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On the Ability of Adaptation and Acclimatization of Organisms under the Hypoxia (Measurement of Living Liver-Cell Potential)

By *Hirokichi Tatsunuma**

As a matter of the experimental plan, the platinum and the glass electrodes were used for the purpose to measure the general potential of the living liver and the cell potential respectively. However, no great difference was found between the data obtained by these two methods.

Generally in these two methods, the weekly transition has shown the high potential giving the significant difference from that of the control, but rather the unstable attitude was noted along with the increase of hypoxia burden. There existed a great difference between the individuals.

On the other hand, the monthly transition seems to suggest the low potential induced by the hypoxia burden with the approach the data of the control, and the stabilized status will thus be created. When the re-acclimatization is given, the platinum electrode gave the approaching figure of the control. Whereas the glass electrode gave the high potential compared to that of the control, and there was the significant difference in the stability, but it was generally of the low potential compared to that of the weekly potential. Platinum electrode was used simply in the blank test, and thus the accuracy is low, but the use of the glass electrode has shown a hint of formation of acclimatization of the cell to the condition of hypoxia.

Looking these facts, two stages namely that of the adaptation and that of the completed status of acclimatization can be assumed in the way of the energy production of liver in the living state as the living body. (Fig. 1, 2, 3, 4, 5, 6, 7)

Such attitude of the cell while still alive will depend finally upon the way of the adaptation and acclimatization of the cells themselves in the hypoxia. The experiment mentioned above can only be conducted in the cardiopulmonary system by having the

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cooperation of the oxygen supply to the cell while alive.

We have a experiment about extracted liver from living body with out cardio-pulmonal cooperation. The liver were broken in a mortar, and it floated in 5cc. of phosphatebuffer solution of C 38° (ph 7.0), subjected to centrifugal separation (3.000rpm, during 30min.) after having been shaken. The fluid extract was transferred to a container. The electrode were immersed in it, which was placed in a desicator, and the pressure was reduced up to 100mmHg.. The recording was made on the progress of the lowering of electric potential during 60 min.. The averages of the initial potential, lowered potential, and final potential were compared.

Potential drop on 1, 3, 5 weeks after acclimatized treatment is compered with non-acclimatized group, but final potential keeps high level.

Further, those of liver extract, to which 0.01 gr. of the reduced glutation was added as a ferment activator, of non-acclimatized mouse gave the similar trend of the drop potential and the terminal potential was kept at 30 mv. Those to which 1.5 mg. of cytochrome c extracted from the heart muscle of the horse was added as a reinforcing factor of the redox system gave a large drop potential with the low terminal potential, and no great difference was found from the group of non-acclimatization, but the small protuberances on the potential curve were found at the positions of +41mv. and −8 mv. as if they are to refuse the simple drop of the curve. The results of these experiments thus obtained seem to suggest that though the reinforcement of the supply of the enzyme by the cardiopulmonary system in the living body was discontinued, the acclimatization of the enzyme system of the cells themselves remained unchanged. (Fig. 8, 9)

The difference in the outlook of the drop potential curve was found between that of the flavin and pyridine systems which are of the carrier systems, and that of ascorbic acid and glutation which are of the standard system. However, there are quantitative as well as qualitative problems in both of the systems, and there exist the great varieties gathered from the large number of the experimental results obtained so far. At any rate, there must be no support from the cardiopulmonary system in this case, because the liver was removed from the body. (Fig. 10)

Having these results, one has to consider the constituents of the living body.

Generally the strict rule governs in the structure of atom and molecule composed

from elementary particles. The orbit of the elementary particles is set, and getting in to the orbit is meant to form the atom and the molecule, and there exists only very little error involved in the atom and the molecule thus formed. There will of course exist the control by the inheritance code at the time of further formation of polymolecules of organisms. Nucleic acids, such as DNA and RNA, are produced regularly assisted by the pair of bases. Up to this stage, it is the pure chemistry of the joint-coupling in the area of physico-chemistry.

However, the constituents of organelles will be formed by gathering the molecules, but are those produced as dictated by the inheritance. But the mitochondria, which is the granule found in aerobic cell, where basic function is the synthesis of ATP by the oxygen respiration, behaves differently in response to the different environment.

This phenomenon actually taken place was due to the fact that the energy needed for gathering the molecules is small, and that the various informations are produced in the course of the development at the stage of small differences existed in an energy. Hydrophobic-interaction was the major activity in the physico-chemistry, and generally almost no joint-coupling is engaged herein.

Water as a solvent gives the strong effect upon the mutual action between molecules of the living bodies in an aqueous solution.

This is to lower the energy of the mutual action between the water molecules, and the entropy of water becomes small, and the contribution to the free energy $F=E-TS$ will be balanced by each other. However, with the approach of the two residual radicals, a part of the water restrained in the structure becomes free, and the entropy will be increased and thus the free energy can be lowered. Stabilized status by such a force of an entropy is the hydrophobic interaction.

Such as further, they have proceeded to construct the cells, and then an organism as a whole. Thus, organelles, mostly created by the hydrophobic-interaction, were under the control of inheritance and environment, and seem to be a model of an organism at this level. Taking mitochondria as an organelles, which basic funktion is respiration, the study on the interaction between various facters in electron transfer on the main line of oxydation-reduction is requested.

However, the clarification is required three dimensionally on the functions and

interactions of all of the substances, such as zymo-protein, substrate, co-enzyme and water as a solvent, from the process of in corporation of substrate mostly by the enzymic activity to the process of release of the product from enzyme.

Mitochondria include the association, electron transfers and membranes, relating to energy transduction. One of them is chemical structure—hydrocarbon metabolic chemistry, phosphorilation on the substrate level, and other is physical structure—atom arrengement in molecule, deviation of direction.

Change of environment will effect upon the metabolic control. The velocity of their interaction will vary according to the location in the stratum of the control of an influential and environmental element. For example, the change of the velocity of transcription will give the slower effect upon the metabolism than those compared with the environmental direct action giving the effect upon the existing activity of modulation.

Namely, the velocity of the realization of biochemical adaptation will differ depending upon the location in the metabolic control state which are created by their adaptation. Enzymic mutation being already active in the cell will make an instantaneous adaptation to be possible.

On the other hand, most of the transamination, made along with the system evolution of protein among the joint-coupling, are those which are fixed to the group by an oppotunistic free movement of the mutation gene being neutral to the natural selection, but the actual living organism is of high adaptation to the environment.

It is assumed that the adaptative evolution must have taken place togather with the neutral evolution even on the protein level, but the long period of time will be needed in the transamination.

Conclusion

1) The measured values of the general potential of the living body and the liver cell potential seem to suggest that the adaptative ability of the acclimatized mouse to the hypoxia burden of the living body will be which is to hold well the high potential, being about 198 mmHg. of atmosphere, for about four weeks by the cooperation of cardiopulmonary system. However, the difference between the individuals can be found.

2) Monthly transition of the general potential of the living liver will be held for four months, and will become stable approaching that of the non-acclimatized mouse.

3) Monthly transition of the potential of the living liver cells of the repeatedly re-acclimatized mouse to the low oxygen level holds the high potential with the significant difference from that of the non-acclimatized group and it will become stable.

From the results obtained above, it is suggested that the state of the acclimatization of the cell electron transfer system remained for over a month. However, the significant difference has been noticed in the drop potential between the liver extracts separated potentially from the living body and the liver cell existed in the living body. The difference will probably be due to the temporary reaction caused by the oxygen supply in the cardiopulmonary system or other some adaptative ability as the living body.

Dealing with the liver as the living body, the oxygen will evenly be distributed to the tissues via the blood vessel and the interstitial fluid, and there can be a possibility of having a high density, not necessarily being in a proportion to the environmental oxygen density. On the other hand, when it is dealt as the liver extract or the piece, the oxygen density in the deep portion thereof will be lower than that of the surface area. The primary reaction of other organs of the living body to the condition of the low oxygen level, such as the attitude of the permanent activity created by the changing state of incretion of the adrenal cortex system, must be different, but this difference can not be found in an isolated chemical system.

Thus, the quantitative as well as the qualitative change will be included only in the enzymic system of the living body, or rather the change will only be restricted to that of the quality in the confined system.

Anyway, the hydrophobic interaction will be the primary system in the mitochondria, which is the organelle within the cell. It will contain the electron transfer system. As the production site of the energy having the oxygen affinity, it will be placed under the control of the environment and will exhibit the adaptability. Further, there will be a significance in having the tissue being higher grade than this as a test material.

However, the physico-chemical reference of the metablic system, for example the

cubic structure of the enzymic system, and the study of the radical and the spine will be needed as a problem of quality. But in the enzymic activity, an electron can collide with others in disorder, but once taken in to this system it will be placed into the characteristic direction, and will be treated by the terminal oxygen affinity.

Thus, the living system in the specific order, being controlled by the environment, will have the energy heading toward the survival by the adaptative ability. Therefore, the lost sight of this energy will lead to the closing of the study in the way of the substance of the adaptative ability.

The living body will generally proceed to the reduction of an entropy, whereas the isolated material will go to the direction of the increased entropy. Thus, the study of an energy for the tissues and organs of higher grade than the mitochondorial level which is mostly constituted by the hydrophobic interaction, will be adequate as an object of the study.

The study on the isolated material from the living body is fairly easy in the physico-chemical method of the modern knowledge, but the study of it in the living body will raise at all times the technically and extremely difficult problem. Therefore the effect on the reference of the investigation of energy in the living body will have to be made equally and constantly on the parallel basis to the study of the isolated chemical system from the living body.

Further, the systematic order and the feed back problem of the living body are being studied and clarified physico-chemically in an isolated system, but at least it will be needed not to lose the eye upon the energy of adaptation to the environment in the direction of survival. The measurement of the liver potential in the living body will have a significance as an index. (common study S. Tatsunuma)