HOMEODYNAMICS

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Keywords: Detoxification, feedback, glucose, gain, homeostasis, pH, organ systems, oxygen, temperature, water.

Contents

Summary

Nothing is constant—in the environment or within organisms or in their cells. Some changes are cyclic and some are stochastic. The organisms have numerous mechanisms, which help them to cope with the changes. The changes in the environment are followed with senses and receptors, and the information collected is summarized and form the basis of the responses. The regulatory mechanisms in the central nervous system control the functions and use feedback information of the parameters monitored. Many of them oscillate, as do the responses in the organisms. The genetic backgrounds of individuals are different—with the exception of homozygotic ones—therefore also the responses are quite variable, too. The energy metabolism of the cells is to meet the consumption in the membranes, nucleic acid, protein and other synthetic processes and secretion. These are regulated by the availability of oxygen, oxygen derived metabolites and adenosine phosphates. Homeodynamic phenomena can be observed in the cells, in tissues, in the extracellular fluid surrounding the cells and in organisms in response to environmental changes, but the same also occurs in ecosystems.

1. Introduction

In physiology one often uses the word homeostasis (literally translated: staying the same)—to explain the tendency in all organisms to maintain constancy of variables like the balance of the important metabolites, to help the functions to proceed. Originally the word was proposed to describe the maintenance of static or constant condition in the internal environment. Actually everything even in the internal environment of living organisms is, however, fluctuating up and down. Nothing is constant—in the environment or within the organisms and their cells. Some changes are cyclic and some are stochastic. Some of the changes are manmade—perhaps already too many. All living organisms must therefore be able to adapt even in polar areas to man-made effectors. Some organisms have very large distributions where they manage to live, or at least to survive, and unfortunately many species are currently close to extinction.

Instead of homeostasis it is better to use the word homeodynamics, which expresses the dynamism—the ever changing state of parameters. The list of controlled variables is long, from processes within cells (intracellular homeodynamics), in cell numbers (homeodynamics of cell numbers), their immediate environment of extracellular fluid (extracellular homeodynamics), and extra corporeal environment (environmental homeodynamics) and ecosystem (ecosystem homeodynamics). The organisms can cope with the changes to certain extent, but when the zone of tolerance is exceeded, they meet difficulties in their zones of resistance, and finally perish. Humans are no exception.

One can describe the oscillations with the term *equilibrium homeodynamics*—when the organism follows fluctuations in the environment like Antarctic ice fish do, or *regulatory feedback homeodynamics*—when the physiological feedback mechanisms control responses in the organisms, like in humans (see *Thermoregulation*). The different functional systems operate in harmony in a healthy organism, but this harmony is lost when the reserves are at first stretched and then exceeded in disease.

The mystic phenomenon of heat that is connected to our body and which disappears after death was shown to depend on the use of oxygen (after its discovery in the air) and the oxidation processes connected to its use. This function needs a control to save the cells from overheating but to provide the energy for so many other processes.

The most important regulated variables for the tissues of aerobic organisms are the availability of oxygen and the release of carbon dioxide. The second most important variables are related to water and ionic balances. The next important category is the essential energy sources like glucose. The temperature where the organism lives has powerful effects on the regulatory mechanisms especially in homeothermic animals, although behavioural regulatory responses are also seen in poikilothermic animals.

Different physiological mechanisms allow mammals and birds to maintain a rather constant body temperature, while the choice of mechanisms is poorer in poikilothermic species like e.g. in fish and reptiles. Homeothermic animals like humans increase the heat production by increasing muscle activity first by shivering and then by motions, but cold adapted people can also activate their brown adipose tissue where substrate oxidation is uncoupled from ATP syntehsis. Brown adipose tissue is rudimentary in other humans expect new born babies Humans also use clothing and they are building houses, which are heated or cooled depending the need.. Many mammals have different furs during cold and warm seasons. In cold periods many are hiding under the snow like the mice and moles. Also some boreal birds use snow to escape the worst winter weathers. Poikilothermic animals have different behaviors like the previous examples to survive. Fish select the proper temperature layers in water and that helps them to survive in hot and cold periods. Snakes seek shelter in soil during winter, and they warm themselves up in sunshine in spring

In animals, the blood distributes water, energy substrates, building blocks of synthesis and also heat, as well as numerous chemical messages. Thus blood circulation contributes to the relative constancy of the immediate environment of the cells in tissues. It also coordinates the functions in the body with its constituents, substrates of energy and hormones. In plants, fluid streams also carry messages.

Evolutionary survival has required measures to deal with the risks that nature and other life forms on this earth pose. Survival requires adaptation to environmental conditions. The largest known terrestial species—the dinosaurs—disappeared after a huge stochastic environmental catastrophe caused by a crash of a meteorite into the earth. But this did not cause the end of other forms of life.

2. Feedback and Gain

The most important regulatory mechanisms in the maintenance of balanced oscillations are feedback mechanisms.

Negative feedback reverses excess levels of any parameter. When the blood carbon dioxide levels increase due to increased metabolism, the pulmonary ventilation is stimulated, and carbon dioxide level is decreased as more of it is released into expired air. Carbon dioxide stimulated ventilation thus has a negative effect on the pressure of this gas in the blood and tissues, although ventilation also provides more oxygen for metabolism and carbon dioxide production.

When blood glucose level increases after a meal, insulin secretion increases from the pancreas. Insulin opens the storage systems in the body, and the glucose blood level falls. Insulin thus has a negative effect on the blood glucose level.

Positive feedback regulation also occurs. In this case, the compensation augments the disturbance—processes speed up when they get started. A good example is the relationship between the resting membrane potential of nerve cells and sodium conductance, by depolarization. If an external stimulus depolarizes the resting potential, this increases the sodium permeability by opening the sodium channels of the membrane. The increase of sodium within the nerve cell promotes the opening of more sodium channels nearby. Luckily the sodium channels automatically close, but the action potential travels over the whole cell membrane, perhaps one meter in the human body. Sodium ions are pumped out again, and the resting state of the membrane is resumed.

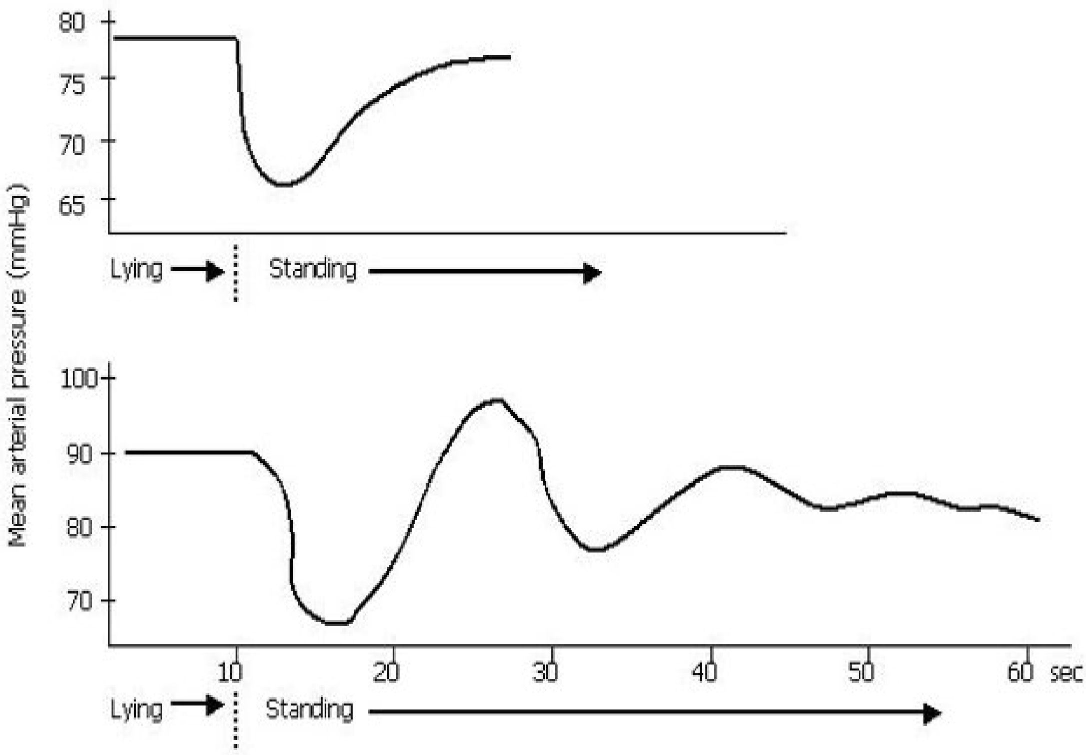

Figure 1. When a person rises up to stand, mean arterial blood pressure drops, but it soon goes up again in normal people. In some people, however, the pressure may oscillate for a short while. Blood pressure is monitored by baroreceptors which activate the brain and sympathetic system.

Haemostasis of the blood is another example of positive feedback. Clotting starts when the blood meets a foreign surface instead of the endothelial lining, e.g. due to a wound. A cascade of enzymes makes the fibrin precipitate and finally the clot to contract. Luckily the fibrinolytic system limits the process and blood clotting takes place only around the trauma area.

Childbirth is also an example of positive feedback. Uterine muscle contractions become stronger with increasing pressure in the uterine cervix caused by the baby’s head, as the signals reach the uterine body.

The level of the most important physiological variables is, however, controlled by multiple regulatory mechanisms. They increase the precision and the flexibility.

One simple example is the thermoregulatory system, which has several components starting from behavior (putting warm clothing on and walking indoors from the cold), closure of surface venous system in limbs, muscle shivering and increased metabolism, i.e. increased heat production regulated by nerves.

The latter may continue indoors until the body temperature has recovered.

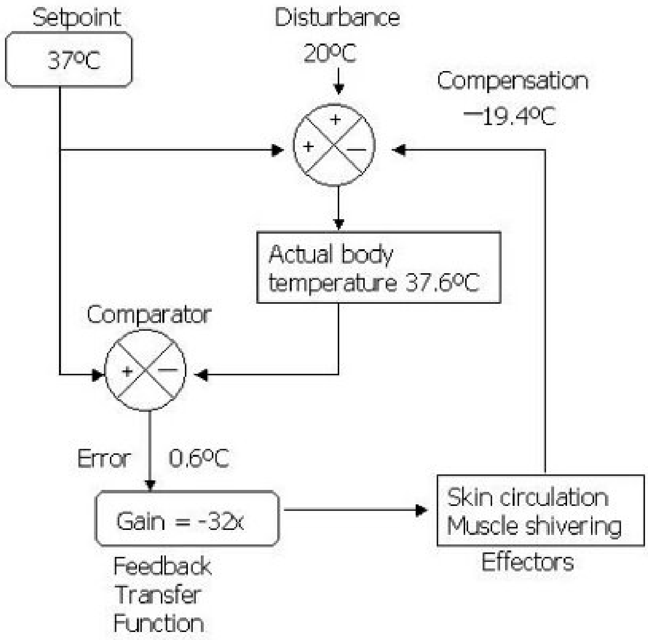

Figure 2. Schematic illustration of feedback and gain, as well as primary effectors (blood circulation in skin and muscle shivering) in thermoregulation. If the person still feels cold in a room, she/he will increase either clothing or heating of the room. Modified from Withers P.C. (1992).Comparative Animal Physiology. International Edition. Saunders College Publishing, Fort Worth

The regulatory mechanisms cause oscillation of the parameters. If we ski in a cold environment and meet a friend and stop to chat, we dissipate heat and after a while feel cold. We therefore soon resume skiing, to raise heat production.

Lung ventilation—regulated by chemoreceptors which follow the carbon dioxide, proton (pH) and oxygen levels in the body—takes place in intervals of a few seconds. The heart beats about once per second at rest. Both frequencies go up when the physical load increases and gradually go down after the work ceases (see *Physiological Basis of Exercise*). There are many hormone levels which oscillate with different rhythms. The cortisol level has a diurnal rhythm. Female menstruations take place about once per month, etc.

Activation of the feedback cycles needs sensors. There are many kinds of monitoring systems (see *G Protein-Coupled Receptors*). As glucose is the key energy substrate of the central nervous system, this is easy to understand. Blood glucose level is recorded at many levels, i.e. in the gut, portal vein and in several areas of the central nervous system. The effectiveness of the feedback system varies in different cases. The effectiveness of the control system in maintaining the constancy of conditions, i.e. the compensation relative to the remaining error is called the gain of the system. In human thermoregulation the gain is –32. This indicates that the body temperature is well regulated. In the regulation of arterial blood pressure the gain is perhaps –7 i.e. it is not so well regulated.

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Biographical Sketches

Chancellor, Prof. (em) Kaarlo Jakob Waldemar Hartiala (formerly Hartman until 1941) was born in 1919 in Hancock, USA. He studied at the University of Helsinki, Finland, where he received his Licentiate of Medicine (M.D.) in 1947, Doctor of Medical Sciences (D.M.S.) in 1951 and Docent of Physiology in 1952. He has been a specialist in internal medicine since 1954 and clinical physiology since 1960. He was resident of internal medicine of Helsinki University Central Hospital in 1951-4, research assistant of physiology at the University of Helsinki 1947-1953.

He was granted as a Rockefeller fellow to carry out postgraduate studies in USA. He studied two years at the Department of Clinical Science, University of Illinois in Chicago and at the Mayo Clinic, Rochester, Minnesota. He served as the first professor of physiology of the University of Turku, Finland 1951-84, President of the University 1970-5, Chancellor 1975-84. Teacher of physiology at the Department of Gymnastics, University of Helsinki; Director of Reseach Laboratory, Lääke Farmos 1959-75.

He was the chairman of the Finnish Olympic Committee and a member of the Medical Commission of the International Olympic Committee. He was the first Chairman of the Medical Commission of the European Committee and the Association of the National Olympic Committees with the task to fight against the doping and violence in top sports.

He retired in the year 1984 from University of Turku.

Dr. Osmo Otto Päiviö Hänninen, D.M.S., Ph.D., Professor of Physiology and Chairman of the Department of Physiology, University of Kuopio, Finland, was born in 1939 in 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 (M.D.) in 1964, Doctor of Medical Sciences (D.M.S.) 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, 1962–1964; Assistant of Physiology, 1964–1965; Laborator of Physiology, 1966–1967; Docent of Physiology, from 1967, and Associate Professor of Biochemistry, 1969–1971, at the University of Turku. He was Acting Professor in the Planning Office, 1971–1972, and from 1972, Professor of Physiology and Chairman of the Department of Physiology, University of Kuopio. He served as Vice-President of the University of Kuopio, 1972–1979; and as President of the University from 1981 to 1984.

Furthermore, he served as Visiting Professor of Physiology at Shanghai Medical University, China, 1991–1992, and at Sun Yat Sen Medical University, Guangzhou, China, 1998–1999; as Foreign Member of the Russian Academy of Natural Sciences, from 1994; and as Secretary General, International Council for Laboratory Animal Science, 1988–1995. He was the President of Societas Physiologica Finlandiae, 1990–1999, 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, comparative biochemical toxicology, muscle metabolism and function, and ergonomics.

He has contributed 266 papers in refereed journals and 72 in proceedings, and written 55 reviews, and 30 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 (32 in biotransformation, 27 in muscle metabolism and physiology, and five others), 12 serve as professors in China, Finland, Greece, Sweden, and USA.