lax conjunctive tissue and numerous connections exist between the muscle and the conduction tissue. Gradually, cellular reabsorption occurs and conjunctive tissue rich in collagen surges, acquiring the appearance of adult transport tissue.

Development of electric excitability and activity of the heart

At the beginning of the embryonic period, the excitability of the cardiac cells is depressed because they have a decreased membrane potential. This is due to low potassium permeability, while the permeability of sodium is similar to that of adult hearts, existing an excess of positive intracellular charges in relation to the mature viscera. The activity of the sodium and potassium pump is low in the initial stages and increases with age (fig. 18).

In the adult, the cardiac action potentials present, after the phase of depolarization, a plateau in which calcium penetrates into the cell, prolonging its duration. The depolarization stage in embryonic hearts is slow, its magnitude is reduced and the potentials lack the plateau. Two distinct mechanisms have been described to explain the late depolarization at the beginning of development in different groups of organisms. In birds, it is due to the entrance of sodium into cells through slow channels, differing from the adult in that they are not sensitive to medicine such as tetrodotoxin. Later, these canals coexist with the fast sodium channels to finally predominate the latter. It is not known if fast sodium channels do not exist in the membrane of the myocytes of birds at the beginning of development, or if they are inactive because of decreased membrane potential. In contrast, the slow potentials in the rat are the result of the entrance of calcium into the cells through channels that can be blocked by substances such as cobalt and manganese. Later, the potentials depend upon fast sodium channels as well as on calcium pores, and finally the first predominate. The change from a rapid phase into a slow phase of depolarization, causes the duration of the action potential to decrease during the first days of development, but afterwards it increases when the plateau phase appears.

Initially, automatism occurs in all the cardiac cells and is of low frequency, but later it exclusively restricts to the cells of the conduction tissue and the frequency increases to a higher value than in the adult. At first, the primitive atrium acts as a pacemaker, but gradually the sinus venosus takes on this function and incorporates into the right atrium. The changes in automatism are parallel to the modifications in the permeability of potassium and can be related to the energetic equilibrium of

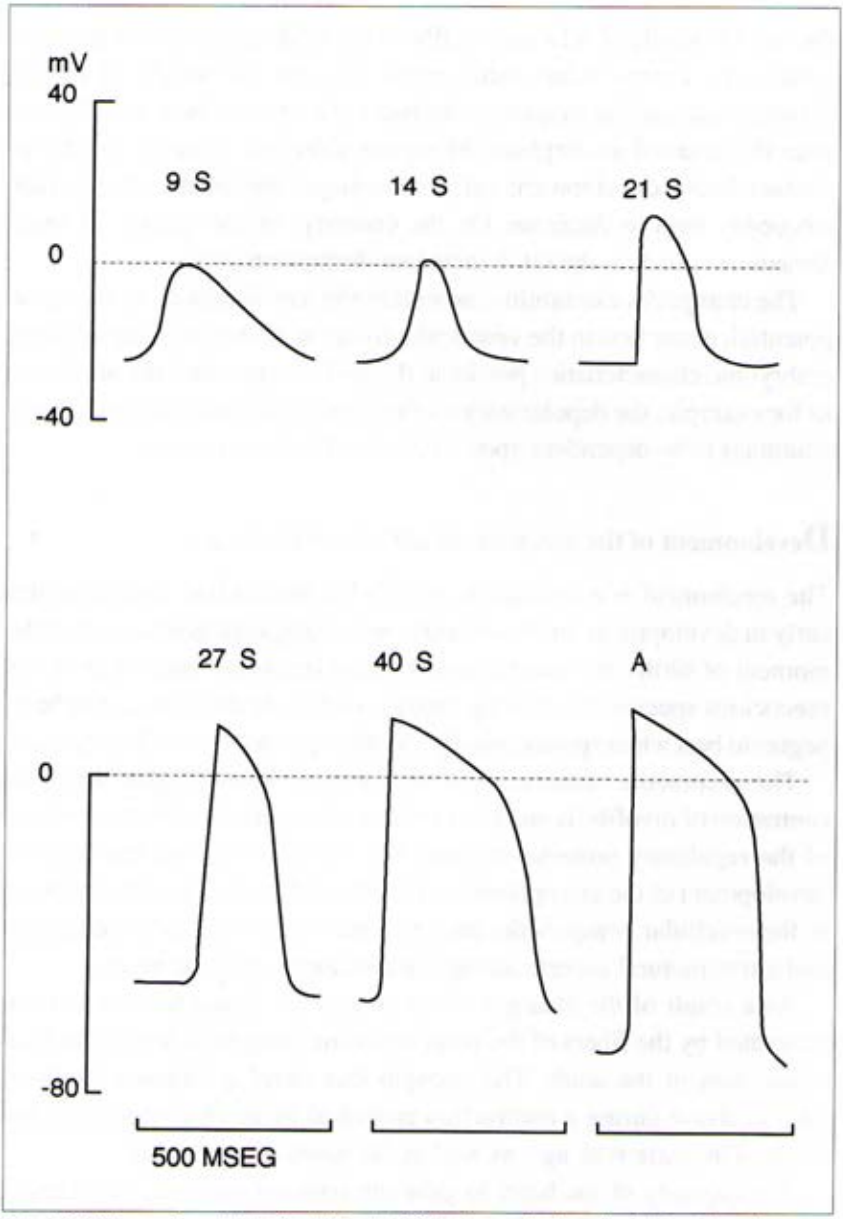


Fig. 18. Ontogenetic evolution of electrical activity in the ventricular cells. Letters above the traces indicate the stage of chick embryonic development expressed as the number of somites and the adult stage.

the cell (its levels of ATP and ADP). In the adult organisms of different species, an inverse relationship exists between the weight of the individuals and cardiac frequency; the heart of a rat beats more rapidly than does the heart of an elephant. However, although corporal weight increases during development, only in the larger species does the cardiac frequency tend to decrease. On the contrary, in the species of small dimensions, such as the rat, it increases during ontogeny.

The changes in excitability, as well as the modifications in the action potential, occur first in the ventricular tissue and later in the atria. Many embryonic characteristics persist in the nodal tissue until the adult age, as for example, the depolarization of the action potential in these tissues continues to be dependent upon calcium and lacks a plateau.

Development of the mechanical activity of the heart

The mechanical and contractile activity of the cardiac viscera begins early in development. In the altricial species (organisms immature at the moment of birth), the heart begins beating relatively late; while in the precocious species, the beating appears earlier. In the human, the heart begins to beat when approximately 8% of the gestation period has passed.

The contractile characteristics of the heart depend upon: the concentration of myofibrils and their level of arrangement; the composition of the regulatory proteins (myosin V1, V2 and V3); and the level of development of the sarcoplasmic reticulum and the T tubes. The changes in these cellular components are described in the section of cellularity and ultrastructural aspects during the development of the heart.

As a result of the changes in the contractile structures, the tension generated by the fibers of the heart at distinct lengths is less in the fetal tissue than in the adult. The strength that develop isolated bands of cardiac tissue during a contraction provoked by its electric stimulation tends to increase with age, as well as the speed of shortening.

The capacity of the heart to generate contraction force, at different fiber lengths due to the volume of blood filling the viscera at the end of the diastole, is represented in the curves of ventricular function. This

response is decreased in the fetus by a low cardiac contractility. After birth, although the contractility increases, a reserve volume of blood does not exist to distend the viscera to a large level. This is because all the liquid is being pulsed to cover the high demand of nutrients. Until after the neonatal period, the curve of the ventricular function, characteristic of the adult, manifests.

In the embryo, the tubular heart generates an arterial pressure of scarcely 1 to 2 mm of mercury that grows, during development to reach at the end of gestation, approximately half the pressure of an adult.

Cardiac output in the fetus is the sum of the combined outputs of the two ventricles, since both pulse blood to all organs and to the placenta, functioning as a system in parallel. This contrasts with the functioning in the series of the two ventricles in the adult heart.

Changes in metabolism

As a difference from fetal skeletal muscle, the cardiac has a greater demand of energy than the adult has. In spite of this fact, its consumption of oxygen is low and quickly increases after birth to higher levels superior than those of the adult, implying that its functioning is greatly anaerobic during intrauterine life. Of the oxygen consumed by the fetal heart, 20% is used in the basal metabolism of the organ and in the development of the electric activity, while the remaining 80% is utilized in its function as a pump. On the other hand, practically the totality of oxygen consumption can be attributed to the oxidation of carbohydrates since the organ does not consume lipids. This contrasts with the metabolism of the adult viscera in which the consumption of carbohydrates is responsible for only 35% of the expense of oxygen and the lipids are responsible for the remaining 65%.

Membrane permeability to glucose in embryonic myocytes is higher than in adults, and the sugar enters through simple diffusion, being its transport exclusively limited by the rate of utilization. Much later, glucose crosses the membrane by facilitated diffusion, and the metabolism of the fatty acids decreases its transport and utilization as an energetic substratum.

The activities of the enzymes of the glycolytic pathway in the fetal heart are comparable to those of the adult viscera and change little during development. The percentage of glycolytic flux converted to lactate is elevated and tends to decrease in the majority of species, although there exists great variation among species, for example: pigs consume lactate instead of producing it.

On the other hand, the activity of the enzymes in the Krebs cycle and the respiratory chain are depressed during gestation and increase during development. The pentose pathway is very active throughout all the phases of cellular proliferation. A deficiency exists in the oxidation of lipids, because the substances that introduce them to the mitochondria are not active.

During the fetal period, synthesis of glycogen in the heart is elevated. The carbohydrates stores descend by the middle of gestation in the precocious species, reaching a high level of maturity before birth. Nevertheless, in the altricial species, whose newborns are very immature, the contents of glycogen in the heart and in other organs continues to be elevated until the moment of birth.

Resistance to hypoxia is much higher in fetal and neonatal hearts than in the adult, because during the intra-uterine life, the organisms develop in an environment with little oxygen; since this gas arrives to the fetus by simple diffusion, following decreasing concentration gradients. The sensitivity of the fetal heart to hypoxia increases during development. Hypoxia decreases the capacity of the cardiac viscera to generate tension during the postnatal stage when the glycogen reserves are poor and this effect can be partially counteracted through increases in the concentration of glucose.

Development of the regulation of cardiovascular activity

Myocardial regulation depends upon growth of its innervation, upon appearance of postsynaptic receptors and upon the maturation of the intracellular mechanisms, permitting a response to the transmitter-receptor interaction. These three events occur independently during the embryonic and fetal development.

The innervation of the heart appears relatively late throughout ontogeny. In the rat, it arrives around the moment of birth, and during the first postnatal week, preceding the vagal fibers those of the sympathetic. The nervous fibers appear first in the sino-atrial region and progress toward the left atrium, the bases of the ventricles, the right ventricular body and the apex. The coronary innervation advances more rapidly than does the rest of the myocardia.

The surge of the receptors precedes the innervation. The molecules receiving the information from the sympathetic system, known as alpha and beta adrenergic receptors, are present from early ontogeny and their appearance precedes that of the receptors capturing the vagal signals, called cholinergic.

The maturation of the intramembranous mechanisms mediating the response to the neurotransmitter-receptor interaction does not appear simultaneously with the expression of receptors. The transducer proteins (G protein) and those in charge of the synthesis of the second intracellular messengers have their own pattern of maturation. The clearest evidence of this dissociation is observed with the stimulation of the alpha adrenergic receptors during distinct stages of cardiac development. At first, its stimulation increasess the frequency and the strength of the heart. As a consequence of innervation the response transforms to a decrease. The change has been associated with the incorporation of an inhibitory transducer protein (Gi protein), which intervenes in the passing of information between the receptor-neurotransmitter complex and the enzymes in charge of synthesis of the second messenger.

Fetal circulation

Fetal circulation differs from that of the adult in that the flow of the blood of the right and left hearts join to irrigate the entire organism and the placenta. This is due to the existence of communication between the atria through the oval orifice, and because the pulmonary trunk is connected to the aorta through the ductus arteriosus (fig. 19). The distribution of blood to the distinct organs differs in the fetus and in the organism after

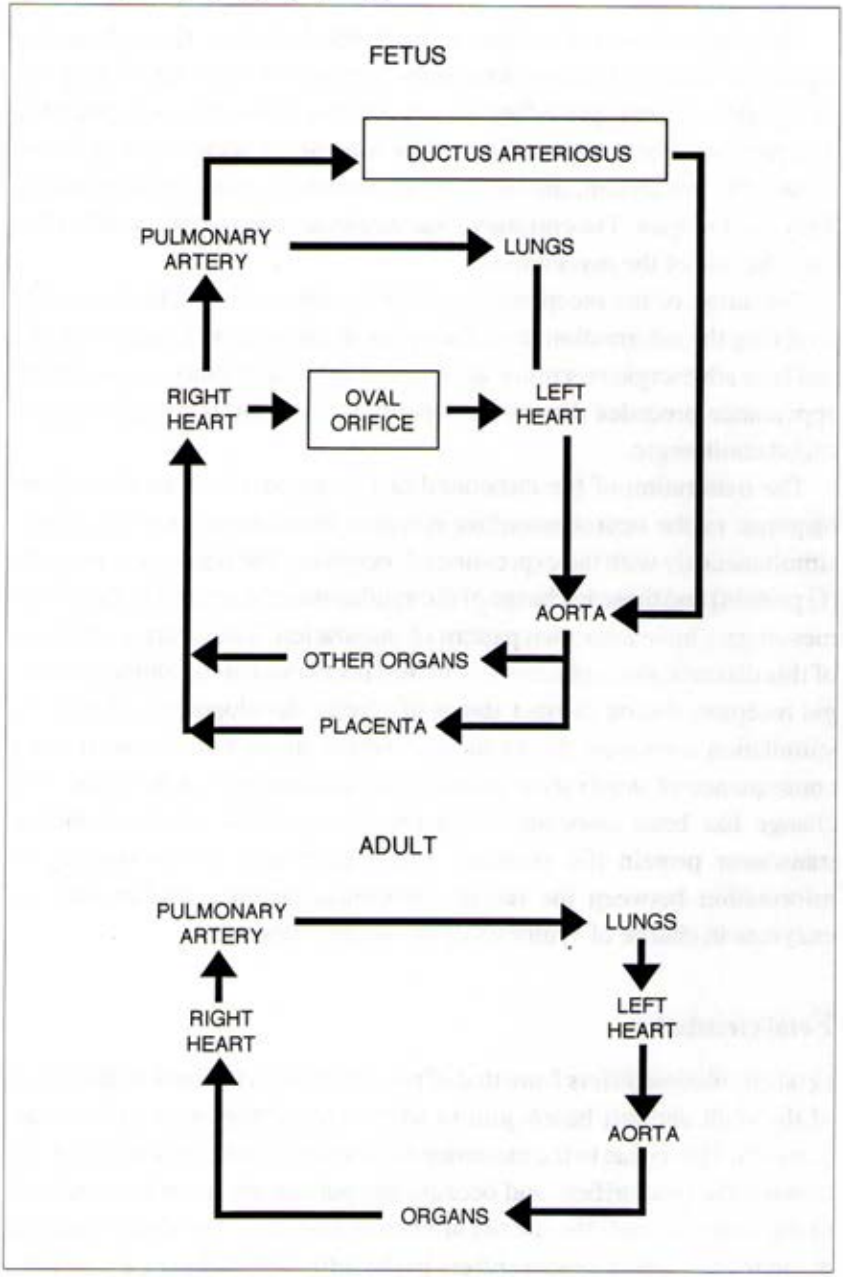


Fig. 19. Comparative scheme of fetal and adult circulation.

birth; 41% of the cardiac output goes to the placenta, which disappears at the moment of birth, and the lungs only receive 7% of the blood, while in the adult, the same quantity of blood passes through them as that which will be distributed to all the other corporal organs.

At birth, the placental circulation is occluded, decreasing the pressure in the inferior vena cava and in the right atrium, reducing the vascular pulmonary resistance and increasing blood flow to the lungs. This produces an increase in the pressure in the left atrium and closes the oval orifice and the ductus arteriosus.

Regulation of the vasculature appears from intra-uterine life, during which there exist cholinergic and catecholaminergic receptors. It is known, for example, that noradrenaline increases blood pressure, produces bradycardia, elevates flow of blood to the heart, the lungs and the placenta, without modifying the cardiac output during the last stage of gestation.

The vascular receptors can be influenced through innervation, by substances secreted by the same organs; or by catecholamines secreted by the adrenal medulla, by the para-aortic ganglia or by organs of Zuckerkandl. Information arriving from the innervation and from the secretion of catecholamine through the suprarenal gland is determined by the activity of superior centers. When the electric activity of the fetal cerebral cortex changes to rapid waves of low voltage, similar to those present during REM (rapid eye movement) sleep, the cardiac activity and the fetal systemic pressure increases. On the other hand, electric stimulation of the hypothalamus produces an increase in arterial pressure and in cardiac frequency. Superior centers receive information from chemoreceptors and baroreceptors located in the carotid and aortic sinuses, which are present and active from fetal life. Even though baroreceptive activity in the fetus is limited, variations are presented in both the cardiac frequency and in the fetal systemic pressure as a result of the denervation of the aortic sinus. On the other hand, other factors have been described which affect the circulation in the organisms during development, such as the variations in the blood volume, angiotensin II, prostaglandin E2 and bradykinin.

THE PHYLOGENY OF THE CARDIOVASCULAR SYSTEM

The principal function of circulation is to carry nutrients to all the cells of the organism and to pick up the products of the cellular metabolism. All living beings need to transport substances from one part of their system to the others; nevertheless, in a large quantity of unicellular and in some simple multicellular organisms a circulatory system is not developed, and both nutrients and wastes diffused between the environment and the interior of the organism. This process of diffusion is facilitated by movement of the cytoplasm of unicellular organisms, of the mesothelium (lax layer of cells in the corporal wall) in sponges, or of the mesoglea (tissue occupying the space corresponding to the coelom) in coelenterates (fig. 20). This movement is, many times, the result of the animal's own displacement. Besides, the environment in direct contact with the organism is renovated by the movement of the cilia, flagella or muscular fibers in these primitive invertebrate.

In those which are not as primitive, but conserve the small size such as the rotifers, the bryozoan and some echinoderm, a circulatory system is not present, the nutrients and the wastes still being moved simply by diffusion. In many of these organisms, particularly the echinoderms, the circulatory system forms a hydraulic skeleton.

The first well-differentiated cardiovascular apparatus appears in the nemertines or flatworms. These marine beings of ribbon form are characterized by the presence of an organ, a proboscis provided with a calcareous stylet, which can be released to the exterior through an orifice behind the mouth. Their circulatory system is formed by two canals united by blood lagoons and some transverse vessels. The flow for circulation is provoked by the movement of the animals and by portions of the vessels which contract in an irregular form.

Once cardiovascular systems appear in invertebrates, two basic types of systems surge: opened and closed. In the first, blood is pulsed by the heart through vessels towards lagoons or cavities of blood to again return to the cardiac viscera. In the closed systems, blood circulates through canals and nutrients and wastes leave or are incorporated at the capillary level, without blood leaving the canal system.

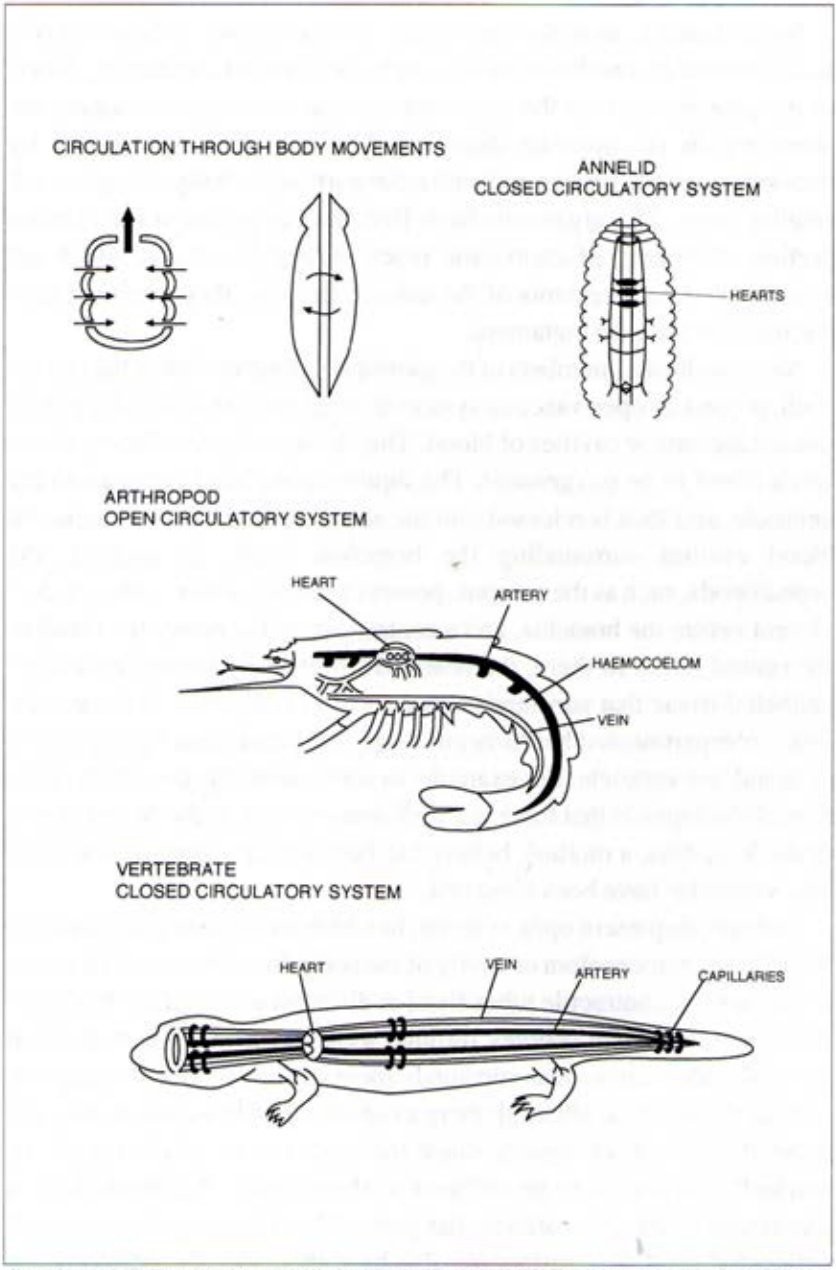


Fig. 20. Schematic representation of the internal transport systems in distinct groups of animals.

In the annelids, as in the earthworm, the circulatory system is closed and is formed by two blood tubes; one in the ventral face carrying blood to the posterior part of the organism and the other dorsal, making the same trip in the opposite direction. These vessels interconnect by transverse vascularization and with other parts of the body through much smaller tubes. The organisms have five pairs of hearts in the anterior portion, consisting of contractile tubes pulsing blood and which are assisted by the movements of the animal. Besides, they present a contractile bulb for each metamere.

Some mollusks, members of the gastropod group including the marine snail, present an open vascular system through which the blood is pulsed toward lagoons or cavities of blood. They have a branchial heart, which sends blood to be oxygenated. The liquid passes from the heart to the ventricle, and then is released into the aorta, which in turn opens to the blood cavities surrounding the branchial heart. In contrast, the cephalopods, such as the octopus, possess a closed system with a cardiac viscera before the branchia, and a central pump that pulses the blood to the central aorta. In them, the hearts are formed by spongy muscular-epithelial tissue that surrounds many small vessels. Also in some mollusks, compartmented hearts begin to appear, constituted by one or two atria and one ventricle. For example, in some cephalopods, which differ from the octopus in that there is a shell present, such as the Nautilus, and in the Neopilina, a mollusk believed to be extinct for many years, up to four ventricles have been observed.

Arthropods present open systems, in which the cardiac viscera pulses blood to the hemocoelom or cavity of the body that harbors it. The hearts are formed by contractile tubes fixed at different points of the body and have pores, known as ostioles, through which the blood penetrates from the pericardial cavity that surrounds them. In some small arthropods, such as the sea flea, although there exists a pulsatile vessel, it does not present a circulatory system, since the organism is small enough for nutrients and wastes to be diffused to the exterior. Arachnids have a segmented heart with ostioles that pulses blood to the pulmonary and pericardial cavities. Crustaceans also have this type of cardiac viscera

and present two aortas, an anterior and a posterior, which carry blood to the corporal cavities and the pericardial cavity (fig. 20). In some of them, accessory hearts are found at the entrance of the branchia and in the feet.

Automatism of cardiac beating in the invertebrates is not given through muscular cells, but depends on the activity of the nerves, therefore its rhythm is said to be neurogenic. There are about ten neurons grouped in ganglia presenting spontaneous activity that determine the rhythm of the heart.

The hemichordates, such as the acron worm, form a small group of marine animals that excavate holes in the sand or mud and are provided with a muscular proboscis. These beings have similar larvas to those of the echinoderms and at the same time are phylogenetically related to chordates, since only in these groups are pharyngeal clefts present. In them, the circulatory system is open and contrasts with the closed system of the chordates, despite their kinship.

In fish, the heart is formed by two cavities that push the blood to the branchia and to the rest of the organism. Important differences exist within the closed circulation of chordates to adapt the organisms to the terrestrial environment, the most important is the division of the heart in two pumps, so that the same quantity of blood that arrives to the rest of the body also reaches the lungs.

In amphibians, the heart contains three cavities. The blood proceeding from the systemic circulation mixes in small proportions with the blood pumped through the lungs at the level of the ventricle. This pushes the major circulation as well as the minor, and the mix of the arterial and venous blood is oxygenated to a large extent at the level of the skin.

Reptiles possess four cavities in the heart, although in some of them the ventricles are only partially separated. In birds and mammalians the ventricles are completely divided into the right and the left (fig. 21).

In the hearts of vertebrates, automatism is given by the muscular cells called nodal. Besides, the cardiac frequency is in direct correlation to the size of the organism and is higher in the smaller-sized animals than in the larger ones.

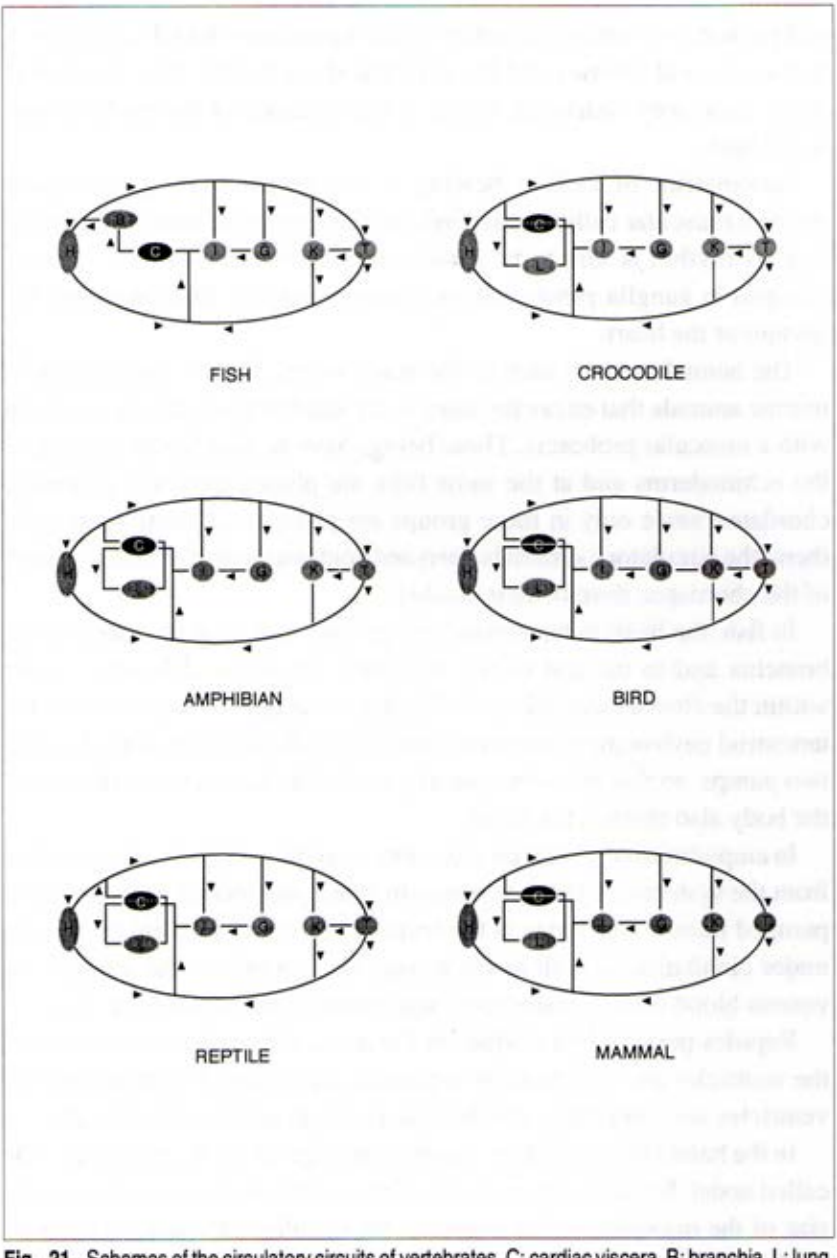


Fig. 21. Schemes of the circulatory circuits of vertebrates. C: cardiac viscera, B: branchia, L: lung, l: liver, G: gut, H: head, K: kidney, T: tail and extremities.

SIMILARITIES AND DIFFERENCES BETWEEN ONTOGENY AND PHYLOGENY

The diversity in the phylogeny of the cardiovascular system is so great that it takes a large amount of work to find the evolutionary tendencies. However, some similarities can be mentioned in the phylogenetic development and the ontogeny of the mammalians, such as the following:

1. The fusion of the blood lagoons to form the circulatory system.
2. The rise of the heart from pulsatile tubes.
3. The separation of the heart into chambers (atria and ventricles).
4. The step of a system constituted by a heart or a pair of them connected in parallel, pulsing blood to irrigate the entire organism to another type of system formed by two viscera connected in series; one to oxygenate the blood and the other to pulse it to the rest of the body.

CHAPTER 5

The Ontogeny and Phylogeny of the Digestive Functions and Nutrition

THE PHYSIOLOGY OF NUTRITION IN THE ADULT MAMMALIAN

The gastrointestinal apparatus comprises: the mouth, esophagus, the stomach and the small and large intestines. It also includes the salivary glands, part of the liver and the pancreas. Their function is to break down food into small molecules and transfer them from the external environment to the internal; where they can be distributed to the cells of the body by the circulatory system. The glucostats, located at the level of the hypothalamus, regulate the acquisition of food; the glucostats of the lateral nuclei stimulate ingestion, and those of the medial nucleus induce animals to stop eating. These structures respond to the levels of glucose contained in the plasma. The majority of food taken in the mouth are large fragments of matter, composed of high molecular weight substances, such as proteins and polysaccharides that are not capable of crossing cellular membranes. Before these substances can be absorbed, they should be disintegrated into tiny molecules, such as amino acids and monosaccharides. This process is carried out by the action of hydrochloric acid and enzymes, which are secreted toward the interior of the gastrointestinal tract. The molecules resulting from digestion cross the membranes of the intestinal cells and penetrate the blood and lymph, a process known as absorption. While this process is taking place, the contractions of the smooth muscle lining the walls of the gastrointestinal apparatus displace the luminal contents through the tract. Finally, the unabsorbed and undigested material is discarded, as well as bacteria and metabolic products, as fecal matter.

The coordination of the movements of the digestive tube depends upon the activity of the two intramural nervous plexi. These are formed by neurons found present throughout the entire length of the digestive tract,

responding spontaneously to the stretching of the walls of the canal. They receive terminations of the sympathetic and parasympathetic nervous systems. The motility of the digestive apparatus is also regulated by gastrointestinal neurotransmitters and hormones, which are synthesized by the same wall of the digestive tube (submucous layer), such as secretin, somatostatin, CCK-PZ (cholecystokinin-pancreozyme), VIP (vasoactive inhibitor peptide), gastrin, bombezine, serotonin, etc.

The digestive system secretes mucus, enzymes, hydrochloric acid and hormones. The rhythm of secretion of these factors and motility depend upon influences, such as the activity of the plexi, nervous excitation and internal secretions.

Obtainment of nutrients during the inter-digestive stage

As humans, we generally eat three times each day, while many other species eat less frequently. Nevertheless, all the other components of our body need a continuous supply of nutrients. Because of this fact, a large part of the nutrients we consume are transformed into carbohydrates, stored in specific organs, from where they are slowly released into the blood stream during lapses between one meal and the next. To assure the continuous administering of nutrients to all cells, the levels of glucose in plasma are maintained constant and are subject to control systems. These control systems accomplish their function by regulating the storage or release of glucose from the carbohydrate reserves established in organs such as the liver, skeletal muscle and erythrocytes.

The most important storage of glucose in vertebrates is in the liver. This organ accumulates carbohydrates as glycogen, which is degraded for the benefit of other tissues, and the main source of energy used by the hepatocytes are fatty acids. Although glycogen is found in other tissues, such as skeletal muscle, its function is to only supply energy locally to these cells when glucose or oxygen are scarce. The erythrocytes of some species also act as storers of glucose. Besides, they compensate the changes in the concentration of glucose in plasma, absorbing this carbohydrate and incorporating it to its glycogen reserves when it is in excess, and releasing it in small quantities when the concentration of glucose is low.

The control systems regulating the utilization and storage of glucose through the distinct organs consist of afferent and efferent components found integrated by the nervous system. Among the afferent elements are the glucostats of the hypothalamus and some peripheral receptors, such as the chemoreceptors of the carotid sinus and of the aortic glomus that respond to hypoglycemia by provoking the secretion of adrenaline, which acts over the liver, releasing glucose. On the other hand, there are glucoregulators sensitive to insulin in the central nervous system as well as peripheral receptors, located in the region that irrigates the pancreaticoduodenal artery.

At least five hormones comprise the efferent part of the control system regulating glycemia. Insulin increases the transport of glucose at the cellular membrane of the adipocytes and of the muscular tissue, and also increases the capture of carbohydrates by the hepatocytes. These effects make the concentration of glucose in the blood decrease. Adrenaline mobilizes the carbohydrates stored as hepatic glycogen, therefore increasing blood glucose. Glucocorticoids inhibit the utilization of sugar by the extrahepatic tissues and facilitate the synthesis of glucose from the proteins and fatty acids, elevating the levels of glucose in the blood. Glucagon stimulates the conversion of hepatic glycogen to glucose and facilitates its secretion into the blood stream. The thyroid hormones exercise a diabetic action over glycemia. There are also numerous neuropeptides that intervene in the glucoregulation, such as the growth hormone, the adrenocorticotrophic hormone stimulating the secretion of glucocorticoids, and another neuropeptide that facilitates the absorption of glucose by the neurons.

On the other hand, there is a central control over the levels of glucose in the internal medium, and it is possible to establish conditioned hypoglycemic reflexes associating the sound of a bell or the smell of mint with insulin injections. These reflexes are similar to those described by the Russian physiologist Ivan Pavlov, who associated in time the ringing of a bell with the arrival of food, provoking an animal to start salivating upon hearing the auditory stimulus. The nervous system also plays an important role in glucose homeostasis through innervation of the liver and of the glands in charge of producing the hormones that intervene in glucoregulation.

THE ONTOGENY OF THE DIGESTIVE SYSTEM AND NUTRITION

Nutrition during the embryonic and fetal periods

Glucose is the principal source of energy the ovule consumes, obtaining it through the circulation while it is in the ovary and from the secretions of the feminine genital tract after ovulation. There exists an increase in the metabolism of glucose in the moment of fertilization and it increases ten times more during the stages preceding implantation. The embryos of two cells in some species need glucose, as well as pyruvic and lactic acid to develop. However, from the stage of eight cells, the embryos of all species develop until forming blastocysts, when they grow in a cultivation medium containing glucose as the only source of energy. The glycogen reserves in existence from the beginning of development degrade after the formation of the blastocyst and totally disappear in the moment of implantation. During gastrulation, glycogen stores are consumed more rapidly by the cells of the dorsal lip of the blastopore than by cells of other regions.

From the moment of implantation to the stage of formation of the first somites, the embryo obtains nutrients from liquid filling the blastocoel and from the uterine cells degraded by the trophoblast to form the decidua that will later compose the placenta.

After the formation of the first somites, the embryos consume more glucose than do the adult tissues. The expense decreases with growth and reaches the level of the adult organisms before the fetal period. The change temporally coincides with a progressive decrease in the production of lactic acid, and is therefore possibly due to a transition from anaerobic to aerobic respiration. However, the consumption of oxygen is maintained constant during this period, and this gas is used most probably in synthetic processes.

The fetus obtains glucose through the umbilical circulation. The mother ingests this carbohydrate with food and it is transported through the intestinal mucous into the blood stream, or is released from the hepatic reserves into the maternal circulation. Glucose is transported to the placenta, where et crosses to the fetal side by facilitated diffusion. The fetal level of glucose in plasma is less than in the maternal plasma, and

the gradient is maintained by the accumulation of glucose as glycogen in the fetal erythrocites of some species. Glucose passes, by simple diffusion, from the blood to the tissues in favor of the concentration gradient that is created and maintained by metabolic activity.

Development of the gastrointestinal tract

Simultaneously with the processes of nutrition, the organism in development forms the primitive intestine, which will be in charge of nutrition from birth. This forms when the embryo folds cephalo-caudally and laterally incorporating part of the vitelline sac (fig. 22). The intestinal epithelia and glands develop from the endoderm, as the muscle and the peritoneum develop from the splanchnic mesoderm. The origin of the secretory cells of the digestive tract is still unknown, it might be nervous, deriving from the neural crests or mesodermic belonging to the digestive tube and expressing the same genes as some neurons.

During histological development of the intestine, numerous mitosis are observed, but little change in cell form is noticed, the epithelia conserving its morphological cuboid apparence. There is an increase in the rate of migration of the cells related to the grade of differentiation.

The primitive intestine can be divided into: the anterior, middle and caudal. From the anterior forms the pharynx, esophagus, the stomach, duodenum, liver and the pancreas. From the middle part forms the jejunum, ileum, the caecum, appendix, ascending colon and part of the transverse colon. From the caudal intestine derive part of the transverse colon, the descending colon, the sigmoid colon, rectum, the high portion of the anal canal and part of the urogenital system.

The process of formation of the mouth and the anus in the first stages is similar. The notochord grows toward the cephalic and caudal region between the ectoderm and endoderm until it arrives at the prochordal plate and the cloacal membrane. These regions are bi-laminar and the endodermic cells are firmly adhered to the supra-adjacent ectoderm, impeding the growth of the notochord. The prochordal plate will form the oral or bucco-pharyngal membrane that, in the moment of the longitudinal fold of the embryo, is placed in a ventral position to form

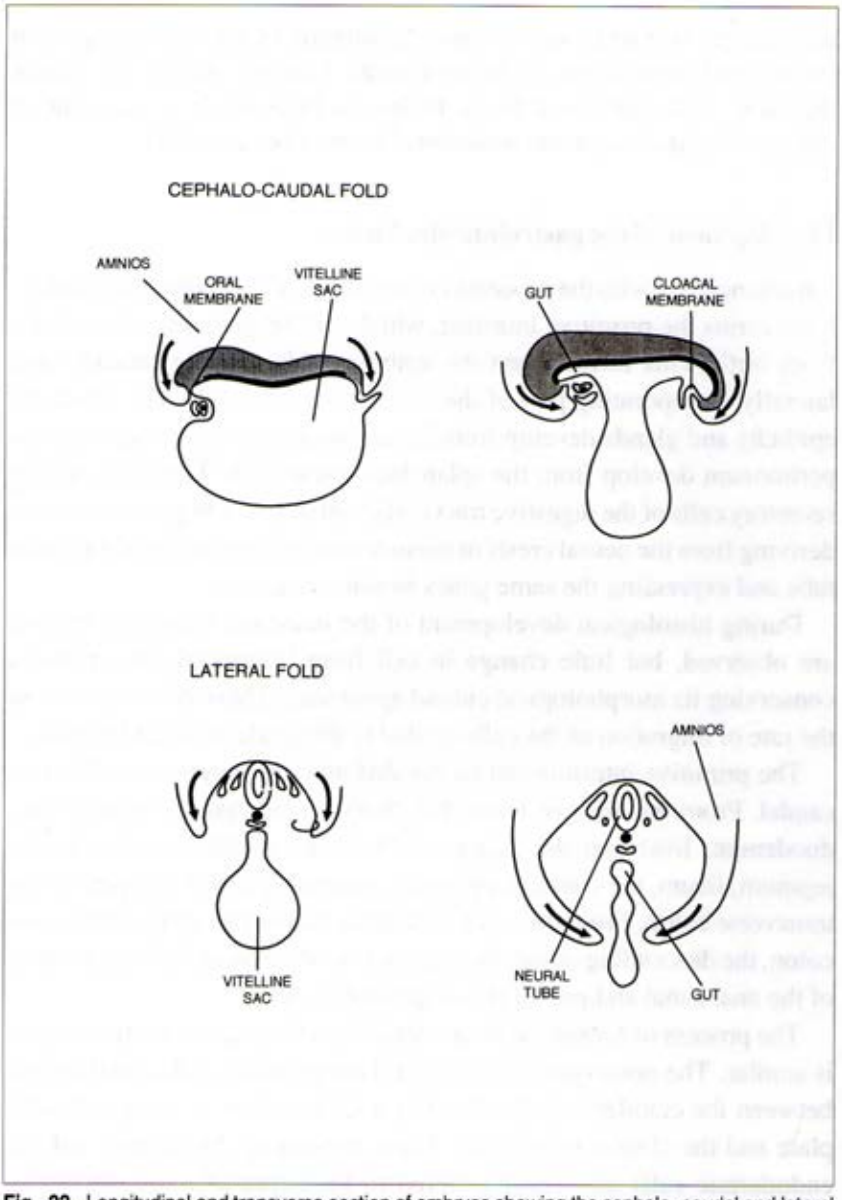


Fig. 22. Longitudinal and transverse section of embryos showing the cephalo- caudal and lateral folds, engulfing part of the vitelline sac to form the anterior, middle and posterior intestine. Also illustrated is the localization of the oral and the cloacal membranes where the openings of the digestive tube will develop.

the mouth. Similarly, during the caudal fold responsible of the formation of the posterior intestine, the cloacal membrane fixes in the ventral position. The oral region and the cloacal membrane perforate to form the two openings of the digestive tube.

At the beginning, the secretion of enzymes occurs in the entire wall of the digestive tube and later specializes in defined portions of the wall with the secretion of a certain type of enzyme. Finally, the accessory glands appear, which are in charge of this function. The secretion is initially regulated by the type of food found in the light of the intestine and later appears the regulation through substrates or hormones circulating in plasma after having been absorbed from the digestive tube.

The hormonal secretions of the digestive tube can be grouped into two families, because they have similar structures; the first is that of the gastrin and the cholecystokinin and there also exists an independent group constituted by the secretin, the vasoactive intestinal peptide (VIP) and glucagon.

It is not until the moment of birth, when villi and microvilli begin to transport nutrients across the intestinal epithelium. In the adult, the epithelial cells divide in the base of the intestinal prolongations and migrate to the point where they will remain to accomplish their function. However, during development, mitosis occurs on the entire surface of the microvilli and the life span of the cells is longer. Not all the transporters of nutrients appear simultaneously. First the glucose and amino acid transporters surge, and much later the transporters of biliary salts, which are not observed until some days after birth, despite the fact that the organism begins to eat milk rich in fats requiring these salts for their absorption. The appearance of the different transporters varies in time in agreement with the level of maturity reached by the species before birth.

In the beginning, the transport of nutrients occurs at all levels of the digestive tube and gradually it becomes the principal function of the duodenum. As an example, it should be remembered that at the beginning of the postnatal period, amino acids are absorbed by the colon and a few days after, these transporters disappear, and the function of absorption is restricted exclusively to the small intestine.

Despite that the absorption of nutrients is poor before birth, feces are formed (meconium) and contain the wastes of the amniotic liquid that the product consumes during the fetal period. The greenish color of meconium is the result of biliary salts that are already secreted but cannot be reabsorbed by the intestine.

It is important to point out here that during the neonatal period there are important changes in the diet of the organisms. Before birth, the product mainly receives carbohydrates dissolved in blood, after birth it receives nutrition mainly from the fatty acids contained in the maternal milk and by the end of lactation diet becomes more varied.

Development of the nutrient reserves

During the fetal period, two stages can be distinguished with functional organizations in charge of glucose homeostasis. In the first of the two stages, each organ depends upon the carbohydrates arriving through circulation and contains a small reserve of it. The mechanisms in charge of glucose homeostasis in this stage are related to the mechanisms that regulate vascular changes. Catecholamines play an important role, provoking a redistribution of blood flow to the distinct fetal organs and increase the arrival of substrates to the brain, heart and liver.

Towards the end of gestation, fetal homeostatic mechanisms evolve. The liver functionally differentiates as the general storer of glucose and accumulates almost the double of glycogen per gram of tissue, as that found in the adult liver. Insulin and adrenaline regulate glycogen stores in the hepatic organ in this stage, in the same way as they regulate it in the adult.

These reserves of fetal glycogen decrease after birth, since they are used to supplying glucose to the fetus during birth, when long periods occur in which the blood coming from the placenta does not arrive. Birth contractions, produce hypoxia, bradycardia and probably hypoglycemia. After birth, the diet of the newborn is rich in fats and low in carbohydrates. This change also contributes to the descent of the fetal glycogen reserves in the newborn. Toward the adult age, the carbohydrate stores increase.

THE PHYLOGENY OF THE DIGESTIVE FUNCTIONS AND NUTRITION

Modalities of nutrition in phylogeny

Although autotrophic organisms exist that synthesize their own food and do not have digestive functions such as plants, the majority of the living beings are heterotrophs, finding nutritious material in their surrounding environment.

It is said that nutrition is microphagic when the ingested particles are very small and are consumed in great quantity. Food is obtained through pseudopods, through systems of filtration or through ciliated surfaces, utilizing mucus to trap the particles. In protozoans, as in the amebas, the nutrients are obtained by engulfing portions of the environment through prolongations of parts of the cytoplasm, forming pseudopods. In the paramecium, the cytopharynx is covered with cilia that conduct food toward the mouth. In the sponges, the internal face of the corporal wall is covered with ciliated cells, which create currents of water to obtain food. These move a volume of liquid, equivalent to the sponge, every minute. The bivalves, like the clams, have branchias covered with cilia, which produce currents, dragging the small organisms to their mouth. The secretion of mucus traps food in the gastropods, as in the snail and the tunicate. Finally, structures specialized in filtration of the environment exist, such as those present in crustaceans. It seems incredible that an organism the size of a whale feeds exclusively by the filtration of small organisms from the medium, which implies the passing of thousands of gallons of water through the filtration system to be able to cover the energetic requirements of the organism.

The nutrition is considered macrophagic when the particles consumed from the environment are of large size. Some animals, such as earthworms and spiders, indiscriminately ingest portions of the world surrounding them, digesting only the useful organic material for their food and discarding the rest of the material that was caught. Others choose food through their sensory organs. Within these, we find the herbivores, which feed on plants, the carnivores that eat meat, the

omnivores who have a varied diet, and saprophytes which consume organic material in decomposition.

There are also organisms that exclusively consume liquid food, like insects and hummingbirds who drink the nectar of flowers; leeches, insects and vampires who feed on blood; and young mammalians who ingest milk.

Modalities of digestion and absorption in phylogeny

Digestion is intracellular when the food is phagocytized and engulfed into a digestive vacuole to which unite the lysosomes secreting enzymes such as glucosidases, acid phosphatases and peptidases. This manner of breaking down food is the most primitive and precedes the appearance of digestive apparatus. Therefore, it is affirmed that the enzymes evolve before the gastrointestinal systems.

Digestion is extracellular when the digestive enzymes empty to cavities that communicate with the external medium and the cells absorb the products of broken down food. Generally, enzymes are hydrolases, meaning that they break the ties of the molecules attaching to them water. In many superior organisms we still find intracellular and extracellular processes.

The process of absorption is similar in almost all organisms. Simple diffusion is the most primitive mechanism and later in evolution there appears: facilitated diffusion, active transport and pinocytosis, or absorption of liquid and particles dissolved in the medium by pseudopods.

Distinct types of digestive secretions in phylogeny

There have appeared distinct types of secretions in the digestive tube that comply with specific functions. The secretion of mucus traps food particles, protects and lubricates the digestive cavities. Anticoagulants are secreted in organisms that feed on blood, and paralyzing substances in spiders and other predators. Later, digestive enzymes are found which can be grouped into different families according to the type of substrate over which they act. The glucosidases, such as amylase, saccharase,

lactase, maltase and cellulase break down carbohydrates. The proteases fracture proteins; lipases fats; RNA and DNA ases break down nucleic acids. Finally, there appear the gastrointestinal hormones. At the beginning of evolution all of the digestive tube secretes enzymes, but little by little glands are distinguished which specialize in secretion.

The control of the digestive functions of transport and secretion is independent for each part of the tract, and are coordinated in the beginning through the quantity and type of foods and products of digestion. Later appears the nervous regulation and that of internal secretions.

Food requirements in phylogeny

The need to consume food depends on the degree of activity of the organisms and on the presence or absence of thermic regulation. In homeotherms, the intensity of metabolism is proportional to the size of the body; when the organism is small its consumption of food is greater, since the loss of heat is increased.

The food requirements of substances that the organisms cannot themselves synthesize are also very varied. Protozoans need to consume pyrimidine; some insects and mollusks require the intake of cholesterol from the medium surrounding them; and in other insects, the incorporation of choline is indispensable. There are essential amino acids and fatty acids (linoleic, linolenic and arachidonic), which are indispensable for mammalians, and in the ruminants there are symbiont bacteria and protozoans that synthesize this molecules. The vitamins also form part of the indispensable requirements of some species of vertebrates.

Digestive systems in distinct groups of animals

Protozoans take in food, which is intracellularly degraded using digestive enzymes, and the products diffuse to other parts of the cell. In some protozoans the acquisition of nutrients is facilitated through the movements of the cytoplasm, as in the case of the amebas that obtain nutrients through phagocytosis (fig. 23). In other unicellular organisms having a

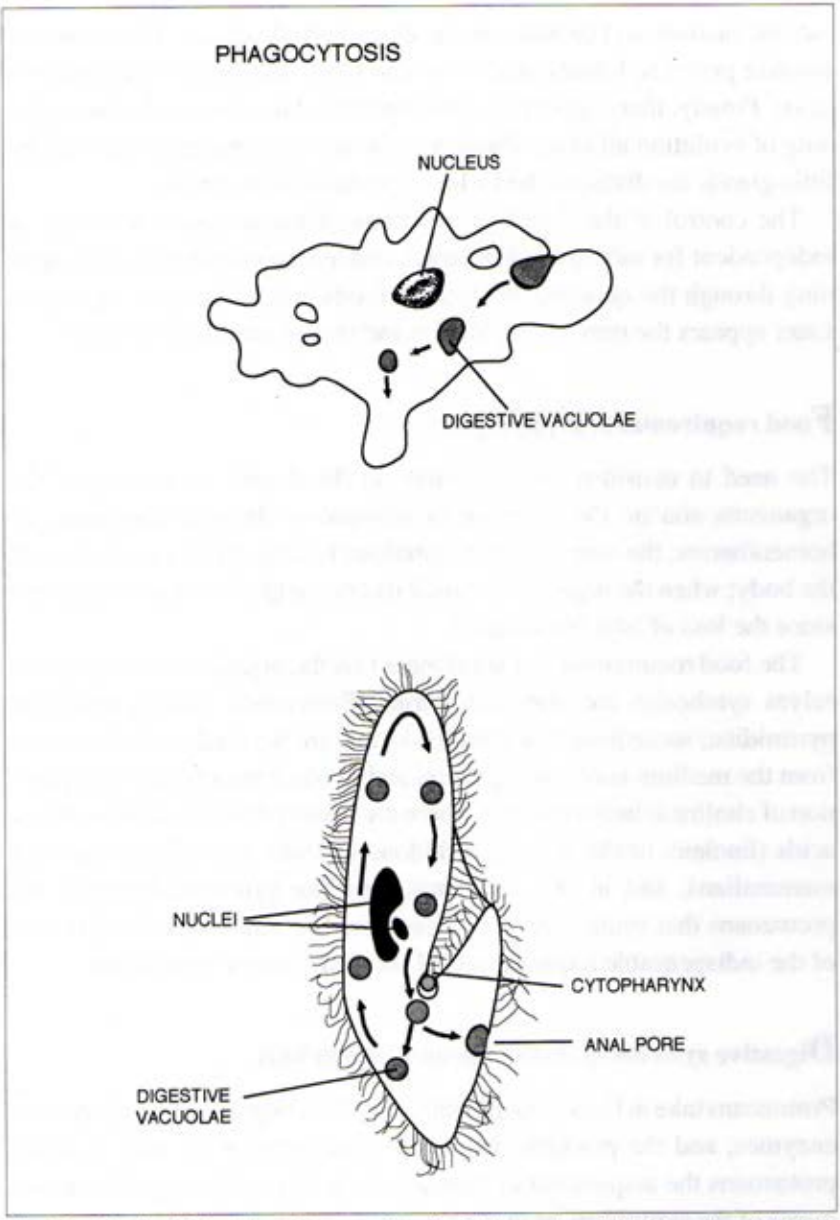


Fig. 23. Digestive Systems in protozoans. Digestion in the ameba with the formation of digestive vacuoles. Digestion in a paramecium showing the mouth, cytopharynx, the formation of the digestive vacuoles, their route and finally their fusion with the plasmatic membrane at the anal pore.

rigid exterior, there is a rhythmic and circular movement of the cytoplasm. In the paramecium, the food enters through the mouth or cytopharynx, whose base forms digestive vacuoles that detach and move through the cell as nutrients are digested and absorbed. The vacuole finally fuses into the cytopyge or anal pore to eliminate the wastes and recycle the membrane (fig. 23).

The flagellated cells covering the internal face of the wall of the sponges take in food from the medium and intracellularly digest it so that later it can be passed to the amebocytes in the corporal wall of the animal. In the coelenterates, as in the medusas, the tentacles capture the prey, passing it through the mouth toward the central cavity, where digestion is carried out through secretion of enzymes. The substances are absorbed by diffusion toward the external layers of the organism. Digestion ends in food vacuoles within the cells and the wastes are excreted through the mouth (fig. 24). In the platyhelminths, digestion is similar to that of the coelenterates, with the difference that the cavity is ramified to facilitate the digestion and distribution of the nutrients.

An important advancement is the acquisition of two openings in the digestive tube, which occurs from the annelids (fig. 24). Later in evolution, the distinct parts of the digestive tube specialize and specific regions, each in charge of either digestion, absorption, secretion, transport or storage of food begin to be distinguish.

In the superior organisms there are numerous cavities carrying out digestion, such as: the mouth, the maw, gizzard, stomach and the intestine. In many beings there also exist symbiotic digestion in which food is fermented by microorganisms lodged inside the larger-sized animals, facilitating their digestion. Termites house protozoans that digest cellulose. The ruminants present a structure known as rumen, in which a large quantity of protozoan and anaerobic bacteria live. In the caecum of many non-ruminant mammalians similar processes occur. In other animals, such as rabbits, there appears coprophagia, permitting a better digestion of food. In these, two types of feces are produced, ones during the day of waste and other nocturnal one that are consumed again.

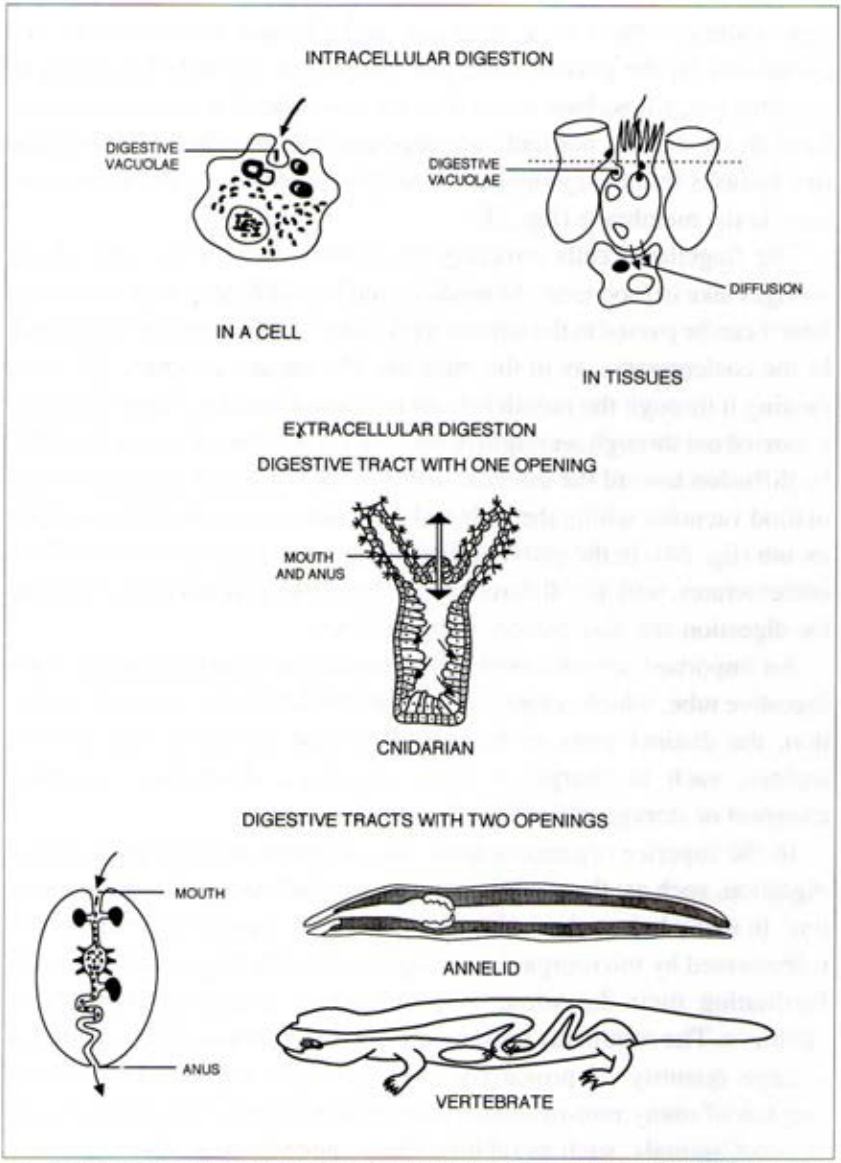


Fig. 24. Schematic representation of the digestive tubes in distinct groups of animals. Intracellular digestion in the protozoans and sponges. Extracellular digestion in a digestive tube with a single opening in the hydra. Digestive tubes with two openings in the annelid and in a vertebrate, observing that the digestive tube each time has more segments specialized in secretion, digestion and absorption.

SIMILARITIES AND DIFFERENCES BETWEEN ONTOGENY AND PHYLOGENY

The diversity in the phylogeny of the digestive system is enormous and the evolutionary tendencies are difficult to find.

Nevertheless, the following similarities can be found between the ontogenetic development of mammalians and phylogeny:

1. The progress of intracellular to extracellular digestion.
2. The step of microphagic nutrition or ingestion of liquids to macrophagic nutrition.
3. The regionalization of the digestive tube in portions in charge of digestion, secretion and absorption.

CHAPTER 6

The Ontogeny and Phylogeny of Respiratory Gas Exchange

RESPIRATION IN ADULT MAMMALIANS

Permanent access to oxygen is a priority for the majority of cells. There is no oxygen storage comparable to that of the energetic nutrients (fats and glycogen) upon which cells depend for a constant supply. Nevertheless, there are certain reserves with a moderated capacity to accumulate oxygen, as is the case of myoglobin in the skeletal muscle.

Some animals have developed organs specialized in the exchange of gases, such as the lungs in mammalians, which connect with the exterior through a series of canals whose interior recycle air. These organs are composed of a closed system in which the gases arriving to the alveoli are always a mix of recently inhaled air from the atmosphere and residual air, filling the respiratory system at the end of exhalation.

The alveoli are covered by two types of cells: the pneumocytes of type I, through which gas exchange occurs and type II cells, specializing in the synthesis of surfactant. This material decreases the superficial tension of the alveoli, impedes their filling with plasmatic liquid, and decreases the energetic expenditure invested during respiratory movements. This secretion is formed by proteins and phospholipids, whose concentrations are very different from those observed in the cellular membranes. The most abundant of them is the phosphatidylcholine.

The motions assuring the renovation of air in the lungs are movements of the thoracic cage and the diaphragm. The respiratory muscles are innervated by motorneurons located in the cervical and thoracic spinal cord. These receive currents generated by the bulbar respiratory centers, constituted by two groups of neurons; the inspiratory and the expiratory. The rhythmic activity of these groups is maintained by the influence of other centers located in the brain stem, known as pneumotaxic and apneustic. Also, the rhythm and amplitude of the ventilatory movements

are permanently regulated by the pH variations in plasma and by partial pressures of oxygen and carbon dioxide (PO_2 and PCO_2). On the other hand, the state of activity (dreaming, exercise, etc.), variations in temperature, alarm, certain hormones and vocalization modulate this function, acting over the neurons of the respiratory centers which permanently integrate information from very diverse origins.

Among the receptors regulating the respiratory necessities are the central chemoreceptors located at the bulbar level, which are sensitive to the pH variations of the hematoencephalic liquid associated with the changes of PCO_2. When the pH decreases in the cephalorachidian liquid, ventilation accelerates. The peripheral chemoreceptors, located in the carotid bodies and in the aortic glomus, increase the frequency of emission of impulses when the PO_2 of the arterial blood decreases or increases the levels of PCO_2. The mechanoreceptors of the superior airways and of the pulmonary parenchyma are sensitive to distention, and when stimulated they emit signals that decrease respiratory frequency.

The transport of oxygen in the internal medium is carried out by dissolution of the gas into the blood, and is facilitated by the presence in the blood of respiratory pigments with high affinity for oxygen such as hemoglobin. This is distributed from the lungs to the tissues, following the concentration gradient of oxygen, which is created and maintained by the metabolic activity of the cells.

THE ONTOGENY OF RESPIRATION

Obtainment of oxygen

From the beginning of embryonic life there is a constant dependency on oxygen. The ovule requires it for its metabolism and obtains it by diffusion from the medium that surrounds it from the moment it is released from the ovaries. During segmentation and gastrulation, the consumption of oxygen is increased and varies in the different parts of the embryo. The animal pole of the gastrula consumes more oxygen than the vegetal pole. This is because the cells of this region contain a lower quantity of vitellus in relation to active cytoplasm, than the cells of the

vegetal pole. During the stage of formation of the first somites, the consumption of oxygen by the embryo remains constant. However, there is possibly a transition of the embryonic metabolism from anaerobic to aerobic during this stage, because of a decrease in the production of lactate and because the enzymes of the respiratory chain of the embryo are not active. It has been explained that the high consumption of oxygen is the result of synthetic processes. While the embryo is small, oxygen is diffused from the liquid surrounding it to all the cells comprising it.

The transport of this gas from the atmosphere to the tissues in the fetus is a sequence of steps requiring a progressive decrease of the pressures of oxygen. This gas is transferred from the atmosphere to the maternal alveoli through the action of the respiratory muscles, which ventilate the lungs and afterwards alveolar air diffuses to the maternal blood. The arterial blood of the progenitor, pulsed by the action of the heart, transports the oxygen from the lungs to the placenta. In the placenta, the gas diffuses from maternal to fetal blood with the help of a special hemoglobin with a higher affinity for oxygen. The blood going from the placenta to the fetus combines in its body with other less oxygenated blood from the fetal body to comprise the liquid that circulates to the organs. Therefore, the fetus lives and develops in a hypoxic environment. Like in the last step, the oxygen diffuses from the fetal blood to the tissues, following the gradient of partial pressure of oxygen that is created and maintained through the metabolic activity of the cells. The transport of carbon dioxide from the fetal tissues to the atmosphere follows the same path, but inverted, and each step is accompanied by a decrease in the pressure of carbon dioxide. The system of gas exchange in the fetus is similar to the branchias of marine organisms. The placenta functions as a branchia whose external environment is the placental blood on the mother's side.

Development of the lungs

At the same time that the process occurs in which the fetal tissues are permitted to obtain oxygen, the fetal lungs differentiate and mature, allowing the new being to oxygenate at the moment of birth. The lungs appear as a crack or cleft in the ventral wall of the primitive intestine, which is converted by the fusion of the borders in a sac. Two bronchopulmonary buds develop from this sac. The left is smaller than the right and

has a lateral direction. Both grow toward the pleural cavities and ramify. The right bud forms two secondary protuberances while the left only produces one. The primary and secondary buds experience a progressive dichotomic ramification. The lungs develop a layer of visceral pleura derived from the splanchnic mesoderm. Simultaneously, the corporal thoracic wall is covered with a plate of parietal pleura derived from the somatic mesoderm (fig. 25).

Pulmonary development can be divided into four stages:

1. Pseudoglandular period: The bronchi and bronchioles are covered with cuboid epithelia and from the microscopic point of view, the lung develops similarly to a gland.
2. Canalicular phase: The lights of the terminal bronchi and bronchioles increase in size and develop the respiratory bronchioles and the alveolar canals. Notably, the pulmonary tissue begins vascularization.
3. Stage of the terminal sacs: This is the time in which the alveolar canals produce the terminal air sacs or primitive alveoli, which are covered in the beginning by cuboid epithelia that flattens to become scaly or flaky. The capillary network proliferates close to the alveolar epithelia and the pulmonary surfactant begins to be synthesized.
4. Alveolar period: The epithelia covering the terminal air sacs thins until a layer of squamous epithelia forms the alveoli (fig. 26).

The development of the lungs is characterized by: a decrease in the average size of the cells; a decrease in the glycogen reserves, which are degraded to use glycerol, resulting in the synthesis of the phospholipids of surfactant; and by the appearance of lamellated organelles in the pneumocytes of type II, increasing the synthesis of the surfactant. There are periods during which the rhythm of cellular multiplication is very elevated. These phases are alternated with stages during which the cells multiply slowly and in which a differentiation of the respiratory epithelia occurs. The periods of pulmonary maturation are brief and happen relatively late during gestation.

Surfactant is synthesized late in the gestation of mammalians and does not appear until the formation of the airways. The appearance of the phospholipids of the surfactant temporally coincides with the presence of lamellated organelles in the epithelial cells, which overlook the alveoli, first appearing phosphatidylcholine and later phosphatidylglycerol.

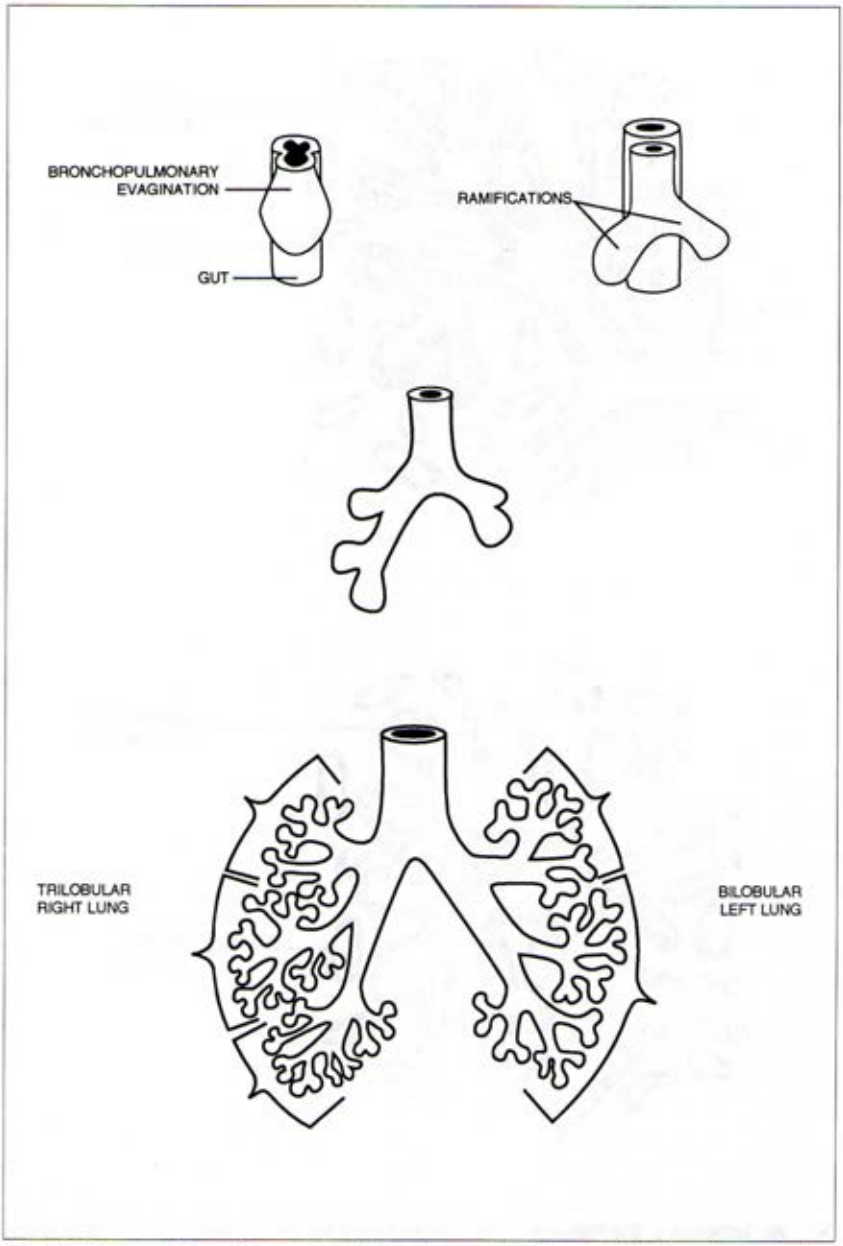


Fig. 25. Representation of the embryonic development of the lungs, which form by evagination of the anterior and posterior intestinal creases that later divide until forming the pulmonary alveoli.

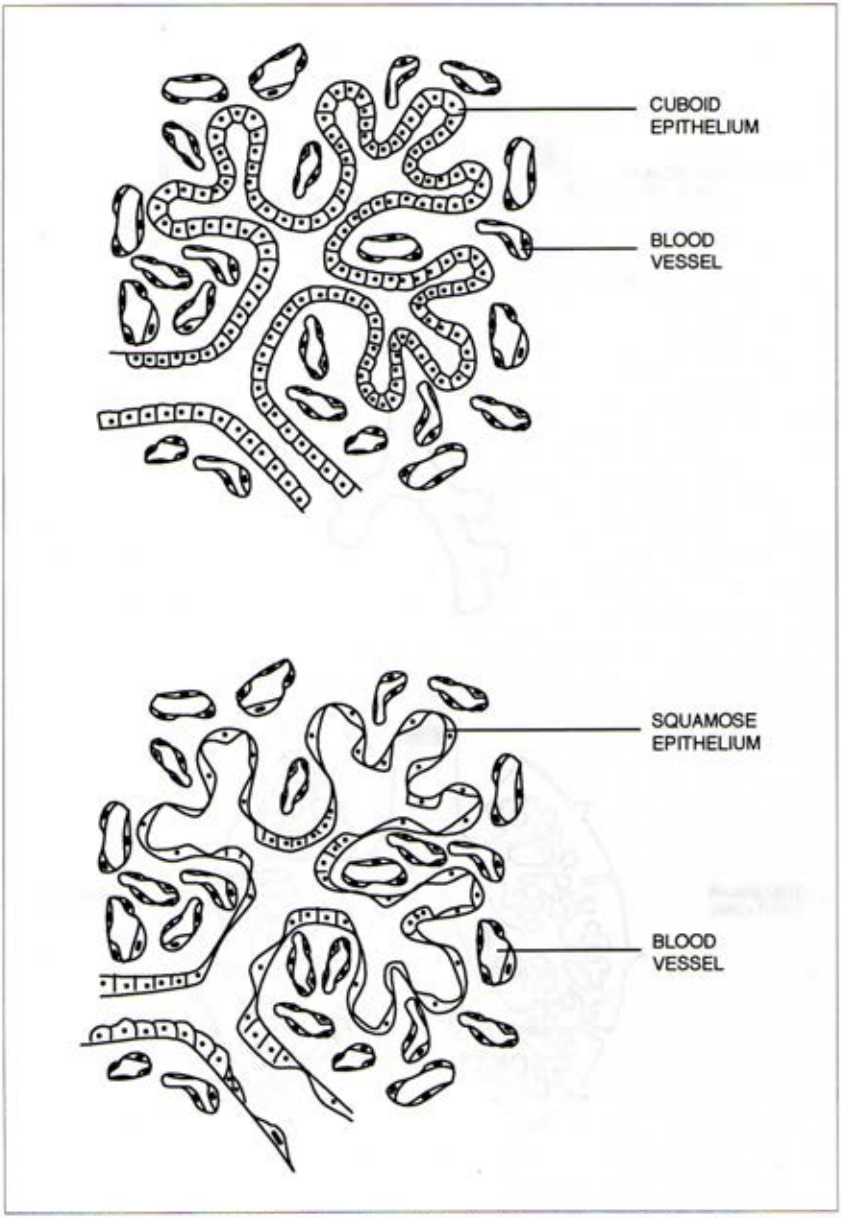


Fig. 26. Schemes of the histological sections illustrating the cellular maturation of the lung with the successive flattening of the cells which overlook the alveoli, making the light of each alveolus more ample each time.

The factors controlling the differentiation of the type II pneumocytes and the biosynthesis of the surfactant have been studied throughout the perinatal period because of their possible clinical applications. A large number of mediators are known to stimulate the synthesis of surfactant. These include the glucocorticoids, the thyroid hormones, estrogen, ACTH (adrenocorticotrophic hormone secreted by the hypophysis), the epidermic growth factor, the adrenergic beta agonists, prostaglandin and cyclic AMP. The effects of the glucocorticoids are better characterized, knowing that they do not directly act over the type II pneumocytes, but instead over the adjacent fibroblasts inducing the secretion of a peptide known as the "fibroblast-pneumocyte factor." The secretion of this substance is preceded by the biosynthesis of its messenger RNA. The fibroblast-pneumocyte factor stimulates the production of phosphatidylcholine and of phosphatidylglycerol by the pneumocytes activating the enzyme cytidiltransferase choline phosphate. The glucocorticoids also increase the synthesis of the surfactant proteins and induce the breakdown of pulmonary glycogen. It has been described that the platelet activator factor increases glycogenolysis in respiratory epithelia.

Before birth, the lungs do not contain air, the alveoli are collapsed and the air canals are filled with fluid known as "pulmonary liquid." This fluid is synthesized in the lungs and exits through the trachea into the amniotic fluid, or is swallowed by the fetus, to finally be reabsorbed after birth.

Respiratory movements occur from before birth; nevertheless, the said movements are not strong enough to open the alveoli, nor to cause the movement of the fluid filling the lungs.

Regulation of respiration

During the prenatal period, the central and peripheral reflexes constituting the control mechanisms of respiration are developed and integrated in such a way that the newborn responds to respiratory stimuli. However, the responses to certain stimuli are different in the fetus from those in the adult. For example, a decrease in PO_2 in the adult increases the rate of ventilation, while in the fetus the respiratory movements decrease with this stimulus. This may be explained by the fact that in the adult, an increase in the ventilatory rate increases PO_2, while in the fetus the

ventilatory movements do not increase the exchange of oxygen but increase its consumption. REM sleep (rapid eye movement) in the adult inhibits respiratory movements, while in the fetus it increases the ventilatory motions or ceases to inhibit them. Response to sensory stimulation is much stronger in the fetus than in the adult.

On the other hand, the chemoreceptors of the carotid sinus mature late during ontogeny, or are inhibited during a long period of development, while the chemoreceptors of the aortic cavity mature before and respond when they are stimulated by a decrease in PO_2 by inhibiting the ventilatory movements.

Pulmonary circulation

Despite the fact that the lungs are already present and that the capillary network is well developed, only between 7% and 10% of the blood passing through the pulmonary artery arrives to them, since lung resistance to blood flow is very high. At the moment of birth, the flow of umbilical blood ceases, stimuli appear and act over the respiratory centers, and the first profound inhalation occurs. Until this moment, the lungs, which have been collapsed and filled with liquid, expand. The increase in the pressure of oxygen relaxes the tone of the pulmonary arteries and allows blood to arrive to them. The fall in the pressure of the right heart is caused by the entrance of blood into the respiratory organs, resulting in the closure of the oval foramen valve and of the ductus arteriosus.

THE PHYLOGENY OF RESPIRATION

Although there exist some anaerobic organisms capable of surviving in conditions where oxygen is not present, this gas is an indispensable requirement for the subsistence of the majority of animal cells. In contrast to the carbohydrates and fats, there are very small oxygen reserves, myoglobin being the most well known. Gases always move according to gradients in their partial pressures and specific transport systems have not been described until now. Cellular metabolism decreases the pressure of oxygen in the cellular interior, creating a gradient that facilitates the diffusion of gas.

During evolution, different strategies have appeared allowing the transport of oxygen and carbon dioxide. In small organisms, respiration is simply accomplished by diffusion through the cellular membrane, of the tegument, or of the skin (fig. 27). At the increase in the dimensions of living beings, the appearance of specialized organs in charge of gas exchange has become indispensable. In general, these organs present a large gas exchange surface, abundant irrigation and a thin-shaped epithelium in contact with the exterior. The main respiratory organs that we find in phylogeny are: the branchia, composed of evaginations of the exchange surface; the trachea, present in insects; and the lungs, developed as an invagination of the exchange area (fig. 27).

Branchia are present in numerous animal groups, such as mollusks, crustaceans, annelids, fish and even during the larval stage in amphibians (fig. 27). In them, the blood has a countercurrent circulation, meaning it is distributed in the manner contrary to which water moves. There are different mechanisms permitting water to come in contact with the branchial epithelium. Among the mechanisms there are included:

1. Branchial movements, such as those present in the aquatic larvas of insects and amphibians,
2. The motions of the cilia of the epithelial cells covering the branchia, as in the case of clams,
3. The water pumps or bucco-opercular displacements of crustaceans and fish, and
4. The constant swimming of the animal, such as in the case of sharks. It is interesting to know that these vicious predators die from asphyxiation if they are immobile for even a short period of time.

The tracheas of insects directly conduct air from the exterior to the cells without the intervention of a circulatory system. There are openings of the tracheas on the entire surface of the body, known as spiracles, which communicate with the atmosphere and allow the entrance of air to circulate through all of the ramifications of the tracheal apparatus. The thick regions in contact with the cuticle, as well as the tracheoles, are filled with liquid and measure up to 0.1 micra, penetrating into the cells as deep as or in close proximity to the mitochondria. The movements of the abdomen of the insect permit the renewal of air inside the tracheal

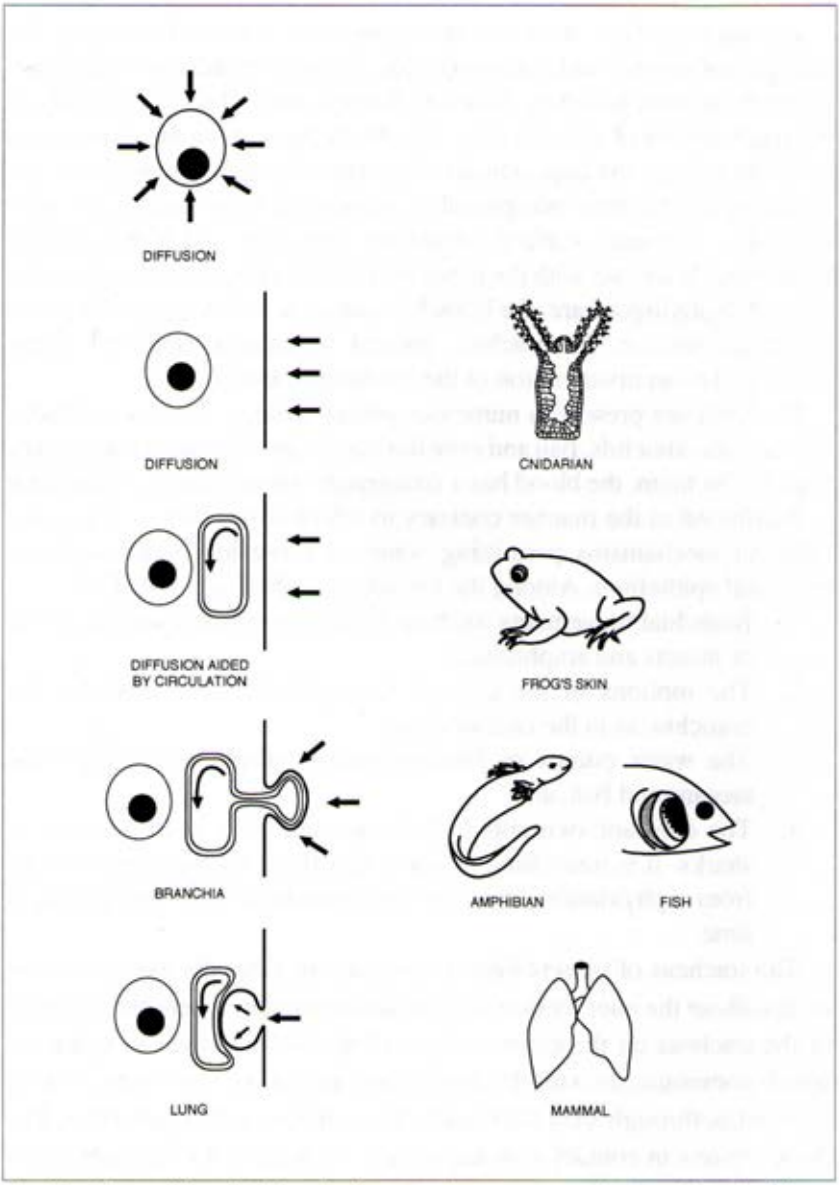


Fig. 27. Scheme of the principal mechanisms assuring gaseous respiratory exchange in different groups of animals. The most simple mechanism is diffusion, which is aided by the the circulatory apparatus. The evagination of the respiratory surface forms the branchia, while its invagination develops the lungs.

system. Inspiration is passive and expiration active (fig. 28). Although the trachea is a respiratory organ adapted to terrestrial medium, many insects and their larvas live in water and the structures have been modified to adapt to this environment. The respiratory canals of aquatic insects have lost the majority or the totality of their spiracles, and the gases diffuse from the water through the cuticles to the trachea, and in this case, their only function is to distribute the gases to the tissues. In some of these organisms, the cuticle flattens, increasing the surface at certain points of its body, and form what are known as branchia. Many aquatic insects only have the openings of the trachea toward the last segments of the body, since the animal lives exclusively in the water and only the rear part of its abdomen sticks out of the water, making contact with the atmosphere. In many of these organisms, some of the trachea are enlarged, constituting true air sacs, permitting the animal to be submerged for extended periods of time and which also facilitate flotation.

The lungs are cavities with respiratory function, communicating with the exterior through a single canal. In crustaceans, the branchial cavity has been transformed into a lung; in isopods such as the pill woodlouse, the pulmonary apparatus is located in the feet and the abdomen; and in amphibians, pulmonary respiration is complemented by gas exchange through the skin.

The first indication of lungs similar to those of mammalians is found in fossil fish as an execration of the anterior part of the digestive tube. In fish, this structure gives origin to the swim bladder that facilitates flotation, while in the terrestrial vertebrates it constitutes the lungs. The swim bladder can be either single or double, and it has been observed that some of its cells secrete oxygen, while others circulate the oxygen from the swim bladder to circulation. This organ also serves for vocalization purposes, or the emission of sounds.

The existence should be remembered of the current and fossil lunged fish, such as the eel and the coelacanth, because lungs are not exclusive to terrestrial organisms. The fish in which air respiration developed should have been exposed to whichever of the following adaptive pressures: the lack of oxygen in water or drought of habitat in which the organism lived. The branchia were maladapted for air respiration, since

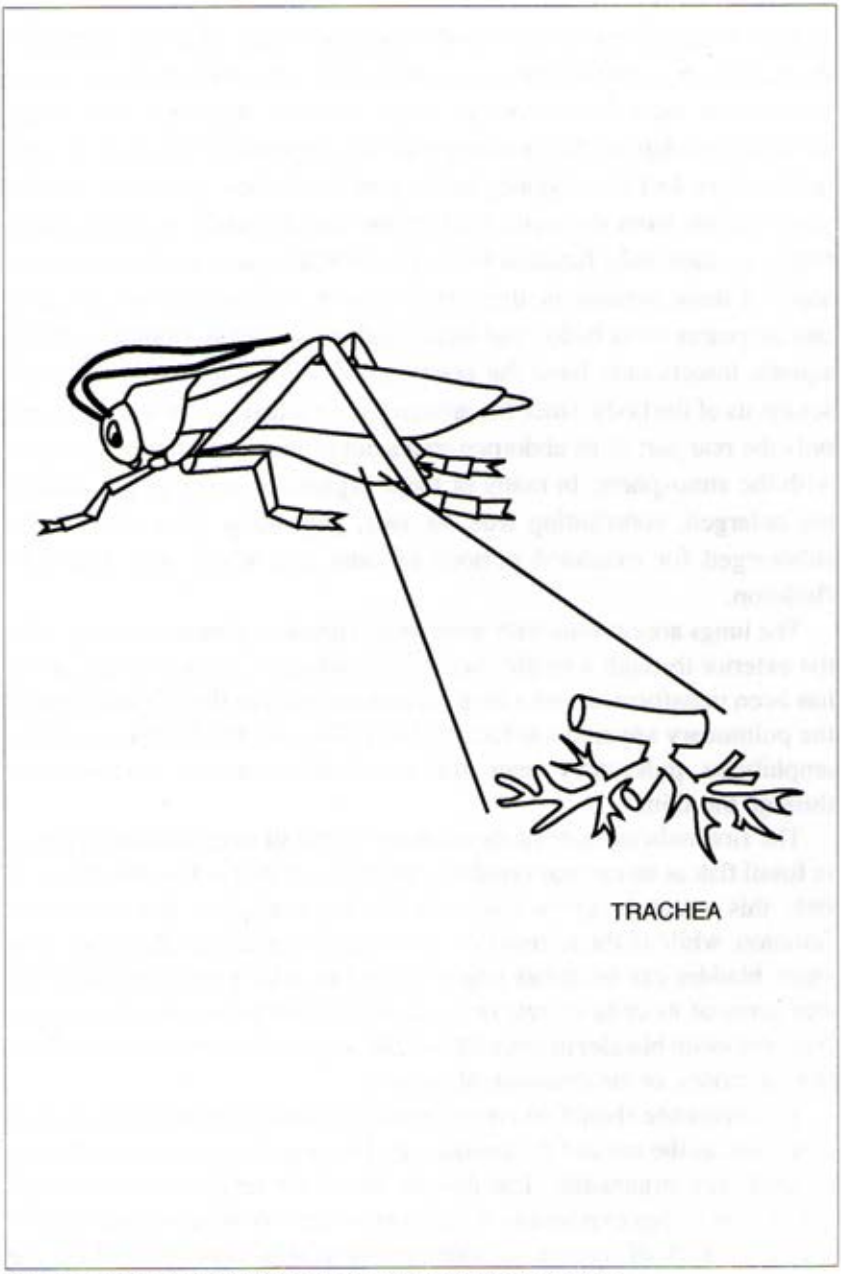


Fig. 28. Schematic representation of the tracheal system of an insect.

they did not have sufficient rigidity and their plates beat against each other in the air. The organisms were able to obtain oxygen through the branchia or, utilized whatever other ample surface in contact with air, and well irrigated to obtain oxygen through such parts as the skin, mouth, or other parts of the digestive tube, until arriving at the current type of respiratory organ.

There are two different types of lungs present in terrestrial organisms: tubular lungs with air sacs, typical of birds, and alveolar lungs, characteristic of mammalians (fig. 29).

The tubular lungs of birds are connected to a system of air sacs located in the bone cavities, which do not intervene in the exchange of gases, but instead permit the passing of air through the lungs. These beings do not present closed alveoli, but have open air capillaries in their two extremes where the transfer of gases occurs. There are two groups of capillaries in which the exchange of gas happens: those which overlook the anterior sacs and those which form the posterior sacs. A respiratory cycle in this type of lungs requires two inspirations and two expirations. In the first inspiration, the inhaled air passes to structures in contact with the posterior capillaries and the air occupying the air sacs passes to the anterior capillaries. In the initial expiration, the gas in contact with the posterior network penetrates the air sacs and the air filling the structures in contact with the anterior capillaries exits to the exterior. The air inhaled during the initial inspiration still permeates through until the end of the first expiration inside the organism, and is not expelled until the following expiratory movement. As the blood is oxygenated in the anterior sacs as well as in the posterior sacs, and the inspired air comes into contact with both, the process of extraction of oxygen is more efficient than in the alveolar lungs (fig. 29). For this reason, birds can be observed flying high above the highest chain of mountains, when at those altitudes mammalians have trouble breathing due to the low partial pressure of oxygen in the atmosphere. It should be noted here that air sacs are also present in some reptiles, permitting them to swell up and appear much larger than their habitual size.

The alveolar lungs in mammalians are closed systems formed by air canals and alveoli, in which the exchange of gases is carried out between the alveolar air and the capillaries. The volume filling the alveoli is a mixture of residual gas that fills the respiratory system at the end of expiration and of the new, recently inhaled air.

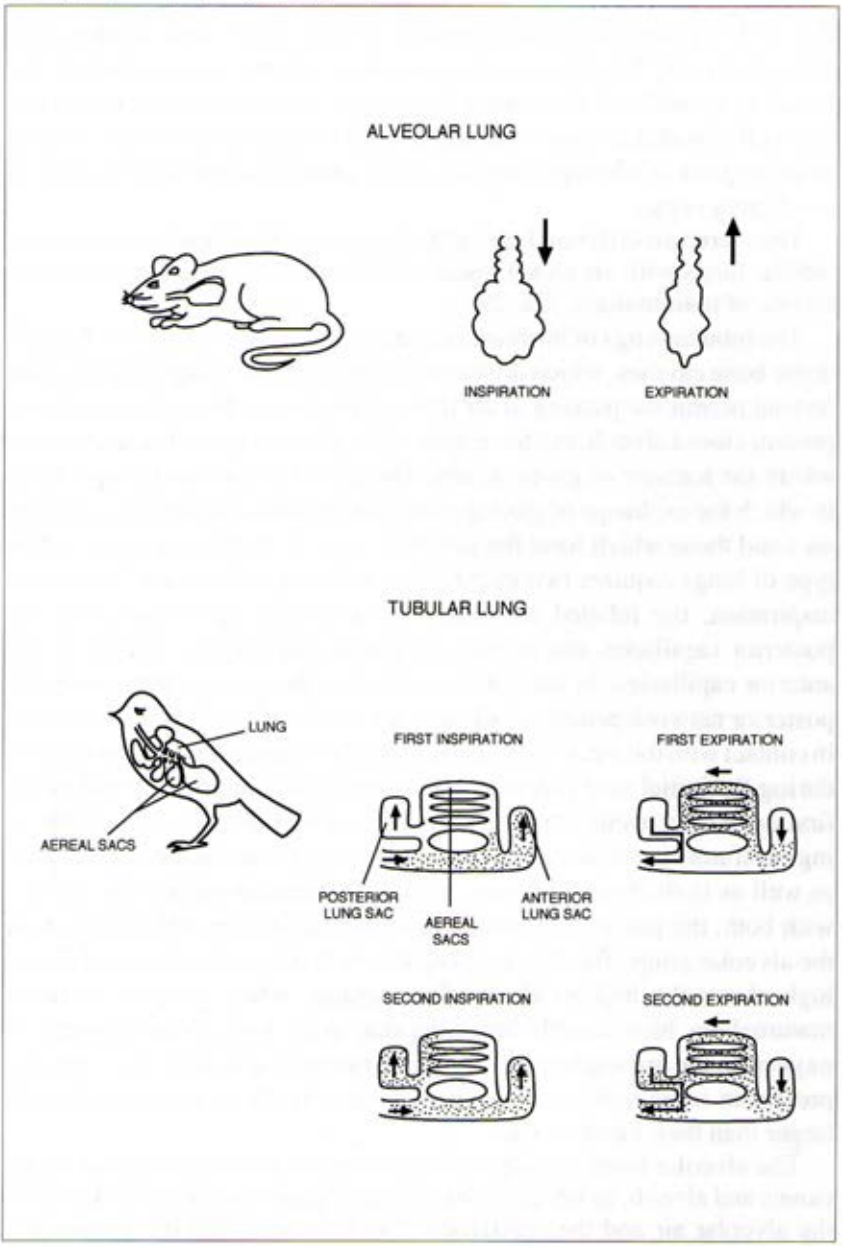


Fig. 29. Scheme illustrating the alveolar lung in mammalians and the tubular lungs of birds with their anterior and posterior sacs, serving in the gaseous exchange, and the aerial sacs.

An important adaptation of the respiratory airways occurs in aquatic mammalians that submerge to great depths where the gases in the lungs dissolve into the blood. At the exiting to the surface and decreasing the pressure that favored the diffusion of the gases into the corporal liquids, bubbles could be formed, which might cause embolism. The difference of a deep sea diver who submerges with lungs filled with air is that the whales and seals have their lungs empty when they sink. In these organisms, the water pressure makes the air in the lungs pass to the high airways, such as the trachea, which are rigid and ample and where the diffusion of gases to the blood does not occur. Also, pulmonary circulation decreases while the animal remains in the depths, and the metabolism of many organs changes from aerobic to anaerobic.

There are also mechanisms to renew air in the lungs. In amphibians, respiration depends on valves in the mouth, on the nostrils, and on the muscles of the fauces. From reptiles, the renewal of air depends upon the movements of the thoracic cage and the diaphragm, and on the maintenance of the intrapleural pressure, which causes the lungs to follow the movements of the expansion and relaxation of the thoracic cage.

Parallel with the evolution of the organs that permit the exchange of gases, the respiratory pigments have developed, which facilitate the transport of the gases, particularly that of oxygen, to all the cells of the multicellular organisms. In invertebrates, the pigments are directly dissolved in the blood or hemolymph. In the more complex organisms, the pigments are included inside the blood cells so that they do not increase the oncotic pressure of the blood or its viscosity. There are also non-circulating pigments located in the organs, such as myoglobin in the muscles. The respiratory pigments are proteins that always have a metal (copper or iron); and may contain a prosthetic group of the type of a porphyrin, such as in hemoglobin; or lack it, such as in hemocyanin.

On the other hand, mechanisms have evolved which permit the affinity of the respiratory pigments for oxygen to be modulated. In mammalians, the decrease in pH reduces the attraction of hemoglobin for oxygen, mechanism known as the Bohr Effect; a high partial pressure of oxygen decreases the affinity of hemoglobin for CO_2, known as the Haldane Effect, and synthesis of molecules in the tissues, such as 2-3 diphosphoglycerate, phosphorylated compounds and inositol phosphate, also modify the affinity of hemoglobin for oxygen. In the cephalopods,

crustaceans and fish, the pH affects the maximum capacity of fixation of oxygen to the hemoglobin, mechanism known as the Root Effect. Hemoglobin has less affinity for oxygen in small organisms having a very rapid metabolism than in the bigger ones with a slow metabolism, and the capillary area tends to be larger in the smaller organisms.

Development of the larynx

The larynx is found in a higher position in monkeys and in children than in the adult human, and during growth and the phylogeny tends to descend, making the length of the larynx increase. Monkeys and children are capable of swallowing and breathing at the same time but do not vocalize, while the human adult has lost the capacity to swallow and breathe at the same time. It has been postulated that this loss has been the price of the complicated language acquired through the centuries.

SIMILARITIES AND DIFFERENCES BETWEEN ONTOGENY AND PHYLOGENY

Although an enormous diversity exists in the types of respiratory apparatus responding to the adaptation of organisms to different environments, in which they inhabit, the following similarities between the ontogeny of a superior mammalian and phylogeny can be mentioned:

1. Increase in the exchange surface and vascularization in the respiratory organs.
2. Decrease of the thickness of the epithelia separating the external from the internal media.
3. Step from anaerobic respiration to aerobic respiration.
4. Evolution of the lungs from the evaginations of the digestive tube.
5. The functioning of the placenta as if it were a branchia irrigated by maternal blood.
6. The branchial arcs have been considered as the most common example of the reminiscences of phylogeny in ontogeny.
7. The evolution of the position of the larynx, permitting monkeys and children to breathe and swallow at the same time.

CHAPTER 7

The Ontogeny and Phylogeny of Blood and the Immune System

THE BLOOD AND IMMUNE SYSTEM IN THE ADULT MAMMALIAN

Blood is composed of a liquid called plasma, and of specialized cells suspended in it. Plasma is extremely complex and consists of a large quantity of organic and inorganic substances dissolved in water. The most important solutes are proteins, constituting 7% of its weight. These vary notably in their structure and function, but they can be classified into three large groups: the albumins, transporting a large quantity of substances combined in the plasma and which are responsible for the oncotic pressure or force assisting the plasma filtered at the level of the capillary to return to the blood stream; the globulins, including the immunoglobulins (antibodies) and the proteins in charge of coagulation. Also in plasma are dissolved nutrients, ions and final products of the metabolism.

The blood cells are: the platelets that intervene in hemostasis; the red globules or erythrocytes whose main function is the transport of oxygen through the synthesis of hemoglobin; and the white globules or leukocytes that include the basophils, neutrophils, eosinophils, lymphocytes and monocytes. This last group of cells participates in the immune functions and in the protection of the organism, defending it against the aggressions of the medium surrounding it.

The phenomenon of immunity was recognized centuries ago when it was understood that a man having suffered certain illnesses was not able to contract them again, meaning, he had become immune to the specific diseases. In superior mammalians, we have innate immune mechanisms and an actively acquired immunity, which is specific to a certain invading

agent and which is based in two types of responses: cellular and humoral, given by the antibodies. These are synthesized and released into the blood and to the tissues in response to a certain proteins known as antigens.

To unleash the response against the antigen, the macrophages take the invader protein, fragment it, and unite the resulting pieces with the molecules of the organism itself, known as the major histocompatibility complex (MHC). They are then exhibited on the surface of its membrane, being recognized by the B lymphocytes, which differentiate into the plasmatic cells, whose function is to synthesize and secrete the antibodies. These are gamma immunoglobulins (Ig), and according to their characteristics, they can be classified into: G, M, A, E and D. The IgG are the most abundant, the only ones which cross the placenta and those which are produced in large quantity when an individual is exposed to an antigen on multiple occasions. The IgM are pentameres formed by five units and are in charge of the response against an antigen the first time we come into contact with it. The IgA accumulate in secretions and the IgE are responsible for the reactions of hypersensitivity and allergy. The antibodies recognize the antigens and precipitate or agglutinate so that they can be phagocytized by the neutrophils or the macrophages. They also activate a group of proteins known as the hemolytic complex, which provokes the lysis of the cells possessing this antigen and induces reactions that facilitate the attack of the invader agents or organism, like the anaphylactic reactions.

The capacity of an organism to produce antibodies with specificity to distinct substances was interpreted for a long period of time from the Lamarksist point of view. In accordance with this interpretation, the information of the environmental stimulus was taken by the organism for its DNA to synthesize an adequate substance with the objective of combating it. In actuality and in opposition to the Lamarksist interpretation, it has been proposed that the organism produces a large quantity of different cells in relation to the antibodies that are elaborated, and from these, the ones that synthesize the correct antibody, are selected favoring their proliferation.

Cellular immunity is in charge of a group of lymphocytes known as T lymphocytes, among which are found: the killer cells, which cripple the invader agents; helper cells, which secrete substances, such as inter-

leukines, favoring the immune reactions; and suppressor cells, which stop the response.

In mammalians, hemostasis is a sequence of rapidly succeeding events occurring to avoid the loss of blood in a lesioned vessel. These events are:

1. Contraction and retraction of the lesioned vascular walls
2. Interaction of the platelets with the altered surface and formation of a platelet plug
3. Activation of coagulation, permitting the formation of a fibrin network, which constitutes the platelet thrombus.
4. Initiation of scarring by the closure of the lesioned vascular layer through the mass conformed by the fibrin and the platelets.
5. Reabsorption of the coagulus by the fibrinolytic system.

THE ONTOGENY OF BLOOD AND THE IMMUNE SYSTEM

Ontogeny of the blood cells

The first blood cells develop from the vitelline sac. Later, the liver and the spleen are converted into the hematopoietic organs, and finally the precursor cells of all the blood corpuscles migrate toward the bone marrow. From the beginning, a large quantity of immature cells of the pathways of differentiation of the distinct groups circulate and gradually they remain longer in the hematopoietic organ, until only the mature cells appear in circulation. For this reason, there are a large quantity of circulating nucleated erythrocytes found in the fetus. Equally, the content of water in the blood is very high in many embryonic and fetal tissues, and so the value of hematocrit is decreased. The quantity of blood cells, in relation to the volume of liquid, increases during fetal and embryonic development.

The expression of the type of hemoglobin contained in the erythrocytes is also modified during growth. In the beginning, gamma globulin chains are expressed, making the fetal hemoglobin more attractive to oxygen than that of the mother and which also facilitate the transport of this gas from the maternal to the fetal blood. Later, the chains of alpha and beta globulin appear, characteristic of the adult blood, and changes the affinity for oxygen.

Ontogeny of the immune system

Immunity in vertebrates is divided into two types: cellular, carried out by the T lymphocytes, which pre-differentiate in the thymus; and humoral, in charge of the B lymphocytes, which compromise to their function in the spleen. The ontogenetic development of these two systems is independent. The thymus, which was considered by Descartes as the shelter of the soul, is the first lymphoid organ to develop. It originates from the tissue in the area of the third branchial arch, and forms a mesh of epithelial character over which migrate the precursor pre-thymic cells of the T lymphocytes. The origin of these precursors is unknown, but they were possible provided by the liver, which in this stage functions as a hematopoietic organ. The thymic gland acts in cellular differentiation in at least two ways: 1) it modulates the transformation of the pre-thymic cells to functional precursor cells of the T lymphocyte; and 2) after these functional cells abandon and migrate to other lymphoid tissues, it regulates the quantity and functional activity of T cells.

In the process of differentiation of the thymus, the cells first localize in the cortex and then slowly migrate toward the medulla. Similarly, their characteristics pass from the thymic precursors to small lymphocytes. From the thymus, the cells migrate toward the peripheral lymphoid organs. During adolescence, this gland disappears when the cells have already been differentiated that will convert into T lymphocytes and will later make up the sub-populations of helper, suppressor and killer or cytotoxic lymphocytes.

Together with the increase in the number of circulating lymphocytes in peripheral blood and with the differentiation of the thymus in the cortex and medulla, appears the response to a lectin, which is used to evaluate the normal activation of the lymphocytes known as phytohemagglutinin. The test of the cultivated mixture of unidirectional lymphocytes (MLC), used to detect differences of histocompatibility, is positive before the appearance of the reactivity to phytohemagglutinin, and is the immune response capable of being detected earlier in development.

The appearance of B lymphocytes also occurs after a period of differentiation in a specific organ similar to the thymus. In birds, this

organ is the intestinal sac, known as the Fabricio bursa or sac, while in mammalians, the organ may be the intestine, the liver or the spleen. The B lymphocytes are in charge of synthesizing and secreting antibodies. The first immunoglobulin capable of being detected in the sac of Fabricio is IgM, followed by IgG and IgA. The IgD is also very primitive, almost as the IgM, and it has been postulated that it may represent a fetal immunoglobulin analogous to the fetal variety of hemoglobin, because the specific functions in the adult are not known.

Despite the rapid development of the T and B cells during embryonic growth, the fetus is not capable of mounting a vigorous immune response to transplanted tissues or antigens. Although immunoglobulins are produced, their title is very low in the fetus. Also, some of the complement factors have been detected in the blood of the umbilical cord, but their levels are much lower than in the maternal blood. The pattern of development of the seric immunoglobulins can be importantly altered when there is an intrauterine infection.

Another transcendental fact that occurs during the intrauterine development of the immune system is the tolerance to the organisms own tissues. A critical stage during growth has been observed in which if alien molecules are present, they will not be recognized as foreign in postnatal life. The alteration in the recognizing of the organisms own tissues in adult life is what generates autoimmune illnesses.

THE PHYLOGENY OF BLOOD AND THE IMMUNE SYSTEM

Phylogeny of the blood cells

Erythrocytes are cells in charge of transporting oxygen to all of the tissues of the organism; however, in the invertebrate, these types of cells are not present and the oxygen is transported through pigments directly dissolved in the blood or hemolymph. The respiratory pigments are proteins wrapping a metal (copper or iron) and may contain a prosthetic group of the type of porphyrin, as in the case of hemoglobin, or may lack it, as in the case of hemocyanin.

In primitive organisms, the pigment does not have prosthetic group and the metal is copper. Annelids and some other mollusks present hemoglobin as blood pigment, while other mollusks and arthropods present hemocyanin. The only group of organisms in which the blood does not contain respiratory pigments are insects, in which the tracheas carry oxygen directly to all the cells of the organism. In insects, the blood or hemolymph only transports nutrients, metabolic waste and hormones.

Annelids are the first invertebrates in which blood globules appear. In this group, the pigments are included inside the blood cells, not increasing the oncotic pressure of the liquid nor its viscosity, making the transport of gases more efficient. The red cells of the primitive vertebrate are nucleated and in the superior species, the nuclei are lost to convert the cells into more specialized ones. The leukocytes appear from the echinoderms and continue developing in the rest of the species.

Phylogeny of the immune system

In such organisms as the bacteria transporter proteins in plasma membrane homologous to proteins that unite peptides of the major histocompatibility complex (MHC) in vertebrates have been observed. Endonucleases are also present in some microbes. These enzymes are capable of destroying the nucleic acids of certain viruses, conferring resistances to determined infections. Nevertheless, it is said that the immune response originates in the organisms with nuclei (eukaryotes) as a solution to recognize its own from foreign. It has been described that protozoans reject the transplanted nuclei of other organisms. Sponges can be broken up and the cells regroup to comprise a new organism. If the cells of different organisms mix, they recognize, and those belonging to the same organism will group together while those not belonging are rejected until a compatible match is found. In coelenterates, necrosis and intolerance of transplanted tissue appear after the foreign cells have been encapsulated. This information indicates that from primitive multicellular organisms there are responses that can be considered as immunologic. In the invertebrates, immunologic responses are due to the presence of coelomocytes or phagocytic cells, aglutinogens (lectins),

inactivators of ciliar movements and to the presence of substances that cause lysis of bacteria, as the terminal components of the complementary system do. These organisms also possibly show the precursors of the major histocompatibility system. However, they do not exhibit a molecule with a functional or physicochemical structure similar to that of immunoglobulins. In light of this fact, it is said that cellular immunity precedes humoral immunity. The processes found in invertebrates may possibly be described as complex mechanisms of defense or innate immunity. The critical characteristics of an acquired immune system, which differs from a simple defense mechanism, are specificity and memory. These two characteristics are not found in invertebrates and exclusively appear in vertebrates. To date, forms of transition have not been found between the defense mechanisms and the appearance of such an acquired immune system.

Although there is a natural humoral immunity in annelids, mollusks and arthropods, the antibodies with specificity, whose synthesis is induced by contact with the antigen, appear for the first time in agnates or fish without mandibles. In these said fish, cellular and humoral immunity manifest simultaneously.

It has been proposed that antibodies originated from a single gene, which duplicated, segmented and recombined to develop the enormous variety of antibodies found in mammalians. Although in fish there coexists cellular and humoral immunity, no lymphocytes are found, except the T and the only antibody expressed is IgM. The following type of molecule expressed in phylogeny is IgG, later appears IgA, and finally IgD and IgE. Not only are the types of antibodies produced limited, but also their quantity, for example: tadpoles only produce 100 distinct molecules of antibodies. On the other hand, the major histocompatibility complex may have evolved independently on at least four different occasions during the phylogeny of vertebrates, which reflects a convergent evolution.

Phylogeny of hemostasis

The hemostatic mechanisms are essential for invertebrates as well as vertebrates. The fact that many invertebrates have an open circulatory system, complicates the situation, since in these organisms the contraction of vessels does not assist hemostasis.

In the invertebrates lacking a rigid exoskeleton and in those which the hydrostatic pressure of extracellular liquids is low (some echinoderms), the principal mechanism assuring hemostasis is simply a contraction of the walls of the body or of the musculature of the vascular walls. When a rigid exoskeleton exists or the blood pressure is high, the blood cells can group together at the site of the lesion to form a pliant hemostatic thrombus as in the sea urchin. In arthropods and mollusks, the cells do not only clump together, but they form a coherent mass. In other arthropods, a protein similar to fibrinogen appears, known as coagulogen, produced and secreted by the blood cells that rapidly break after a lesion occurs (explosive cells of the crustaceans or coagulocytes in some insects). The knowledge of coagulation mechanisms in invertebrates remains unknown to date, but the information we posses suggests that this type of response should have evolved on multiple occasions independently during the course of phylogeny. Coagulation mechanisms exhibited by invertebrates are biochemically different from those mechanisms found in vertebrates; for example, heparin inhibits coagulation in vertebrates, but it does not in invertebrates. The elements of coagulation associated to blood cells are still found in fish and in the remaining vertebrates, independent circulating factors of coagulation are found.

SIMILARITIES AND DIFFERENCES BETWEEN ONTOGENY AND PHYLOGENY

Despite the differences observed in distinct animal groups in phylogeny, which are the result of the adaptations to distinct environmental conditions, we find the following similarities between the ontogeny of superior mammalians and phylogeny:

1. The red blood cells in the beginning are nucleated, and later lose this structure.
2. First appear the unspecific immune responses and later the specific responses.
3. Initially surges the cellular response and later the humoral response.
4. IgM is the first type of antibody to be present in both types of development.

CHAPTER 8

The Ontogeny and Phylogeny of the Hydro-mineral Equilibrium

THE HYDRO-MINERAL EQUILIBRIUM IN THE SUPERIOR ADULT MAMMALIAN

In the superior mammalian, the functional unit of the kidney is the nephron, which is composed of different regions: the glomerulus, the proximal convoluted tubule, Henle's Loop and the distal tubule that ends in the collector canals of the kidney. The glomerular portion of the nephron is where the water, salts and some organic molecules cross the cellular wall of the blood capillary and the cellular wall of the nephronic capsule. This filtration depends directly upon the blood pressure existing in the glomerulus. While filtered fluid flows from the capsule through the tubular portion of the nephron, the following substances are reabsorbed at diverse levels: water, glucose, different proteins, chlorine ions and other molecules, while the tubular cells secrete the following substances to the filtered fluid: urea, magnesium and potassium ions, being the urine the final product.

The capacity of the kidneys in mammalians to produce hypertonic urine, in relation to blood, depends on a countercurrent flow system transferring sodium ions from one part of the renal tubule to the other; consequently, an elevated level of sodium can be maintained in the medullar part of the excretory organ. A large part of the active transport of sodium ions takes place through the ascending portions of Henle's Loop. Sodium moves to the intercellular liquid to enter from there the descending portion, thus it tends to move in a circle, creating a gradient in the medullar portion of the kidney. Due to the high concentration of

ions, water tends to cross the walls of Henle's Loop and of the collector tube, which pass through the renal medulla, reducing the volume of urine.

The control system of the functioning of the kidney is extraordinarily complex and depends upon the activity of the nervous and endocrine cells. Primary regulation takes place in the brain, whose hypothalamus has osmoreceptor cells that control the release of the antidiuretic hormone or vasopressin. These nervous cells respond to alterations in the osmotic pressure of blood plasma, which flows through the brain, producing a compensating adjustment in the quantity of vasopressin released by the neurohypophysis. The antidiuretic hormone affects the collector tubules by increasing the reabsorption of water.

There are more agents controlling the contents of urine. Aldosterone produced by the cortex of the adrenal gland determines the reabsorption of sodium ions in the distal tubules of the nephrons. The secretion of aldosterone is regulated by angiotensin II, produced when the kidney releases renin, which acts over a plasmatic alpha globulin, modifying it into angiotensin I. Angiotensin I is then transformed into angiotensin II by the convertor enzyme. Angiotensin II, besides affecting the release of aldosterone, also induces the contraction of the smooth muscle cells in the kidney and in the walls in the blood capillaries and in other parts of the body.

THE ONTOGENY OF THE HYDRO-MINERAL EQUILIBRIUM

During the first phases of development, before implantation, hydro-mineral equilibrium is carried out by diffusion from the embryo to the fluids found in the uterus. From the formation of the placenta, this organ is in charge of the hydro-mineral equilibrium, although an exchange of small levels of water at the chorion persists. The waste elements diffuse from the fetal plasma to the maternal circulation and it is the kidney of the mother that finally eliminates the embryonic metabolic products. The fetus generates a large amount of urea, since its rate of oxidation of amino

acids is elevated. The rate of absorption of amino acids at the umbilical cord level is superior to the fetal consumption of these types of molecules. The renewal of proteins per kilogram is more in the fetus than in the adult. In general, it can be affirmed that organisms in development produce more urea than mature organisms. The fetus also excretes ammonia, and the concentration of salt is elevated in the uterine vein at the beginning of development, and tends to decrease. The salt is possibly produced more by the uterus and placenta, than by the fetus that uses it. Similarly, the volume of corporal liquids is higher in the embryonic and fetal period than in the adult organism.

Formation of the kidney

Although during embryonic and fetal life the function of the hydro-mineral equilibrium is carried out by the placenta, the kidney begins to develop early and will be the organ specialized in this function after birth. This gland develops from the intermediate mesoderm, from the coelomic epithelia and from the cloaca. The intermediate mesoderm at each side of the vertebrate column migrates in a ventral sense and loses its connections with the somites. These tissue masses are called nephrotomes and fuse with those from the nearest cephalic and caudal somites to form the nephrogenic cords. These cords produce longitudinal bilateral convexities toward what will be the coelom, called urogenital borders (fig. 30).

In the cephalic part of the nephrogenic chords develop the pronephros, which is an accumulation of cells with a canal running in the caudal sense that opens into the cloaca. This tube, known as archinephric, primary ureter or Wolff's Canal, forms the urospermiduct in the inferior vertebrates and originates a part of the masculine genital tracts in the superior vertebrates. The pronephros is a transitory structure and not a functional one.

The mesonephros later develops at the height of the gonads. The differentiation of this structure depends upon the inducing action of the primary ureter or the Canal of Wolff. In the nephrogenous chords form

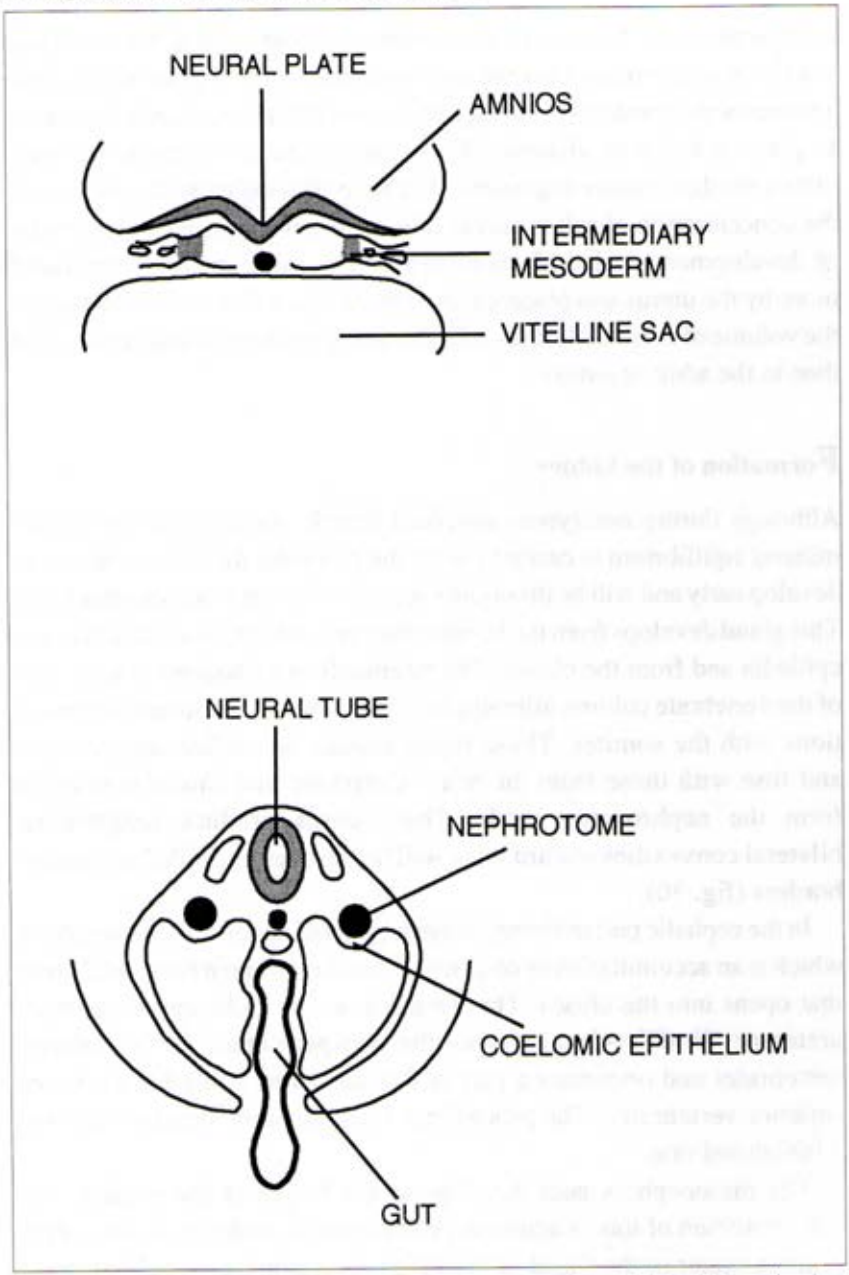


Fig. 30. Localization in the embryonic disc of the nephrotomes from which the kidneys develop.

tubes, converting into mesonephric vesicles. Each one of these vesicles stretches and acquires an "S" shape. The tubule of each mesonephric vesicle grows in the lateral sense, and comes into contact with the pronephric canal. At their other end, each tube expands and invaginates with a capillary network. The middle portion grows and folds to form the proximal convoluted tubules, Henle's Loop and the distal tubule (fig. 31). The mesonephros develops in a cranio caudal sense and degenerates in the same sense (fig. 32). In the case where the mesonephros does not develop, the gonads never differentiate.

The metanephros finally appears, generating from two regions: on one side the metanephric vesicles, which are dorsal buds of the mesonephric canal close to the outlet of the cloaca, which form the secondary ureter, the renal pelvis and the collector tubules. On the other side, the metanephrogenic mass, of mesodermic origin, forms the nephrons in a manner similar to that observed in the mesonephros (fig. 32). The only difference is that the distal convoluted tubules are not in contact with the canal of the pronephros, but with the collector tubules. The bladder derives from the vesico uterine canal. After birth, new nephrons are no longer formed: the nephrons only grow and the cells constituting the walls of the tubules degenerate and die to be substituted.

Even though the embryonic and fetal kidney is not totally functional, during gestation the processes of urine formation already begin to occur. The following facts have been observed during development: 1) The quantity of sodium filtered tends to decrease; 2) The capacity of Henle's Loop to reabsorb sodium chloride (NaCl) is reduced; 3) The clearance of water decreases more rapidly than does the elimination of ions and wastes; 4) The sensitivity to aldosterone of the tubules increases and although this hormone is present early on, its effect over the composition of urine is poor; and 5) The osmoreceptors regulating the secretion of the antidiuretic hormone by the posterior hypophysis are active from the end of gestation.

The urine produced by the fetus is hypotonic in relation to the plasma, despite the volume of extracellular liquid being elevated. To be eliminated, it passes to form part of the amniotic liquid.

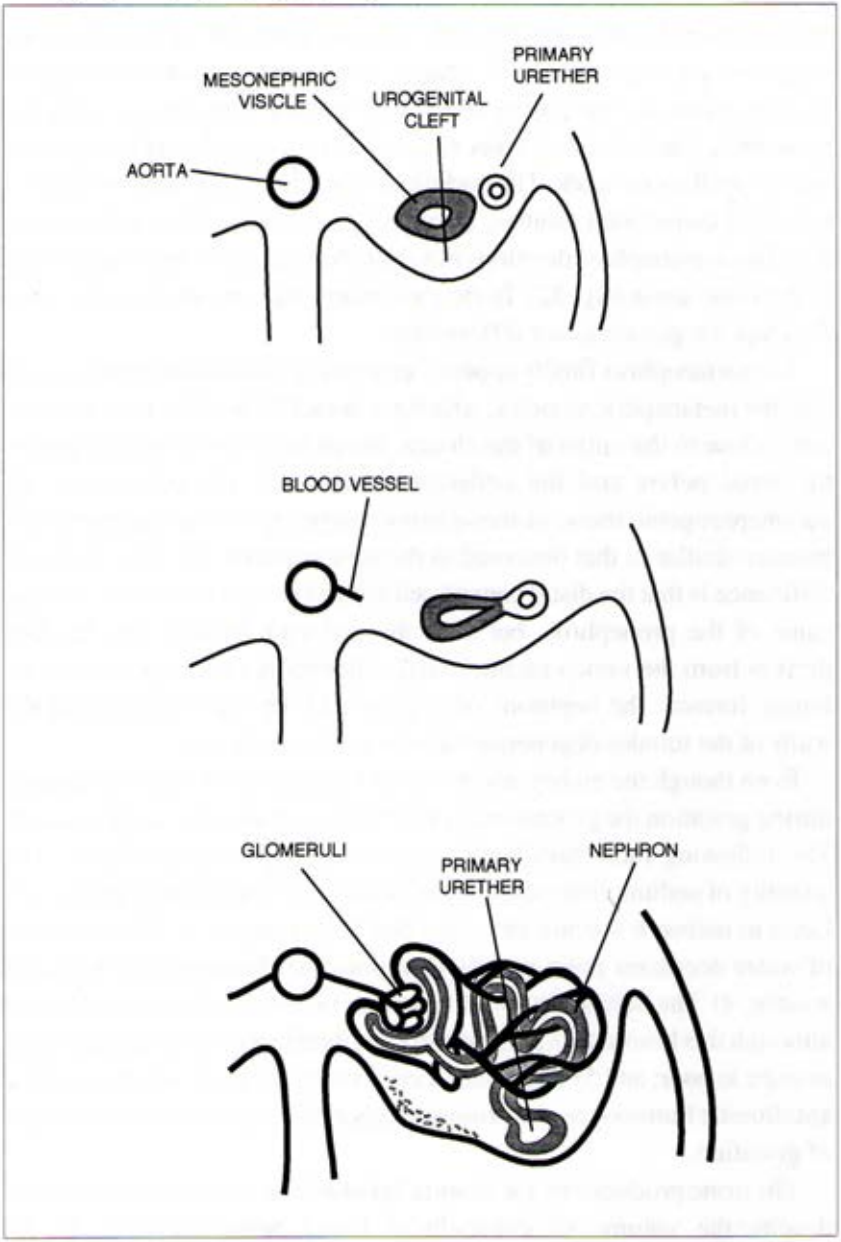


Fig. 31. Development of the nephrons and their contact with the primary urether and with the renal capillaries.

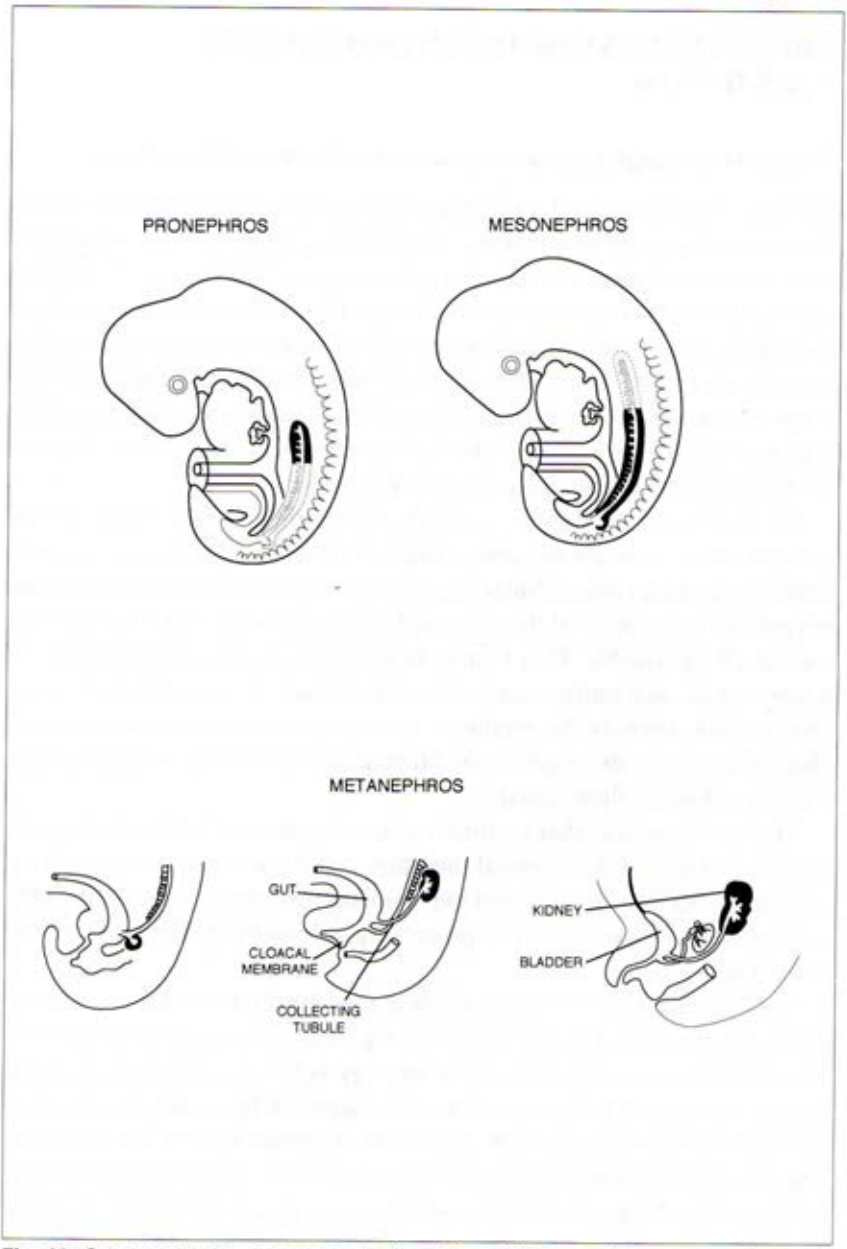


Fig. 32. Scheme showing the progressive formation of the pronephros, mesonephros, and metanephros as well as the collector tubule and the urinary bladder.

THE PHYLOGENY OF THE HYDRO-MINERAL EQUILIBRIUM

Adaptive strategies according to the environmental medium

The term 'hydro-mineral equilibrium' refers to the osmotic balance and the constant maintenance of the extracellular volume. The organisms have developed diverse strategies to maintain it, which vary in accordance with the environment in which they live. The beings inhabiting a marine medium confront a constant loss of water in their organism and an entrance of ions, since the medium is hyperosmolar in relation to their corporal liquids. Those beings living in fresh waters swell through the entrance of water into their bodies and continuously loose ions. Finally, the terrestrial beings are subject to dehydration.

To survive in a marine medium, some invertebrates such as the coelenterates, crustaceans, and certain vertebrates like manta rays and sharks, present an intracellular liquid in osmotic equilibrium or are even hypertonic in relation to the oceans, being more salty than the external medium they inhabit. This is mainly achieved by the accumulation of wastes, urea and amino acids. It is important to mention that some invertebrate, such as the medusas, belonging to the coelenterates, exchange ions with the medium by storing the less dense of ions in their interior, allowing them flotation.

Marine organisms that maintain a concentration of intracellular ions different to that of the external medium, avoid the loss of water and the entrance of ions through varied mechanisms. One process is to avoid the exiting of the corporal liquids, presenting aglomerular kidneys, as is the case of many fish.

Another mechanism found in some maritime birds consists of compensating the loss of water by increasing their consumption by between 5 and 33 liters per day. One more strategy is the development of rectal glands, salt glands and ion elimination systems at the kidney level and at the level of the branchia. Chloride cells eliminate ions in the branchia. The salt glands found in the beaks of marine birds secrete a concentrated solution of sodium chloride through the eyes, giving the impression that the bird cries. These structures present complex intracellular spaces, creating ionic gradients to facilitate the reabsorption of water.

Organisms inhabiting fresh water confront the problem of the entrance of liquid and the loss of ions. To counteract the income of water, elements are found from organisms such as the protozoan, like the contractile vacuole, which can or cannot be nurtured by the endoplasmic reticulum. To avoid the exiting of solutes, the fresh water invertebrates have developed active transport systems to capture ions at the level of the branchia. These systems are similar to those attrapping ions in marine organisms, but the direction of the flow is opposite. Adult insects inhabiting ponds have ionic absorption systems in the digestive tube and in the rectum, while their larvas absorb ions through the anal papilla.

In the vertebrates, fresh water fish drink little, eliminate diluted and abundant urine, and present chloride cells in their branchia to introduce ions to the corporal liquids. Amphibians also form diluted urine and incorporate ions through the skin. The permeability of this surface is regulated by the antidiuretic hormone.

There are many organisms capable of living in either salt or fresh water, and in them, the flow of water and of ions invert to accommodate the change from one medium to another. These organisms are known as euryhyalines, in contrast to the stenohyalines only capable of living in waters with a very narrow range of salinity. Euryhyaline organisms born in fresh water and which migrate to salty waters are known as anadromes, and those organisms born in salty waters and which migrate to fresh waters are known as catadromes. In preparation for the change from one medium to another, the organisms suffer a series of corporal changes on the level of the kidney and of the branchia, known as smoltification. Other living beings depend upon their behavior to support the changes in the salinity of the medium. Such is the case of many fish that bury themselves to protect from the dilution of salt in the body upon passing from salt water to fresh water.

The organisms living on land suffer dehydration problems. To combat dehydration, insects have developed an impermeable cuticle that covers their skin. They have also created a gradient of ions and nitrogenous wastes (uric acid) through active transport in the colon, permitting the reabsorption of liquid. Insects also possess a curious system of water transport, independent from the ionic gradients.

Amphibians normally do not drink, and by having a permeable skin, resolve the dehydration problem by reabsorbing practically all the water

in the urine. They are also capable of surviving after having lost up to 40% of their corporal liquid. Frogs in the desert utilize their urinary bladder for water storage. Reptiles drink a lot and have a thick skin covered with scales, however, never excrete a concentrated urine and possess salt glands to eliminate ions. Finally, in birds and mammalians, Henle's Loop has been developed, permitting the reabsorption of filtered water.

In some superior vertebrates, similar to the deer such as the elan that live in the desert, the corporal temperature rises as it increases in the medium to avoid evaporation of the corporal liquids, and the beings live as if they had a fever. For the brain to support an increase in body temperature, a modification is present in circulation. The modification allows the warm blood from the body to loose temperature as it passes through hundreds of small vessels in the carotid bodies that are in contact with the colder venous blood coming from the nasal airways that has lost temperature by respiratory evaporation.

In the plant kingdom, there have also developed mechanisms to adapt to the type of medium that they inhabit. Some marine botanical species are eurybathic (capable of living in both salt water and fresh water). The terrestrial plants have developed cuticles, which are thicker in the desert plants. They have mechanisms to store water and the stomas regulate transpiration through holes.

Participation of hormones in the control of osmolarity of the corporal liquids is found in crustaceans. The brain of these organisms secretes a factor to increase the concentration of chlorine in the corporal liquids and the rate of sodium absorption. In nemertines (tape worms), it has been observed that when the cephalic ganglion is extirpated, osmoregulation rate slows down. Also possibly in annelids there are neurosecretions intervening in the hydro-mineral equilibrium. The main hormones with osmoregulatory functions in different groups of organisms are vasotocin arginine, prolactin and antidiuretic hormone.

The loss of water is useful to eliminate nitrogenous products. Aquatic organisms with large surfaces in contact with water directly eliminate ammonia. In other organisms forming concentrated urine, stored in the bladder, urine is eliminated which is less toxic, producing it to form ammonia and CO_2 in the liver. Ammonia is only used as a buffer in the renal tubules. In insects, reptiles and birds, uric acid is eliminated.

Evolution of the organs specialized in osmoregulation

As previously mentioned, the primitive process for hydro-mineral conservation is simple diffusion and the organs initially in charge are the contractile vacuoles of the protozoans. Contractile vacuoles are also found in sponges.

The nephridia of the invertebrates can be divided into protonephridium and metanephridium. The first are simple or ramified tubular structures opening to the exterior through a nephrostome. Its internal extreme is closed and is covered by solenocytes (cells with a large cilium toward the light of the protonephridium) or by flame cells (cells with a group of cilia undulating toward the light of the protonephridium), creating a negative pressure to drain the extracellular liquid through ultracentrifugation. The protonephridia are characteristic of the acoelomated organisms, such as the platyhelminths and the coelenterates (fig. 33).

The metanephridium is formed by ramified tubes opened on both ends. The internal end is in contact with the coelom through a ciliated funnel and by filtration produces an isotonic liquid, which is later transformed through reabsorption and secretion. Around the tube is a capillary network.

The Malpighi corpuscles of insects are tubular evaginations of the terminal part of the digestive apparatus, whose distal extremity opens to the hemocoel. The tubes are covered by ciliated epithelial cells with a large quantity of mitochondria and of muscular cells, giving them motility. They do not function through ultracentrifugation, but only by the active transport of sodium, potassium, uric acid and water. The Malpighi tubes are also in charge of the secretion of silk, with which many insects construct their cocoon during the pupa phase (fig. 33).

In some invertebrate and fish, the branchia and the anal glands intervene in the hydro-mineral equilibrium, capturing and excreting salts through the chloride cells in the epithelia of the primary lamellae.

The functional units of the kidney, or the nephrons, appeared early in the evolution of the vertebrates. Each one was originally a drainage canal from the body cavity, or coelom, to the exterior. A collection of blood capillaries later evolved, uniting to a part of the canal and interrupting the connection of the tube with the coelom. After this, the canals began

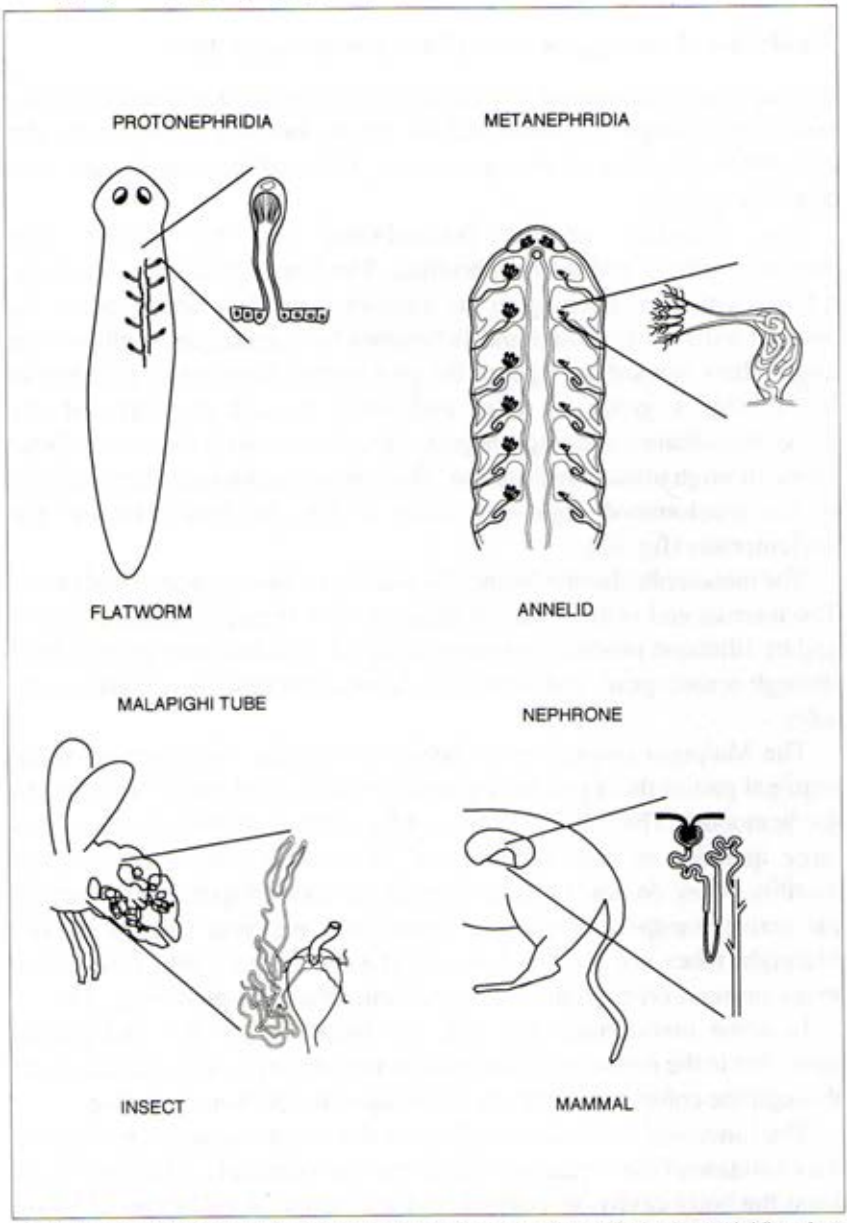


Fig. 33. Distinct excretory organs in phylogeny. Scheme of a typical protonephridium in a platyhelminth; sketch of a metanephridium characteristic of an annelid; scheme of a Malpighian corpuscle of insects; and a diagram of a nephron of a mammalian.

to eliminate liquids and molecules they filtered from the blood capillaries to the cavity of the canals. The most primitive kidney that we currently know of is that in the larvas of lampreys, in which there is a glomus (a tangle of blood vessels) in the wall of the coelom, close to the point where each nephron opens. There are similar glomi and nephrons in the cyclostome, whose corporal liquid has the same osmotic pressure as the sea, but with differences in the ionic concentration accumulating in the body and in the environmental medium. In the adult lamprey, as in all superior vertebrates, the glomus is inserted in the extreme or the funnel of the nephron, receiving the name glomerulus.

The kidney in the vertebrates finally appears, which is a mesonephros in the case of amphibians, and a metanephros in the remaining groups. Henle's Loop is only found in birds and in mammalians, and the quantity of nephrons that contain the structure, known as a juxtaglomerular, is higher in the more evolved organisms.

SIMILARITIES AND DIFFERENCES BETWEEN ONTOGENY AND PHYLOGENY

Despite the enormous variety of the systems in charge of hydro-mineral equilibrium, which have evolved throughout phylogeny to adequate the organism to the medium it inhabits, the following similarities can be noted between the phylogeny and ontogeny of the superior mammalian:

1. The development of a pronephros, later a mesonephros and finally, a metanephros is repeated in the ontogeny of mammalians and in the evolution of vertebrates.
2. Similarly, there arises an excreting organ independent of the vascular compartment which changes to an excreting organ linked directly to the circulatory system, in ontogeny as well as in phylogeny.

CHAPTER 9

The Ontogeny and Phylogeny of the Functions of Reproduction

THE REPRODUCTIVE FUNCTION IN THE ADULT MAMMALIAN

Masculine sexual physiology

The essential function of reproduction in the male is the production of sperm, or spermatogenesis, and its placing in the genital tract of the female. The organs producing the sperm, the testicles, also carry out endocrine functions, or, the production of the main masculine hormone, called testosterone. Each testicle is composed of different types of tissues, collaborating in spermatogenesis and endocrine functions, which are respectively the seminiferous tubes and the interstitial cells. The relationship between the two basic functions is of great importance since the formation and development of the gametes requires testosterone, but the production of testosterone does not depend upon spermatogenesis.

All the aspects of the masculine function of reproduction are controlled directly or indirectly by testosterone or by the gonadotropines of the anterior hypophysis, which are: the follicle stimulating hormone (FSH) and the luteinizing hormone (LH). These internal secretions receive their name based upon their effects known in the female, but their molecular structures are exactly equal in both sexes. FSH and LH exercise their effects in the testicles, while testosterone presents an ample spectrum of actions not only in the testicles, but also in the accessory reproductive organs, in the appearance of the secondary sexual characteristics, in reproductive behavior and in metabolism.

Feminine sexual physiology

In contrast to continuous production of sperm in the male, the maturation and liberation of the germinal feminine cell, or ovules, is cyclic and intermittent. This pattern is true, not only in respect to the development of the ovule, but also of the structure and function of the entire feminine reproductive system. In human beings and in primates these cycles are called menstrual.

The ovary, similarly to the testicle, has a double responsibility: it produces the ovules and secretes the two feminine sexual hormones, called progesterone and estrogen. The regulatory system controlling the development of the ovule, ovulation, and the formation of the luteal body, is analogous to that described for to the testicular function. The anterior hypophysial gonadotropins (FSH and LH) are present and estrogens carry out important roles. However, the general scheme is more complex in the female, since it includes a second important gonadal hormone, progesterone, and a hormonal cycle that contrasts with the stable and continuous rates of masculine hormonal secretion. Two phases can be distinguished in the menstrual cycle: the follicular, in which the follicle grows before liberating the ovule and the luteal, in which the follicle stays in the ovule after ovulation, growing until it involutes. FSH is more concentrated in the plasma of the female in the initial part of the follicular phase of the menstrual cycle, later decreasing during the rest of the period, except for a transitory peak presented halfway in the cycle. LH is constant during the major part of the follicular phase, but some hours before ovulation it increases and then later decreases slowly and progressively during the luteal phase. The pattern of estrogen is more complex: after remaining more or less low and stable during the development of the follicle, it increases, reaching a peak before the levels of LH rise. Such a peak is followed by a fall, after which a second phase of increase due to its secretion through the luteal body is observed, and finally there is a rapid declination during the last days of the cycle. The pattern of progesterone is the most simple of all, given that during the follicular phase the hormone is not secreted, but little after ovulation, the luteal body begins to secrete it and its production decreases as the structure involutes.

Upon initiating the ovarian cycle, the endometrium, lining the internal part of the uterus, grows under the influence of the increased concentration of blood estrogen. This phase of the uterine cycle is known as the proliferative stage. After ovulation, the secretory type of the endometrium develops through the combined action of progesterone and estrogen. This secretory period ends with the disintegration of the luteal body. The decrease in the concentration of these hormones deprives the highly developed endometrial lining of its hormonal support, constricting the blood vessels, and the endometrium begins to shed, initiating the menstrual flow. Estrogen and progesterone do not act exclusively over the uterus, but also induce the appearance of the secondary feminine sexual traits and sexual conduct.

THE ONTOGENY OF THE REPRODUCTIVE SYSTEM

Determination of sex

Sex in mammalians is genetically determined from the moment of fertilization of the ovule. In these organisms, the males are heterozygotic (they produce two types of gametes) and the females are homozygotic (they produce only one type of gamete). The type of spermatozoid that fertilizes the ovule determines the genetic sex of the offspring. From before the first division of the fertilized egg, the germinal plasma can be distinguished, from which will develop the germinal cells of the organism in formation.

Germinal cells

In the beginning, the gametes of the mammalians are observed in the base of the vitelline sac and allantoides and are pulled when the embryo folds to form the middle intestine. The cells leave the wall of the middle intestine, using an enzymatic method, and once they have abandoned it, they use signals in the matrix, mainly fibronectin, and direct cellular contacts to find their direction toward the gonadal crest. There are also chemo-attractive systems, which indicates their destiny. In birds, the gametes are initially located in the opaque area of the cephalic portion of the embryo, and later they pass into circulation to reach the gonadal crest.

Formation of the undifferentiated gonad

The undifferentiated gonadal crest is composed of cells of the stroma, derived from the mesonephric region, which degenerates, by the mesenchymatous epithelial cells covering the coelom and by germinal cells that slowly invade them (fig. 34). These cellular groups organize to form the stroma and the sexual epithelial chords. In females, these sexual epithelial chords form the primordial cells and the pregranulosa cells, and the stroma differentiates into the cells of the theca and the interstitial cells. In the males, the stroma originates the connective tissue, the muscle and the Leydig cells.

Differentiation of the gonad

The formation of the gonad is passive in females, while in the males a masculinization factor is needed in order for the male gonad to mold. In the beginning, this factor was thought to be a surface antigen known as HY. It was later postulated that it could be the product of the expression of a gene known as ZFY (zinc finger protein of Y, or a protein containing a finger of zinc on the Y chromosome), which is a transcription factor. It is currently known that it is not the ZFY gene, but a gene known as Sry (sexual region of Y, or a sexual region of the Y chromosome), which is exclusively expressed in males and whose transcription coincides with the critical stage of development of the gonad; expressed even when there is not an invasion of the undifferentiated crest by germinal cells. The differentiation of the masculine gonad is characterized by a separation of the chords from the surface by morphogenetic movements of mesenchymatous tissue, by which it is invaded and through angiogenesis (fig. 35). The stroma of the gonad also secretes a fibroblastic growth factor assisting the said movements, and another hormone known as antimüllerian aiding in the differentiation of the gonad as well as the genital tracts, and testosterone begins to be secreted.

Important ultrastructural changes occur in the masculine gonad, such as the appearance of an endoplasmic reticulum in the cells of the stroma, which synthesize the masculine factors. The Leydig cells have mitochondria with tubular crests, great quantities of glycogen, drops of lipids and smooth endoplasmic reticulum. Upon arrival at the gonad, the

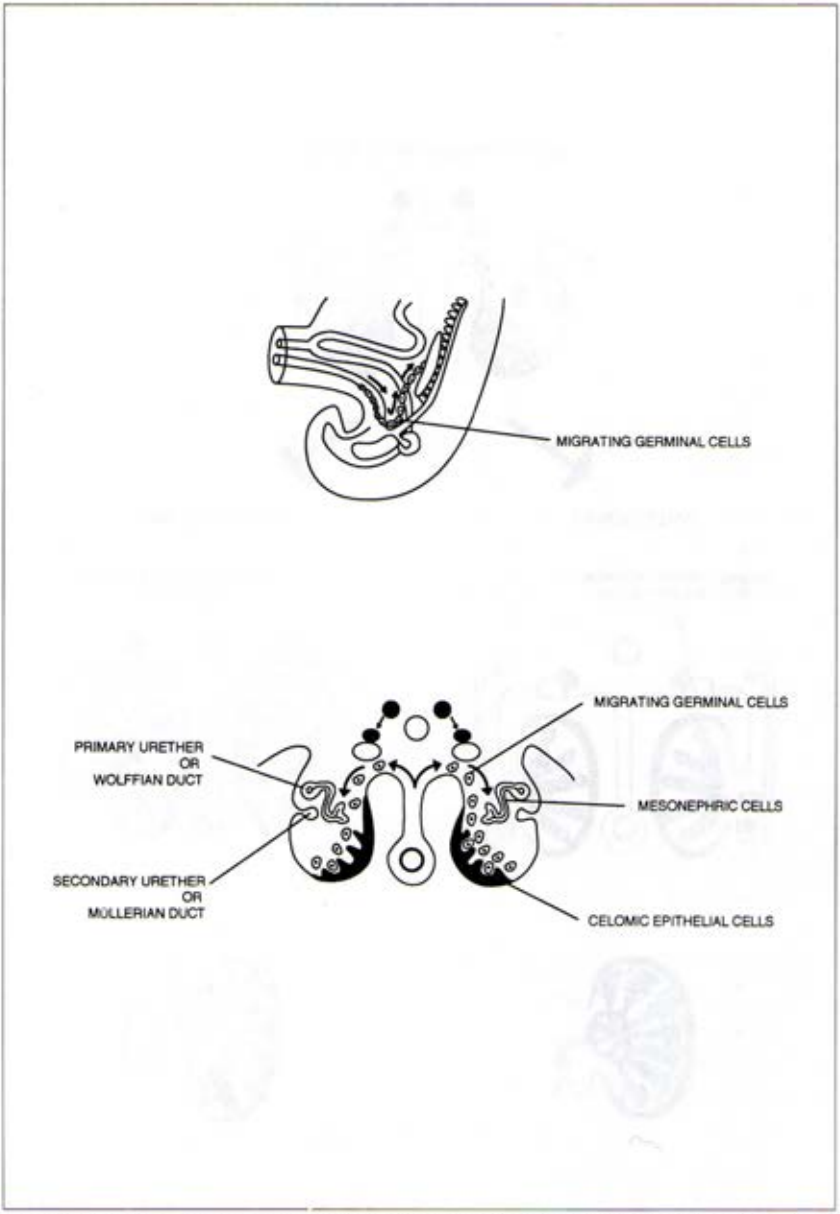


Fig. 34. Scheme showing the migration of the primordial germinal cells. Localization of the coelomic epithelial cells, migration of the germinal cells, formation of the primary and secondary urethers.

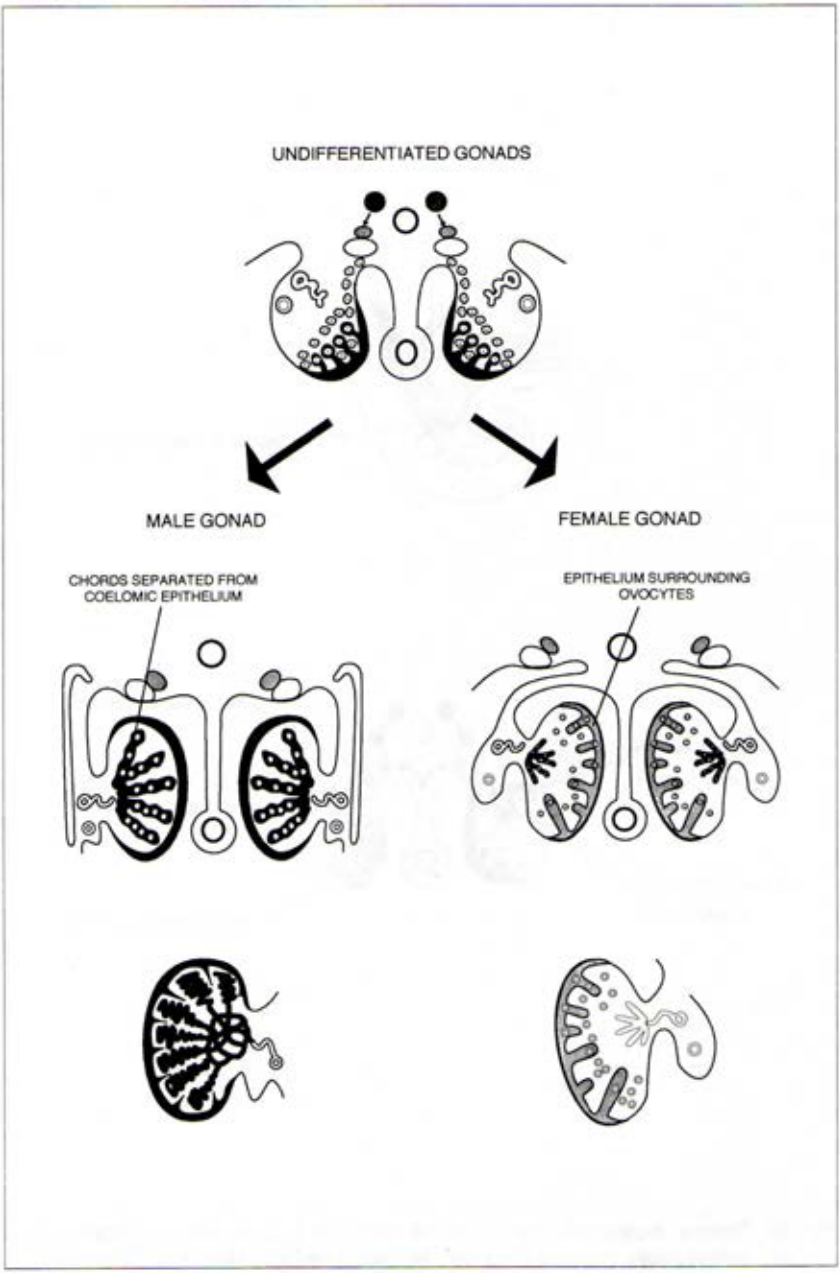


Fig. 35. Development of the undifferentiated gonad to a testicle or an ovary.

gametes begin a stage of mitotic division, which is why they are known as prospermatid M, and later enter into mitotic arrest, where they are known as prospermatid T. It should be noted that the mitosis of germinal cells begins from the period of migration.

The ovary maintains an undifferentiated state for a long time and the first indication of differentiation is the beginning of meiosis with the appearance of synaptonemal complexes. The ovocytes are much smaller and less differentiated in the periphery. The basal plate penetrates toward the medulla and the epithelium slowly surrounds each ovocyte. If the ovocytes do not migrate, the differentiation of the gonad and the stroma will not appear in the ovaries. This contrasts with the differentiation of the testicle in which the Leydig cells appear even though there are no spermatocytes. Therefore in females, if there are no ovocytes, the hypothalamus-hypophysis-gonad axis will never be established (fig. 35).

In the ovary the ovocytes enter meiosis to initially delay the first meiotic division in the stage known as "diplotene." Afterwards, the division process continues until producing the elimination of the first polar body and later makes a second stop during prophase 2. Meiosis only ends when fertilization occurs in adult life. A hormone secreted by the gonad known as inhibin and the antimüllerian hormone intervene in mitotic arrest.

Formation of the tracts

During the formation of the kidney, a pronephric canal is constructed, acting as an inducer in the differentiation of the mesonephros, and finally constitutes the Canal of Wolff. There also develops a paramesonephric canal through the invagination of the coelomic epithelia, forming the Müller canal. In male organisms, this degenerates and the epididymus, the seminiferous tubules, and the seminiferous vesicles develop from the Wolff canal. From the urogenital cavity develops the prostate. The induction of masculine genital tracts depends upon testosterone and another hormone also secreted by the gonad. The differentiation of the urogenital cavity is not subject to testosterone, but to two enzymes whose appearance precedes the differentiation in the structure. The cells of Muller's canal die or differentiate into mesenchymatous cells. The establishment of the hemotesticular barrier and the transformation of the chords in tubes occurs after birth. The hemotesticular obstacle is com-

prised by the unions between the Sertoli cells, in which the membranes are superimposed, presenting union fibers and in which the cisterns of the endoplasmic reticulum are located parallel to them. In these unions, only ribosomes are observed on the side of the cistern facing the cytoplasm. This type of disposition does not permit the passing of ions and the barrier creates a micro-environment toward the interior of the seminiferous tubules (fig. 36).

In females, the Wolff canal degenerates and the Müller canal persists. Again, this stage is passive and depends upon the absence of testosterone. The Müller canal develops into the Fallopian tubes and the uterus and vagina develop from the urogenital cavity (fig. 36).

Sexual differentiation of the encephalon

The administration of androgens during the first days of postnatal life produces masculine behavior, even in genetically and gonadally feminine subjects. It has surged that feminine conduct is a result of the absence of estrogen in the brain of females, since this hormone is restrained and destroyed by a hepatic fetoprotein. In masculine organisms, testosterone is not captured by this enzyme and then penetrates the brain, where it is converted into estradiol, which is in charge of masculinizing conduct. Again, the determination of feminine behavior is a passive process, while masculine acting depends upon the presence of testosterone.

THE PHYLOGENY OF THE REPRODUCTIVE SYSTEM

Determination of sex

The factors imposing sex in invertebrates are unknown. In fish, amphibians and reptiles the elements determining the sex of the organism are temperature and/or the behavior of the individuals in the same species.

Sex in birds and mammalians is genetically established from the moment of fertilization of the ovule. In birds, the females are the heterozygotic (they produce two types of gametes) and, consequently determine the sex of the descendants, while in mammalians, the males are heterozygotic, and the type of spermatozoid fertilizing the ovule is what determines the sex of the descendants.

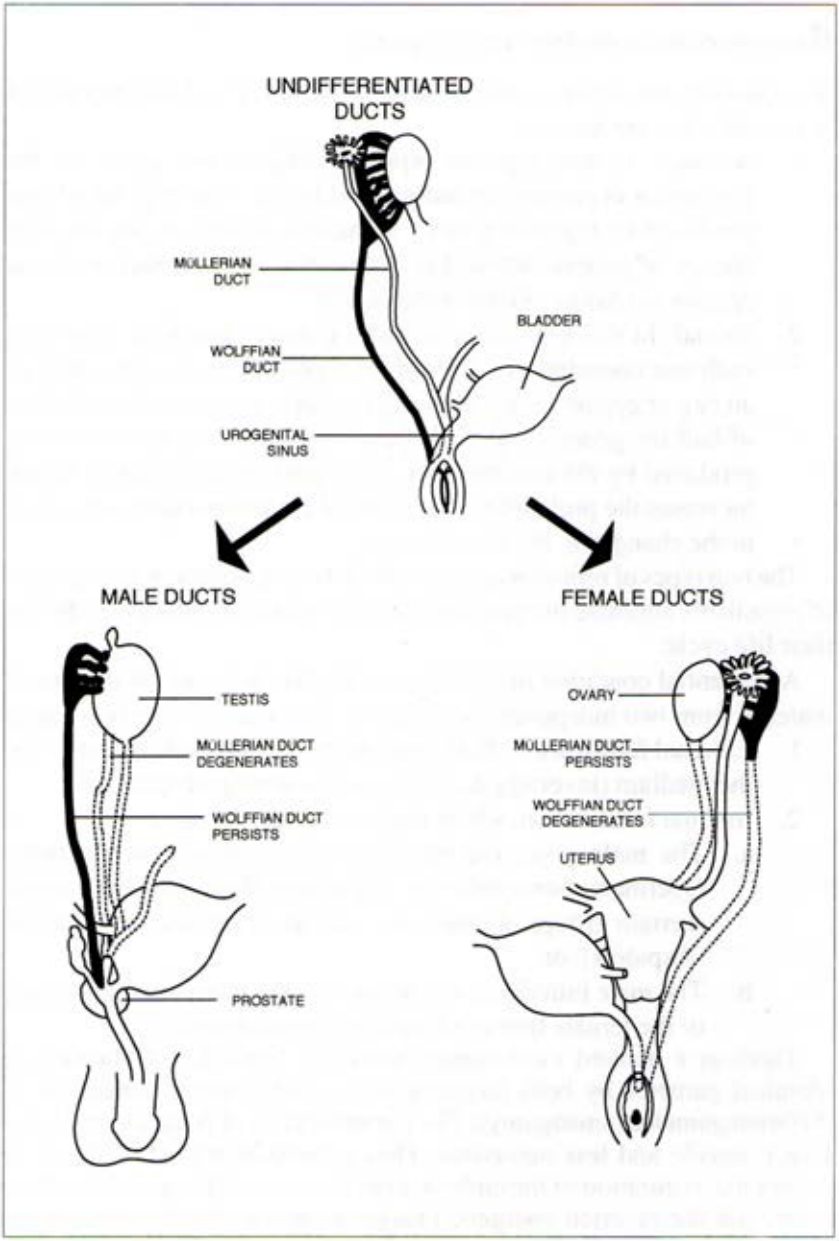


Fig. 36. Development of the masculine and feminine internal genitals from the Wolff and Muller canals.

Reproduction in distinct animal groups

Reproduction assures the continuance of a species. Two basic modalities of reproduction are known:

1. Asexual: In this type of reproduction, all the genes of the progenitor organism are transmitted to the offspring, which are produced by bipartition or by gemation. Mutations are the only source of genetic variability, permitting the adaptation of the species to changes in the environment.
2. Sexual: In this type of reproduction, two individuals intervene, each one contributing a half of their genome in the formation of an egg or zygote. The adaptive advantage, compensating the loss of half the genetic material of each progenitor, is the variability produced by the combination of the traits of the parents, which increases the probability that some of the descendants will adapt to the changes in the environment.

The two types of reproduction are not exclusive, and numerous groups of organisms alternate between asexual and sexual reproduction during their life cycle.

An essential condition in sexual reproduction is the union of genetic material from two independent organisms. This can occur in two ways:

1. External fertilization: Both progenitors release their gametes into the medium (invertebrates, fish and some amphibians); and
2. Internal fertilization, which may occur in two ways:
   a. The male gives the female a sac containing his gametes (spermatophore) and she introduces them into her vagina (certain groups of mollusks, such as squid, and the majority of spiders); or
   b. The male introduces his sperm into the interior of the vagina of the female through specialized sexual organs.

There is a marked evolutionary tendency from the production of identical gametes by both progenitors (isogamy) to the formation of different gametes (anisogamy). The germinal cells of females tend to be larger, sessile and less numerous. They possess nutritious material to permit the maturation of the embryo until an advanced stage of development, and the inverted energetic charge in each ovule is strong to the female. In contrast, the gametes of males are small, mobile and numerous, therefore their inversion in each gamete is reduced.

In all invertebrates, although gonads are present, their only function is to produce gametes. The endocrine functions of these organs do not appear until the chordates, initiating in this group the regulation of somatic and behavioral characteristics by the sexual hormones. Possibly the most important adaptation of the gonads within the chordate group is found in birds. To alleviate weight during flight, in many birds atrophy occurs to one of the reproductive organs, and only the gonad continuing its development functions in adult life.

Some species are capable of reproducing throughout the entire year; however, the majority of them only do it during some seasons, waiting for the appearance of certain conditions in the medium to initiate reproductive activity. In the majority of hermaphroditic organisms, producing both masculine and feminine gametes (with exception of platyhelminths and some plants), the two types of cells mature during different periods of time and generally crossed fertilization occurs between two individuals. Another example of seasonal reproductive behavior is constituted by livestock. Cattle respond by increasing synthesis and secretion of sexual hormones to the reduction of light and darkness cycles, reproducing in the Fall so that their offspring will be born in the Spring or Summer, when there is an abundance of food. Continual reproductive activity appears relatively late in the evolution of mammalians.

It should be remembered that species are ecologically grouped into r strategies (reproductive) and k strategies (caring) according to their method of reproduction. The r species produce a large number of descendants, dedicating little time to their care, while k species have very few offspring, but give them much attention.

Evolution of sexual conduct

Some form of sexual behavior has been observed since unicellular organisms. The ciliated organisms, such as the paramecium, do not present sexual dimorphism and under normal conditions, reproduce by bipartition. However, in special situations, two paramecia unite their oral surfaces and exchange micronuclei. They later separate and each one divides into two daughter cells. From the ciliated organisms, sexual conduct evolves, each time taking on more complex and varied patterns.

The superior plants produce gametes that are carried by the wind or by water, or posses complex, well-developed structures, such as flowers that attract insects, birds and mammalians who disperse their gametes. Some sessile animals, such as sponges, coral and echinoderms, release their gametes into the water and leave them to chance. In terrestrial and aquatic organisms there appears a type of specific behavior of the parents, known as sexual conduct. This form of acting shows early on the phylogenetic scale. Its function is to rectify that both progenitors belong to the same species and to opposite sexes, decreasing the aggression between the members of the pair and increasing their capacity to respond sexually.

In parallel to the evolutionary tendency toward anisogamy, there is an inclination from similar sexual behavior in both progenitors to distinct conducts. The inversion of a high level of energy in the production of few feminine gametes is accompanied by a receptive behavior, and the females tend to capture the egg to care for it and protect it. Males look to fertilize a large number of females. Since the ovules are limited, the males fight to obtain them, and develop anatomical, physiological and etiological mechanisms to demonstrate to the females their normality, physiological adequacy and capacity to help them care for their offspring. As examples of these mechanisms can be cited: the chants of numerou insects; the coloring and dances of the fish; the croaking of frogs; the coloring, dances and singing of birds, and many times the battles for territory, also seen in the mammalians. This phenomenon determines sexual selection.

The males of many species also develop mechanisms to attract the females, assuring that their gametes are the only ones to fertilize the females. Many insects (dipters and coleopters) remain copulating for more than and hour, although their sperm is passed to the female in the first few minutes. This mechanism impedes the female to pair with another male so that the spermatozoids of both do not compete for the ovules. The males of the rodents secrete a coagulant substance that forms a vaginal thrombus in the female, impeding the access of the spermatozoids of other males. Some masculine rats, in the presence of pregnant females, emit an odor, provoking abortion and permitting them to copulate. Lions kill the litters of the female of other males to be able to copulate with her.

Although the ovules never cease to be a limiting factor, on some occasions, females attract males and are the object of sexual selection. This situation occurs in the species where the males actively intervene in the care of the offspring and in those in which the appearance of the secondary sexual traits of the males requires an important energetic inversion. One of the mechanisms females use to attract males is to extend their receptive period of copulation.

From the previous paragraphs it can be deduced that polygamic conduct (mating with many females during a reproductive period) appears in the following situations:

A. A marked anisogamy exists;
B. When the territories are rich in food and free of predators, permitting the female to care for her litter by herself;
C. In the case where the offspring are precocious and do not require a prolonged period of care by the parents; and
D. In those situations when a high risk of predation exists, increasing the probability of survival of the family if it is divided.

Monogamy (the female and male remain united during at least one season to care for the litter) is favored by:

A. Short periods of mating, not permitting the search of various partners;
B. Poor territories, requiring the two adults for the search of food for the family; and by
C. The presence of predators, requiring both parents to defend their offspring.

The type of reproduction plays an important role in the formation of societies. There is a higher probability of perfect collectivities, with a high level of coordination and without conflict, when the individuals are identical or genetically similar. Examples of this type of society are the colonies of sponges, coral, bryzoans and tunicates, which form by asexual divisions. These groups of organisms only use sexual reproduction to construct independent colonies, but never within the same group. Insects living in colonies, such as bees and wasps, use in the formation of communities a variant of sexual reproduction, parthenogenesis, in which the second polar body is used for fertilizing the ovule, creating almost identical descendants of the progenitors (note that worker bees are all female). In the species using sexual reproduction, societies are almost never found, except for Man and primates, which have sufficient intelligence to remember family relations and to establish alliances.

SIMILARITIES AND DIFFERENCES BETWEEN ONTOGENY AND PHYLOGENY

The similarities in the ontogenetic and phylogenetic development of the reproductive function are difficult to find. Not even at the level of determination of the sex or the formation of the gonads have similarities been found, nor in the construction of the tracts or of the hormones. A possible explanation for this fact is that the rest of the functional systems favor the survival of the individual, while reproduction supports the survival of the species. Possibly through this, the reproductive system is more specific in each species, and is found in higher relations with the environment in which the organisms live.

CHAPTER 10

The Ontogeny and Phylogeny of the Endocrine System

THE ENDOCRINE SYSTEM IN THE ADULT MAMMALIAN

The endocrine and nervous systems constitute the principal means of communication in the body, the messengers being the hormones and the neurotransmitters, which regulate cellular function. Classically, internal secretions, or hormones, were considered to be chemical substances synthesized by a gland and secreted into the blood stream, which transported them to specific sites (target organs) of the body where they exercised their action. Currently, this definition has ceased being so strict, because there are substances that are neurotransmitters, but at the same time are secreted into the blood stream and exercise their actions at distance; there is no clear line between what is a hormone and what is a neurotransmitter. If a neurotransmitter acting over a neighboring cell can be considered as a hormone, then many other substances modifying the behavior of neighboring cells, without passing through circulation, would possibly fall under the same classification. Within these regulators we would find: the autocrine secretions, which regulate the same cells that produce them, and the paracrine, which control the neighboring cells.

On the other side, the nervous system regulates the endocrine production of numerous glands, but at the same time, many of the hormones have the brain as their target organ. Each time, it has become more difficult to define the boundaries between the nervous and the endocrine systems, and so there has been much talk of a neuroendocrine system. Originally, only glandular tissues were considered as endocrine organs, but currently, the heart may even be proposed as a gland since it secretes

an atrial natriuretic peptide, which passes to circulation and decreases the reabsorption of sodium at the renal level. The kidney also functions as an endocrine organ. It secretes renin, which triggers the synthesis of angiotensin II, causing the constriction of the smooth vascular muscle, and secretes erythropoietin, which regulates the production of red blood cells. Two other examples are the liver, which secretes somatomedines, and the duodenum, which produces gastrin. Evidently the boundaries of endocrinology are still unclear to date.

THE ONTOGENY OF THE ENDOCRINE SYSTEM

Generalities

The study of the ontogeny of the endocrine system is very complex. Since we do not have the boundaries of adult endocrinology clearly defined, the situation in the embryo and the fetus is complicated even more.

According to the classic definition of a hormone, we can limit ourselves to study the appearance of the glandular tissues and of the simple feedback systems as well as those with a hierarchical control in which the hypothalamus, the hypophysis and the glands intervene. During ontogeny, in order for these systems to regulate the functions of the organisms, a gland in charge of secreting the hormones, must have matured and begun to synthesize molecules. These should be secreted into the blood stream and be recognized by the target organ, which should be capable of responding to the stimulus. These events do not always occur at the same time in development, and often, although the gland has already appeared, its secretions are not present or the target organs are not yet capable of responding to them.

However, if we limit ourselves to only studying these aspects, we omit a great quantity of events during development that are controlled by chemical substances that could be possibly considered as hormones. The primitive precursors of the internal secretions may have been the intracellular messengers throughout the first stages of division. Later there surged the paracrine secretions, known as inducers, and the chemo-at-

tractive substances, determining irreversible changes, which may be considered as the first functions of the hormones. An example of these substances would be the factor secreted by the notochord, inducing the development of the neural plate.

On the other hand, the study of the ontogeny of the endocrine system is further complicated. The effects of some substances, classically considered as hormones,are not always the same in the organisms in development and in the adults. Many of the internal secretions of adults play important roles in differentiation and in the induction of irreversible changes of the organs in early stages of development, and much later their function in metabolic regulation appears.

Another important aspect in the ontogeny of the endocrine system in mammalians is the problem of the autonomy of the offspring in relation to the mother. The embryo or fetus has, for the most part, autonomous endocrine functions. Nevertheless, changes in the female progenitor may alter some aspects of the fetal endocrine functions. For example, although maternal insulin does not pass to the fetus, the changes in glycemia are reflected in him. A diabetic mother determines an elevated glycemia in the fetus and high glucose levels, force the pancreas of the offspring in development to secrete a higher quantity of insulin.

A chapter about the ontogeny of the endocrine system should also mention the function of the placenta as a hormone producing organ. The placenta is capable of modifying maternal hormones and secreting them to the side of the fetus and vice versa, altering fetal hormones. Its participation is particularly important in the synthesis of estrogens, since it is a known fact that birth is induced by an increase in the concentration of estrogen, in relation to progesterone, by the end of pregnancy. In primates, the maternal cholesterol arrives at the placenta where it is converted into pregnenolone. This passes to the fetal suprarenal gland where it is transformed into dehydroepiandrosterone (DHEA) and is sulfated into DHEAS. It later returns to the placenta, where is converted into estrogens. In some species, the DHEAS secreted by the suprarenal gland passes to the liver, where they are converted into alpha hydroxy 1 DHEAS before being used by the placenta for the synthesis of estrogens. This last process plays an important role during birth, since it increases the synthesis of prostaglandin by the uterus and promotes the degenera-

tion of the luteal body while decreasing the secretion of progesterone. The estrogens also increase the number and sensitivity of the receptors to oxytocin in the uterus. It has been proposed that the increase in the capacity of the organ to synthesize and secrete estrogen is the result of an increase in the concentration of cortisol by the fetus, by the mother or both.

Ontogeny of some endocrine glands

Hypothalamus-hypophysis-gland axis

The hypophysis, located in a small depression in the base of the cranium, underneath the hypothalamus, is a gland constituted by two parts. In the embryo, its anterior lobe is formed as an excrescence of the mouth, while the posterior lobe grows downward from the bottom of the brain. The two parts unite and the anterior lobe partially develops around the posterior. The anterior portion loses its connection with the mouth, but the posterior maintains its junction with the hypothalamus. Despite that the anterior lobe of the hypophysis is not united with the hypothalamus, certain cells of this structure secrete "releasing factors" toward the portal hypophysial blood system, regulating the secretion of the hormones by the adenohypophysis. Examples of them are: CRF (corticotropin releasing factor), regulating the secretion of ACTH (adrenocorticotrophin hormone), and TRF (thyrotropin releasing factor), which determines the production of TSH (thyroid stimulating hormone).

The anterior lobe of the hypophysis contains at least five types of cells differing in the shape, size and class of granules present in their cytoplasm. Each type produces and secretes a different hormone, such as the growth hormone, prolactin, ACTH, TSH, FSH (follicle stimulating hormone), LH (luteinizing hormone), or MSH (melanocyte stimulating hormone). Some of these internal secretions have effects over the peripheral organs and others regulate the production of glandular hormones. ACTH regulates the secretion of the suprarenal gland; TSH regulates the secretory activity of the thyroid, and FSH and LH determine the secretion of hormones of masculine and feminine sexual glands.

During ontogeny, the hypothalamus does not induce the differentiation of the hypophysis, but its size is smaller in the absence of hypothalamic factors. The portal hypophysial system, which transports the releasing factors, appears late, but the hypothalamic secretions surge before this has been established. The production of some agents of the hypothalamus, such as CRF (corticotropin releasing factor), is modulated by the reactions of alarm from before birth, and there exists a period after birth in which this response disappears, to manifest again later.

The hypophysis does not participate in the differentiation of the target glands, nor in their capacity to synthesize hormones in small concentrations, but importantly adjusts the mass synthesis of hormones and their release. Atrophy of the hypophysis occurs in the absence of feedback control through the hormones secreted by the target organs. At the beginning of development, the internal hypophysial secretions are released without any regulation by the hypothalamus and their rhythm of release is pulsatile. This autonomous capacity of secretion of the gland decreases with development at the same time that it increases the negative feedback control by the hormones secreted by the target glands.

Suprarenal gland

The suprarenal glands, situated at the superior extreme of each kidney, are combinations of two completely independent glands: the adrenal medulla secreting both adrenaline and noradrenaline, which promote various useful responses when confronting urgencies; and the adrenal cortex producing the glucocorticoids (cortisol and corticosterone), which regulate the conversion of amino acids into glucose, the mineralocorticoid (aldosterone), which adjusts the metabolism of sodium and potassium, favoring the reabsorption of sodium in the renal tubules, and sexual hormones. The production of glucocorticoids and of sexual hormones are regulated by hypophysial ACTH, and the products of secretion of the adrenal gland determine the production of the hypothalamic and hypophysial secretions through feedback mechanisms.

The suprarenal cortex develops from a group of cells of the coelomic epithelia. In a similar way that there is in the hypophysis an initial stage in the secretion of this gland, which is independent of regulation by the adrenocorticotrophic hormone (ACTH), the suprarrenal gland has a period of autonomous production of hormones. The hormones secreted during this stage have the function to induce the differentiation of other organs. In fact, there is a peak in the secretion of glucocorticoids that precedes that of ACTH by the hypophysis.

The following effects of glucocorticoids have been described over the differentiation of distinct tissues:

1. They induce the beginning of accumulation of glycogen by the fetal liver;
2. They determine the synthesis of the pulmonary surfactant (factor which decreases the superficial tension in the alveoli, impeding their collapse), from the glycogen found stored in the type II pneumocytes in the lungs;
3. Develop the appearance of the phenyletanolamine-N-methyl transferase (PNMT), enzyme in charge of the synthesis of adrenaline from noradrenaline in the suprarenal medulla; and
4. They induce the migration of the hepatic hematopoietic cells towards the bone marrow.

From a certain stage in development, the continuation of the maturation of the suprarenal cortex is dependent upon the hypophysis. If the gland is extirpated, the adrenal glands will atrophy, modifying its distribution of lipids and decreasing its concentration of ascorbic acid.

On the other hand, the suprarenal medulla, which is the main source of circulating catecholamines in the adult organisms, embryologically derives from ectodermic cells of the neural crests and from nervous fibers extending from the last eight paravertebral sympathetic thoracic ganglia and from the first two lumbar. These cells migrate toward the groupings of coelomic epithelia found in the cranial part of the mesonephric kidney which will constitute the fetal suprarenal cortex.

Histologically and biochemically, the adrenal medulla remains immature during the entire fetal life; however, some cells found in proximity of the blood vessels mature and begin to synthesize or secrete catecholamines. At the beginning, the only catecholamine synthesized is noradrenaline and only towards the end of gestation is the presence of

adrenaline detected. The existence of glucocorticoids is necessary for the appearance of the phenyletanolamine-N-methyl transferase (PNMT) in the chromaffin tissue, in charge of methylating the noradrenaline to form adrenaline. Glucocorticoids also facilitate the release of the catecholamines from the fetal suprarenal medulla.

In the organisms in development, there is an additional source of catecholamines constituted by the extramedullary chromaffin tissue, located in the Zuckerkandl organs or the pre-aortic paraganglia. These bodies, formed by large masses of chromaffin tissue, are situated at the sides of the aorta at the height of the inferior mesenteric artery and are formed from the ectodermic cells that migrate from the neural crests. During the fetal period, these organs increase enormously in size and disappear during the first days after birth. In contrast to the suprarenal medulla, the extramedullary chromaffin tissue is poorly innervated and only synthesizes noradrenaline. The formation and degradation of this catecholamines are much slower than in the adrenal medulla. However, towards the end of gestation, these organs contain approximately double the amount of catecholamines found in the suprarenal medulla.

Toward the end of intrauterine development, factors such as asphyxia, hypoxia and hypoglycemia increase the secretion of catecholamines in the fetus of the sheep. The first two conditions produce a decrease in the concentration of noradrenaline in the extramedullary chromaffin tissue, but do not modify the levels of catecholamines in the suprarenal medulla. As the Zuckerkandl organs are not innervated, the effect of these stimuli would be directly through a humoral via. In the sheep, where the innervation of the suprarenal medulla is profuse and appears in the last third of gestation, asphyxia and hypoxia provoke, beside the direct response of the extramedullary chromaffin tissue, a medullar effect through the splanchnic nerves appears. Hypoglycemia produces a decrease of the concentration of catecholamines in the suprarenal medulla, but does not modify its level in the extramedullary chromaffin tissue. This consequence is mediated by the splanchnic nerves and appears only in certain species, such as sheep, in which the innervation of the suprarenal medulla matures toward the end of gestation.

During fetal life, the most important effect of the catecholamines is the modification of the quantity of blood stored in the placenta and its distribution to distinct fetal organs. In these, the noradrenaline causes a

redistribution of the blood flow favoring the heart and the brain, but decreases the current to the placenta and the muscles. Adrenaline and noradrenaline, in smaller levels, increase the concentration of glucose, lactate, amino acids and free fatty acids in the blood of the fetal lamb, activate the enzymes intervening in the gluconeogenic and glucogenolytic pathways and inhibits the secretion of insulin.

Thyroids

The thyroids are a pair of glands located in the anterior face of the neck, united by a straight isthmus of tissue situated in front of the trachea, immediately underneath the larynx. The thyroids consist of two groups of cuboid epithelial cells disposed in follicles or empty spheres bordered by a layer of cells. The cavity of these contains a gelatinous colloid, secreted by the epithelial cells, in which a part of the process of the synthesis of hormones occurs. The follicular cells secrete a protein to ward the colloid, known as thyroglobulin, which is iodized and later phagocytized, breaking into the fragments constituting the thyroid hormones. The main ones are: thyroxine (T4), triiodothyronine (T3), and the reverse triiodothyronine (T3r). The fundamental effect of these secretions is to accelerate oxidative processes that release energy in all the corporal tissues. The first has a higher biological activity. Many peripheral organs take in circulating T4 and through deiodization produce T3 and T3r.

Once released, the thyroid hormones travel united to a plasmatic protein known as TBG (thyroid binding globulin). The appearance of thyroid hormones in blood is regulated by the TSH secreted by the hypophysis, whose production is under the control of thyroxine and triiodothyronine.

Within the thyroid gland are other cellular groups in charge of secreting other hormones. The parathyroids are four masses of cells adhered to the thyroid gland, producing the parahormone, which is in charge, together with the derivatives of vitamin D, of the control of the metabolism of calcium. The glands also produce another secretion, known as calcitonin, which is secreted by the C cells of the thyroid follicles.

From the embryonic point of view, the thyroids are formed as an invagination of the bottom of the buccal cavity. This loses contact with

the oral cleft and while the neck, extends, the gland is shifted toward the caudal portion. Later, it is invaded by the cells of the fifth pharyngeal sac, which will form the parathyroid glands and the calcitonin producing cells.

Histologically, in the beginning of development the gland is composed of a solid mass of cells without colloid or follicular structure. Gradually the canaliculus appear between these masses of cells, and central spaces form in their interior, which are filled with colloid, as the follicles grow. Nevertheless, the surge of thyroglobulin (protein secreted toward the colloid from where the thyroid hormones are synthesized) precedes the appearance of the follicular space.

During intrauterine life, the placenta concentrates iodine, which accumulates in the blood, however, it is impermeable to the thyroxine (T4), triiodothyronine (T3), TRH (thyrotrophin releasing hormone, secreted by the hypothalamus) or TSH (thyrotropin or thyroid stimulating hormone secreted by the hypophysis), in the majority of species. Only in the rat does thyroxine cross the placenta. The capacity of the gland to capture iodine precedes the potential to synthesize hormones.

In the fetal period, the activity of the hypothalamus-hypophysis-thyroid axis is higher than in the adult. The levels of TSH and thyroxine (T4) are elevated, but the concentration of triiodothyronine (T3) is low. Distinct explanations have been proposed for the low levels of T3 in the fetus, including: A) deprived peripheral deiodization, B) a high renal clearance of T3, C) a rate of production different in the thyroid of T3/T4 and D) an activation of the pathway of deiodization for production of reverse T3 (T3r).

The change in the concentrations of fetal thyroid hormones to the pattern of the adult has been attributed to distinct causes, including: 1) the increase in the partial pressure of oxygen in the plasma at the moment of birth, 2) to hemodynamic changes, 3) to the adaptation to a lower environmental temperature at the moment of birth and 4) to a transformation in the activity of the autonomous nervous system. On the other side, it has been observed that the fall in the concentration of thyroxine precedes birth and this situation is the secondary consequence of the mechanisms that trigger birth, including an increase in the concentration of cortisol.

The thyroid hormones have important effects on growth and differentiation of the organism in development, for example, in the absence of thyroid hormones there are metal and skeletal deficiencies (cretinism). It has been observed that the thyroid hormones are also indispensable during some periods of differentiation, known as critical phases. Thyroid hormones are involved in the maturation of the type II pneumocytes, of the intestine, in the appearance of ossification centers in bones, in the development of components of the skin, such as hair follicles and sebaceous glands, and in the development of the nervous system.

The pancreas

Dispersed between the acinar cells of the pancreas, which secrete the digestive enzymes, there are a million or more islands of endocrine tissue, called the islets of Langerhans. These contain two types of cells, which can easily be distinguished in the histological sections. The beta cells secrete insulin and the alpha cells secrete glucagon. These two internal secretions participate in the control of the plasmatic levels of glucose, which at the same time is the most important regulatory factor in their hormonal production.

Embryologically, the pancreas is derived from the primitive intestine. The intestinal epithelial cells form bulbar structures surrounded by mesodermic tissue. From them develop the independent pancreatic lobes, one dorsal and one ventral, which are united by the flexions and rotations of the stomach until they fuse completely. The cells of the Langerhans islets may develop from the intestine or be of neural origin, invading the gland. From early embryonic stages insulin exists in the pancreatic rudiment and its concentration increases bi-phasically until reaching adult levels before birth. However, the secretory granules of the beta cells do not appear in the rat until the end of embryonic development; despite that the hormone is synthesized early, it is not secreted until the posterior stages of development are reached. The plasmatic concentration of insulin begins to increase at the end of the embryonic period, or at the beginning of the fetal period, and increases toward the end of gestation. In some species there is a small decrease in the plasmatic levels of insulin before birth. In the newborn, the plasmatic concentration of insulin is approximately eight times higher than in adults.

The differentiation of the cells of the acinus follows a pattern of development independent from that of the Langerhan's islets. In general, the secretion of insulin precedes that of pancreatic enzymes.

The fetal beta cells are only sensitive to the levels of glucose toward the end of the fetal period or in stages prior to birth. The secretion of insulin responds to the stimulation of the autonomous nervous system before birth. When pancreatic cells are cultivated in media with distinct concentrations of acetylcholine and adrenaline, they change the secretion of insulin. ACTH (adrenocorticotrophic hormone) and the secretions of the suprarenal cortex alter the capacity of the beta cells to respond to glucose, modifying the secretion of insulin.

Insulin regulates the levels of blood glucose in the fetus and exercises control over the accumulation of hepatic glycogen before birth. Its mechanism of action over the hepatocytes is still unknown and apparently its effect is secondary, since it does not intervene in the initiation of glycogen storage or in its synthesis, but impairs its degradation.

The effects of insulin over other fetal organs are practically unknown. Apparently in some species it decreases the levels of blood glucose, and the hearts of embryos are sensitive to insulin from early stages. We do not know the effect of insulin over the nervous system, despite that the hematoencephalic barrier begins to function after birth.

THE PHYLOGENY OF THE ENDOCRINE SYSTEM

From unicellular organisms, hormones are found that act as intracellular messengers, since their function as elements of communication between cells is impossible. Insulin exists in protozoans, while thyroxine (T4) appears in coelenterates and in medusas. It should be remembered that plants also have hormones, such as indoleacetic acid, cytokinin and gibberellin, which regulate the processes of growth, flowering and fructification.

Although there exist internal secretions in invertebrates, there are no glands present until vertebrates. In invertebrates, the hormones are produced by gastrointestinal or nervous cells, therefore it is said that the

systems are, in reality, neuroendocrine or enteric, and that in evolution they preceded the appearance of the endocrine system. In spite of the brusque changes that have occurred in the evolution of the glands, the sequences of the hormones practically remain identical and for example, the insulin found in unicellular organisms is similar to the insulin found in mammalians.

In the evolution of the internal secretions: the autocrine cells that produce substances for autoregulation appear first, later arise the paracrine, modifying the behavior of neighboring cells; and the last to appear are the neuroendocrine and endocrine messengers, acting at a distance.

The same as in ontogeny, in phylogeny there are secretions that participate in the induction of differentiation, and which regulate the irreversible processes, such as metamorphosis and molting of many organisms. On the other hand hormones participate in the regulation of reversible processes, such as metabolic function. The first type of effects preceded the evolution of the second.

Examples of hormones regulating reversible processes

In insects there is an internal secretion that determines the dilution of the urine produced by a cluster of neurosecretory cells in the ganglion of the first abdominal segment. The plant hormones regulate reversible functions, such as the production of flowers and fruits. Finally there are pheromones, substances secreted by the exocrine glands toward the environment, whose function is to modify the conduct of other animals of the same species and their effects are reversible.

Examples of hormones participating in irreversible processes

The rigid exoskeleton of many arthropods does not permit progressive growth. To be able to increase in size, these organisms must detach from their cuticle and synthesize a new exoskeleton of larger dimensions. This process is known as molting or ecdysis, and is controlled by a steroid hormone known as ecdysone. This substance is secreted by the neural

ganglia called prothoracic glands. For their maturation, these glands depend upon the presence of a neurohormone secreted by the cardiac body, which is composed of the expanded extremes of the axons of a bundle or cluster of neurons, known as the intercerebral gland.

There is also an internal secretion known as juvenile hormone, in charge of inhibiting the growth of the wings and gonads of the larvas and pupas of insects. This hormone is a terpene produced by a cluster of cells located behind the brain, known as the alate body. The concentration of this secretion decreases during the phases of successive molting.

An additional evidence of the irreversible effects of the hormones in phylogeny is constituted by the thyroidal secretions determining the metamorphosis of amphibians. Tadpoles fed with thyroid glands suffer an anticipated and rapid transformation. On the contrary, the larvas without thyroid never present metamorphosis. If the tadpoles without thyroids are administered thyroxine, the phenomenon then appears. The presence of the hypophysis, as well as the hypothalamus, is indispensable in regulating the secretion of the thyroidal hormones. In fact, a certain amphibian of Mexico, the axolotl, does not suffer metamorphosis, since its thyroid glands are incapable of responding to TSH, or its peripheral organs are incapable of responding to thyroxine.

Phylogeny of some endocrine glands

Phylogeny of the hypothalamus-hypophysis-gland axis

The structure evolutionarily preceding the hypophysis may be an ectodermic depression in front of the mouth of the Amphioxus in its juvenile stage. In the adult, the surface of this structure is covered by ciliated cells and establishes communication with the mouth, where it creates currents of water. In the urochordates, the neural gland is said to be homologous to the hypophysis. This is a nervous gland embedded in the layer between the syphons. It is in the lampreys where a hypophysis similar to that of the rest of the vertebrates is seen for the first time, and in it, the anterior, middle and posterior lobes are already distinguished.

Phylogeny of the suprarenal gland

Elements similar to the adrenal glands have been seen for the first time in cyclostomes, such as the lampreys. They are composed of two series of small and irregular steroidogenic bodies located besides the abdominal veins and arteries, including the chromaffin cells. In fish, the adrenal glands are located in the kidney or on top of it, but the chromaffin cells remain at the sides of the vessels. In amphibians, reptiles and birds, the suprarenal glands are formed by dispersed steroidogenic and chromaffin components. It is not until mammalians that the gland, cortex and medulla can be distinguished.

Phylogeny of the thyroid gland

The presence of T4 has been described in the coelenterates (medusas), although in them there still does not exist a thyroid gland or any structure resembling a thyroidal follicle. Possibly, the functions of the iodoproteins in the invertebrates are metabolic. It has also been described that iodine is fixed by some algae and invertebrates, passing to form part of the exoskeleton and/or part of the pharyngeal cavity.

The first outline of a thyroid gland appears in the protochordates (the tunicates and the Amphioxus) and in the cyclostomes (such as the lampreys), where there exists a primitive glandular structure on the bottom of the pharynx, known as a subpharyngeal gland or endostyle. This organ produces mucus that mixes with food; however, there are cells which trap iodine and generate residues of iodized tyrosine. These residues have the functions of hormones and are secreted in exocrine form to the intestine to be absorbed by the blood stream. Little by little in evolution, the mucus producing cells disappear and the cells fixing iodine predominate. The gland invaginates and loses contact with the pharynx. Possibly the adaptive pressure that made the fixer cells of iodine become dominant also constituted the element for the adaptation to fresh water in the protochordates.

The shape of the thyroid gland presents important modifications in the entire group of chordates. In the agnates, it is a compact structure without an axis in the regulation of its function and the thyroid hormones have been associated with metamorphosis and sexual maturation. These organisms have elevated levels of T3 in their corporal liquids after having suffered metamorphosis and the function of this hormone is not known.

The cartilaginous or elasmobranchial fish, such as sharks and manta rays, have a compact thyroid gland, while the bony fish have thyroidal tissue dispersed in a large number of corporal structures, from the eyes to the ovaries. The thyroidal hormones in these organisms are related with the migration associated to reproduction and in the smoltification or the changes to adapt from fresh water to salt water. T3 also provokes the deposit of guanine in the skin of fish, giving them a silvery coloration and therefore favoring mimetism. In fish, the plasmatic levels of T3 are elevated and the levels of T4 are very low. They do not have the plasmatic transporter protein of thyroidal hormones (TBG), therefore hormones pass rapidly to the target organs and their half life in the corporal liquids is very short.

In amphibians, T3 regulates sexual maturation and metamorphosis, also provoking a thickening of the skin, which favors their survival on land. In reptiles, the thyroidal hormones participate in sexual maturation, as they do in birds. However, in birds they also regulate migratory phenomena, the consumption of oxygen and the production of heat.

In all the vertebrate species, except for mammalians, the effects of the thyroidal hormones are largely antagonized by prolactin. Also, in all the chordates, except mammalians, the thyroidal hormones travel in the blood stream attached to albumin. It is not until mammalians that TBG (thyroid binding hormone) is found. In mammalians, the main function of the thyroidal hormones is to regulate the metabolism, increasing the consumption of oxygen and the production of heat.

Phylogeny of the pancreas

In lampreys, the exocrine pancreas is incorporated within the intestine and the endocrine is embedded into the mucous layer, as isolated cells. In the elasmobranchia, although well-defined islets are already found, the structures are buried in the wall of the intestine. The vertebrates constitute the only group in which a pancreas appears with both endocrine and exocrine functions. Amphibians are the first group in which a gland independent of the digestive tube is observed, and the structure is present up through the superior mammalians. The pancreas in inferior mammalians has a diffuse organization and lobes are only distinguishes in birds and in superior mammalians.

SIMILARITIES AND DIFFERENCES BETWEEN ONTOGENY AND PHYLOGENY

The study of the ontogeny and the phylogeny of the endocrine system is a very ample field and sprinkled with surprisingly similar information. The following similarities can be cited:

1. Originally, the glands were included in the digestive apparatus, or formed part of the neuronal ganglia to later separate as independent endocrine systems.
2. In their beginnings, the secretions emptied out toward the digestive tube or cavity, and later into the blood stream.
3. The role of the hormones is initially to regulate irreversible processes related with differentiation and the growth of the organism, and the control of reversible processes as its main role later predominates.
4. It is repeated in ontogeny, as well as in phylogeny, the sequence of autocrine secretion to paracrine, and finally to endocrine.
5. The sequences of amino acids in the peptidic hormones are very conserved in ontogeny and in phylogeny, differing from large changes which occur in the expression of other proteins (hemoglobin, myosin, etc.).

Annex: A Catalog of the Animals

Monera kingdom

Unicellular organisms lacking a nucleus or procaryotic. Ex.: bacteria.

Protista kingdom

Nucleated unicellular organisms that are able to group together to form colonies. Ex.: the ciliated organisms, such as the paramecium; the flagellated organisms, such as the euglena; and the colonial flagellated organisms, such as the volvox.

Animal kingdom

Phylum porifera: Its body consists of two layers of cells with a large quantity of pores through which they cross. They are marine and sessile. Ex.: sponges.

Phylum coelenterata or cnidaria: They are formed by two layers of cells separated by one layer of gelatinous material. they have digestive cavity in the form of a sac with an opening or mouth. Present radial symmetry and tentacles with adherent cells.

Class hydrozoa: Single individuals or colonies with an undivided digestive cavity and simple sense organs. Ex.: the hydra.

Class scyphozoa: Independent individuals that float or swim. Some species have sessile stages within their life cycle. The digestive cavity is divided and they have complex sensory organs. Ex.: medusas.

Class anthozoa: Independent individuals of massive colonies. They present and exoskeleton and in their life cycle do not have floating or swimming stages. Their digestive cavity is divided. Ex.: corals.

Phylum ctenophora: Marine. Free-living organisms that swim by means of eight rows of cilia and do not have adherent cells.

Phylum platyhelminth: Have a free life or are parasitic. Have a flat body with bilateral symmetry. Their structure consists of three layers of cells and they can or cannot have a simple or divided digestive cavity.

Class turberllaria: Live freely, generally present a ciliated exterior. Ex.:planarian.

Class trematoda: Parasites without external cilia. Feed by suction and have a digestive apparatus. Ex.: a fluke.

Class cestoda: Parasites without external cilia and without a digestive system. Ex.: tapeworms.

Phylum mesozoa: Parasites of the platyhelminths, mollusks and annelids. Have a very simple structure and no digestive system.

Phylum nemertinea: Large, flat, unsegmented worms. Have a digestive system with two openings.

Phylum aschelminth: Live freely or are parasitic, with bilateral symmetry and a coelom.

Class rotifera: Microscopic, with bilateral symmetry and numerous cilia around the mouth.

Class gastrotricha: Microscopic and live freely. Have cilia on their ventral surface and their body is covered with flaky cuticles.

Class kinorhynch: Small marine organisms with a spiny proboscis. Their body surface is covered with cuticle plates, forming rings.

Class priapulida: Freely living marine organisms. Present spines in the mouth region. the body is covered with rings of cuticles.

Class nematomorpha: The juvenile forms are parasites of arthropods, and the adults are free living. Have reduced digestive tubes.

Class nematoda; Free living or parasites, 30 species parasite man. They have a cylindrical body with bilateral symmetry, digestive tract with mouth and anus and no circulatory system. Many are decomposers. Ex.: intestinal worms.

Phylum acanthocephala: The juvenile forms are parasites of the arthropods, and the adults are parasites of the intestines of vertebrates. Lack a digestive apparatus.

Phylum bryozoa: Marine organisms living in fixed colonies. Have a digestive tube in the form of a 'U,' with a mouth surrounded by a crown of tentacles.

Phylum brachiopoda: Marine organisms, symmetrical with a spiral formed by two pieces that lodge a pair of arms with tentacles.

Phylum phoronid: Marine, inhabit caverns in the mud or the sand. Have a pair of arms with tentacles and a digestive tube in the form of a 'U.'

Phylum chaetognatha: Marine swimmers or floaters. Have bilateral symmetry and a straight digestive tube.

Phylum mollusca: Marine, fresh water or land dwellers. Have either bilateral symmetry or an asymmetrical. Have a crease of tissue over their body known as a mantel, which frequently secretes a spiral calyx. They are not segmented and have well-developed digestive, circulatory and nervous systems.

Class amphineura: Marine, with a shell composed of eight overlapping plates. Do not have a distinguished head.

Class monoplacophora: Marine, with a single shell with an apex curve. Have wide and flat feet. Are found in great depths. Ex.: neopilina.

Class gasteropoda: Marine, fresh water or land organisms. Some have a helicoid shell and have a clearly distinguished head. Ex.: snails.

Class scaphopoda: Marine with a shell in the form of a tube or cone show tentacles on the head to trap food.

Class pelecypoda or bivalvia: Marine or fresh water. Some lived fixed to the floor or buried in mud or sand. Present shells of two pieces. Ex.: clams.

Class cephalopoda: Marine with a small internal shell. In some cases they have external helicoid shells with internal subdivisions. Have tentacles on the head. Ex.: octopus and nautilus.

Phylum annelida: Marine, fresh water or terrestrial with bilateral symmetry and a segmented body. Lack appendages or they are lacking articulations. Possess a ventral nervous chord.

Class polichaetes: For the most part are marine, bury themselves or construct caverns. Have a pair of appendages in form of paddles on each segment.

Class oligochaeta: Mostly freshwater or terrestrial. Appendages small or lacking. Ex.: earthworms.

Class hirudinea: Flat, without appendages, and have suction discs on every appendage. Ex.: leeches.

Phylum arthropoda: Marine, fresh water or land organisms. Have bilateral symmetry and a segmented body, although the segments are frequently fused. the body and appendages are covered by an exoskeleton. Have a central nervous chord.

Class onychophora: Are tropical, terrestrial organisms with the shape of a worm. The segmentation is poorly developed. They have a large quantity of characteristics of the annelids and the arthropods.

Class crustacea: Possess two pairs of antennae and their respiration is branchial. Ex.: shrimp, crayfish and crabs.

Class arachnida: Lack antennae, the segmentation is reduced and they have four pairs of feet. Do not possess mandibles. Ex.: spiders and ticks.

Class diplopoda: Have a pair of short antennae. Their body is totally segmented and has two pairs of feet on each segment. In a transverse cut their body is round. They decompose organic material, mainly in the forests. Ex.: millipedes.

Class cheliopoda: Have a long pair of antennae. Their body is flat and totally segmented, with a pair of feet on each segment. Ex.: centipedes.

Class insecta: Possess a pair of antennae, and their body is divided into a head, thorax and an abdomen. Have tree pairs of feet. Some of the most important are:

- Orthoptera: crickets
- Isoptera: termites
- Anopleura: fleas
- Lepidoptera: butterflies
- Diptera: flies
- Coleoptera: beetles
- Hymenoptera: bees and wasps

Phylum echinodermata: Marine organisms with radial symmetry in which the radiating segments are known as arms. In their larvae stage they have a bilateral symmetry. They have an internal calcareous skeleton protected by numerous spines. The possess a system of tubes filled with water that intervene in feeding and in locomotion.

Class crinoidea: Live fixed to surfaces and have a large number of very ramified arms. Ex.: feather stars.

Class asteroidea: Have five arms united at the body by very wide bases. Ex.: sea stars.

Class ophiuroidea: Possess five large arms, which are sometimes ramified, and which are clearly distinguished from the body. Ex.: brittle stars.

Class echinoidea: Spherical with a disc shape and without arms. Have spines, long or short, and superimposed plates. Ex.: sea urchins.

Class holothuroidea: Cylindrical, without arms and with a mouth surrounded by tentacles. Lack spines and their skeleton consists of particles embedded in the skin. Ex.: sea cucumbers.

Phylum hemichordata: Marine, have a worm shape and a distinguished proboscis, which they use to bury themselves in the mud or sand. They have a dorsal nervous chord and pharyngeal sacs. They do not present a notochord.

Phylum chordata: Marine, fresh water or terrestrial beings with a bilateral symmetry. They have a dorsal nervous chord and a notochord underneath, which may disappear during development. There are various pharyngeal sacs in the throat region. There are segmentation outlines in the arrangement of the muscles.

Subphylum urochordata: Marine, with free living larvae and sessile adults. The notochord and part of the nervous system disappear during development.

Subphylum cephalochordata: Marine, translucent and free living. Present a well-developed dorsal nervous tube, a notochord and pharyngeal sacs in the adults. Ex.: amphioxus.

Subphylum vertebrata: The notochord is replaced by vertebral column during development. The anterior part of the nervous tube widens and is protected by either bone or cartilage.

Class agnatha: Without mandibles or fins. Cartilaginous skeleton and a heart with a ventricle. Ex.: lampreys.

Class chondrichthyes or elasmobranchii: Cartilaginous skeleton. Five or more externally distinguished pharyngeal sacs. The heart has a ventricle. Ex.: sharks and manta rays.

Class osteichthyes or teleostei: For the most part the skeleton is formed by bone. Covered pharyngeal sacs and are not externally visible. Heart with a ventricle. Ex.: fish.

Class amphibia: The larvae are aquatic with branchia or gills, and the adults are terrestrial with lungs. Generally present two pairs of appendages, although they may be small or absent. The heart has one ventricle. Ex.: frogs.

Class reptilia: Adults and juveniles have lungs. Eggs with shells and a membrane in the egg stores water. Two pairs of appendages, which may be absent. Skin with scales. Heart with a partially divided ventricle. Ex.: turtles and snakes.

Class aves: The scales are modified to feathers. The anterior extreme of the appendages is changed to form wings. Heart with two ventricles. Ex.: birds, chickens and penguins.

Class mammalia: The scales are transformed into hairs. The present mammary glands that secrete milk. The heart has two ventricles. The most important orders are:

- Monotremes: ornithorhynchus and echidna
- Marsupials: kangaroos and koalas
- Insectivores: anteater
- Chiroptera: bats
- Primates: monkeys and Man
- Edentate: armadillos
- Pholidota: pangolin
- Rodentia: rats and squirrels
- Lagomorpha: rabbits
- Cetacea: whales
- Carnivores: tigers and lions
- Proboscidea: elephants
- Sirenia: manatees and seals
- Perissodactyla: rhinoceros
- Artiodactyla: hippopotamus and deer

Bibliography and Recommended Readings

General References

Ontogeny

Battaglia, F.C., Meschia, G. (1986), *An Introduction to Fetal Physiology*. Academic Press, Inc., Orlando, Florida, USA, pages: 257.

Jones, C.T., Nathanielsz, P.W. (1985). *The Physiological Development of the Fetus and Newborn*. Academic Press, Inc., Orlando, Florida, USA, pages: 837.

Moore, K.L. (1975). *Embriología Clínica*. Interamericana. México, D.F. México, pages: 368.

Houillon, Ch. (1977). *Embriología*. Omega, Fourth Edition, Barcelona, Spain, pages: 184.

Phylogeny

Rieutort, M. (1982). *Physiologie animale 1. Les cellules dans l'organisme*. Masson, Paris, France, pages: 256.

Rieutort, M. (1982). *Physiologie animale 2. Les grandes fonctions*. Masson, Paris, France, pages: 281.

Schmidt-Nielsen, K. (1979). *Animal Physiology, Adaptation and Environment*. Cambridge University Press, Second Edition, New York, USA, pages: 560.

Tresguerres, J.A.F. (1992). *Fisiología humana*. Editorial Interamericana, First Edition, Madrid, Spain, pages: 1216.

Guyton, A. (1991). *Textbook of Medical Physiology*. Saunders, Eighth Edition, Philadelphia, USA, pages: 1014.

Mountcastle, V.B. (1980). *Medical Physiology*. The C.V. Mosby Co., St. Louis, USA, pages: 1999.

Ganong, W.F. (1975) *Review of Medical Physiology*. Seventh Edition. Lange Med. Pub. Los Altos, California, USA, pages: 587.

Villee, C.A. (1974). *Biología*. Sixth Edition. Nueva Ed. Interamericana. México, pages: 821.

Megglitsch, P.A. (1972). *Invertebrate Zoology*. Oxford University Press. Second Edition. New York, USA, pages: 834.

Barnes, R.D. (1974). *Zoología de los invertebrados*. Nueva Editoral Interamericana. Third Edition. México, pages: 826.

Weicher, Ch. K., Presch, W. (1975). *Elements of Chordate Anatomy*. McGraw Hill Book Co. Fourth Edition. New York, USA, pages: 526.

Wolfe, S.L. (1980). *Biology of the Cell*. Wadsworth Pub. Co. Second Edition. Belmont California, USA pages: 544.

Introduction – The Historical Points of View

Ontogeny

Houillon, Ch. (1977). *Embriología*. Omega. Fourth Edition. Barcelona, Spain, pages: 184.

Evolution and phylogeny

Mayr, E. (1963). *Evolutionary Biology. en: Animal Species and Evolution.* Harvard University Press: 1-11.

Dobzhansky, T., Ayala, F., Stebbins, G.L., Valentine, J.W. (1977). *Evolution.* W.H. Freeman and Co. San Francisco. USA. Chapter 1: The nature of evolution: 1-19.

The parallel between ontogeny and phylogeny

Gould, S.J. (1977). *Ontogeny and Phylogeny.* Belknap Harvard. U.S.A.

Chapter 1 – Mechanisms of Differentiation in Ontogeny and Phylogeny

Ontogeny

Rutter, W.J. (1980). *Control of Cellular Differentiation: Overwiew.* Ann. N.Y. Acad. Sci.: 263-264.

Loewenstein, W.R. (1980). *Junctional Cell to Cell Communication and Growth Control.* Ann. N.Y. Sci.: 39-455.

Robinson, K.R., McCaig, C. (1980). *Electrical Fields, Calcium Gradients and Cell Growth.* Ann. N.Y. Acad. Sci.:132-138.

Cone, C.D. (1980). *Ionically Mediated Induction of Mitogenesis in CNS Neurons.* Ann. N.Y. Acad. Sci.: 115-131.

Soltoff, S.P., Cantley, L. C. (1988). *Mitogens and Ion Fluxes.* Ann. Rev. Physiol. 50: 207-224.

Van Mierop, L.S.H. (1979). *Morphological Development of the Heart. en: Handbook of Physiology, Sección 2, The Cardiovascular System, Vol. 1.* Berne, R.M., Sperelakis, N., Geiger, S.R. (eds.) Bethesda, Maryland. Am. Physiol. Soc. 1-28.

Phylogeny

Gould, S.J. (1982). *Is a New and General Theory of Evolution Emerging? En: Evolution Now: a Century After Darwin.* Maynard Smith, J. (ed) W.H. Freeman Co. USA, 129-145.

Mayr, E. (1963). *Evolutionary Biology. en: Animal Species and Evolution.* Harvard University Press: 1-11.

Dobzhansky, T., Ayala, F., Stebbins, G.L., Valentine, J.W. (1977). *Evolution.* W.H. Freeman and Co. San Francisco. USA. Chapter 1: The Nature of Evolution: 1-19.

Ayala, F.J. (1978). *The mechanisms of evolution. en: Evolution. A Scientific American Book.* W.H. Freeman and Co. San Francisco. USA: 14-29.

Rennie, J. (1993). *DNA's New Twists.* Sci. Am. 266: 88-96.

Mechanisms producing a parallel between ontogeny and phylogeny

Gould, S.J. (1977). *Ontogeny and Phylogeny.* Belknap Harvard. U.S.A.

Chapter 2 – The Early Stages of Ontogenetic and Phylogenetic Development

The early stages of ontogenetic development in mammalians

Moore, K.L. (1975). *Embriología Clínica.* Interamericana. México, D.F. México, pages: 368.

Houillon, Ch. (1977). *Embriología.* Omega. Fourth Edition. Barcelona, Spain, pages: 184.

The outline of phylogeny

Megglitsch, P.A. (1972). *Invertebrate Zoology*. Oxford University Press. Second Edition. New York, USA, pages: 834.

Weicher, Ch. K., Presch, W. (1975). *Elements of Chordate Anatomy*. McGraw Hill Book Co. Fourth Edition. New York, USA, pages: 526.

Barnes, R.D. (1974). *Zoología de los invertebrados*. Nueva Editoral Interamericana. Third Edition. México, pages: 826.

Chapter 3 – The Ontogeny and Phylogeny of the Nervous System

The ontogeny of the nervous system

Salas, M. (editor) (1991). *Ontogenia Neural, aspectos comparativos y mecanismos de regulación*. Sociedad Mexicana de Ciencias Fisiológicas, Universidad Nacional Autónoma de México. México, pages: 346.

Skoglund, S. (1969). *Special Emphasis on Central Growth and Differentiation with Nervous System*. Ann. Rev. Physiol. 49: 321-334.

Harris, W. A. (1981). *Neural Activity and Development*. Ann. Rev. Physiol. 43: 689-710.

Edelman, G.M. (1986). *Cell Adhesion Molecules in Neural Histogenesis*. Ann. Rev. Physiol. 48: 417-430.

Rutishauser, Jessel (1988). *Cell Adhesion Molecules in Vertebrate Neural Development*. Physiol. Rev. 68(3): 819-856.

Sanes, J.R. (1985). *Roles of Extracellular Matrix in Neural Development*. Ann. Rev. Physiol. 45: 581-600.

Kennedy, H., Dehay, C. (1988). *Le développement du cerveau. en: La recherche en neurobiologie*. Editions du Seuil La Recherche. Paris, France, pages: 318-346.

Cowan, W.M. (1979). *The Development of the Brain*. Sci. Am. 241(3):106-117.

The phylogeny of the nervous system

Hille, B. (1984). *Evolution and Diversity. en: Ionic Channels of Excitable Membranes*. Saunders Associates Inc. Publ. Chapter 16: 371-383.

Sagan, C. (1977). *The Dragons of Eden. Speculations on the Evolution of Human Intelligence*. Ballantine Books, Random House Inc., New York, USA, pages: 271.

Chapter 4 – The Ontogeny and Phylogeny of the Circulation of the Internal Medium

The ontogeny of the cardiovascular system

Sperelakis, N. (1989). *Developmental Changes in Membrane Electrical Properties of the Heart. en: Physiology and Pathophysiology of the Heart*. Sperelakis, N. (ed) second edition. Kluver Academic Press, USA, pages: 595-623.

Rudolph, A.M., Heymann, M.A. (1974). *Fetal and Neonatal Circulation and Respiration*. Ann. Rev. Physiol. 36: 187-207.

Guarner, V. (1994). *Desarrollo de la función cardíaca y su relación con el metabolismo durante el período perinatal*. Arch. Inst. Cardiol. Mex. 64: 73-80.

The phylogeny of the cardiovascular system

Martin A.W. (1974). *Circulation in Invertebrates*. Ann. Rev. Physiol. 36: 171-186.

Chapter 5 – The Ontogeny and Phylogeny of the Digestive Functions and Nutrition

The ontogeny of the digestive system and nutrition

Buddington, R.K., Diamond, J.M. (1.989) *Ontogenetic Development of Intestinal Nutrient Transport.* Ann. Rev. Physiol. 51: 601-620.

Lee, P.C., Lebenthal, E. (1983). *Early Weanling and Precocious Development of Small Intestine in Rats: Genetic, Dietary or Hormonal Control.* Pediatr. Res. 17: 645-650.

The phylogeny of the digestive funtions and nutrition

Dockray, G.J. (1979). *Comparative Biochemistry and Physiology of Gut Hormones.* Ann. Rev. Physiol. 41: 83-95.

Jorgensen, C.B. (1975). *Comparative Physiology of Suspension Feeding.* Ann. Rev. Physiol. 37: 57-79.

Chapter 6 – The Ontogeny and Phylogeny of Respiratory Gas Exchange

The ontogeny of respiration

Strang, (1977). *Growth and Development of the Lung: Fetal and Postnatal.* Ann. Rev. Physiol. 39: 253.

Rigatto, H. (1984). *Control of Ventilation in the Newborn.* Ann. Rev. Physiol. 46: 661-674.

Bourbon, J. et al (1987). *Biochemical Maturation of Fetal Rat Lung. A Comprehensive Study Including Surfactant Determination.* Biol. Neonate 52: 48-60.

Read, D.J.C., Henderson-Smart, D.J. (1984). *Regulation of Breathing in the Newborn During Different Behavioral States.* Ann. Rev. Physiol. 46: 675-685.

Walker, D. W. (1984). *Peripheral and Central Chemoreceptorsin the Fetus and Newborn.* Ann. Rev. Physiol. 46: 687-703.

The phylogeny of respiration

White, F.N. (1978). *Comparative Aspects of Vertebrate Cardiorespiratory Physiology.* Ann. Rev. Physiol. 40: 471-499.

Chapter 7 – The Ontogeny and Phylogeny of Blood and the Immune System

The ontogeny of blood and the immune system

Stites, D.P., Caldwell, J.L. (1978). *Phylogeny and Ontogeny of the Immune Response. en Basic and Clinical Immunology.* Fudenberg, H.H., Stites, D.P., Caldwell, J.L., Wells, J.V. (eds) Lange Med. Pub., USA, pages: 1441-154.

The phylogeny of blood and the immune system

Stites, D.P., Caldwell, J.L. (1978). *Phylogeny and Ontogeny of the Immune Response. en Basic and Clinical Immunology*. Fudenberg, H.H., Stites, D.P., Caldwell, J.L., Wells, J.V. (eds) Lange Med. Pub., USA, pages: 1441-154.

Roitt, I.M., Brastoss, J., Male, D.K., Fontan, F. (1993). *Inmunología. Capítulo 15: Evolución de la inmunidad*. Ediciones Científicas y Técnicas. Editoriales Masson y Salvat. Third Edition. Barcelona-México, pages: 1501-1516.

Chapter 8 – The Ontogeny and Phylogeny of the Hydro-mineral Equilibrium

The ontogeny of the hydro-mineral equilibrium

Robillard, J.E., Nakamura, K.T., Ayres, N.A. (1985). *Control of Fluid and Electrolyte Balance During Fetal Life. en: The Physiological Development of the Fetus and Newborn*. Jones, C.T., Nathanielsz, P.W. (eds) Academic Press, England, pages: 527-532.

The phylogeny of the hydro-mineral equilibrium

Potts, W.T.W. (1968). *Osmotic and Ionic Regulation*. Ann. Rev. Physiol. 30: 73-104.

Shoemaker, V.H., Nagy, K.A.(1977). *Osmoregulation in Amphibians and Reptiles*. Ann. Rev. Physiol. 39: 449.

Truchot, J.P. (1990). *Respiratory and Ionic Regulation in Invertebrates Exposed to Both Water and Air*. Ann. Rev. Physiol. 52: 61-76.

Taylor, C.R. (1974). *El elan y el orice. en Vertebrados: estructura y función*. Selections from Scientific American. H. Blume Ediciones, Madrid, pages. 225-233.

Schmidt-Nielsen, K. (1974). *Las glándulas salinas. en Vertebrados: estructura y función*. Selections from Scientific American. H. Blume Ediciones, Madrid, pages. 235-240.

McClanahan, L.L., Rubial, L., Shoemaker, V.H. (1994) *Frogs and Toads in Desserts*. Sci. Am. 270 (3):64-71.

Chapter 9 – The Ontogeny and Phylogeny of the Funtions of Reproduction

The ontogeny od the reproductive system

Byskov, A.G. (1986). *Differentiation of Mammalian Embryonic Gonad*. Physiol Rev. 66: 71.

Wilson , J.D. (1978). *Sexual Differentiation*. Ann. Rev. Physiol. 40: 279-306.

McLaren, A. (1991). *The Making of Male Mice*. Nature, 351: 98.

The phylogeny of the reproductive system

Peter, R.E., Crim, L.W. (1979). *Reproductive Endocrinology of Fishes*. Ann. Rev. Physiol. 41: 323-336.

Licht (1979). *Reproductive Endocrinology of Reptiles and Amphibians*. Ann. Rev. Physiol. 41: 337-352.

Drews, D. (1994) *Animal Sexuality*. Sci. Am. 270(1): 96-103.

Chapter 10 – The Ontogeny and Phylogeny of the Endocrine System

The ontogeny of the endocrine system

Nathanielsz, P.W. (1976). *Fetal Endocrinology, An Experimental Approach.* North Holland Publ. Co. New York.

Jost, A. (1975). *The Fetal Adrenal Cortex. Handbook of Physiology. Endocrinology VI,* Chapter 8, USA: 107-115.

Dussault, J.H., Ruel, J. (1987). *Thyroid Hormones and Brain Development.* Ann. Rev. Physiol. 49: 321-334.

Jost, A. (1966). *Anterior Pituitary Function in Fetal Life. en: The pituitary Gland.* Harris, G.W., Donovan, B.T. (eds): 299-323.

Jost, A. (1970). *Hypothalamo-hypophysial Relationships in the Fetus. en: The Hypothalamus.* Martini, Motta, Fraschini (eds): 1-11.

The phylogeny of the endocrine system

Nail, H.D. (1982). *The Evolution of Peptide Hormones.* Ann. Rev. Physiol. 44: 615-625.

Greenberg, M.J. (1982). *Invertebrate Neuropeptides: Native and Naturalized.* Ann. Rev. Physiol. 44: 615-624.

Valverde-R, C., Aceves, C., Navarro, L. (1993). *Hormonas a la edida y para toda ocasión.* Science and Development 111: 22-33.

Index

Esta edición consta de 1,000 ejemplares y
se terminó de imprimir el mes de junio
de 1996 en Litográfica Maico, S. A. de
C. V., Paz Montes de Oca 48,
03340 México, D. F.

The idea of a parallel existing between ontogeny and phylogeny came from Aristotle and although it drew enormous prosperity through the end of the 19th century it later witnessed a disastrous fall. However, many researchers have recently taken back this proposal to reevaluate the mechanisms that create the parallel and to analyze the events from the historical and epistemological points of view. There does not currently exist any work where, one by one, the ontogeny and phylogeny of each function of the animal organism is analyzed constituting the aim of the present book.
A large quantity of fascinating and interesting aspects of physiology are included in this work. It analyzes the different physiological solutions that the organisms have found in order to survive in different current terrestrial environments, the place where they evolved and the manner in which their ontogenetic development occurred. Trying to analyze in detail every aspect of physiology in the adult, its evolution and its embryology would be a never ending chore, thus this book only gives a general view of this field. The work attempts to advance with a perfectible investigation, hoping to reach a definitive and final explanation in time. We hope that the critics of students in other professional fields will help us to extend and improve our research.

ISBN 968-6779-13-2

Información Profesional Especializada, S.A. de C.V.
Francisco Márquez 127 Colonia Condesa 06140 México, D.F.