BOLK'S COMPANIONS FOR-THE STUDY OF MEDICINE



EMBRYOLOGY

Early development from a phenomenological point of view

Guus van der Bie MD

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BOLK'S COMPANIONS

Embryology

Early Development from a Phenomenological Point of view

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Guus van der Bie MD

About the author

Guus van der Bie MD (1945) worked from 1967 to 1976 as a lecturer at the Department of Medical Anatomy and Embryology at Utrecht State University in the Netherlands. As a family physician since 1976, he has recognized the importance of phenomenology and Goethean science for understanding the human being in health and illness. Next to his practice he stayed involved in teaching medical students at Utrecht State University and physicians, and therapists. In 1998 he was one of the originators of *Renewal of Medical* *Education*, a project of the Louis Bolk Instituut to produce a complement to the current biomedical scientific approach of the human being.

Since 2002 he is a teacher of Complementary Medicine and Medical Humanities at the Medical School of Utrecht State University and teaches anthroposophic medicine at the University of Witten/Herdecke (Germany). He is a member of the Medical Section of the School of Spiritual Science at the Goetheanum, Dornach, Switzerland.

About the project

The project *Renewal of Medical Education* aims to produce Companions that demonstrate how the insights of current biomedical science can be broadened by using the Goethean phenomenological method. This method innovates current concepts and expands the understanding of biochemical, physiological, psychological, and morphological factors in living organisms and their development in time and space, and in health, illness, and therapy. The project is commissioned by the Kingfisher Foundation, which aspires the development, application, and publication of the Goethean phenomenological research method in the widest sense, to complement and innovate the accepted scientific view and research method.

BOLK'S COMPANIONS FOR THE STUDY OF MEDICINE complement current medical education, specifically disclosing human qualities in the fundamental biomedical sciences of today.

BOLK'S COMPANIONS FOR THE PRACTICE OF MEDICINE contribute to a scientific phenomenological basis for integrative medicine and integral psychiatry.

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Preface

In his book *Lifelines* Steven Rose states: "The challenge to the opponents of biological determinism is that, while we may have been effective in our critique of its reductionist claims, we have failed to offer a coherent alternative framework within which to interpret living processes."

We have the same challenge with regard to morphology and embryology. It is imperative to offer a satisfactory alternative framework. In trying to remedy this problem we have striven for to reach two goals: first, to indicate an 'alternative framework' in morphology, and second, to show that the alternative framework which characterizes dynamic quality in morphological phases opens new possibilities for interpreting morphological processes. We achieved the characterization of the dynamic quality in morphological phases by using a phenomenological approach to morphology, and then interpreting this with the help of Goethean science. We think a new framework will be helpful if it can be shown to refer to functional entities in biology. In this case, many facts and details can be seen in a context and understood as belonging to recognizable phases of development. We chose *the dynamic quality in morphological phases* for this purpose since it allows us to see coherence in the facts. *The dynamic quality in morphological phases* can be shown to refer to functional processes in biology.

This results in new concepts in morphogenesis. These new concepts recapture an understanding of morphogenetic factors in living organisms and their development in time and space. This gives us, for instance, a possibility of understanding the relation consciousness and behavior to the shape of the body.

We hope that this framework will be helpful for medical students, who have to learn and remember many morphological details.

Experience has taught us that an overview of the whole makes remembering the details easier. We present this module in an effort to aid medical students and others to take in the wonderful world of embryology and remember it better in later study and work.

We want to emphasize that this module does not replace the textbook on embryology. The information in the module is compact and presupposes the knowledge contained in regular textbooks.

 \rightarrow Morphogenetics is the study of how form and shape develop

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This module in the series **BOLK'S** COMPANIONS FOR THE PRACTICE OF MEDICINE was written at the Louis Bolk Instituut, Driebergen Holland. It is a result of the stimulating exchange of ideas with my colleagues W. Schad, Chr. van Tellingen, G. Verhaagen, H. Vögler, J. van der Wal and R. Zech. I am most grateful to them for their valuable comments, and I am glad we are not at the end of this exciting journey. The next subject to be studied is organogenesis. I hope our cooperation in studying organogenesis will be equally fruitful.

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Guus van der Bie MD, Driebergen April 2001.

1. Introduction

Early development in human embryology

Embryonic development can be divided into different developmental phases. Like every biological developmental process, embryological development is a process in time and as such the visible stages appear as a continuous process in time. Stages and phases are in fact artificially produced by the observer. Therefore, the observer has to be aware of the criteria he or she uses in differentiating the various phases.

When we look at the developing plant, for instance, it can be seen to grow according to a particular time pattern which is structured by morphological and functional changes. We classify its phases based on these morphological and functional changes.

The term 'phase' is used to define and describe a time period during which a particular process takes place. In plant-life, for instance, we can discern germinating, growing, and flowering as clearly different processes and we use a particular term for each phase. Each process (germinating, growing, and flowering) represents a particular aspect of plant development resulting in particular plant products or plant parts.

However, the differentiation of phases is not just a result of observation, it also has a counterpart in the process of conceptualization in the human mind: i.e. we recognize a group of phenomena as belonging to a particular process. The changes in the described processes determine whether development is at one phase or another, and visible phenomena belonging to certain stages can be seen as belonging to one larger developmental phase. A phase therefore may cover different stages.

Here we shall try to find the *characteristic features of different phases* in embryology by using Goetheanistic phenomenology as a scientific approach: morphological and biological phenomena in different organisms are studied and compared in order to find out what the characteristics of their relationships are, what they have in common and how they are different.

Comparing the development of various organisms makes it possible to discover what can be taken as the same process in different organisms. This enables us to recognize general laws and stages in morphogenesis. This method shows us what determines visible phenomena. When we give processes a particular name, e.g. 'cell differentiation', 'organogenesis' or 'programmed cell death' we should be aware that we are using a superimposed conceptual framework. Every individual cell's life is embedded in processes of a 'higher' level; it 'obeys' the laws specific to what is to be developed as an expression of the superimposed process of the higher level (for instance gastrulation).

It is also important to be aware of the way the Goetheanistic scientist approaches an object. In analytical science, the scientist has the attitude of 'onlooker'. In Goetheanistic science, the scientist works with a participative attitude. He participates consciously in what is going on in morphological processes. This kind of consciousness enables the scientist to recognize movement and gesture working in morphological processes. In contrast to the usual scientific approach of analysis and reduction we may broaden our view in Goetheanistic science, in the sense of taking in the 'whole' of the phenomenon and their context.

Note!

It is important to note that Goetheanistic science finds characteristic morphological differences between minerals, plants, animals and human beings. This is due to the fact that a macroscopic point of view is chosen. In his scientific approach, Goethe was looking for the 'archetypal phenomenon'. This archetypal phenomenon represents the dynamic quality of a specific morphological phase.

When we look from the point of view of molecular biological, it is evident that morphological differences between minerals, plants, animals, and human beings disappear for our consciousness. From a scientific point of view there is no necessity to make a choice between the two points of view. It should be emphasized that it lies in the freedom of the scientist which point of view is chosen. Integration of both points of view is possible within the realm of Goetheanism.

We have taken Langman's *Medical Embryology* as a basic text which exemplifies medical science as it is taught in medical schools today. In that sense our effort should be considered to be an attempt to follow contemporary medical education, showing that a

goetheanistic approach can complement and augment modern scientific approach and study.

It is common nowadays to give a bio-molecular explanation of life processes in morphology. Studying molecular biology, particularly genetics, makes us aware that even genes in their complicated and marvelous structures and functions need an explanation in their own right. Understanding protein metabolism is quite different from understanding *morphogenesis*, and describing the protein metabolism that takes place during morphological development does not mean that the description is an explanation of *how form and shape develop* (morphogenesis).

Morphogenesis is the subject of this publication. The central question that gives this study its particular form is: are we able to understand individual cell differentiation and morphological development in relation to specific superimposed processes? By discriminating different phases of development we are immediately confronted with the coherence of multiple phenomena that are part of one superimposed process, for instance a process such as 'gastrulation' (see 5.2.2).

This scientific approach has many practical implications. Molecular biology gives an explanation of processes in substances; however, this cannot fully explain morphology or consciousness.

The specific laws of life processes and mental capacities can be recognized as differentiating forces in embryological development and morphology. The Goetheanistic scientific approach opens up the possibility of understanding the relation between bodily form, life process, and mental capacity.

2. Gametogenesis

2.1. Morphology

Gametogenesis provides a good example of a dynamic quality in morphogenesis as a superimposed process, as described in the preface. In gametogenesis the process of polarization is the working principle 'behind the actual facts'. In studying this process, you can clearly experience the difference between observing visible facts and stages, and the mental process of thinking about those observations. The concept of polarization remains invisible for the physical eye, but it becomes nonetheless 'visible' with the help of our thought process.

2.1.1. Gametogenesis

Gametogenesis starts with the primordial germ cell. From this stage on, differentiation into the oocyte in the female organism, on the one hand, and the sperm cell in the male organism, on the other, is a process of increasing divergence. We can list a great number of properties of the primordial cells, which in subsequent differentiation develop in opposite directions in oocytes and sperm cells.

For instance when we look at:

	Oocyte	Sperm cell
cell volume	+++	
condensation of DNA		+++
mobility		+++
total number of produced cells	400	Numerous +++
localization in the abdomen	Inside	Outside
temperature needed for differentiation	Warm	Cool

We see immediately that a pronounced polarization takes place.

The process of polarization includes germ cell differentiation in opposite directions.

However, there is at the same time a reciprocal development in germ cell differentiation. We can see this by looking at the relevant cell properties mentioned above: cell structures that become more important, dominant, or clearly expressed in one cell (oocyte) become less important in the other cell (sperm cell), and vice versa. While developing in completely opposite directions, *there is a strong inner relationship between the two processes*, which is expressed by the reciprocal characteristic of the process. The inner relationship within this development can help us understand the process of polarization and the reciprocal attraction between oocyte and sperm cell. All phenomena and characteristics of the polarization of the two gametes can be summarized as follows: the oocyte tends to specialize and unidirectionally differentiate to express the features and qualities of the *cytoplasm* of the normal cell. The spermatocyte, on the other hand, exhibits the qualities and 'behavior' of the *nucleus of the cell*.

2.1.2. Fertilization

Fertilization is a necessary condition for the development of a new human being. The main process that creates the conditions of fertilization is polarization. It will become clear that any polarization can be understood as creating conditions and possibilities for new development. We will learn to understand that processes such as the polar differentiation of embryoblast and trophoblast, epiblast and hypoblast, ectoderm and endoderm in later phases of embryonic development, create new possibilities in development. Thus gametogenesis can be considered as a basic exemplary phenomenon which points to the creation of new possibility: the development of the zygote.

Fertilization takes place the moment both gametes are at the end of their life and development. At fertilization both oocyte and sperm cell each can live only one or two more days and then will die if fertilization does not take place. Therefore they can be considered to be cells on the 'edge of life and death'. The only function they have left is to give away their complete physical substance in fertilization.

This phenomenon again is very instructive. It shows that specialization and the possibility to develop in many directions (multipotentiality) are opposite qualities. Specialization means

2.2. Summary and conclusion

→ Gametogenesis can be taken as an example of a coherent process (phase) of differentiation showing many stages. Germ cell differentiation can be qualified as a process of polarization. In Goethean science, polarization can be taken to be an archetypal phenomenon at the beginning of a new phase in biological development.

3. First week of development

3.1. Morphology

3.1.1. Fertilization

The process of fertilization has several consequences. One is the fact that the number of chromosomes becomes 'normal' (diploid) after the fusion of the haploid gametes. Also the sexual identity of the organism is determined. We will discuss a number of further phenomena of the first week of development and then try to characterize these phenomena as belonging to a first phase.

3.1.2. Cell membrane continuity

During fusion the continuity of the membrane of the oocyte is intact. This is one of the most important phenomena during the fusing of the gametes. It is well known that continuity of the cell membrane is a condition for cellular life. As shown in necrosis and apoptosis, any form of membrane destruction leads to the end of cellular life. During fertilization there is not a single moment of dehiscence in the cell membrane, as shown in figure 3.1. The fusion of the gametes is a threefold process, in sequential order: fusion of the cell membranes, fusion of the cytoplasm of both cells, and fusion of the nucleotic substances. That means there is a complete fusion of substance of both gametes.



Fig. 3.1. Fusion of the two gametes and continuity of the cell membrane (from Langman, 1995)

3.1.3. Zona pellucida

After fertilization, the zona pellucida undergoes a striking change. From the moment of fusion of the gametes onwards, the zona pellucida changes to become an impermeable membrane, separating the zygote physically and physiologically from the environment.

3.1.4. Cell cleavage

As a result of fertilization, cleavage is initiated. From this moment on, the zygote will develop a number of daughter cells called blastomeres. Characteristic for this process is the fact that during cleavage each new cell (blastomere) contains half the volume of cytoplasm of the mother cell. This process will go on until a specific ratio is reached between the cell volume and the volume of the nucleus: the volumetric *ratio between nucleus and the cytoplasm* has gained a value characteristic of the human organism in question. The amount of cytoplasm of the zygote is so large that this does not take place till the zygote reaches the 16-cell stage. This specific ratio is a necessity for the cell to have the bio-activity to continue, including protein synthesis. During the process of cleavage the overall size of the zygote does not change, as shown in figure 3.2.

3.1.5. Compaction

About four days after fertilization, the formed cluster of blastomeres, now called the morula, undergoes the process of *compaction*. In compaction the peripheral cells begin to stick together in much closer contact than before, forming a more dense structure. It is a process comparable to epithelialisation. These peripheral cells will give rise to the trophoblast. The inner cell mass will give rise to the embryo proper, and is therefore called the embryoblast.



Fig. 3.2. Development of the morula and compaction (from Vögler, 1987)

3.1.6. Embryopause

Another impressive phenomenon in the early embryology of certain animals is embryopause. In humans this phenomenon has not been observed.

Embryopause is a situation in which the morula interrupts its development at the stage just before implantation. This stage can exist for a long time in the uterus of a kangaroo or in deer. This is a well-known phenomenon in biology. In either animal, the zygote develops to the stage just before implantation, and then a developmental pause sets in. Before going on to further development or differentiation, implantation is delayed for a longer period of time.

In deer this can occur when mating has taken place in autumn (Deer 1 in fig. 3.3). When fertilization takes place during the spring rutting season, the zygote develops and implantation occurs without any delay (Deer 2 in fig. 3.3). Pregnancy will be completed in the normal time frame. When fertilization has taken place during the autumn rutting-season, the morula is stored in the womb, 'waiting' for the spring rutting-season, and from a specific moment embryonic development goes on to implantation. Pregnancy in either case will be completed and concluded at about the same time.

In the kangaroo, fertilization may occur after mating, even when the kangaroo is already bearing a cub in its pouch. The zygote then interrupts its development just before implantation. From the moment the cub in the pouch leaves the shelter, the zygote starts implanting in the uterine wall. The moment of birth is fixed by that moment (fig. 3.3).



Fig. 3.3. Embryopause

3.1.7. From fertilization to implantation: a special period of time?

In all viviparous animals, the first morphological phase in embryological development starts at fertilization and continues on to implantation taking about one week (4 - 7 days). However, the duration of pregnancy varies for different species and under different circumstances (see above). For instance, in mice pregnancy takes 21 days, in elephants it takes 21 months. Yet this first morphological phase, from fertilization to implantation takes about the same time in either animal: one week. The same applies in deer and kangaroos when a correction is made for embryopause. Therefore, the morula phase has its own time cycle which is not dependent upon that of pregnancy. This is characteristic for this first phase of development.

3.1.8. The development of twins

We know from identical twin development that monozygotic twins can develop from spontaneous cleavage of the morula. This is due to the fact that morula cells are multipotent, meaning that each morula cell can grow into a complete and healthy organism. In fact, the process of cloning is done at this stage and can take place only at this stage as soon after this the morula cells lose their omnipotence by differentiating. Therefore, the *morula* as a whole, or even a single morula cell, can be taken to have the *capacity* for determining the *physical* development of an individual organism.

When the morula enters the uterine cavity, fluid appears in the cell mass. During this process the outer cell mass partly loses contact with the inner cell mass, forming a single cavity. Thus, the blastula is formed and implantation can occur. In the meantime, the zona pellucida, which was until now the peripheral physical surrounding of the zygote, disappears.

The blastula stage is the last stage in which the possibility for monozygotic (identical) twin development exists. As shown in fig 3.4. nearly 99% of twins develop before or at this stage of development. When twin formation starts later, there is a very high risk of pathological and often fatal development. It is evident that the phase during which the basis for autonomous biological development can occur, is over.



Fig 3.4. Monozygotic (identical) twin development at different stages (from Langman 1973)

3.2. Summary and conclusion

3.2.1. Morphology

We will first sum up the above-mentioned phenomena from a morphological (form and shape) point of view.

The main developmental issues of the 'first week' are:

Fertilization

Fertilization causes fusion of the cytoplasm and nuclei of both gametes; it results in a diploid genetic status, while the cell membrane stays intact.

Development of the morula

Morula cells are multipotent; the zona pellucida becomes impermeable after fertilization, giving the embryo a firm boundary. While the oocyte functions as an organism open to the environment, the zygote is to be taken as a self contained organism.

In some animals embryopause can occur. Monozygotic twin formation can take place.

3.2.2. Goethean aspects

We can look at these phenomena also from the Goethean point of view, which allows a further characterization of the first week of development.

The physical condition

The phenomena of the first week are manifestations of a special phase. This phase results in the creation of the physical circumstance for further development. Its dynamic tendency is centripetal (see chapter 8.2.1)

The morula (and the young blastula) can be considered to be 'living' organisms; yet it is striking that this 'life' does not have a biological clock or evident growth or intense metabolism like most biological processes. There is only a short period in early development during which it is possible to preserve the embryo by freezing. This is at the morula stage. When we freeze the embryo, *we preserve mainly the physical condition for development*, a status that can 'wait' for implantation. In doing so we create an artificial embryopause.

Relation to time and metabolism

The 'first week' has the characteristic of the seed of the plant. Seeds can be stored for a long time, keeping their germinal force over many years. There is no imperative biological clock or active metabolism, as we know them in biologically active organisms.

Is the seed alive? It is a special way of being alive: *the physical material phase of life, living 'outside of time' and having no active metabolism.* The situation of living outside of time and having no active metabolism is well known in inorganic substances. It is the 'physical way of being alive'.

→ The first week as an embryonic phase results in the physical condition for autonomous biological development.

4. Second week of development

4.1. Morphology

First we will describe the different phenomena of the second week, then we will summarize and characterize them again, and find the characteristics of this phase.

4.1.1. Growth

From the moment the blastula comes into contact with the uterine mucosa, the blastocyst grows rapidly. This is a new impulse. It is a real leap in development. Growth, which now happens in the sense of increase in volume and cell mass, is obvious. This growth is not the same in different parts of the blastocyst. In this phase of development growth primarily takes place at the periphery of the blastocyst, as can be seen in figure 4.1.

4.1.2. Differentiation

The trophoblast develops rapidly in a centrifugal direction. At the same time it will undergo histological differentiation into two layers: the cytotrophoblast, consisting of well-differentiated cells, and the syncytiotrophoblast, in which individual cell structure is lost.

The embryoblast also differentiates into two layers: epiblast and hypoblast.



Fig. 4.1. Development of the blastocyst from day 7 to day 15 (from Blechschmidt 1968)

4.1.3. Metabolism

Metabolic conditions necessarily change when an organism starts to differentiate and grow. An active metabolic process is needed.

Nutrition (blood) and secretion (secretory products) are important signs of an increased metabolism. In the syncytiotrophoblast, vacuoles fuse to form lacunae. Cells of the syncytiotrophoblast cause erosion to the maternal blood vessels. Cells in the lacunae will, from about the twelfth day, come into contact with maternal blood. *Blood circulation* can be seen as a phenomenon belonging to the form of increased metabolism that the blastocyst needs.

Production of HCG by trophoblast cells prevents degeneration of the corpus luteum. This means that the embryo is not only active on a morphological level but also on a *physiological level*. The production of HCG is the secretion process that enables the blastocyst to interact physiologically with the maternal organism, thereby tremendously enlarging its 'biological environment'. This process has its morphological counterpart in the peripheral expansion of the trophoblast. Both processes show an invasive tendency. Giving up its own boundaries, morphologically and physiologically, the embryo comes into contact with a wider periphery.

4.1.4. Bilaminar germ disc

The differentiation of the embryoblast in the second week results in the formation of the bilaminar germ disc, the next developmental stage of the primitive embryonic body. Because of the round shape of amnion and primitive yolk sac, their contact surface constitutes a circular-shaped bilaminar disc. This means that there is *radial symmetry in the embryonic disc*.

When we look at a 12-day-old blastocyst we can also find this radial symmetry in the total 'body form'. The only morphological differentiation of the germ disc and of the blastocyst as a whole is the coming into existence of a new *polarization*. The former polarizes to become epiblast and hypoblast. The latter polarizes into an embryonic pole (where the germ disc is situated) and an abembryonic pole (figure 4.1B).

4.2. Summary and conclusions

4.2.1. Morphology

We will first summarize and characterize the morphological phenomena again.

Growth, cell differentiation, and an increased, blood-dependent metabolism are taken as phenomena of vital activity. The blastocyst in this phase of development is an organism capable of self-regulation. This is a property of all typical biological processes. From the moment of implantation onwards, the *'biological clock'* regulates the vital processes of the blastocyst. This indicates that the blastocyst has its own *vital organization*.

The striving to become more and more peripheral is illustrative of a tendency to be limitless. This tendency is opposite to the one seen in the first week of development. Therefore we conclude that the developmental impulse of the first week is morphodynamically completely different from the second week's impulse. Morphodynamics of the first week are therefore not continuous with those of the second week.

4.2.2. Goethean aspects

Looking at the development of the first week, we compared the morula with the seed of a plant. The second week shows a different pattern that we can compare with the phase of a *plant in a germinating and growing phase*. Growth, cell differentiation, metabolism, and a specific pattern in time (biological clock) become manifest. This phase of plant life interacts intensively with the environment and has a tendency to be limitless.

> → When we state that embryonic development can be divided into different phases, each having a specific characteristic, the second week shows morphological and physiological features of a germinating and growing plant. Thus, the physical substance of the first week comes 'to life' in the same way plants are alive.

5. The third week of development

5.1. Morphology

5.1.1. Development of axial symmetry in the germ disc

During the last days of the second week the connecting stalk 'migrates'. This 'migration' takes place during the enormous growth and differentiation of the germ disc that characterizes the third week of development. The position of amnion and definitive yolk sac,, including the germ disc, changes rapidly in relation to the mesoderm lining the inner wall of the chorion. By the end of the third week the connecting stalk is a mesodermal bridge between chorion and germ disc. It is attached to the embryoblast where amnion and definitive yolk sac come together. In later stages it will emerge as the future caudal region of the embryonic body.

This process puts an end to the radial symmetry of the germ disc. The germ disc becomes elongated at the future caudal end. Through this development there will be only *one axial line in the embryo* from now on, making the embryonic body a *bilaterally symmetrical structure* (fig. 5.1a, 5.1b), with the form of a leaf. The left and right sides of the embryonic body are fixed from this point on.

5.1.2. Primitive streak and mesoderm

The primitive streak develops in the dorso-caudal part of the epiblast in the mid-axial region (fig. 5.1c, 16th day). From now on the formation of the mesoderm and the notochord will occur with the invagination of epiblast cells through the primitive streak and primitive pit.

Results of these new developments are the trilaminar germ disc, a central axis, and bilateral symmetry of the embryo.



Fig. 5.1. Dorsal view of morphological changes in the germ disc in the third week of development (day 16 – day 19) (from Langman 1973)

5.1.3. The cylindrical body form, the folding processes

In the 17 day old embryo we can distinguish three directions: a dorso-ventral direction (epiblast-hypoblast), and, after development of the axial structures, a caudo-cranial direction, and a left and right side.

The germ disc now starts folding around a transversal axis in a cephalo-caudal direction (fig. 5.2) and around a longitudinal axis in a ventro-lateral direction (fig. 5.3). An enormous expansion in all directions of the amnion takes place at the same time. During this process the embryonic body will gradually become a separate structure freely floating in the amniotic fluid. The last connection with the environment will be the umbilical cord, which develops from the connecting stalk. The former 'open body form' will be changed into a cylinder-like 'closed bodily form' (fig. 5.2).



Fig. 5.2. Cephalo-caudal folding process (from Langman 1973)



Fig 5.3. Lateral folding leading to a cylindrical body form: view from cranial direction (from Langman 1973)

In figures 5.2 and 5.3 only the morphological changes resulting from the folding processes are shown. It is also important to note that simultaneously the total body volume increases.

5.1.4. Differentiation of the internal organs

The first organ to develop is the heart. Angiogenic cell clusters appear in the late presomite embryo on day 17 or 18. The most cranial part of the intraembryonic mesoderm gives rise to these cell clusters that will form both blood cells and vascular cells. *The beginning of heart development initiates the development of all other internal organs.* Liver, kidney, gut, and many other organs start their development immediately after the appearance of the heart. The development of the internal organs starts a new phase in embryonic life. In the third week the embryo again makes a tremendous leap.

The most dynamic region of development is once more at the very center of the embryo: the germ disc. During the previous phase (second week) development was directed towards the periphery. But building internal organs means changing to a centripetal tendency again (see chapter 8.2.3), as in the first week!

Organ	First day of development	
Heart	17	
Central nervous system	18	
Liver / Gall bladder	18	
Kidney	22	
Somites	20-30	
Lungs	25	
Gonads (indifferent)	23	
Thyroid gland	33	
Pancreas	30	

5.2. Summary and conclusions

5.2.1. Morphology

The body of a 17-day embryo has a *median axial structure* (primitive streak and notochordal cells) and is involved in the process of *gastrulation*, i.e. forming an inner cavity, an inner space. Both are highly specific processes of animal embryological development. The change from radial symmetry to *bilateral symmetry* and the differentiation of *mesoderm* support this interpretation. Mesoderm is tissue that gives rise to muscles, bones, tendons, and cartilage. These tissues are all precursors for structures, which are in some way connected with the ability of the organism to move.

Morphologically, an 'inner world' develops between ectoderm and endoderm.

5.2.2. Goethean aspects

The most important differences between plant and animal organisms are the formation of an *internal body cavity, the differentiation of internal organs, and the capacity to move freely.* The word 'gastrula' means little stomach. Therefore the word gastrulation is very meaningful. It makes clear that the phases of forming the body cavity and of forming the internal organs are due to the same underlying dynamic process. In the animal world, gastrulation is a universal phase of development. Figure 5.4 shows this phase for different animals and the human being. They have their own developmental speed and form but they have two things in common: gastrulation and differentiation of an internal organ system. Animals which have developed a digestive system ('stomach') digest external substances, build up 'internal organs', and change the environment by excreting metabolic products: an 'inner' world develops and interacts with an 'outer' world. Digestion can be taken as the archetypal phenomenon of creating a relation of an 'inner' world to an 'outer' world.



Fig. 5.4. The gastrula form as an archetypal phenomenon and the beginning of unfolding (from Poppelbaum 1933)

Gastrulation can be seen as *the* archetypal phenomenon of animal morphology (see 6.2.2). In Goethean science, the archetypal phenomenon is analogous to the axiom in mathematics. It is remarkable that organisms with a very different evolutionary history and different genetic structures can develop the same characteristic macroscopic stages and phases.

A second aspect of this phase is the development of a nervous system and a movement system in animal organisms. Animals develop sense organs, a nervous system and muscles, which all enable them to 'communicate' on a more or less conscious level with their environment. Perception, awareness, and reaction are components of the interaction of the individual organism with its environment. This interaction is comparable with the substantial interaction of the digestive system with the environment. Animal life and behavior are highly determined by the specific form of the body and animal instinct. For that reason, the gastrula form can be taken as an emanation of processes according to determinism.

From a phenomenological point of view, the external form induced by the *folding process* can be understood as a *'gastrulation of the whole body's form'*.

Folding and gastrulation of the body can be understood as a manifestation of 'animalization' of the body. The outer world enters the organism by ingestion or perception, will be integrated by digestion or assimilation, and the organism interacts with the outer world by excretion or reaction.

→ This phase of the developmental process can be described as animalization of the body.
6. Embryonic period

6.1. Morphology

The emergence of the external form of the body

6.1.1. Folding process

The start of cephalo-caudal and the lateral folding mark the end of the third week. Over the following two weeks segmentation and somite formation occurs. The embryonic body becomes maximally curved over the primitive umbilical cord, as shown in figure 6.1 A. For most mammals and many other animal organisms, this external body shape exists more or less as a final morphological stage of the body. They will never reach the 'upright' body form characteristic that human beings have. Also monkeys and apes, considered closest to humans, show remnants of the cephalo-caudal folding in their external bodily form and vertebral column. Although primates can for a few moments walk and stand upright, they are not able to develop the upright posture of the human organism. The reasons for this inability to maintain an upright posture will be discussed.

6.1.2. Process of unfolding

From the 4th and 5th week of human embryological development onward, the folding process of the third week is partly unfolded to reach the typical human external bodily form: upright posture. Figure 6.1B shows the effect of the unfolding on the external form of the body. Unfolding creates a morphological movement opposite to flexion. This is superimposed on the folded bodily form of the early embryonic period.

Animals considered to be close to human, being such as apes and primates, have an unfolding process too. There are important differences between the unfolding process in apes and primates and the human being, as is shown in figure 6.3. In apes and monkeys, unfolding occurs in the brain, skull and pelvic region and in the pelvic organs. Therefore the vertebral column never reaches a completely upright position. In humans, however, unfolding does not occur in the region of the head and the pelvic region. In humans, unfolding is important in the development of the cervical, thoracic and lumbar part of the vertebral column.

This means that in apes and monkeys the unfolding process is polarly opposite compared to man: unfolding is prominent in the skull and pelvic region, and does not persist in the vertebral column. In humans unfolding is prominent in the vertebral column and inhibited at the level of the pelvic region (fig. 6.2) and skull (fig. 6.3).

Only human beings have a stable upright posture. The perfect rectangular relationship of the frontal, sagittal and horizontal planes in the human body is due to the persistence of the unfolding process of the vertebral column.

 \rightarrow From the fourth week on the embryonic body becomes specific human.



Fig. 6.1. Coming into appearance of the external bodily form

Figure 6.1. shows the development of the external body form, adjusted for growth.



Fig. 6.2. The human body: the unfolding of the vertebral column is completed (from Verhulst, 1999)



Fig. 6.3. Inhibition of unfolding in humans: the skull (from Verhulst , 1999)

6.2. Summary and conclusions

6.2.1. Morphological considerations

When we look at the development of the external bodily form of the germ disc, two main processes, starting at the end of the third week (18th day), can be recognized: a *folding* process, followed by an *unfolding* process. Many details of topographic anatomy can be understood when we take these two processes into account, especially when we look at the skull and pelvic region, on the one hand, and the vertebral column, the trunk and the internal organs, on the other.

6.2.2. Goetheanistic aspects

Folding and gastrulation were recognized as typical characteristics of 'animalisation' of the body (see 5.2.2).

The unfolding processes of the trunk induce the uprightness as shown in figures 6.1 and 6.2. In the human being, the upright form is realized in its completion by *unfolding*. Characteristic for this phenomenon is that as a result the following joints are situated in the same frontal plane: atlanto occipital joint, shoulder joint, hip joint, knee joint and ankle joint.

Comparative anatomy shows that the process of unfolding the processes of limb development and the development of the human brain are related to one another.

Unfolding results in upright posture, limb development in the characteristic human limbs, i.e. the basic (not instrumental) architecture of limbs and human brain development results in an unequalled quantity and quality of brain tissue. Each of these phenomena can be taken as highly specific and unique for human development. Only the human being is able to maintain these morphological features lifelong.

Parallel to this morphological differentiation, determinism looses hold of human behavior, as will be discussed in chapter 7.5.

→ The upright bodily form can be understood as a manifestation of the characteristic human capacity to be free of instinctual behavior.

7. Characterizing four processes of development

Dynamic qualities in different embryological phases

7.1. introduction

In our Introduction we stated: "we have striven for two goals: first, to indicate an 'alternative framework' in morphology, and second, to show that the selected alternative framework which characterizes dynamic quality in morphological phases opens new possibilities for interpreting morphological processes." In this chapter these dynamic qualities will be described more in detail. Here we shall try to make clear that a dynamic point of view opens a possibility to understand many facts in embryonic development as belonging to one dynamic process. These dynamic processes work during a specific period of time. Within this specific period, the embryo realizes a special phase of its development.

Early development in human embryology shows four characteristic phases, which start successively at about the beginning of the first, second, third, and fourth week of development (see Ch. 3, 4, 5, 6). Each phase is a result of specialized morphological and physiological processes.

Morphological development as described in the chapters 3, 4, 5 and 6 will be discussed again here this time from a Goethean point of view.

The phenomenologist Louis Bolk, advised the use of the 'macroscope'. In saying that, he pointed out that a coherent understanding of biological facts needs more than just a microscope. A microscope allows us to discover many exciting details. An inherent insufficiency of this method is that the coherence of facts and their relation to each other does not become visible. Louis Bolk's macroscope is the better instrument to find this coherence and the interrelations. The macroscope is, of course, our thinking process. One of the techniques in using the macroscope is the comparative method. Comparing different kingdoms in nature and the respective behavior and laws to which the individuals in different kingdoms are subjected, gives the possibility to reach a coherent overview.

7.2. The physical state of individual development

7.2.1. Physical substance in biology

Every living organism has a physical identity. The smallest mono-cellular organism and the most complicated multi-cellular organism each has its own physical boundaries and its own physical substance. Within the physical world, an organism forms a kind of enclave that contains its own substance. Physiological processes influence these substances, their concentrations and their composition, and determine the processes in which the substances will be involved. When physical substance is taken out of the organism, it is part of the world again and obeys the physical laws of inorganic nature. These laws will not make this substance into a new organism. That means that this substance 'returns to' the phase of being merely dead inorganic substance. The laws of inorganic nature are different from the laws of the organism. For this reason, substance appears in a different context in the surrounding inorganic world to that of the organic world.

It is important to make a difference between the physical state and the physical space. Physical substance is always a condition and a necessity for the physical state of being (see 3.1.2). Physical substance is, of course, an object in space. That does not mean, however, that as an object in space it has an orientation in space. A piece of stone has no front or back, no left or right side. Even a nice piece of quartz does not have an orientation in space, it has no above or below. We can give it any possible orientation in space.

7.2.2. Surface and boundary

Any object in space has a surface or boundary. Physical substance is contained within this surface or boundary.

During the first week of development, the cleavage divisions make many surfaces. In that first phase, the zona pellucida acts as a firm boundary for the zygote. After the process of compaction, the zygote has a new possibility to form a firm external boundary. Having 'a skin' belongs to being alive, and every organism will try to keep its boundaries intact during its lifetime. Within these boundaries organic laws are at work to form the organism.

An organic boundary has many biological functions and *plays an active role* within the physiology of the organism.

A piece of quartz has a surface that *does not act* as a boundary separating the realm of organic laws from the realm of physical and mathematical laws. Crystal surfaces are physiologically inert.

→ We may conclude that the physical state of development can be characterized as physical substances that will be organized to fit into the development of an organism, and that the physical state tends to have surfaces and boundaries.

7.3. Physiological processes of individualized life and metamorphosis

Physiological processes in living organisms proceed according to a 'biological clock' and are subject to metamorphosis.

7.3.1. A structure in time

The 'biological clock' is a universal phenomenon of the physiology in living organisms. It can be found by investigating the *changes* in quantity and quality of the physical substance of an organism. It will be seen that these changes show a specific pattern in time. This means that any organism shows fluctuations in the composition of the substances within its boundaries in time.

These fluctuations are highly specific for each organism, and are mainly induced by the sun. The sun sets the organic rhythms, therefore the sun is called the 'time setter' (in German: Zeitgeber) in chronobiology. Each organism has its own relation to the sun cycle. I.e. that there is a characteristic relation of living organisms to the cycle of day and night. The physical composition of an organism is very specific for the day- or the night-situation. Photophosphorilation and photosynthesis in plants, and circadian rhythms in humans and animals are examples of how time regulates the physical composition and processes of organisms.

Organisms have the possibility to ingest substance one moment and excrete it the next. For this, a fluid condition, in the form of a watery solution, is necessary. Ingested and excreted substances can be seen to be 'floating in the organism'. This floating substance circulates through the organism, conforming to the physiological laws and the 'time pattern' of the organism, or it can circulate in nature, obeying natural laws.

7.3.2. Metamorphosis

A second phenomenon in the realm of life is 'metamorphosis'. Metamorphosis is the development of different bodily forms of an organism during life. Not only the physical substance changes in an ongoing process, even the *form of the body* changes. Embryology is the science par excellence to study changes in the form of the body: *metamorphosis*. The human body undergoes formative change every day. After the embryological period, during which time metamorphosis is impressive, the changing of the bodily form slows down, but it never stops, not even for one day.

→ Organic vital processes are subject to a specific time structure and a morphological development (metamorphosis); this characterizes life processes.

7.4. Life processes and consciousness

7.4.1. Consciousness, physiology, and reflexes

The state of consciousness can influence metabolism. Psychological events can change the physiology of metabolism in a split second. Fear, anger, and happiness are well known for their physiological effects. They each represent a different state of consciousness as well as a psychological experience. Acceleration of the heartbeat, sweating, trembling and many other physiological events occur, induced by psychological events which go hand in hand with heightening or lowering of consciousness.

The immunological status of the body is also highly influenced by feelings of discomfort

or of well-being. The first diminishes the immunological status, the latter enhances it. These and other phenomena demonstrate a close relation between psychological events and physiological response.

All organisms with a certain level of conscious awareness have contractile (muscle) elements and a nervous system. That is the basis of any reflex cycle: perception leading to a reaction. We can destroy this cycle by destroying either the nerves or the contractile part of the cycle.

It is important to emphasize that there is a difference between plants and animals reacting to stimuli. Plants react slowly and do not have contractile elements or nervous tissue. Much of their reaction can be understood as 'growing movement'. It is not 'reactive motion' evoked by the impact of the perception in the way a reflex takes place in animal life. Plants react mainly with biochemical and humoral processes, while neural reactions are characteristic of animal life.

Plant life can be described in terms of biochemistry and morphology only. It is, however, not sufficient to describe animal life in this way. In animals psycho-neuro-pharmacology plays an added role in biochemistry.

7.4.2. Psycho-neuro-pharmacology

Animals are the only suitable test objects when drugs such as tranquilizers or psychostimulants are tested. The testing requires the existence of an independent consciousness and psycho-neuro-pharmacology in the test object. Plants are useless for testing tranquilizer effect.

Psycho-neuro-pharmacology depends on highly specialized organs. Brain and nervous tissue are not the only necessary organs. Thyroid gland, parathyroid glands, kidneys, liver, pancreas, gonads, adrenals and pituarity gland are also organs necessary for conscious life, perception, and movement. They form the basis for psychopharmacological processes. The development of mesoderm and the beginning development of nervous tissue, internal organs, the muscle system and sense organs (chapter 5) characterize the end of the third week of development. Gastrulation was described as the archetypal phenomenon of 'animalization' of the organism. When we take into account the foregoing, concerning

psycho-neuro-pharmacology, the characteristic of the third phase of development is that it is a specific 'animalistic' phase of development.

7.4.3. A relation between the inner and outer world

Conscious awareness creates an 'inner world' for the organism. Perception penetrates into this inner world from outside. Behavior (reactive impulse) takes the opposite route: it starts in the inner world and results in an activity in the outer world. That process can be described in terms of biochemistry, physiology, and neuromuscular events. Conscious experience, however, can only be described as a psychological phenomenon.

→ The existence of conscious experience in addition to physiological processes and the possibility to influence physiology by means of psychological events is characteristic for animalization.

7.5. Consciousness, behavior and determinism

Animal organisms are highly specialized. Specialization takes place both on a morphological and a functional level, and these levels are linked together. The result of specializing in this way is twofold. On the one hand, animals have unique and specialized skills for perception and reaction; on the other hand, the loss of developmental possibilities is evident. Animals are unequalled in their specific skills, and at the same time condemned to only one way of living. A high level of specialization of an organism goes together with loss of the possibility to use the body for multiple functions. This type of specialization we would like to characterize as instrumental specialization. In instrumental specialization mainly the sense organs, the trunk and the limbs develop in a specific way.

Perception and reaction are strongly determined by morphology and physiology. From the moment we know how animals behave in the context of their instinct, their behavior is highly predictable. Instinct can be characterized as 'determinism of perception and reaction'. The human body is not a tool for specialized instrumental functions. Sense organs, jaws, teeth, hands and feet are not fit for just a few functions, like smelling, chewing, grasping, or running. Human behavior is not necessarily predictable. It is exactly the unpredictable that makes human beings special.

Human creativity is most remarkable. Characteristic of this creativity is the freedom to act. Human beings 'can do whatever they want'. Animals 'must do what they can do'. Human beings can 'learn to observe what they want to observe', animals 'must observe what they are fit for'.

In looking at human morphology, Louis Bolk came to the conclusion that the human body shows the unique tendency to avoid instrumental specialization. The possibility for further and ongoing development can be likened to the embryological state. Embryos have the greatest possibilities of development and specialization.

According to Bolk, human morphology shows clearly that the possibility for ongoing development, even into adulthood, is inherent in the shape of the human body.

That means that the human body has a form which corresponds to early phases of development. Early stages of animal limbs do have five digits. In the course of animal development one or more segments can become rudimentary. In many beasts of prey (e.g. the lion) four digits develop and specialize into claws. In onehoofed animals (e.g. the horse) only one digit develops completely and specializes to become a hoof; the other digits are rudimentary (fig. 7.1).

Human physiology and psychology make clear that the aspect of 'not being specialized' is not only a bodily morphological issue. Human physiology and psychology show a great variety and a striking lack of determinism.

Yet it cannot be denied that humans have a high degree of specialization.

Evolution can be divided into a natural and a cultural aspect. On the cultural level, evolution of humans is in full swing.

The impetus for natural evolution was metamorphosis on a biological level. In cultural evolution the possibility of metamorphosis is also the basis for development. It is striking

to see that in the realms of knowledge and social life metamorphosis is as vital for development as it has been in natural development.

Humans have 'internalized' the epicenter of metamorphosis as a part of their organization.

→ Psychological and mental ability characterizes the human being's specialization.

This ability creates a 'multipotent organism' for which the highly specialized organisms of animals do not fit. Therefore, the biological status of humans indicates that there is a possibility to be free of determinism. Freedom, however, can be realized only in the inner life, where self-awareness guides metamorphosis.

→ Only humans have a lifelong possibility for ongoing development; only humans can overcome the force of determinism and enter the realm of freedom.



Fig. 7.1. Limb development in A: Human B: the Lion C: the Horse (from Verhulst, 1999)

8. Four qualities in early development: morphodynamics

8.1. General aspects

From a *morpho-physiological point of view*, early human development can be divided into different phases. It is important to emphasize that a new developmental impulse affects the complete morphological and physiological results of metamorphosis of previous phases. This means that such an impulse marks the starting point for a new developmental quality. From then, on this new quality works throughout the whole organism. When the biological clock starts working, the whole organism is taken into a time process. When the folding processes start, the whole organism is involved, and the same happens when unfolding takes place. Morphological development often shows opposing dynamics in different phases. Observation of the different phases clarifies the different dynamic processes.

8.2. Relation between center and periphery

8.2.1. Morphodynamics in the first phase

When the zygote develops into a morula, the morphodynamic process is cleavage division. This process mostly has a centripetal direction. Development is oriented towards its own center, and during this phase the blastomeres increasingly stick together.



Fig. 8.1. Morphodynamics in the first phase

8.2.2. Morphodynamics in the second phase

After nidation a strong centrifugal dynamic can be seen in the development of the trophoblast.

Development of the second week, therefore, is oriented towards the periphery.



Fig. 8.2. Morphodynamics in the second phase

8.2.3. Morphodynamics in the third phase

If trophoblast formation does not come to an end, development will become pathological. This pathological development results in a hydatiform mole.

When the trilaminar germ disc is formed, development changes direction again to become a centripetal process. Morphological changes are focused in the germ disc. Invagination and formation of the mesoderm are remarkable for their central position in the body of the embryo.



Fig. 8.3. Morphodynamics in the third phase

8.2.4. Morphodynamics in the fourth phase

The folding processes are neither merely centripetal nor centrifugal. The formation of the body cavity involves the shaping of a hollow form. This process can be characterized as follows:



Fig. 8.4 A Morphodynamics in the fouth phase: folding

The unfolding process has the opposite direction:



Fig. 8.4 B Morphodynamics in the fouth phase: unfolding

9.1. Phases of development

In order to find a new framework within which to interpret living processe in the preface we started our aim: 'we chose the dynamic quality in morphological phases for this purpose'. We emphasized that: 'the dynamic quality in morphological phases can be shown to refer to functional processes in biology', subsequently we demonstrated that these functional processes give rise to the shape of the body, specific possibilities for behavior and for the development of consciousness.

In this synopsis figure 9.1 show in a scheme the different aspects of the four phases in early human development. It should be emphasized that each new phase embodies a metamorphosis of the foregoing one, and is the beginning of an ongoing process throughout the development of the organism. Development is not a summary of different stages. When a new phase starts the whole embryo enters a new morphodynamic process. It is important to be aware that the fourth phase goes on till the moment of birth.



Fig. 9.1. Schematic representation of chapters 6 and 7: turning points in development and the processes involved and the different phases of development.

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How these questions are answered depends on the scientific method we use. In this publication two methods are used: the current scientific method to learn about anatomical facts and the phenomenological method to understand the meaning of these facts.

Human morphology can then be understood as an expression of the unique and characteristic qualities of the human being.

This results in new possibilities for understanding the relation between consciousness, psychology, behavior, and morphological aspects of the body. Can physiology give more insight into the living human organism than the mere facts reveal at first? Is the level of activity the same for all organs? Are the vital qualities at work in organs unique for organisms and limited to biological activity? Can we find a scientific basis to research the coherence between organ systems?

By enhancing the current scientific method with phenomenological points of view we can find meaning in the facts and understand them as an expression of life itself. The phenomenological method makes the relation between organs visible and comprehensible. It approaches scientific facts from the point of view of their coherence and can give totally new insights this way. What emerges is a grasp of the interrelations between biological processes, consciousness, and nature.



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The phenomenological method of systems biology makes it possible to examine physiological and pathological processes in terms of the processes themselves. This results in a characterization of the various phases of the wound healing process. Out of this, new insights into the origin of health and disease emerged that also offer possible leads for medical practice.



Respiratory System Disorders and Therapy From a New, Dynamic Viewpoint

Christa van Tellingen MD Guus van der Bie MD (eds.) Publicationnumber GVO 08

In this Companion, the experience of three of our own patients with asthma and pneumonia is used as backdrop for our study of airway disorders. Nearly all of us have had some experience with respiratory disease, given that colds, flus, sinusitis, and bronchitis are so common. Most physicians and therapists know people with asthma and pneumonia from own experience and will readily recognize the descriptions we provide.

The experience with these patients leads us through a study of airway disease which eventually opens up to a wider view with new insights and innovative avenues of treatment for respiratory disorders in general.

Our research has alerted us to the part rhythm plays in the healthy respiratory tract and in the treatment of its disease. Rhythm, consequently, is the subject of the final paragraphs of this Companion.



Depressive Disorders An Integral Psychiatric Approach

Marko van Gerven MD Christa van Tellingen MD Publicationnumber GVO 09

The treatment of depressive disorders is increasingly under scrutiny. We classified the risk factors of depressive disorders according to the scientific method applied in systems biology and phenomenology. The ordering in four biological levels that resulted from this, helps clarify the causes of the disorder. Together with the developmental history, it can lead to an individualized treatment of the patient, tailored to his or her specific situation. The treatment aims at restoring the deficient forces of selfhealing.

This Companion presents a working model based on this methodological approach, as well as a variety of case histories to illustrate how applying this model can aid diagnosis and treatment in practice. Tables are added ordering well-researched regular and integral treatment methods according to the four biological levels.

Embryology

Can we give a scientific basis to our feeling that humans have unique human features? Are the human mind and the human organism 'nothing but' another variation of animal life? Can we find answers for these questions that satisfy both head and heart? How these questions are answered depends on the scientific method we use. In this publication two methods are used: the current scientific method to learn about biological facts and the phenomenological method to understand more about the meaning of these facts.

Early embryological development can teach us about the unique and characteristic qualities of the human being.

The result is, for example, a possibility to understand the relation between consciousness, psychology, and behavior and the shape of the body.

LOUIS BOLK