GENERAL PHYSIOLOGY

Osmo Hänninen
Department of Physiology, University of Kuopio, Finland

Keywords: Behaviorome, functional reserves, normal values, organ systems, physionome, proteomics, variability

Contents

Summary

Physiology studies the wholeness of functions of the healthy organisms. The functions of all the components contribute to health. Whatever is the stimulus, it causes a response. For instance the electric signals generated in the heart spread all over the body. Also other organs send electric signals, although the signals generated by the sensory organs and central nervous system have more definite actions. Eating comprehensively activates the body and contributes to functions of every cell. It is becoming increasingly well understood that the body functions as a whole, including the mind. The Chinese medical tradition has understood this for thousands of years. The harmony of the body has also been considered important in the old Indian medical knowledge. Developments of modern methods, especially genomic, proteomic and biophysical methods, as well computing and data storage, have increased the possibilities of following body functions in depth. Biophysical methods have facilitated learning about human pathophysiology, e.g. from heart rate and pulsations of arteries, with accuracy that was never previously possible. From bits of western data we are able to understand the old masters of the ancient past, and the East and West can find each other, at least in physiology. Physicists have estimated that only some 4% of the total

content of the universe is conventional matter, some 23% so called black matter and the majority is just energy. We can assume that if something similar is true in living organisms, many discoveries also await description in human functions.

1. Introduction

The direct translation of the word physiology means the logic (science of reasoning) of nature. The three Chinese characters of the word physiology are life, logic, study, i.e. the study of the logic of life (Figure 1).

Figure 1: Physiology, i.e. life-logic-study calligraphic characters in Chinese (Dr. Zhiyong Ming)

Hippocrates (460-377 BC) used the word physiology to describe the healing power of nature, and Aristotle (384-322 BC) used it to describe the functions of organisms. We must be thankful that the Persian Abu Ali Sina (better known as Avicenna in Europe) (980-1037), the physician of the Islamic world, collected the old Greek and Roman wisdom and extended it during the Dark Ages of Europe (see Figure 2). He also included the old Persian understanding of life phenomena into his scripts. One of those old beliefs is non-visible communication (telepathy) between people over distances.

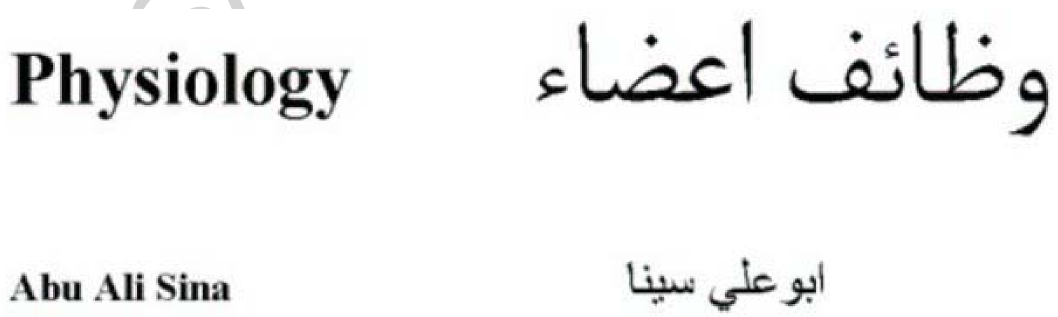

Figure 2: The word physiology written in Arabic to honor Avicenna's, or better Abu Ali Sina's, work in saving the physiological and medical knowledge from the Greek and

Roman times and extending that during the Dark Ages of Europe. His name written in Arabic is also shown.

Apparently independently, the ancient Chinese sages found many interesting features of human physiology. Today it is possible with electromagnetic devices to detect the bioactive points, which have traditionally been called the acupuncture points of Chinese traditional medicine. Also the meridians, which the Chinese discovered a few thousands of years ago, can be located due to their electromagnetic properties. Chinese thinking is based on the balance of opposing and complementary energies, which are either in or out of balance. Representatives of traditional Korean medicine also say that their traditional medical thinking is based on functional balance and its disturbances. Similar thinking can be found also among traditional Finnish healers. Traditional Chinese and Korean physicians say that western medicine is based on abnormalities of organ structures, i.e. morphology and chemistry. Perhaps one can say that the eastern traditional medical thinking is based on physics and physiology. It seems now that Eastern and Western medical knowledge are approaching each other.

At present physiology is the branch of science, which studies how the parts i.e. cells, tissues, organs, organ systems and the wholeness of healthy organisms, work, and how these functions are regulated. This governs both internal and external functions.

As physicists have estimated that only some 4% of the total content of the universe is conventional matter, some 23% is so-called black matter and majority of the content in universe is just energy, we can expect that many major discoveries also await their finding in the functions of the human body. Our knowledge is thus but a small island in the ocean of unknown.

The key phenomena in the internal functions of animals are those which let the internal milieu of the cells and the organism oscillate within certain safe limits.

As most of the metabolic reactions take place in water solution, several mechanisms regulate its intracellular and extra-cellular balance. The availability of water dictates the survival of plants, and they make the life of animals possible. The rains contribute to the seasonal cycles of vegetation and the breeding periods of animals. Evergreen trees can survive very low temperatures, for example in boreal regions in Siberia and Canada. There are many mechanisms which the species use to stay alive even when their internal water is in subzero (Celsius) temperatures. The majority of species are unable to survive in such conditions.

Metabolic reactions take place with the aid of protein catalysis. Enzyme proteins are able to lower the activation energy of their substrates. As some enzymes are very powerful and catalyze destruction of proteins, lipids and nucleic acids of the cells themselves, they are synthesized in inactive forms and only become active in the right place and right time, as do digestive enzymes and those which regulate blood coagulation and dissolution of the clotted blood. Many enzymes are highly specific—lock and its specific key model—and only targeted substrates can react. There are, however, both specific and non-specific inhibitors. The toxicity of many heavy metals like lead and mercury is due to their ability to react with thiol groups in enzyme proteins. The enzymes are denatured when the temperature is increased, but they are denatured also by low temperatures as ice crystals are formed. Many enzymes use metal ions as their activators. Iron is necessary for several enzymes which catalyze the use of oxygen. Many enzymes of energy metabolism need complex organic molecules as their coenzymes (see *Enzymes: The Biological Catalysts of Life*). Their building blocks are not necessarily made, for example, by human tissues. We need them as vitamins, which plants provide in our diet. Most reactions in energy metabolism take place in membranes. The choloroplasts in plant cells and mitochondria, where the conservation of solar energy and release of chemical energy take place, respectively, have been independent organisms which the ancient host cells have engulfed (see *Autotrophic, Heterotrophic and other Nutritional Patterns*). The intracellular membranes give spatial order to chains of collaborating enzymes, and as they have different functions similar to, for example, organs of the human body, they are called organelles.

Recently it has been found that nucleic acids are also able to contribute to the catalytic phenomena. RNAs can function like enzymes, which previously were considered to be catalytic proteins only. RNAs can also contribute to redox chemistry by using the same coenzymes as oxidoreductase enzymes. Nucleic acids can be used also to block the reading of the genome. Recent discoveries on RNA interference (RNAi) indicate that small molecular weight segments have powerful effects on gene regulation in animals, plants and many fungi. Short interfering RNAs can down-regulate genes at DNA level and below with several mechanisms, even triggering messenger RNA elimination and arresting messenger RNA translation to proteins.

The relatively constant volume and composition of intracellular fluids takes place with the aid of various homeodynamic mechanisms (see *Homeodynamics*). These regulate the entrance of substances into cells, their metabolic control and the release of products and wastes. As the cell membrane is semi-permeable and cells contain a lot of proteins and many metabolites compared to the outside fluids, there are numerous transport systems in the cell membrane. Most of the intracellular proteins have a negative net charge. The transport channels pump ions and regulate the entrance of different substrates into the cell. Water and gases like oxygen and carbon dioxide pass through the membranes without difficulty. The cells have high concentrations of potassium. In multicellular organisms, tissue fluid surrounds the cells. This fluid contains a lot of sodium and chloride ions. The entrance of sodium into the cells is limited. The differences in ion concentrations between the intracellular and extracellular spaces cause a potential difference across the cell membrane. This is called resting potential. If a thin electrode is introduced into human muscle fiber, one finds that the intracellular space has a negative charge of about -90 mV compared to the extracellular fluid. The permeability of the cell membrane for potassium ions is about 40 times greater than that for sodium—the main cation of the extracellular fluid. When nerve cells—and other cells—are stimulated, the ion permeability increases, some potassium ions flow out and some sodium ions flow in, and the charge across the cell membrane changes temporarily as the ion pumps soon correct the balance and repolarization of the membrane takes place. This oscillation of the membrane potential is called action potential. During that time it is said that the membrane is depolarized. As the nerve cells and muscle fibers are long, the action potential travels all over their membrane. This carries rapid messages, for example from nerve cells to muscle fibers. The neurons also secrete specific compounds, which transfer the stimulus to the next cell or effector cells at the end of the information chain. In addition to the electrical signals the cells communicate also with light signals. This mechanism is still rather poorly known.

The composition of the extracellular fluid fluctuates but again within quite a limited range. Thus the concentration of hydrogen ions is maintained within rather narrow limits—varying in human blood less than 0.5 pH units. pH is the negative logarithm of the hydrogen ion concentration. High hydrogen ion concentration, as in the human stomach, denatures most proteins, but gastric peptide splitting pepsin needs that high hydrogen concentration to become and stay active. Most of the enzymes which catalyze the key reactions of metabolism function, however, best at neutral pH i.e. their activity optimum is at or near pH 7, as the three dimensional configuration of their peptide chain is sensitive to pH. This makes the expression easier, but one must remember that a change of one pH unit means a tenfold change. The osmolarity of the tissue fluid varies also within quite narrow limits. In hypotonic fluid the cells will swell and finally the cell membrane will break. In hypertonic environment they will shrink. The glucose concentration is highly regulated in humans. The actions of the organisms towards the external milieu help in keeping the internal milieu within the limits, as external resources are needed for everyday life as well as for reproduction and growth. Again there are many homeodynamic mechanisms contributing to the wellbeing of the organisms (see *Homeodynamics*) If the homeodynamic imbalance continues, and the control mechanisms cannot bring back the balance, the outcome may threaten life.

The functions of all the cells, organs and their systems, in any organism, contribute to the internal milieu and to the health of the organism. The organ systems can be grouped in different ways. Blood, cardiovascular and lymphatic systems with sensory and nervous, as well endocrine systems, form the means of communication. In addition the cells also communicate by electromagnetic means. The respiratory and digestive systems provide the essential raw materials and with the urinary system they are also responsible for the excretion of wastes. The protection of the body takes place in the skin and mucous membranes as well as in immune system complemented with metabolic defense in many organs. The locomotor system comprises the muscles, bones, joints and tendons, as well as fascia with respective sensory and motor nerve systems. All the organisms have their reproductive systems. None of the systems work independently, and health is the sum of all the functions.

Physiology has a very difficult task to meet as the regulatory mechanisms are multiple and overlapping at the cellular, tissue, organ and whole body level. Luckily new recording and mathematical methods help in the analysis of their functions and their interaction i.e. the physionome of the complete organism. This means that physiology is the most challenging and interesting area of life sciences.

The number of cells varies in organisms from one to myriads. As multicellular organisms are also built up from cells, their metabolic behavior can be estimated. It has been found in this regard that the formula:

$$y = x^a$$

can be helpful (*y* and *x* are variables and *a* is a constant exponent). The exponent ¾ appears to work in organisms from unicellular organisms to animals and plants.

Organisms can also host many other species. Humans carry in their body many more micro-organism than there are own cells. This increases the research challenges, as interaction of the organisms within individuals in health and disease is crucial. The organisms form colonies and other social systems and share different functions together, like for example a colony of ants or bees—or indeed a community of humans. Sociophysiology is its own area of research.

It has been said that each species which exists is a special physiological experiment that has proved a success. It has been estimated that only one out of ten currently extant species has yet been described. For instance nobody knows all the species living in the human gut. This means that the physiological knowledge is still very limited. It also indicates that comparative physiology may reveal, over time, many more secrets of life than are now understood.

The growth of knowledge is fast. It has been said that 50% of the knowledge having medical meaning is renewed every 5 years, and nobody knows which 50%. There are thus many phenomena, which only await their revealing, even in our own body. The need for research work is thus nearly endless, as the environment constantly changes our responses.

Some people tend to think that only one study is enough. Unfortunately both the genetic backgrounds and the environmental factors greatly vary. The progress in understanding is slow, and studies must be repeated several times before we comprehend what we have perhaps found. One of the great physiologists of the past, Robert Tigerstedt once wrote “Truth will be revealed only to those who doubt”.

Anatomy—the study of structures—is one of the sisters of physiology, as many functions take place in the organs and tissues. It is, however, already now known that there are phenomena, which take place without structure. Some of the energies travel all over within our bodies, as do the electric signals of the heart. Some of the signals can be detected even outside us like thermal radiation and magnetic fields. We are also transmitting signals at least in the form of infrared light. On the other hand the significance of organs had been recognized in ancient Rome—it was recorded that “functio creat organon” i.e. function makes the organ.

Physiology is an integrative science. The functions of the different organ systems complement each other. Physiology is especially concerned with the regulatory systems. Pathophysiology is the study of disturbed functions, which lead to abnormalities and finally abnormal structures. All the functions are controlled by numerous different mechanisms both at the local level and also centrally by regulatory mechanisms. Neural systems work fast and humoral systems a bit slower. There are probably other control systems with different physical and chemical substrates. The Chinese described the meridians thousands of years ago. With electrophysiological recordings we can trace them, but so far no anatomic basis has been described.

-
-
-

Bibliography

Avicenne (Al-Husayn Ibn ‘Abd Allah Ibn Sina) (1956). Poème de la Médecine, Cantica Avicennae Edited by H. Jahier and A. Noureddine, Société d’édition ”Les Belles Lettres”, Paris, 210 pp. [Good summary of the Greek, Roman, and Persian-Arabic understanding of physiology and medicine.]

Helmuth L. (2003). Fear and Trembling in The Amygdala. Science 300 (5619) 568-9. [Short summary of the present understanding of stress effects on brain functions and structures. In many societies fear is part of everyday life. This article presents in concise form the present understanding of the physiology of brain mechanisms.]

Huether S.E. and McCance K.L. (2000). Understanding Pathophysiology. Mosby, St. Louis, MO, USA, 1195 pp. (A comprehensive description of the most common health problems and their genesis and laboratory and other findings].

Macer D.R. (2002). The next challenge is to map the human mind. Nature 420, 121 [An introduction to the behaviorome hypothesis i.e. how the human mind works].

Roy S., Khanna S., Bickerstaff A.A., Subramanian S.V., Atalay M., Bierl M., Pendyala S., Levy D., Sharma N., Venojärvi M., Strauch A., Orosz C.G. and Sen S.K. (2003). Oxygen sensing by primary cardiac fibroblasts. Circulation Research 92, 264-271. [Mammalian cells—at least cardiac fibroblasts—are able to sense oxygen levels and adapt accordingly. This study shows that in cell cultures oxygen level is probably too high compared to physiological tissue levels].

Schmidt-Nielsen K. (1998). Animal Physiology. Adaptation and Environment. Fifth Edition. Cambridge University Press, Cambridge, UK. 612 pp. [A helpful textbook which already has a long tradition in comparative animal physiology].

Schultz S.G. (2002). William Harvey and the Circulation of the Blood: The Birth of a Scientific Revolution and Modern Physiology. News in Physiological Sciences 17, 175-180. (A good summary of the historical turning point in the understanding of how the human body works and how circulation takes place)

Silverthorn D (2001) Human Physiology. An Integrated Approach, Second Edition. Prentice Hall, Upper Saddle River, New Jersey, USA, 816 pp. [Good textbook: a treatise of human physiology in a new way of presentation. A lot of good illustrations].

Stewart K.J., Hiatt W.R., Regensteiner J.G. and Hirsch A.T.(2002) Exercise Training for Claudication. New England Journal of Medicine 347 (24) 1941-1951. [This article describes the physiology of arteries and pathophysiology of peripheral arterial problems as well as reporting how exercise training promotes metabolism, circulation and functional abilities].

Taiz L. and Zeiger E. (2002) Plant Physiology. 3rd Edition. Sinauer Associates. Pp 690. [This book gives a good overview of plant physiology. It is also available in electronic form at address http://www.plantphys.net].

Waugh A. and Grant A. (2002). Ross and Wilson Anatomy and Physiology in Health and Illness. Ninth Edition, Churchill Livingstone (Elsevier Science Ltd), Spain, 484 pp. [A well-written traditional book for nurses, with good illustrations].

Biographical Sketch

Dr Osmo Otto Päiviö Hänninen, DMS, Ph..D., Professor of Physiology, Chairman of the Department, University of Kuopio, Finland. Born 1939, Lahti, Finland. He studied at the University of Helsinki and the University of Turku, Finland, where he received his Master of Sciences (Biochemistry) in 1962, Licentiate of Medicine (MD) in 1964, Doctor of Medical Sciences (DMS) in 1966, and passed his dissertation in biochemistry for his Ph.D. in 1968. He has also studied genetics. He has been a specialist in sports medicine since 1986. He served as the Research Assistant of Professor K. Hartiala, 1962–4; Assistant of Physiology, 1964–5; Laboratory of Physiology, 1966–7; Docent of Physiology, from 1967, and Associate Professor of Biochemistry, 1969–71, at the University of Turku; Acting Professor in the Planning Office, 1971–2; and from 1972, Professor of Physiology and Chairman of the Department of Physiology, University of Kuopio; Vice-President of the University of Kuopio, 1972–9; and President, University of Kuopio, 1981–4. Furthermore, he served as Visiting Professor of Physiology at Shanghai Medical University, China, 1991–2, and at Sun Yat Sen Medical University, Guangzhou, China, 1998–9; as Foreign Member of the Russian Academy of Natural Sciences, from 1994; and as Secretary General, International Council for Laboratory Animal Science, 1988–95. He was the President of Societas Physiologica Finlandiae, 1990–9, and has been President of the International Society for Pathophysiology and a Member of the Executive Committee since 1994, and the Treasurer of the International Union of Biological Sciences since 1997.

His special interests in research are:

- Biotransformation and adaptation to chemical loading, biomonitoring of toxicants, and comparative biochemical toxicology.
- Muscle metabolism and function.
- Ergonomics.

He has contributed 266 papers in refereed journals and seventy-two in proceedings, and written fifty-five reviews, and thirty books or book chapters. He serves on the editorial board of four international journals and is at present the European Journal Editor of *Pathophysiology*.

Of his post-graduate students (thirty-two in biotransformation, twenty-seven in. muscle metabolism and physiology, and five others), twelve serve as professors in China, Finland, Greece, Sweden, and USA