#### Kikuo CHISHIMA

throcyte from yolk-spheres in frog. Now we found, further, that though, at the carly stage of development, the primordium of brain, m, spinalis and eye are derived from the invagination of ectoderm, thereafter the cells composed of them are derived from yolksphers by means of the new-formation of mesenchymal cell but thenceforth they are derived from the derivatives of erythrocytes,

- (2) Moreover we have confirmed that the all of the early elements of notochord, digestive canal, liver, pronephros, heart-wall, erythrocyte, and of blood vessel are derived from yolk-spheres, at first, through the following transitional phases: yolkspheres → aggregation of yolk-spheres → appearance of melanin pigments in the yolk-sphere-mass → fragmentation and fusion of yolkspheres → in the each yolksphere-mass there appears a vacuole-like primordial nucleus surrounded by melanin pigments → primordial cell with faint basophilic nucleus sorrounded by yolks-pheres (the so-called yolk cell) → yolklysis, and transform into mesenchymes or other embryonic cells, nucleus contain synthesized DNA.
- (3) However, thenceforth the cell of liver, nephrotic tissue, heart-muscle, tail-muscle and several other tissues in tadpole or in adult frog grow upon the continuous supplying of respective blastocytes derived from erythrocytes.
- (4) Cartilage cells show transitions from mesenchyme and notochord-tissue. The mesenchyme cells are derived from yolksphere-mass through a transition described above.
- (5) Typical phases of mitotic division of the embryonic cells can be scarcely seen, while there are so abundant and clear transitions from yolkspheres into embryonic cells that we can find no reliable evidence of the mitotic continuity between the elements of certain germ-layer and the respective tissue-cells.
- (6) It is highly probable that the polypotencies of embryonic cells derived from yolkspheres or blood cells are induced or determined by the so-called "field" where they are localized.
- (7) From the above-mentioned results we can not escape from the conclusion that the segregation of germ-layers is not necessarily accompanied by any determination of fates or restriction of potencies of the embryonic cells. Thus the cellular elements of adult are not descendants of the germ layer's elements.

## (F) Blood Clotting and Erythrocytes

 The Role of Erythrocytes and Blood Platelets in the Blood Coagulation (with 18 microphotographs, in English) Research Bull of College of Agric, Gifu-Univ. no. 1, pp. 107-117, 1951

#### Summary

(1) Studies on the mechanism of blood clotting with special reference to the behaviour of erythrocytes in two species of mammals and six species of oviparous vertebrates were carried out by means of comparative researches on actual me-

#### The Origin, Behaviour and the Differentiation of Blood Corpuscles and Certain Other Cells,

chanism of blood clotting in living animals, in vitro, blood smear preparations and on the sections of blood clots,

- (2) This observation showed that agglutination, viscous metamorphosis and disintegration of erythrocytes are very important factors in blood coagulation.
- (3) The close parallel between the blood coagulation promoting factors and the accelerating factors of crythrocyte-destruction supports the opinion that the process of blood coagulation, has direct relation with disintegration of crythrocytes.
- (4) Most of the components of the so-called "clumps of agglutinated and disintegrated platelets" in mammalian blood clot and the clumped mass composed, chiefly, of lymphocytoid elements in coagulated blood of oviparous vertebrates are merely a product of disintegrated erythrocytes in loco.
- (5) Cell content extruded from disintegrated crythrocytes may change rapidly its characteristics, especially their staining properties and colloidal state and become a jelly-like mass,
- (6) There are many evidences that a greater part of fibrin or fibrin mass may be derived from the viscous metamorphosis of erythrocytes or disintegrated erythrocytes themselves.
- (7) Fibrin strand plays a considerably important rôle in blood clotting in mammals but it may not be essential elements in oviparous vertebrates. Furthermore there are evidences that the fine fibrin mesh within the section of blood clot may be a residual product of denaturated protein by fixative agents.

#### An Additional Note

The continuation of this paper, the part two, will be published in the near future,

The present author intend to describe, in the part two on the essence of the following three monographic books written by the present author;

- Basis of Neo-Biology, Vol. I. —Genetics, Embryology and Evolution in relation to the Origin of Germ Cells—, (in Japanese with English "Suggestion"), 1957, 462 pages, 207 illus, (MEIBUNDO CO, LTD, TOKYO).
- (2) ——, Vol. II, -Origin of Life, Cells and Blood Corpuscles—, (in Japanese with English Summary), 1958, 490 pages, 200 illus, (MEIBUNDO CO, LTD, TOKYO).
- (3) Re-examination of the Orthodox View as to the Intramedullary Haematopoiesis— The Reversible Differentiation of Blood Corpuscles—(in Japanese with English Summary), 1954, 133 pages, 39 illus (IGAKUSHOIN CO. LTD. TOKYO).

In addition to these three books the present author is in preparing to publish, in the near future, a book "Basis of Neo-Biology, Vol. III, Differentiation, Organization, Histogenesis and Evolution of Blood Corpuscles, Cells and of Microorganisms".

## PART II

THE SECOND PRINCIPLE: THE REVERSIBLE DIFFERENTIATION BETWEEN BLOOD CORPUSCLES AND FIXED CELLS OR TISSUES, AND ITS PRACTICAL APPLICATION TO HUMAN BEINGS

CHAP. I. The Outline of the Reversible-Differentiating Capacity of Blood Corpuscles and its philosophical meaning

(I) Red blood corpuscles

As previously described in the First Principle on the differentiating capacity of red blood corpuscles in the vertebrates including human beings, the red blood corpuscles of various vertebrates including human beings differentiate into all kinds of sematic cells or tissues as well as germ cells under the well-no-urished condition. Of course, this fact has never been imagined in the domains of the oxthodox medical and biological sciences.

And then, on the contrary, the fixed tissues or cells differentiate reversely into blood corpuscles under the ill-fed condition, or under the abnormal conditions, such as in inanition or fasting, at reduced diet, at diseases, and after profuse bleeding. It was in 1953 when the present author found this fact and published first. Since then the present author has demonstrated it through subjecting to

various kinds of biological tests, making it public at every opportunity. (See K. Chishima's Monographs and papers described later).

Moreover, in the development of an embryo, the erythrocytes or mesenchyme cells are newly formed from the yolkspheres of an ovum which is generated from the erythrocytes of the mother. In other words, the yolkspheres of an ovum differentiate reversely into erythrocytes. Then, they differentiate into all kinds of somatic cells or germ cells according to the induction of their fields.

These facts may be concisely expressed as follows:

Reversible differentiation between the blood corpuscles and the fixed elements (see Figs. 2-1, 2, 3)

- Under the well-fed condition
   erythrocytes —— > all kinds of cells and tissues
- Under the ill-fed condition erythrocytes ← all kinds of cells and tissues
- 4) In the development of an embryo crythrocytes ← ova and yolkspheres
- 5) Under the pathological condition erythrocytes — cancer cells, cells in the inflammatory region, and connective tissue in wound healing.
- 6) In fasting, semi-starvation, and after profuse bleeding
  erythrocytes cancer cells, cells in inflammatory region, germ
  cells, fat, muscles, and the other somatic cells
  of the intestinal organs
- As mentioned above, the reversible differentiation between blood corpuscles and somatic cells or tissues in the developmental stage of an embryo or under the abnormal conditions, such as the ill-fed condition, fasting, semi-starvation, and diseases, has not yet been known. But, in this author's opinion, if it is put to practical use, this principle will surely be of great use in the prevention

against and the treatment for diseases, even though it is quite different from the orthodox dietetic point of view.

Fig. 2-1 Reverse differentiation from the yellow bone marrow (fatty tissue) of a chick staved for 4 days.

a...the so-called polynucleated giant cell which arised from yellow bone marrow.

b···erythrocytes and the so-called erythroblests.

Fig. 2-2 Reverse differentiation from the brain cell (ganglion cell) into several number of erythrocytes in the frog starved for 35-days. (show by the arrows). (K, C.)

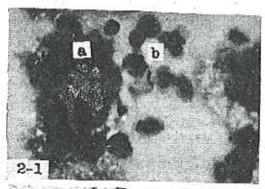
Fig. 2-3 Revese differentiation from the liver cell into many of crythrocytes in the liver of young goat starved for 7-days.

Fig. 2-4 Reverse differentiation from erythroblast(redifferentiated from yellow bone marrow)

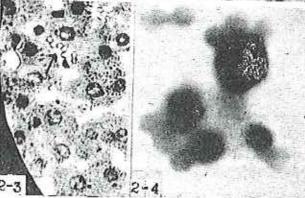
> es by meanse of budding-like process. (Femur of cat starved for 12-

into erythrocyt

days). (K. C.)







(II) The extramedullary haematopoietic theory is a misunderstanding of the reverse differentiation from the fixed tissue elements into the blood cells.

It has been generally believed that under the various abnormal conditions, extramedullary haematopoiesis take place in the various parts of the body, such as abrenal, the spleen, gonads, the liver, muscle, the aorta, veins, etc.

And it is said that, under the condition of leukemia, infection, diseases, chronic poisoning, and after the repeated bleeding also takes place extramedullary haematopoiesis.

And in the so-called extramedulary heamatopoietic center, there appear, at first, heterophil and eosinophil myelocyte-like cells or megakaryocytes, and finally erythroblasts or erythrocytes in the center.

It is a fact that there can be seen such a histological features as described above, but the interpretation about these phenomena is not correct.

Because there is no reliable evidence of the mitotic proliferation of the myelocytoid elements or of megakaryocytes in the so-called haematopoietic center, so that the mechanism of the increasing in number of these cellular elements can not be explained.

Furtheremore, there is another question that by what means, those newly arised myelocytes and erythrocytes can be entered into the closed typed blood vessels?

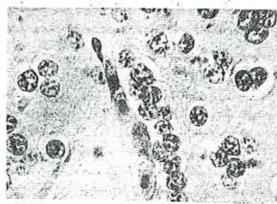
These selfcontradictions as to the extramedullary hemopoletic theory have not yet been solved.

But it may be easily solved by my new second principle, that is to say, the so-



(A) Reverse differentiation from the yellow bone marrow (fat) of a chick starved for 4-days, into blood corpuscles. (K. C.)

called extramedullary haematopoictic centers are nothing but a reverse differentiating phase from the fixed tissue elements including adipose tissue into erythrocytes through the intermediate stage, namely myclocytoid elements.



(B) Reverse differentiantion from the ganglion cell (shown by the arrow) of a frog starved for 35 days, into several blood cells. (K.C.)

## (III) "A reversible view" of a matter corresponds to correct science and philosophy

In modern medical science and biology, "the irreversibility of a phenomenon" is regarded as a postulate on the principles of physics.

For it is presumed that "the Second Law of Thermodynamics (Law of increasing of entropy)" governs all natural phenomena including life phenomena. According to this law, heat changes from a high condition to a lower condition, and all phenomena, with the passage of time, change irreversibly from an orderly to a less orderly, or to a more chaotic state.

Thus this interpretation of entropy necessarily leads to the conclusion that the entropy of the universe increases gradually as time passes, until at last it reaches the state of heat equilibrium, and all motions come to a stop, and the world of death appears. This law, as well as the First law of thermodynamics, is regarded as an iron law in modern physics.

The second law is often called "the principle of Carnot & Clausius", applied to a closed system, or an insulated system from the heat energy of the outside, and the probability of this law is approximated to "one". We cannot

deny the probability that there may exist some very rare exceptions as it is not so absolute one.

For it has not yet been completely proved that the whole universe is a closed system. Neverthless, it seems that biologists and medical scientists in our time are contentedly dependent upon physics, believing this physical law to be a golden law, and have no doubt that even life phenomena are governed by this law.

But, as a matter of fact, all life phenomena, such as development, growth, reproduction, sensibility, and evolution, change from simplicity. (homogeneity) to complexity (heterogeneity), or from equality (a chaotic state) to distinction (a more orderly state), although organisms can be classified as belonging to an open system, the life phenomena show a tendency as if their entropy is decreasing against the second law of thermodynanis during the organisms are growing.

#### (IV) Rejuvenation and fasting

It is said in biology that, if a jelly-fish is released in the sea water without food, it gets smaller and smaller, and goes backward the early stage of development, or a lump of cell. This phenomenon is biologically called as "degrowth".

This phenomenon may be said to be a kind of rejuvenation, due to starvation. And this corresponds exactly to the Second principle of this author that there is a reversible differentiation between the blood corpuscles and all kinds of somatic cells or tissues under the starved conditions.

In the development of an embryo, the increasing in number of its cells has been considered by orthodox scientist, as a result of mitotic cell division, but, according to the present author's studies, in the development of an ovum containing a large amount of yolk, such as frog eggs, the young cells(blood corpuscles and mesenchymal cells) are not proliferated by mitotic cell division, but they are newly formed through the Aggregation, Fusion, and Differention of yolkspheres.

+ Furthermore, in this case yolk which is a derivative of the mother's blood cells, differentiate reversely into blood corpuscles or mesenchymal cells in the development of the embryo, because the yolkspheres are produced through the degenrative change of the mother's blood cells.

This author will take the case of fasting, which has been widely conducted customarily as a religious discipline in the world from ancient times. In our time fasting is fairly practiced in order to train one's body and mind, promote one's health, improve one's constitution, and purify one's spirit. This is an evidence that fasting is of great use in differentiating somatic cells, muscles, fat, and the tissues of the viscera reversely into blood corpuscles, in excreting waste matter or noxious matter deposited in the body, and for sake of purifying, refreshing, and rejuvenating all the tissues of the body.

And the bio-medical grounds for these effects of fasting will be explained theoretically by the Second Principle presented by this author.

It seems that biological scientists in our time are contented with the fact that biology is now dependent upon physics and chemistry, since organisms including human beings disintegrate and disperse themselves ultimately through the process of their senility and death, according to the Second law of thermodynamics, and, as a result, entropy increases.

But this author has some doubt about this theory. For, when they reach their sexual maturity, oranisms produce thir progency, the supporters of the next generation, by reproduction.

In other words, an individual in the adult stage reverses to the primitive stage, or to the stage of spermatoza and ova, and then from the fertilized egg produces an embryo, and it reaches the adult stage again through the development of the embryo. This cycle repeats itself.

Namely, this means the continuous recapitulating development of an individual from a parent to a child, a child to a grand-child, and a grand-child to a great-grand child, ........., This is a reverse phenomenon, and may be said to be the most adequate thinking for the explanation of all natural phenomena, as well as life phenomena, which corresponds exactly to "Bio-dialectic" advocated by this author: it is a dialectic saying that one's hody and mind should be regarded as an indivisible entity. In our time we are required to "aufheben", or unify, the material dialectic and spiritual dialectic, and form a new dialectic. Moreover, this corresponds exactly to the "Haeckel's law", or to the phenomenon that an organism recapitulates briefly the process of its evolution or phylogeny in the process of its ontogeny. The reverse or recapitulation in

this case does not mean a simple repeat of the same phase, but a form of the cubic, spiral motion. That is to say, an organism evolves or develops continuously from generation to generation, but recapitulates as a spiral movement.

This philosophy is different in essence from the so-called formal logic which has been believed, by allmost all of the scientists belonging to the orthodox biology and medical sciences. Moreover, biodialectic and the reverse, repetition principle may be applied to the explanation of all cosmic phenomena, including life phenomena.

This philosophy may be also adapted to the interpretation of the forms of all motions and changes in the universe from a micro cosmos, or from an atomic world, into a macro cosmos, (or a spiral nebula).

The history of the evolution of the globe and oranisms on the earth must be dialectical. For, unless it is endorsed that the globe and organisms have repeated destruction and formation many a time from ancient times, there will still remain a great number of phenomena on the earth which are inexplicable.

For instance, seeing the periodic law of atoms (evolution of atoms) discovered by Mendelefev in 1869, we can know that the evolution of atoms in an inorganic world has, strangely, a regular, periodic arrangement. In addition to this,
the reversible reaction in chemistry may be said to be a proof of this principle
of the periodic repeat in the natural world.

The following phenomena cannot be understood without the aid of this philosophy saying that they all should be regarded as the repetition of the wavy, and spiral movement in the formation of the globe and life: there are the phenomenon that in the evolution of an oranism, ontogeny repeats phylogeny briefly, the phenomenon of orthogenisis, and the mysteries in the development of an oranism.

It seems that Bergson, the prominent French philosopher, in 1907, and Bertalanffy, the eminent theoretical biologist, in 1952, both had some unconvincing feeling about the application of the Second law of thermodynamics to oranisms.

Provided that a new principle is established in future which can unify or include physics and life science, it will probably be a biodialectical one.

For dialectic must be based upon reverse, repeat, and spiral.

# CHAP. II Practical Application of the Reversible Differentiation of Blood Corpuscles under the Starvation or Fasting Condition.

- (1) Rejuvenation, health-recovering, and cancer treatment through fasting therapy and cure by reduced diet
- (a) Plus dietetics and minus dietetics

Dietetics in our time has a strong tendency to stress chiefly the plus-side of nutrition, neglecting its minus-side. As a result, various chronic diseases, as well as gastroenteric disorders and obesity, have greatly increased in number, due to overnutrition or overeating.

Therefore, now we must renew our understanding of the minus-side of nutrition, such as fasting, semi-starvation, and temperance in eating.

(b) The relation between cancer, and semi starvation or reduced diet

The common hospitals in every country of the world were extremely quiet, or had very few patients, during the Second World War, especially about the time when people had a great difficulty in obtaining food. And it is proved from statistical data that both the occurrence rate of cancer and the death rate from cancer were comparatively lower in the warring countries, such as England, America, Germany, and Japan, in war time, especially about the time of the difficulty of obtaining food. Naturally, the occurrence rate of gastroenteric disorders and other diseases, and the death rate were comparatively lower as well.

But, as the food supply has got more favourable in post-war days, various diseases have rapidly increased in number mainly owing to overnutrition and over eating. Today, hospitals in every place are very busy, or almost filled with patients. Perhaps this may be chiefly attributed to the following facts that the modern dietetics has a strong inclination to the plus-dietetics, and there are many people who believe it without due consideration, while they are ignorant of correct food control.

This may be shown from the results of the studies of some scientists in

Europe and America on the relations between the prevention and cure of cancer, and the quantity and quality of food.

The following are the results that research workers obtained by their biological experiments, who investigated the relations between the occurrence rate of breast cancer among one group of mice compelled to reduce their diet and that among another group of mice allowed to eat their fill:

Reduced Rations and the Occurrence Rate of Breast Cancer in Mice.

Research workers	Reduction of food	Occurence rate of cancer
Sivestsen & Hasting('38)	16%	18%
	0	88%
Viscler('42) & White('44)	1/3	0%
1800 (180) (1800 (1800 (1800 (1800 (1800 (1800 (1800 (	0	67%
Bischoff & Long('38)	1/2	the lowest percentage

## Reduced Rations and the Occurrence Rate of Carcinoma

Moresch in 1909 and Rous in 1914 respectively published that the occurrence of carcinoma might be restrained by reduced rations.

# Reduced Rations and the Relapse Rate of Cancer after the operation

- Rous in 1915 published that the relapse rate of cancer after the operation was much lower when reduced rations were taken before the operation.
- 2) Sugiura and Bennedict in 1926 published that the occurrence rate of cancer after the operation in thirty-seven test mice were as follows:

Reduction	Relapse rate	New occurrence rate
0	18 (48%)	15 (41%)
1/2	6 (16%)	6 (16%)

## Obesity and Cancer Mortality

The following datum is the result obtained by Dublin in 1932, who investigated the relations between obesity and cancer mortality about 192,000 persons at the age of more than 45:

Body we	ight :		Mortality
	nt heavier	(than the average)	9per cent more (than the average)
15-24			24 "
more than 25		#	29 "
5~14 per cei	it lighter	( <b>W</b> )	3per cent fewer
15-50	"	T.	15 #

From the above results of studies on cancer, we may say that the occurrence rate of cancer, the relapse rate of cancer, and the death rate from cancer, have a higher tendency under over-nutrition than under reduced nutrition. But we should not jump at the conclusion that cancer is related especially with the quantity of food, for cancer is often dependent on the other combicated factors, such as mental stress, food quality, stimuli by carcinogenic factors, lack of exercise, and an unnatural life.

# (II) The dangers of blood transfusion after the surgical operation of cancer or other diseases

It is a well-known fact in modern medical science that in order to supply them with nutrition. blood transfusion is given to patients under malnutrition suffering from cancer or chronic diseases. Similarly, blood transfusion, as you know, is given to patients after the surgical operation or after profuse bleeding caused by traffic accidents or external wounds. But, on the other hand, the part of blood, especially the part of crythrocytes, is not understood correctly in modern medical science, while in dietetics the plus-side of nutrition is made

too much of. Consequently, the patients are exposed to the great danger of developing serum hepatitis after blood transfusion, even though the fresh blood of an adaptive blood type is transfused. Especially, when they are enervated, the patients are in much more danger of developing serum hepatitis. For, even if the blood type of the donor and that of patient are identified, there is the possibility that a certain refusal reaction or an antigen, antibody reaction may occur due to an individual difference in the composition of protein in blood between each other. Besides, in case a great quantity of blood transfusion is given, erythrocytes, the volume of which occupy 45 per cent of blood, or more, will probably stagnate in the parts of the body, such as carcinoma and the liver, where the blood stream runs very slowly, erythrocytes differentiate into cancer cells or liver cells, corresponding to each part, and cause cancer or liver hypertrophy or hepatitis.

And then cancer will get worse, and serum hepatitis or cirrhosis will occur in the liver. This expresses the presumption that the dangers of blood transfusion may be far greater than the common medical scientists have thought.

Moreover, there is the possibility that we may be infected with syphilis or malaria by blood transfusion.

In the present-day medical science, it is supposed that serum hepatitis will occur only in the case of a blood-donor carrying the viruses of serum hepatitis in his blood. But in this author's opinion, a virus is not the cause of discase but the effect of disease, for viruses are produced from the pathological, the dving, and the dead cells of a living body. Consequently, it is possible that a giant molecule, which can be called an elementary body of protein in the protoplasm of blood cells or somatic cells, synthesizes spontaneously DNA in the cell, and generates viruses in the cells. Therefore, there can be no frash blood that is entirely free from the viruses of serum hepatitis. Today, there are many Puritans in the world who are driving a movement against blood transfusion in conformity with their religious doctrine. This means in a sense that we should avoid blood transfusion as far as possible, from true haematology or from this author's bio-medicine. And it is desirable to use a substitute for blood such as Ringer's solution, Ringer-Lock's solution, physiological salt solution, PVA, and the other blood substitutes, all of which must be free from blood cells or protein.

Modern medical scientists may be very difficult to understand a new haematology presented by this author, but a wise man, in any case, will reject blood transfusion, and use blood substitutes in order to keep his own life.

## (III) Fasting, Rejuvenation and Obesity-cure

Obesity is a phenomenon caused by the fact that when the digestive organs are sound, are ingesting nutrition greedily, and, consequently, haematopoiesis in the intestines is very active, excessive blood cells are stored up in large quantities as fat cells and fatty tissue under the skin or in the surroundings of the viscerals or in the tissues.

Conversely speaking, person must be learned that the fat, at first, and then muscles or tissues of the viscerals, differentiate reversely into blood cells, respectively through fasting or semi-starvation or reduced diet.

It has been neglected by scientists that the fat and muscles not only dissolve themselves into its components as an energy source, but also differentiate reversely into blood cells, and they are useful in resupplying blood cells.

This redifferentiation of fat and muscles into blood cells is performed in order that a living body may supply blood cells when haematopoiesis in the intestines is almost checked, or extremely reduced, due to fasting or reduced diet.

Fasting and reduced diet remove waste matter or noxious matter stored up in the body, refresh tissues or cells, and relieve the digestive organs, recover vitality, and renew, or purify, blood or body cells.

Futhermore, fasting and reduced diet are useful in promotion of health or rejuvenation because they prevent the putrefaction of the contents of the stomach and intestines, and the toxin of bacteria from being absorbed into the blood. Thus, we may say that most of the various diseases (gastroenteric diseases and others) in our time arise from the compositeness between overeating of animal food, lack of exercise, mental stress, and an unnatural life.

And the Second Principle presented by this author will prove theoretically that minus-nutrition has good effects on the prevention against and the treatment for such diseases as cancer, hypertension, cerebral apoplexy, asthma, neurose, hepatitis, pancreatitis, neuralgia, diabetes, heart diseases, gout, empynema, dermatitis, suppurative inflammation, and other various inflammations.

There is the proverd, "To get fat is to get old". This is true from a biomedicical point of view. Therefore, it is necessary that we should usually carry out strictly the principle of "three S" at meals, or sometimes practise the fasting, if possible. (The "three S" represents "Saishoku" in Japanese for vegeterisnism in English, "Shōshoku" for reduced diet, and "Soshaku" for mastication.) This author calls this "an amortization plan of fasting", and is now advising the sick or the sickly persons to practise this principle.

## The dangers of medicine for obesity-cure

This author hears that in America more than 1000 fat doctors have a large practice by administrating the rainbow diet pills for getting lean to fat women.

And these pills are classified into the seven colours.

These coloured pills contain a toxic substance which is an obstacle to the digestive organs and diminishes the appetite, a medicine for curing it, digitalis for preventing the heart from growing weak, thiazide diurectics for promoting the urination of the kidney, and a medicine for the brain or the nerve, respectively. By the way, the "Life" on Jan. 26, '67 says that not a few of the women who had taken these coloured pills for more than one year continuously died suddenly from paralysis of the heart.

We may say that one who takes the pills uncritically in order to get lean, has not any correct wisdom of life. Originally, one's growing fat proves that one's digestive organs are sound, and one's powers of digestion and absorption are very large. Neverthless, if one uses the pill habitually in order to get lean, neglecting this fact, it will either spoil one's digestive organs, or promote one's metabolism abnormally. It is evident that either case is unnatural, and causes ill health.

Therefore, one who wants to get lean should do nothing but carry out strictly reduced diet, vegetarianism, and moderate exercise or muscular movement, instead of committing the above folly. This also expresses that one should just go counter to the principle of domestic animals fattening, which requires the following three conditions: that is, to eat well and much, to set limits to exercise in the dark, and to avoid stimuli from the outside far as for as possible. Performing fasting or reduced diet at times makes better one's health, one's looks, and one's form, and then make one's life longer. Besides, they are useful in doing mental training and promoting intellectual activity.

Professor Mackey once showed that he made a comparative experiment of one group of white rats forced to reduce their diet, and another group allowed to eat their fill, and, as a result, the former lived more than twice as long as the latter.

There has once lived not a man of the macrobians, or long-lived men, who was both an epicure or a great eater, and an idle fellow.

CHAP. III. Original papers in English and Abstracts from Monographs and Parpers (in Japanese with English résumé) On the reversible differentiation between erythhrocytes and the certain fixed tissue elements.

#### (A) Papers

(1) ON THE DIFFERENTIATION AND DE-DIFFERENTIATION FROM ERYTHROCYTES INTO OVARIAN ELEMENTS, AND ON THE RE-DIFFERENTIATION FROM YOLK MATERIAL INTO ERYTHROCYTES IN CHICKENS AND RABBITS.

Kikuo CHISHIMA\*

(Received for Publication, October 1, 1952)

#### INTRODUCTION

Ever since the publication of his papers in 1947, the present writer has been asserting that, in vertebrate forms, the erythrocytes with very wide prospective potencies, differentiate into (i) lymphocytes (Chishima '47 a, b, '51 a, b, d, '52 a, b, c.), (ii) neutrophiles, eoslnophiles, and basophilic granulocytes (Chishima '47 a, b, '50 a, b, '52 a, b), (iii) bone marrow elements (Chishima '49 '51 a) (iv) so-called mesenchyme cells-B (which differs from mesenchyme cells-A of blood island in embryonic yolk sac) (Chishima '47 a, '52 c), (v) connective tissue cells (Chishima '47 b, '50 c, '52 c), (vi) epithelial cells, muscular tissue (Chishima '50 c), (vii) fat cells and fatty tissue ('47 a '62 a, c), (viii) macrophages (Chishima '50 c, '51 b) (ix) plasma cells (Chishima '49 '51 a), (x) pigment cells and cartilage cells (Chishima '50 c), (xi) gonadal elements ('47 '52 c), (xii) elements of Wolffian body in chick embryos (Chishima '51 c) and (xiii) hepatic cells in chicken, rabbits and goats (Chishima '51 b).

I have learned, recently, of the following important publications; (1) "Secretion of red blood corpuscles by eosinophiles in intestinal walls of herbivorous animals" (Duran-Jorda '47-'51), (2) "Blood cells (Green cell type in Ascidian) serves as nutritive cells

<sup>\*</sup>Laboratory for Zootechny, Faculty of Agriculture, Gifu University, Japan Reprinted from Research Bulletin of the Faculty of Agriculture, Gifu University No. 2 (Merch 1953)

or nurse cells for the tissue (yolk and muscle)" (George '39) (3) "New formation of crythrocyes from yolk-sphere in chick embryos" (Lepeshinskaya '37-'50), (4) "Differentiation of germ cells into four cell strains" (Weiss' 50), (5) "The fate and differential potency of lymphocytes (Andrew and Andrew '48, Fatr '51), (6) "The phenomenon of crescent-expulsion of erythrocytes" (Neuda) '49, '50, (7) "Initimate histogenetic interrelationships of elements of germinal epithelium, egg cells and follicle cells in mammals" (Dawson et al '51 a, b), (8) "The derivation of true lutein cells in Porcupine from granulosal and stromal cells" (Mossman and Ilse Judas '49). The new ideas of several authors mentioned above are very startling and support in part my opinion.

It seems most probable, that the generally accepted opinion as to the origin, functions and fate of erythrocytes has not yet been substantiated with adequate evidence. On the contrary, it includes many fundamental questions and contradictions.

The purpose of this report is to show that the erythrocytes with poly-potencies differentiate or de-differentiate into ovarian elements and erythrocytes arise from yolk material in chicken reversely.

#### MATERIALS AND METHODS

The observations here presented are based upon the examination of the ovaries from 87 chick embryos, 15 chickens, 7 adult laying here, and 5 adult female rabbits.

These animals were strong and healthy. Some of these adult animals were injected intravenously with 28 cc. of a 50% physiological salt solution of colloidal carbon ink, and then the animals were killed at various intervals ranging from one hour to 4 days after the single injection.

The animals were killed by cutting of jugular vein, the ovaries removed were fixed in Bouin's fixative or in a 10% solution of formalin and sectioned serieally at 5-10 $\mu$ , and stained with Delafiel's or Mayer's hematoxylin and cosin. Some of the vascular walls of ovarian follicles of laying hems were removed from the follicles which already had been fixed, and from it expanded or spread preparations, or the preparations sectioned transversely were made and stained with hematoxylin and eosin.

Observations on hematopoiesis in the blood islands of the chick embryos were carried out on the stained sections or on the living blood islands which were removed from yolk sac, and were cultured (slide-cover-glass method) under the microscope-thermostat at 39° C.

#### RESULTS

- (1) Three modes of the growth of follicle in chick and hen
- The first mode of the growth of the primary and growing follicles in young chickens and in laying hers.

In a previous paper (Chishima '62) the writer stated that the so-called primordial germ cells arise and grow by means of the fusion of mesenchymatous elements of germinal epithelium.

It is true, as has been claimed by other authors that there can be no transitions from one of mesenchyme cell into a primordial germ cell, however, there can be seen clear transitions from fused mesenchymatous elements of germinal epithelium into a primordial germ cell, and further it grows at expense of other crescent shaped mesenchyme cells attached closely on it's surface (Fig. 9) Origin and growth of a primary follicle is, principally, the same as that of primordial germ cell.

Many of microscopic follicles without stalk are found on the periphery of the ovaries of chickens and laying hers. (Fig. 29)

It was levealed from the observations of sections, that the primary follicle is composed of an aggregated mass, the oval or round in shape, of several hundreds or more of the extravascular blood cells (composed chiefly of crythrocytes and of a few leucocytes).

This crythrocytic mass then is transformed into a mass of small lymphocytoid cells. Then the small lymphoid cells localized at the inner portion of the mass gradually show the sign of their de-differentiation into the lipoidal substance or the yolk material.

At the same time, there arises a large clear ove-nucleus in the cavity, and at the periphery of that cavity (in cytoplasm of ovum) there appears a newly formed granulosa layer showing a transition from lymphoid elements of that mass.

And other lymphoid elements situated on the surface of this mass show transition into the flattened, elongated fibroblast, and then into the connective tissue elements which also ultimately de-differentiate into the yelk material. (Pigs. 1-2, 4-6)

The inner most layer of primary follicles, the granulosa layer, shows relatively uniform size, shape and arrangement of its components, but that layer of growing follicles varies in thickness according to its position, and often shows, in some portion, its degenerating feature (enlarged vesicular nuclei, decreasing of stainning capacity, vacuolized or cloudy appearance) of the granulosa cells.

From present studies, the existence of the so-called vitelline membrane could not be confirmed, even though it has been schematically figured by many authors.

On the granulosa layer we could not find the existence of the minute canaliculi through which yolk formation materials may be transported, as has been supposed by some workers. Furthermore, no definite clear boundary-line between the theca and the vascular layer of the growing follicle-wall can be recognized.

In other words, they are continuous each other, each is composed of the connective tissue elements, fibroblasts, lymphoid elements, scattered erythrocytes and blood vascular system containing blood cells. And, all transitions from erythrocytes into the yolk substance can be seen through the mesenchymatous elements of the germinal epithelium, lymphoid elements, fibroblasts, connective elements and granulosu cells.

And the degeneration (de-differentiation) from granulosa cells into the yolk substance can easily be observed. (Figs. 4-7)

#### (2) The second mode of the follicular growth.

Beside the first mode, the follicle grows by another mode, that is, the fusion of two or more follicles into one.

From the observations of ovarian sections we often found that the thin pressed walls of two or more small follicles, standing closely together, are degenerating and often show their fusion into one follicle through the disappearance of the walls of this contacted area. (Figs 1-A, 29)

In this case, at first, the fused follicle is polyovular, that may due to the incorporation of the ovum or ovums originating from the several follicles.

The ovums in a polyovular follicle are almost always differ each othes, in their size and developmental stages and show no mitotic figure.

In a polyovular follicle the old and large ovum often show a degenerating feature, but on the contrary, the small and young ones do not show such a sign. From this fact it is most probable that a polyovular follicle arise from the result of fusion of follicles and only one of the smallest and youngest of these ovums survives and the others are degenerated.

It is generally agreed that the ovarian follicle moves actually toward the periphery of the ovary in accordance with its growth. But this seems to be incorrect, because the relative position of the growing follicle may be shifted by its growth or by means of fusion and additional growth without its own movement.

It is a most important fact that even though the follicles grow very rapidly there can hardly be seen the mitotic proliferation of all follicular elements.

From these facts, the orthodox view regarding the follicle growth, which is based on initotic proliferation of the ovarian elements, is highly improbable.

#### (3) The third mode of follicle growth

Transverse sections of young growing follicles often show the blood pouring directly, into the follicular cavity through the open end of the capillary which is located in the inner vascular layer of the follicule wall. (Figs. 1-c. 6, 8,) And the crythrocytes poured into the follicular cavity are mingled with yolk material and shows transition into the yolk material through the stage of the so-called nurse cells or yolk nucleus. (Figs. 30, 32, 33)

However, this mode of follicular growth plays less importance than the first and second modes, especially in mature follicle.

## (II) The large and mature follicles in laying hens and the yolk formation.

It is a well known fact that the follicles in the laying hen show extraordinarily rapid growth and attain a larger size than that of other animals. So that it is said that a follicle weighing less than I gm. increases to an ovulatory size of about 16 gm. for only 9 days.

Thus the prodigious work of transportation and synthesis of yolk building materials in such a short period of time leaves us no doubt as to the existence of an initimate relationship between the uneven development of the vascular system of follicle wall and the blood.

Recently, Nalbandov and James ('48) studied extensively the vascular system of mature follicles in laying hens. My observations agree in many points with their findings.

Prom my observations the structure of the mature follicle wall reveals the following striking features.

- (1) The expansion preparations of the follicle walls showed that the whole surface of follicle walls was covered with extraordinarily developed, intercommunicated and flattened vascular mesh-work or bands. (Fig. 27) Since the flattness of the blood vessels was also observed on the transverse section of the follicle wall (Figs. 7, 11, 34), it probably was due to the tension of accumulated yolk material.
- (2) The distribution of the arteries on the surface of the follicle wall is relatively simple. On the contrary, that of venous system (venous sinuspid) shows strikingly disproportional development than that of arteries.

From this fact, it is reasonable to consider that the blood current in the venous sinusoids of the follicle wall is most probably, stopped or stagnated.

A stopped or stagnated condition of the blood is a most favorable condition of the differentiation of crythrocytes as has been observed by the writer.

In fact, erythrocytes contained in such a stagnant venous sinusoid often show transitions into lymphoid elements which, in turn, show transitions into yolk material (Fig. 7)

- (8) A large and somewhat flattened artery in an expansion preparation of the mature follicle wall often involves two or more small capillary-like blood vessels parallel to them, and some of these small blood vessels contain lymphoid elements only, which show transitions from erythrocytes. (Fig. 3)
- (4) Another characteristic feature of the arteries in expansion preparation of the follicle wall bears resemblance in structure to the vein, e, g, a relatively thin vessel wall composed of degenerating components.

It is also a note-worthy fact that these afteries often expand and branch into the small vessels at the lower half of the follicle.

And these arterial branches often are transformed, directly into venous sinusoids without passing through the capillary, and many extravasated erythrocytes can be seen here and there.

- (5) A transverse section of the stalk of a mature follicle reveals that the several numbers of typical arteries and volus and their degenerating forms are being transformed into yolk substance.
- (6) The transverse section of the mature follicle wall shows 2 or 3 layers of a vascular system, but there is no clear distinction between, the se-called outer, middle and inner vascular layers. Therefore it seems, rather continuous. (Fig. 31)
- (7) The venous sinusoids in the inner vascular layer are somewhat flattened and the components of this layer together with involved blood show transitions into connective tissue elements and the elements of the inner most layer of it, and further, they show transions into the granulosa cells. (Figs 7,31) The so-called basement membrane of follicles also shows transition from the elements of flattened thin, innermost capillary layer.

Both the elements of the wall and the included blood cells of the venous

sinusold at the middle or outer vascular layer also often show a sign of degeneration, (Fig. 31)

In a mature follicle, the direct extravasation of blood into the follicle cavity is less in degree than that of a smaller, growing follicle.

The process of the differentiation and de-differentiation from erythrocytes in a mature follicle into yolk material is the same as that of the growing follicle. (Figs. 7-8, 9-13)

- (8) The granulosa layer is not necessarily composed of a single layer of typical, unifrom glanulosa cells, but it varies in thickness of layer and the developmental stage of its elements, thus in some areas there has no granulosa layer.
- (9) Some venous sinusoid of follicular wall contain small lymphoid elemnts only.

This type of venous sinusoid shows transition, on one hand, from the venous sinusoid which contains arythrocytes, and, on the other hand, into the connective tissue layer, from which further shows evidences of de-differentiation into yolk substance. (Figs. 7, 34) (10) The degeneration of granulosa cells is a most common thing, on the contrary, there is no evidence of their mitotic or amitotic proliferation. (Figs. 7, 10, 11)

- (11) Yolk spheres lying immediately under the granulosa layer are relatively small in size but they increase in size and staining ability with cosin, as they get away from the granulosa layer by the condensation of cloudy yolk substance. So that yolk spheres are formed. Therefore, the mechanism of the formation of yolk spheres seems to be a concervation process. (Figs. 7, 51)
- (12) The region of stigma of the matured follicle contains very few capillaries. This, probably, is due to the physical pressure of yolk substance on that area.

#### (III) Results of Carbon Injection

Five laying hens were subjected to single intravenous injections (into the wing vein) of colloidal carbon. From this experiment it was revealed that the carbon particles were rapidly (after 24 hours) removed from the circulating blood. The most active sites of the de position of carbon particles was liver and spleen.

Histological examination of the transverse section of the follicle walls after 24 hours of a single injection showed that the carbon particles were deposited, and scattered here and there mainly on the surface of the follicular walls, and some others were ingested in the se-called macrophages (Figs.10,11) However, such a typical macrophage can not be seen in a normal condition, so that it seems probable that these macrophages are only a derivatives from fused blood cells (with the adsorbed carbon particles) which have activated its phagocytic activity by foreign colloidal carbon and by physiological stagnation of blood current.

In the small sized follicles, the carbon particles were found even in the inner vascular layer, sometimes, a small amount of carbon particles was found in the blood flowed into the follicular cavity.

Examination of the wall of a large follicle after 72 hours of a single injection showed that the carbon particles were found, mainly, on the inner vascular layer, and on the granulosa layer.

However, in a small amount, of carbon was found on the outer most layer of follicle well and on the surface of yolk, (Figs 12, 13)

It is of interest, that the masses of carbon particles which were found in the follicular wall of the hen which had received a single injection of colloidal carbon 72 hours before were larger in size than those of the hen which had been injected 24 hours before.

In the former case the blood cells mingled with carbon particles showed the sign of de-differentiation into yolk substance.

No evidence of passing out of carbon particles through blood vessel walls could be seen. On the contrary, there were many evidences that the injected carbon particles were scattered about in the interstices of follicle walls or follicular cavities through the degeneration of the wall of venous sinusoids or through the open ends of capillaries together with the blood contained in it.

From the above described facts, it may be interpreted that the blood cells (mainly crythrocytes) begin to degenerate into yolk material in the course of about 3-4 days in laving hens.

#### (IV) Re-differentiation from yolk spheres into erythrocytes in chick embryo.

Recently, I have learned that Lepeshinskaya ('37-'50, quoted by Kusano, '51) has already published papers on the new formation of erythrocytes from yolk material in a chick embryo.

My work presented here, however, is carried out independently of Lepeshinshaye's work, and deals with a wider range (viz. reversible differentiation between crythrocytes and yolk material.) than her works.

From observations on the stained sections of the blood island of chick embryos at 48 hours incubation, the writer found that the erythroblasts may arise from yolk material through the following three possible modes; the first mode, is the concervation of very minute yolk apheres.

The yolk material is composed of yolk spheres varying in size from  $1\mu$  to  $40\mu$  or more. The faint basophile substance appears at first in the yolk material by condensation (fusion) and concervation of the minute yolk particles. These basophile substances show a somewhat cloudy, mottled appearance in the early stage, and then they are transformed into triangular or cup-shaped, light stained nuclei which often adhere on one side of large yolk spheres. These elements correspond to the so-called "periblast nuclei" of Lillie ('18,) and they show, further, transitions into explicit through its rounding up process. (Fig.  $13-p_1-p_5$ ) From the observation on the tissue culture of yolk and blood island, the writer found that the so-called periblast nucleus shows neither the evidence of a self-moving capacity, nor its own mitotic proliferation. Therefore, we can not escape from the conclusion that the so-called periblast nuclei from which erythroblasts may be arosed in loco by means of coacervation of minute yolk particles.

The second mode, is the formation of crythroblast from large yolk spheres. After the appearance of "periblast nuclei" a large yolk sphere decreases its staining capacity with cosin, then the spheres give rise to several small yolk spheres and a cloudy neutrophilic substance through a sporulation-like process and liquefaction of it. In this monera-like substance then appears some faint basophilic substance, of which some are fine strands and others are granular in shape. The basophilic matter subsequently forms meshes surrounding the clear spaces which often contain the mottled neutrophilic substance (derivative of yolk sphere) or yolk spheres. As the basophilic substance increase in amount the mesh and basophilic granules condense into several number of angular, nuclei with spicules or fine strands on their surface. This nuclear element undoubtedly corresponds to the so-called mesenchyme cell, but the writer defines it as "mesenchyme cell-A" to ditinguish it from "mesenchyme cell-B" which is a derivative of erythrocytes and found in an embryonic body.

These angular shaped nuclei then are transformed into typical crythroblasts with thin, light basephilic cytoplasm through their rounding up process. (Figs. 13, a-f)

Mesenchyme cell-A situated on the surface of the mass of crythroblasts becomes to the so-called endothelial cells due, probably, to the mechanical tension. The blood island formed by this mode is not necessarily covered in all its surface with endothelial cells. On the contrary, it often shows a continuance of underlying yolk material.

The third mode, is the sporulation or segmentation of the yolk sphere. This mode was found on the sections of the blastoderm of hen's egg after 6 days or upward of incubation. In each large yolk sphere (about 20-10 $\mu$  or more in diameter) lying adjacent to the blood island there arise, at first, several numbers of small cosmophilic yolk spheres which are almost equal in size and shape to crythroblasts. These small yolk spheres then are scattered by the liquefaction of the wall of the large yolk sphere.

Inner part or on the outer surface of these small yolk spheres, then, arise minute, basophilic granules, and they increase in number and size, and at last show transition into a spherical, deep basophilic nucleus of a mammalian normoblast-like cell. The mass of the elements of this type may be reserved to a primordium of blood island, because it is located in a closely adjacent and homologous position to blood island, and furthermore there is apparent transitions between the erythroblasts in blood island and the elements of this mass.

Above mentioned three modes of new formation of crythroblasts from yolk-material can be observed in the blastoderm of incubating eggs ranging from 2 to 21 days. Some crythroblasts in the blood island even show mitotic figures (mitotic index is about 5 % in average) yet the mesenchyme cells, the precursor of crythroblast, show no sign of their mitotic proliferation. From these facts we can not escape from the conclusion that crythroblasts are derived from yolk sphere in situ. This phenomenon is strange, yet it is a fact. As to the detail of this matter, the writer will publish in another paper.

 (V) Differentiation from arythrocytes into ovarian elements and yolk material in rabbit,

From the studies of serial sections of normal adult rabbits it was revealed that the erythrocytes in ovaries, also, show every transitions into all elements of the follicule and from which, further, the follicular liquid (which corresponds with avian yolk material) is derived. However, the manner of differentiation of non-nucleated crythrocytes in rabbits and other manners markedly differs from that of nucleated crythrocytes of chickens and other lower vertebrates. That is to say, the rabbit's crythrocytes in the vein, ve-

uous sinusoid or in interstices of ovarian follicles, at first, aggregate and fuse together with each other and produce an eosinophilic homogeneous mass, the monera-like substance. Most probably, it has been referred to as an artefact derived from crythrocyte-hemolysis. However, there is certain evidence that this did not originate in a technical error, since on the same field of a preparation some crythrocytes contained in arteries of peripheral region of ovary still retain their untouched normal features. From this fact formation of the monera-like mass of crythrocytes is thought to be conditioned by cellular circumstances and the time factor. (Figs. 2, 16, 17, 18, 23, 36) In these monera-like masses, then, there appear several numbers of vacuole-like, clear, round spheres, accompanied with decreasing of staining ability (loss of hemoglobin) of the mass. These vacuoles subsequently acquire intensive basophilic staining capacity and become a mass of small lymphold elements. (Figs 23, 36, 37) Such phenomena were also observed by the writer on living crythrocytes cultured with liver cells in rabbit.

In general, the behavior of crythracytes in vertebrates, show four characteristic behaviour, namely (i) Thigmotaxis, the tendency to adhere to the surface of other material, (ii) Aggregation, (iii) Fusion with others, (iv) Coacervation, arising of new cells from a fused mass of crythrocytes. The writer designates, in short, these four stages, as the "TAFC or AFD phenomenon of crythrocytes."

The aggregated lymphoid elements, so-called lymphoid tissue, in the follicle wall or in ovarian stroma always show transitions from erythrocytic monora-like substances through a "TAFC phenomenon". (Figs. 14, 16, 18, 24, 25, 37)

Pibroblast or connective tissue cells, usually, located on the surface of ovary or ovarian follicle, or in ovarian stroma at where, they may receive mechanical pressure from surrounding tissues. (Fig. 36) In these sites connective tissue cells clearly show transitions from lymphoid elements resulting from the "TAFC phenomenon of crythrocytes."

It is a most common thing that in many parts of the ovarian tissue, there are spindle-shaped fibroblast or lymphoid elements with eosinophilic cytoplasm. It is no doubt, a stage of TAFC phenomena. It is a very important fact, that notwithstanding the ovary shows rapid growth and contains immense numbers of degenerating cells, mitotic figure of the ovarian elements can hardly be seen.

At the periphery of the ovary of an adult rabbit there are clear transitions from erythrocytic monera into an ovum or into a primordial follicle. A primary follicle surrounded by extravasated (free) erythrocytes and connective tissue elements is composed of vascular layer, granulosa layer and of follicular liquid. (Figs. 14-25, 35-37) And there can be seen every transition among these elements. In the theca of rabbit's follicle, there are large, clear somewhat polyhedral-shaped cells which often contain one or more small lymphoid elements or even some erythrocytes. (Fig. 20)

This type of cell shows transition from a mass of several erythrocytes contained in venous sinusoid or interstice of the follicular wall. The modes of the growth of follicle in rabbit does not differ. In principle, from that in chick, but the second mode of growth found in chick could not be observed in rabbit.

A tabbit's follicle more frequently includes the accessory small follicle within it

which contains larger numbers of small lymphoid cells or lymphoid follicle cells than that of hen. This difference is probably due to the slower differentation of erythrocytes in the rabbit overy than in that of the hen.

From the above mentioned fact, it appears quite certain that in a rabbit's ovary the ovum, follicular liquid (homologous with avain yolk material), granulosa cell and all other ovarian elements also are the resultants of the "TAFC phenomena of crythrocytes,"

#### DISCUSSION

It is generally agreed that the erythrocytes are such highly differentiated cells functioning only as of carriers of oxygen and carbon dioxide, that they degenerate in spicen or liver within about 14 to 127 days of their life span, and in mammals the erythrocytes lose the nucleus during maturation, but in all lower vertebrates they retain the nucleus. It is also a common opinion that erythrocytes in adult animals arise from the hemocytoblasts in red bone marrow through the miltotic proliferation and maturation of it.

It seems very strange to me, however, that such an orthodox view (as to the origin and fate of crythrocytes) although it involves disagreement with many facts, yet has been supported by many hematologists and biologists.

There is no one, so far as I am aware, who has pointed out (i) the differential capacity of etythrocytes, (ii) reversible differential capacity between etythrocytes and the ovarian elements.

If one would observe thoroughly the behaviour of the living blood cells in vivo or in vitro, and would try to reexamine the stained preparations from a dynamic point of view perfectly free from orthodox, he will find that my view, even if it appears very curlous, is neverthless based on fact.

Recently Weiss ('50) has published an unique opinon regarding the differential capa city of the "germ cell" into four main directions. I agree with him, and I think his "germ cell" really corresponds to blood cell. He also said, "we must form the babit, for instance, of viewing the shape of a given cell, tissue or organ not as a static feature, but as a phase, trasitory or terminal, in a continuous chain of transformations." His idea, I believe, is quite correct. If this idea were perfectly understood, it would not be surprising to find that the growth of ovarian follicle and the accumulation of yolk material are at the expense of other cells, as I have mentioned above.

However, at the present time, it is a generally accepted view that; (1) cell proliferation depends entirely upon their mitosis or amitosis, (2) the growth of a given cell includinging ovum is due to the absorption of putrient materials through the cell wall, (3) crythrocytes are the most highly differentiated cells with no differential potency. However, if these dectorines were pursued thoughtfully to their ultimate end and were compared faithfully with the facts, one would find that these orthdox views conflict with facts in many important points. It goes without saying that the fact is first and doctorine second.

There are the following four theories regarding the mechanism of yolk formation;

- The deutoplamic granules are brought to be laid by chromidial material extruded from the nucleus. (Hertwig)
- (2) The lipoids of yolk pass bodily into the cell by secretion from the Graafian follicle, especially from the corona radiata.
- (3) Formation of yolk by mitochondria (Monterosso '15, Russo '12 quoted by Corne '26; van der Stright '23)
- (4) However, the most widely accepted opinion, that is the yolk forming substances which may be in fluid state, are transported into ovum through the canalicular projection of the nurse cells. (Lillie '18, Brambel '30, Wilson '25 Wotton and Village '51)

These four theories may be true in part, but I think, that they can not explain perfectly the extraordinarily rapid accumulation of yolk substance, especially in chick's overy,

Riddle ('11) has studied the formation, significance and chemistry of the white and yellow yolk of ova, by means of Sudam III feeding, and has shown that the yellow yolk was formed during the longer period of high blood pressure, and the white yolk during the briefer nocturnal period of low pressure, but he does not show any evidence as to the mechanism of the transportation of yolk materials into the ovum.

My coinion regarding the followist growth by means of the third mode (additional deposition of yolk by the transition of the follow wall elements) is supported by the numerical coincidences between the eight to nine concentric layers of white and yellow yolk (Chishima '31) and the days (about nine days) during when the most part of the yolk is accumulated.

Nolvandov and James ('49) say, "It is highly improbable that any transfer of yolk building materials can occur from the middle venous layer, both because of its distrace from the selectively permeable membrane of the ovum and the follicle and because of the thickness of the walls of its venous vessels." This opinion is most probably correct. Moreover, the writer could not find any clearly defined vitelline membrane on the surface of the growing follicle in laying bens and rabbits.

The so-called canalicular projection of the nurse cell in mammallian follicle very probably corresponds to the de-differentiated product of the blood cells contained in the open type capillary of the inner vascular layer of the follicle wall.

Wigglesworth ('48) said. "the essential continuity of the organism is independent of the cells, but deputs on a chemical continuity." I agree with him in this respect. Mossman and lise Judas ('49) stated "The fundamental importance of the concept of the essentially embryonic pluripotential nature of both ovarian epithelium and stroma in deviation and transformation of various ovarian elements, and in the regenerative ovary these capacities is stressed." The "pluripotential and embryonic elements in ovary" considered by them, undoubtedly, correspond to my "lymphoid (mesenchymal) elements

derived from erythrocytic masses through "TAFC phenomena." The writer's conceptions, further, are supported by following data of the excellent authors, though they are earlier investigators. Balfour ('78) and, Bereden and Jullis (quoted by Marshall '22) stated, "embryonic ovum may develop at the cost of others". Miss Lane-Claypon (quoted by Marshall '22) also says, "this cannibalism on the part of the young ovarium is not surprising, if the cell at all its stages of development grows and fattens at the expense of other cells. In the young ovaries, it is starting the first stage of growth and must devours other cells; later on, during the growth of the follicle, it lives upon the follicle cells."

It is a strange thing that despite the fact presented by these authors who had already published the unique conceptions, it has been neglected or discarded by most investigators until the present day. However, I received from Prof. George an important paper (George '39) dealing with the blood of the Ascidisms. In that paper, he says, "sections give histological support for the view that a large proportion of blood-cells serves as mutritive cells or nurse cells for the tissues" "It seems probably correct to look upon the hyaline vacuolated cell of the blood, and doubtless the green cell type, as essentially comparable to follicle cells around the eggs and test cells embeded in the substance of e.cs". Gailard ('50) emphasized the ultimate and significant histologic interrelationships of derivatives of the germinal epithelium, egg cells and the first layer of follicles in human ovary. (Quoted by Dawson and McCabe '51). Dawson and McCabe ('51) described that the ovarian interstitial cells may be derived from granulosa cells may be derived from interstitial cells (lymphoid elements).

Ruth McCium; Jones ('49) has bentifuly demonstrated the rat ova of which cytoplasm contained various amount of the injected carbon particles. Unfortunately she looked upon it as an artifact, but it seems to that the contaminated ovum may have arisen through a "TAFC" phenomena of crythrocytes mixed with injected carbon. Shemin and Rittenberg ('46) (quoted by Ashby '48) concluded, that the life span of the human red cells is about 127 days. But this conclusion is based on the indirect method using isotope N<sup>15</sup>, therefore, the actual manner of the destuction of erythrocyes has not yet been demonstrated.

My observations on the sections of liver (Chishima '51) or ovaries of hem and rabhits (present work) which were stained vitally with colloidal carbon revealed that the elements of liver or ovary showed the evidence of transitions from crythrocytes through the "TAFC Phenomenan". Then, a question may arise as to whether the derivatives from crythrocytes contain iron or not. It is already a recognized fact that the reaction of iron contained in red cells or in fixed cells is so labile and variable that the existence of so-called "masked iron" (Bensley and Bensley '38, quoted by Wimsatt '49') is known. It is also known that the so-called hemophages in liver and spleen contain iron but then they becomes Iron free cells.

Wislocki and Wimsatt ('47) found that the epithelium of the yolk sac of bat contained hemosiderin which has shown iron reaction to turnblue. It is also generally accepted that the yolk of hen's egg contains iron though a lesser amount than that of crythrocyte. It is not surprising that the level of iron content in the derivatives of crythrocytes is lower than that of crythrocytes, because iron contained in crythrocytes probably can be freed from it and be transferred into blood scrum or tissue fluid during their "TAFC phenomena".

Hartroft ('51) observed the existence of orange-brown pigment in cirrhotic liver of rat fed with colin deficient food, and he considered this pigment an antecendent sign of fatty formation. The present writer has also often observed the orange-brown pigment, resembling that described by Hartroft, in ovarian stroma and in follicular walls in heathy, laying hers. Furthermore, this pigment was located in the region at where the follicular elements are undergoing change to the yolk material.

From these facts, too, there is no denying the differential and de-differential possibility from erythrocytes into the lipoidal yolk material. And, furthermore, the possibility of the reversible differentiation between crythrocyte and yolk sphere can not be denied. This fact is of great importance, even though it has not yet been noticed by any other investigator.

#### SUMMARY AND CONCLUSION

- (1) New observations are here presented concerning the follicle growth and the yolk formation in the ovaries of chick, hen and rabbit. Emphasize has been placed on the following accounts that have not yet been described or have been misinterpreted: (1) erythrocytes differentiate into ovarian elements which then de-differentiate into yolk material, (ii) erythrocytes in blood island of chick embryo arise spontaneously as a resultant of the re-differentiatiation of yolk material, (iii) the growth of ovary or ovarian follicle is not due, exclusively, to the mitotic proliferation of the proexisted ovarian elements as has been generally accepted.
- (2) Vascular systems of the growing and mature follicle walls in laying hens showed the following characteristics; (i) strikingly disproportional development of venous system to arterial system, (ii) blood stream of venous system shows significantly the sign of physiological stagnation or stoppage, and the blood cells included in it often show transition into yolk material through lymphoid or mesenchymal stage (iii) open type vascular system can be seen commonly, and the extravascular crythrocytes also show transitions into yolk material.
- (3) Ovum and primary folicles in chick and rabbit show transitions from an aggregated and fused mass of lymphoid or mesonchymal elements which further show transitions from crythrocytes.
- (4) Three possible modes of follicle growth in chickens and hens are recognized. First, the fusion of small follicles into one. Second, de-differentiation from elements of the

follicle wall, (including blood cells, vessel wall, connective tissue cells and granulosa cells etc.) into yolk materials. Third, yolk formation from blood and blood cells poured directly into follicular cavity through the open end of cappilary, but this mode is rather less important than the former two modes.

(5) The mode of growth of the ovarian follicle in adult rabbits is the same, in essential points, as that of hens. But the differential process of erythrocytes in the rabbit differs from that of the hen. In chick and hen an erythrocyte differentiates, at first, into a small lymphoid element and then it is transformed further, into all kinds of ovarian elements, and at last, into yolk material. While a non-nucleated erythrocyte of rabbit is not transformed directly into a small lymphoid element, but through "the AFD phenomenon of erythrocytes". That is to say, several numbers of erythrocytes come together and fuse into a homogeneous, eosinophillic, monera-like sudstance. In this mass, then, sppear several vacuoles. Accompanying the decrease in eosinophillic staining capacity of the mass, these vacuoles acquire basophilic staining capacity and at last they become lymphoid or mesonchymal elements.

Subsequent behaviour of these lymphoid elements in rabbit's ovary is the same as that of hen,

- (6) Mitotic figures of the ovarian elements in chick, hen and rabbit are so extremely sare that the mitotic proliferation of ovarian elements can not be considered as a main factor of the extraordinarily rapid growth of the ovary and its follicles. On the contrary, there are sufficient evidences that the ovarian follicle may grow at the cost of all kinds of the ovarian elements derived from erythrocytes.
- (7) Erythrocytes in blood island of chick embryo have newly arisen from yolk material through re-differentiation process, the concervation of yolk material, but not by means of mitosis nor amitosis. Consequently, the possibility of the reversal differentiation between crythrocyte and yolk sphere can be concluded.
- (8) The origin and the fate of erythrocytes in ovary are discussed.

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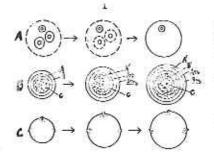
Acknowledgment also due Prof. T. Yamada and S. Goto for affording every facili-

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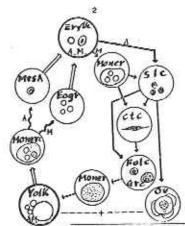


Fig. 1 Schemate illustration of the three modes of the growth of the ovarian follicles in laying hon.

- A. The first mode. Several primary follicles fuse into one.
- The Second mote. Additional growth cit follicle by means of the de-differentiation from all elements of follicle wall into yolk material.
- C, The third mode, overflowing of the blood into the follicular cavity through the open ends of the capillaries of follicle wall. And transformation from that blood and blood cells into the yolk material.

A "granulosa layer; B, "theca and vascular layer of foilicle; C, ovum and yolk material; A' newly formed layer of yolk derived from do-differentiated A (granulosa layer),; B', newly formed layer of yolk derived from B layer; At; Newly formed granulosa layer which is derived from the differentiated B layer (theca and its vascular system); An, newly formed granulosa layer from differentiated Bn layer; Bn, newly formed layer (theca and its vascular system).

Fig. 2 Schematic Illustration of the reversniple differentiation between yolk material and enythrocytes.

-->...Differentiation. --->...De-Differentiation. -->...Re-Differentiation. ------Coaccevation.

A. aves: AM. aves and mammal: ctc. connective tissue cell: Eogr. Posinophilic granules or spheres (Proerythrocyte stage) in rabbit: Eryth, Prythrocyte: Pole, follicle cell: Grn, Gronulosa cell: M. mammal: MesA, Mesenchyme cell A: Moner, Monera-like substance: Monere, Monera-like substance in which vacuoles emerged through coacervatio process of it. Ov. ovum: Yolk, yolk sheres and yolk material.

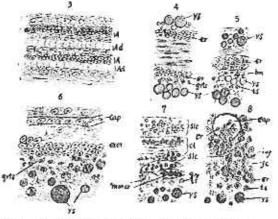


Fig. 8 An artery on the expansion preparation spreads of a follicle wall of laying hen-showing two arterioles (Λ) and, two degenerating remnants of arterioles (Λd; are contained in it.

Fig. 4 Transverse section of the wall of a large follicle in a laying hea-

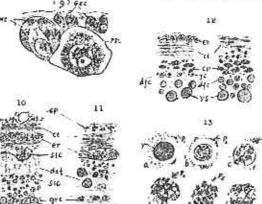
Fig. 5 Same other continual region with that of the Fig. 4. Showing the erythrocytic layer (Fig. 4) Joining with the yolk layer (Fig. 5), and the connective tissue thesa

of the Fig. 4 is joined with venous sinusold of the Fig. 5.

Fig. 6 The same material from the Fig. 5. Showing the transition from extravascular crythrocytes into yolk spheres.

Fig. 7 Transverse section of the wall of a mature follicle in a laying hen, to show the transitions from crythrocytes contained in the veneus sinusoids into yolk spheres through transitional phases, small lymphoid, connective tissue monera-like substance and into grammers cell stages.

Fig. 8 Transverse section of small follicle wall in laying hen, showing overflowing of crythrocytes from the open end of a vessel into follicle cavity, and showing the transitions from 197 fee crythrocytes into yelk spheres.



A artery; Ad. degenerating remnant of arteriole; bm. so-called basement membrane; eap, capillary; Ct connective tissue layer; er, erythrocytes exer, extravasated erythrocytes; fc, so-called follicle cell, the homologue with granulosa cell; grfs, transitional phase from granulosa cell into yolk material; iwf, inner most wall of follicle; moner, monera-like substance derived from de-differentiation of granulosa cells; Ys. Yolk sphere,

Fig. 9 Germinal epithelium of a chick embryo at 6 day of incubation, showing the so-called primordial germ cell (p. g. c) whick grows and fattens at the expense of mesenchymal elements (MC) which is homologue of germinal epithelial cell (GEC).

Fig. 10 Transverse section of a large follicle in a laying hen which had received a single injection of colloidal carbon and was sacrificed 24 hours after the injection, showing the injected carbon located on the surface of the follicle wall.

Fig. 11 Another continuous region of the same preparation of Fig. 10.

Fig. 12 Transverse section of a large follicle in a laying hen which had received a single injection of colloidal carbon and was sacrificed 72 hours after the injection. Notice the size and localization of the masses of carbon particles. Abbreviation of Figs. I-12 Cp' carbon particles; det, degenerating connective tissue; dec degenerating follicle cell; to, follicle cell; gr, granulosa cell; s i c small imphoid clement; Ys, yolk sphere.

ig. 13 R-differentiation-phases from yolk sphere (y) into erythroblasts (f) through intermediate phases (b. c. d and c). b. transition from yolk sphere into monera-like substance; c-d, monera-like substance in which arose vacuale-like body; e, mesenchyme cell stage; f<sub>L</sub> etythroblast arose from the vacuale-like dody. Y, yolk sphere; P<sub>0</sub> primordium of "Periblast nucleus; P<sub>2</sub> and P<sub>3</sub> Periblasts, P<sub>4</sub> mesenchyme cell-A; P<sub>5</sub>, erythroblast.

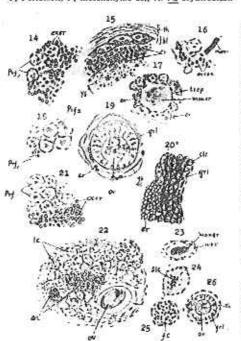


Fig. 14-26 Ovarian follicles in adult rabbits. Abbreviation of the Figs. 14-26 ib, vascular layer; ctc, connective tissue: er, erythrocytes ercoa, mesenchymal elements arised from crythrocyte monera through concervation; exer, extravascular erythrocytes; fc. follicle celli gri, granulosa layer; lc, lutein cell-like clear cellimoner, monera libe pristance; Ov. evenus Prin primary follicle; Prin advanced stage of primary follicle; slc, small lymphoid element; th, theca; tsep, transitional stage of vessel walli wby, wall of blood vessel: Ys, yolk sphere.

Fig. 14 Part of overian stroms, showing the existence of extravascular crythrocytes (exer) and the transition from crythrocytes' mass into primordial follicle.

Fig. 15 Transverse section of the follicle wall, showing (i) the existence of extravascular erythrocytes, (ii) Erythrocytes and erythrocyte-monera contained in vascular system, and transitions from these elements into yolk material.

Fig. 16 Part of follicle wall, showing the transformation of the monera-like substance and primordial follicle from the mass of aggregated crythrocytes.

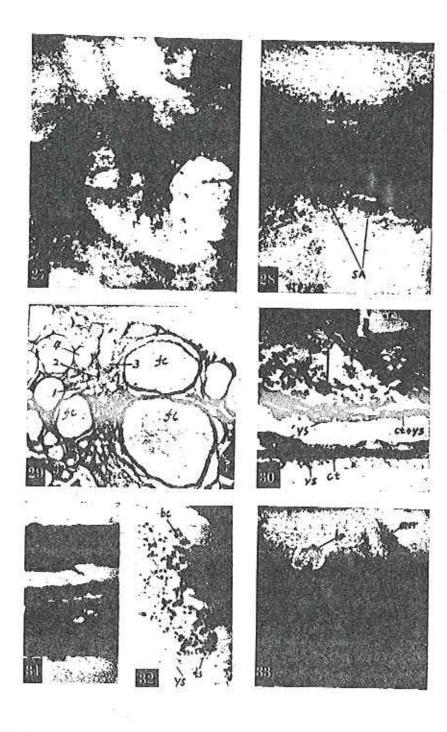
- Fig. 17 Transformation from stagnated blood vessel with its contents, into primary follicle showing the monora-like substance (a derivative of aggregated crythrocytes contained in blood vessel) and the vessel wall elements being transformed into granulosa layer.
- Fig. 18 Part of follicle wall, showing transitions from erythrocytes mass into primordial follicles.
- Fig. 19 A primary follicle, showing an ovum containing many of degenerating follicle cells, and showing the transition from the thecal element into the granulosa layer.
- Fig. 20 Clear cells in the follicle wall, these elements show transition, on the one hand from crythrocytes mass and, on the other hand, into the elements of glanulosa layer.
  - Fig. 21 The same as fig. 14.
- Fig. 22 An atresia follicle containing many clear cells which also show transition from the mass of several crythrocytes. An ovum included in this follicle shows its resemblance to a stagnated and degenerating blood vessels.
- Fig. 23-26. A series of transitional phases from stagnated blood vessels containing the orythrocyte-monera, (fig. 20) into a primary follicle (fig. 20).
- Fig. 27 Expansion preparation secured from a mature follicle in a laying hon, showing almost all of the follicle surface covered with flattened vascular system.
- Fig. 28 A large artery found on the same preparation as fig. 27. It contains several of small arteries (SA), and an degenerating aftery (dA), which contains no blood cells.
- Fig. 29 Peripheral portion of the ovary of young chick of 2 months old, showing transitions from a most of blood cells (1) into the somewhat large fellicle (fc) through the successive stages (1, 4 and 4) of most of small prime dial collicies.
- Fig. 30 Portion of a large follicle wall in a laying hear showing the transitional phases from connective tissue layer (ct) and from vascular layer including blood cells (vsd.) into yolk sphere (Ys). There can be seen clear evidence that the erythrocytes and yolk spheres are mingled with each other and show transitions between these two elements, (Ys + er).
- Fig. 31 Transverse section of a mature follicle of laying hen, showing that there is no clear distinction among so-called outer, middle, and inner vascular layers. On the contrary, it is rather continuous.
- Fig. 32 Section of a small follicle cavity in a laying heat showing the erythrocytes (bc) which flowed out are being transformed into yolk sphere (ys) through the fusion and de-differentiation stage (ts) of erythrocytes.
- Fig. 33 Transverse section of a small follicle from the same material as fig. 32, showing the existence of blood vessels (bv), the extravascular erythrocytes (exer), the blood flowing into follicle cavity (fole) through open end of a capillary and the transition from poured blood cells into the so-called degenerating follicle cells (dfc).
- Fig. 34 Transverse section of a mature follicle of laying hen showing the transformation from somewhat flattened venous sinusoid (vs) into degenerating venous sinusoid (dvs), (ii) the inner vascular layer (icl) also begin to de-differentiate into yolk material from its inner surface, and (iii) the stratified pattern of periphery of yolk (ysi) which, most probably, has arisen from the de differentiation of previous vascular layer.
- Pig. 35 Peripheral part of ovary of an adult rabbit, showing the transition from aggregated small lymphocytoid elements (1) derived from crythrocyte monera into primordial follicle (2), two small follicles are about to fuse into one and the follicle wall is at a stage undergoing to

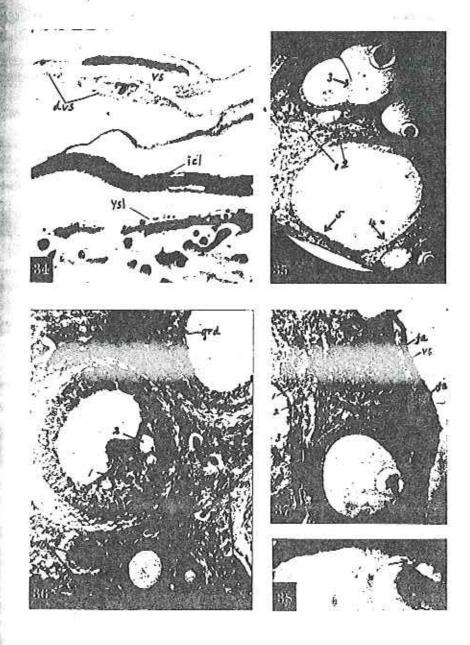
degeneration (3). And showing the granulosa cells at different stages in their development, via, degenerating stage (4) and lymphocytoid stage (5).

Fig. 36 Section of ovary of an adult rabbit, showing the transition from a mass of folicle cells (1) into a follicle ilquid (2); and showing the degenerating granulosa cells (grd); stagnated and degenerating blood vessels (bvm) containing crythrocytes monera-like substance; and a somewhat larger one(bvd) also contains two degenerating blood vessels which show transition into primary follicle.

Fig. 37 Peripheral part of every of an adult rabbit showing the transitions from a mass of lymphoid elements (1) contained in venous sinusoid into primordial follicle (3) through intermediate stage (2), and the transition from the elements of venous sinusoid (vs) into primordium of follicle (fa).

Fig. 38 A region of fig. 37 is presented under higher magnifying power. It shows the degenerating phase of granulosa cells into follicle liquid material.





(3) Reversible Differentiation between the Erythrocytes and the Bone Marrow Elements Under the Normal or Starved Conditions By. K. Chishima. (Okajimas Folia Anatomica Japonica, Anatomisches Inst. der Keio Univ. Tokyo, Japan. Band 25, Heft 3. Sept. 1953. pp. 119~148) See this volume, Part V.

#### (B) Monograph

- (1) Reexamination of the intramedullary hemopoietic theory. —A theory of the reversible differentiation between the blood cells and the bone marrow elements—(In Japanese with English résumé) pp. 1~133. By K. Chishima(Pub, Igakushoin. Tokyo, 1954) See volume 4 of this series books.
- (C) Abstracts from the papers in Japanese with English résumé.
- (1) Reversible Differentiation between the Hepatic Cells and the Blood Cells under the Well-fed or the Starved Conditions. (in Japanese with English résumé 15 microphotographs). Research Bull. Facult. Gifu Univ. no. 5. pp. 203~214, 1955.

#### Résumé

The behaviour of the hepatic cells during the growth or the de-growth of liver in mammals (rabbits, goats, cats, and dogs), birds(chickens) and amphibia (frogs) under well-fed or starved conditions were studied by means of comparative examination of serial sections(H. E. staining) of normal and treated livers (intravenous injection of colloidal carbon). The result obtained can be summarized as follows:—

- (1) The surface of the venous sinusoid of the liver is, if any, not invariably covered with endothelial cells. So that hapatic cell often contacts directly with erythrocytes. Therefore, it can be said that the capillary system of liver is rather an open type.
- (2) It was found in the venous sinusoid, that the erythrocytes under the well-fed conditions show transitions into hepatic cells. The differential process in the bird is as follows; erythrocyte → small lymphocyte → endothelial cell or Kup-

ffer cell → young hepatic cell → hepatic cell, while, in mammals, an aggregated mass composed from several or more of erythrocytes → an eosinophilic fused-mass of crythrocytes (monera-like substance), but it then acquires polychromatic staining ability → small lymphoid nuclei, poly or polymorph nuclei or the so-called macrophage (hemophage) phagocytosed the erythrocytes arise spontaneously in the mass → transform into young hepatic cell or cells according to the size of the mass → hepatic cell or cells.

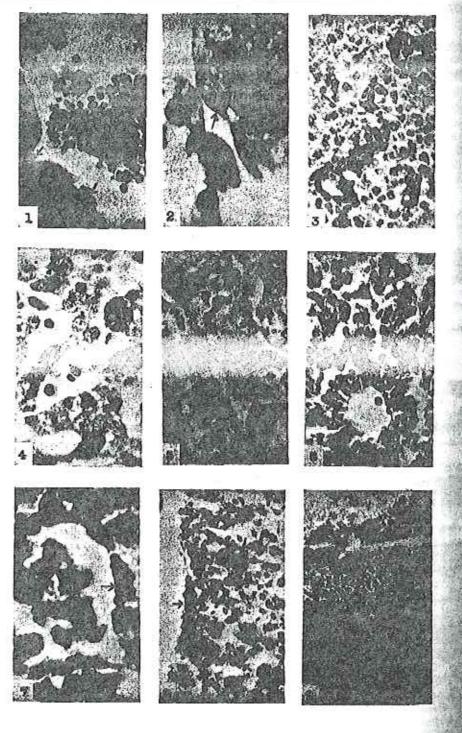
- (3) The blood cell-cords localized in the interstices of the hepatic cords often show transitions into hepatic cords through the same way as described above. Such differentiation of crythrocytes may start, most probably, by the physiological stagnation or stoppage of the blood current within the venous sinusoid. Evidences favouring the view also were obtained by, i) experimental results of intravenous injection of colloidal car bon, ii) cell culture of hepatic cells mixed with crythrocytes, and by iii) centripetal pattern of hepatic cords toward the central vein.
- (4) The large syncytial macrophage seems to be a reaction type of the blood cells to the irritative foreign substance (carbon), and the macrophage stored carbon particles does not show normal differentiation into hepatic call. Thus, after their degeneration, the released carbon particles aggregate together with others and become larger mass, and they remain in the hepatic parenchymo as long as four months or more.
- (5) 'There can hardly be seen the typical mitotic figure of hepatic cells in the postnatal liver. And the evidence favouring the previous worker's view that the growth of liver due mainly to i) increase in size of individual hepatic cell, or ii) increase in relative volume of interstitial tissue of liver have not confirmed.
- (6) It is a generally accepted opinion that the crythrocytes in the liver are often phagocytosed by hemophage (or macrophage), however, it may not be a true phagocytosis, but is only an intermediate differential stage from a fused blood cell-mass into hepatic cell or cells.
- (7) Melanin-like pigment resembling the so-called cerroid substance was often found in the liver elements of animals observed, especially in the frog. Such pigment-formation may be closely related both to the degeneration and redifferentiation of crythrocytes.
- (8) Under the starved or under-fed conditions, the liver decresses in size owing, in parts, to the degeneration and atrophy of the cells, and in the other parts to the decresse in number of blood cells which is, in my view, the ground substance of hepatic cell-formation. And under the same conditions, the bepatic cells show the following order of reverse transitions into erythrocytes; in mammals, increase in polychromatic staining capacity of cytoplasm of hepatic cell→normoblast→several or more of nonnucleated erythrocytes through budding and sporulation-like process; (in bird and amphibia) elongation of cell→spindle cell→nucleated erythrocyte.

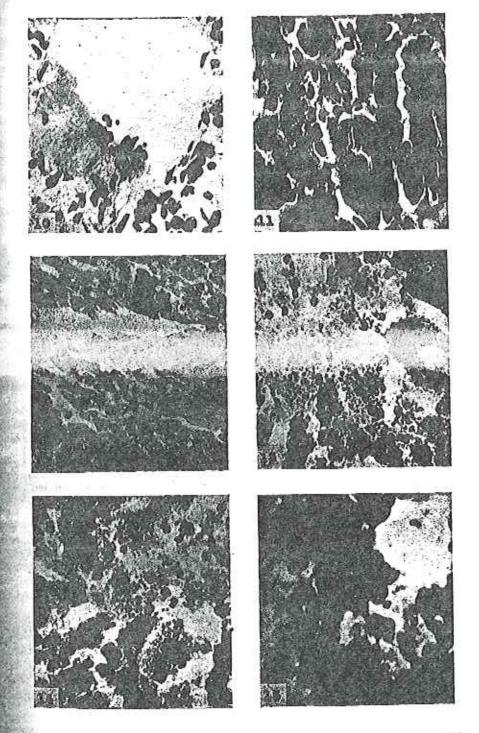
- (9) The view that the bile is secreted from hepatic cells is not valid. The results of present studies shows that the bile may be derived from the degenerated hepatic cells.
- (10) The so-called "crythropoicsis in the embryonic liver" is, most probably, a misinterpretation of the "differentiation from crythrocytes into hepatic cell (my view)". At the most early stage of liver formation in frog the hepatic cells arise from yolk sphere through mesenchymal stage.
- (11) The possibility of reversible differentiation between crythrocytes and cellular elements of the liver was discussed.

#### Explanation of figures

- A venous sinusoid of a chick embryo at 8 days of incubation, showing the adhering of erythrocytes to the surface of hepatic cells, and their transforming phase into hepatic cell. Erythrocytes adhered to the hepatic cells show the sign of transition into young hepatic cell (arrow). ×200
- High power magnification of a part of the same section of fig. 1, showing the transition from endothelial cell into hepatic cell. (arrow). ×2000
- Liver of a rabbit-embryo, showing the transitions from erythrocytes (dark staind) into, hepatic cells through small lymphoid cell stage. ×650
- Liver of a larvae (at 4 days after hatching) of Ross nigro meculate, showing transitions from yoth sphere (dark mass) into hepatic cell through measuredryme. x600
- Liver of an adult hen which received single intravenous injection of colloidal carbon and has killed after 1 hour the injection, showing the blood cells localized in the sinusoid were blackened by the carbon particles injected. ×600
- Liver of an adult hen which was sacrified after 24 hours the single injection of colloidal carbon. Notice the so-called macrophages are larger than that of fig. 5. x600
- Liver of a hen treated as the same manner as that of fig. 6, showing the existence of carbon laiden macrophage (arrow) within the wall of central vein. x2000
- Liver of a hen which was killed after 72 hours of single injection of colloidal carbon, showing the carbon laiden cells (arrow) exist in the hepatic cords and the wall of central vein.
- Liver of hen which was killed after 4 months of single injection of colloidal carbon, showing the existence of many of hugo carbon masses, especially at the periphery of blood vessel. ×200
- A bile duct of Rana nig. starved for 4 days, showing the bile (gray) contains an erythrocyte, several of small lymphoid elements and degenerating hepatic cells. x600
- Liver of a frog (Rosa nig.) starved for 10 days, showing the reverse differentiation from hepatic cells into crythrocytes through spindle cell-stage. Notice the large melanin pigment masses. ×600
- 12. The same material as the fig. 11, showing the clongation of hepatic cells. ×600
- Liver of a young goat under partial insultion, showing reverse differentiation from hepatic cells into erythrocytes. ×600
- 14. The same material as the fig. 13. ×600
- High power magnification of an area of fig. 13. ×1500

(2) Relation between the Origin of the Ovum and the Degenerating Differentiation of the Blood Cells in Amphibia (in English with 22 microphotographs) Research Bull, Facult, Agric, Gifu Univ., no. 7, pp. 205-211, 1956 (Omitted)





## PART III

THE THIRD PRINCIPLE: THE SPONT-ANEOUS GENERATION THEORY OF BA-CTERIA AND ITS PRACTICAL APPLIC-ATION TO EVERYDAY LIFE

## CHAP. I. ON THE ORIGIN OF LIFE

## (I) The Outline of the Third Principle

The following phrases have been considered as a steadfast truth in biology since Virchow, Pasteur, and Strasburger began to persist in them.; "Omnis cellula e cellula" "All cells from cells", "Omnis nuclei e nuclei ("All nuclei from nuclei ."All chromosomes from excomosomes, and All organisms from organisms".

It is needless to say that there is no child without the parents.

But in the case of the origin of life, it is illogical to discuss the highest organism, mankind, and the lowest microorganism on the same evolutinal level. However, almost all of the present-day biologists have been denying the spontaneous generation of life on the earth.

But such an opinion is contrary to the fundamental principles of the correct evolutionism. In spite of this logical contradiction, almost all of the modern hiologists have been believed blindly the Pasteur's theory since Pasteur won that famous controversy with Pouchet on it in 1859.

Even Oparin, who is well known for his studies on the origin of life, declared in 1947 and in 1955 that even a bacterium never generates itself spontaneously on the earth today. (The controversy between Oparin and this author will be described later.) In 1954 the present author published for the first time on the paper "A Contribution to the Spontaneous Generation Theory......On the Relationships between the New-formation of the Oöcyte or Metozoite of Chicken Coccidiosis and the Blood Cells" (See Research Bull. Agr. Gifu Univ. No. 3, 1954; and the more detailed description on this problems are included in "Basis of Neo-Biology vol. II. —On the origin of life, cell and blood corpuscle—pp. 105~140. Mebundo. Tokyo. 1958, This monograph is repulished in the first volume of K. Chishima's serial complete works)

This author reported in this paper the fact that the occyte or mebozoite of coccidium belonging to protozoa was derived from bacteria generated spontaneously in the intestinal content by the putrefaction of blood cells, and Protozoa were newly formed through the aggregation and fusion of these bacteria. This author added in it that when crythrocytes begin to putrefy, bacteria generate themselves spontaneously in the interior of crythrocytes, using protoplasm as a material, even though neither bacteria nor their spores invade the cells. Thereafter, this author published the book "Neo-Biology." The Origin of Life, Cells, and Blood Corpuscles (Vol. II), as a collection of the results of this author's studies on the spontaneous generation of bacteria, in white this author described that he had often surrounded in gentralize

bacteria spontaneously by using various materials and methods.

So far as this author knows, this is the first paper that has ever been published in Japan and at abroad against the orthodox theory since it was established by Pasteur.

Whether a bacterium generate itself spontaneously without the mother bacterium, or the spore, or not, has been not only the central problem of life from the time of ancient Greece, is but also the most important problem related to the prevention against and the therapy for infectious diseases, and virus-diseases in medical science, and the putrefaction, preservation and utilization of food in dietetics.

Now, this author will describe the summaries of controversics from ancient times on the possibility of the spontaneous generation of life, criticize them, and explain the outline of the results of this author's studies on it. And also this author will suggest that we should set up a fundamental revolution against modern medical and biological sciences by applying the Spontaneous Generation Theory of bacteria or viruses to everyday life, or to prevention against infectious diseases, promotion of health, and the cures for various diseases.

- (II) The Controversies on the Spontaneous Generation

  Theory and Criticism on them
- (1) The history of the controveries on the spontaneous
  generation theory from ancient times

The controversies on the spontaneous generation theory originated in the religious or philosophical thought on the origin of life in ancient Egypt and Babylonia. And then in ancient Greece, Thales (640? 546? B.C.) who is called the forerunner of modern science, Anaximander (611? 547? B.C.), and Xenophanes (560? 480? B.C.), all thought that life is spontaneously generated, by chance, out of the mud of the sea bed by aid of heat, light, and it. Two handrat sears been Plate 427? 537? B.C. tablished its groundary and the spontaneous generation theory, but Anaximander and the others maintained the spontaneous generation theory, from an ideological point of view. And their theory have held its prominent position in the circle of philosophy from the Middle Ages to modern times.

In the meantime, it so happened in the Middle Ages that Needham, the English priest, who was in favour of the spontaneous generation theory, had disputed with Spallazani, the Italian priest, who was against it, on spontaneous generation, but Buffon (1707-1788), the French biologist, who sympathied and cooperated with Needham, advocated it positively.

In modern times, I. Kant (1724-1808) denied the spontaneous generation, but G. Hegel (1770-1831), F. Shelling (1775-1854), and I., Oken (1779-1851) were in favour of the spontaneous generation theory. It seems to me that, from a dynamic point of view, Hegel was superior to Kant in this point.

In 1809, in the beginning of the 19th century, J. Lamarck (1744-1829), the French biologist and forerunner of evolutionism, described exactly in his "Philosophie Zoologique" (Philosophy of Zoology) his supporting opinion of the spontaneous generation theory of life. He, who published his leading opinion

of evolutionism in organisms just fifty years earlier than C. Darwin (1809—1882), the famous English evolutionist, and naturalist, had foresight rather than Dawin, from his supporting opinion of the spontaneous generation theory of life. For despairing of searching for the origin of microorganisms eve if in the early stage of biology, Darwin began, in his evolutionism, with amoebae and bacteria, as a starting point. But on the contrary, Lamarck suggested the possibility of the spontaneous generation of life from his surpassing intuition.

Talking of modern times, most of the biological scientists believe right the opponents of it, such as Platon, Kant, Spallanzanie, and Pasteur (described later), different from this author.

But, as a matter to settle whether either opinion is true or not, this author will present here the summary of the results of his study on the Spontaneous Generation of bacteria. And before the description of the results of his study, this author will give a table of the history of the controversies on Spontaneous Generation and especially, the outline of the controversy between Pasteur and Pouchet on Spontaneous Generation, which may be called "an epoch-making

A Comparative Table of the Proponents and the Opponents of the Spontaneous Generation Theory of Life

Proponents	Opponents	Remarks
Ancient Greece		
Thales (640? -546? B. C.) Anaximander (611? -547? B. C.) Empedocles (490? -430? B. C.) Aristotle (384-322B. C.)	Plate (427 ? +347 ? B, C.)	The proponents in this time thought simply that bees and maggots are spontaneously generated out of the mud or a piece of meat. Indeed, this may not be true, but is continuous, and dynamic in a sense.  On the other hand, the opponents were ideological, and formal.

Middle Ages (5-15C.)		
R. Descartes (1596~1650)		The theory was pro- minent in the Middle Ages. In about 11C., they still thought that frogs and loaches are spon- taneously generated out of the mud, Their way of thinking was religi- ous, and metaphysical.
17~18C.		
J. Needham Buffon (1707 ~ 1788)	F. Redi (1620-1697) L. Spallanzani	It was not until about this time that the scientific researches started.  The controversy between Needham and Spaniantam is well known. It is said that the former was a pious priest, but the latter was a foxy minded man according to de Cruif's (1941) description.  Buffon was a prominent biologist. In about this time, the three German biologists, Schwan, Sehultz, and Dush, tried
		to prove the impossibi- lity of the Spontaneous generation through their

G. Hegel (1770~1831) F. Schelling (1775~1854) L. Oken (1770~1851)	1. Kant (17241808)	experiments, but failed in all, owing to the unknown causes.  Seeing the differences in opinion between these four philosophers, we can know that Hegel's dialectic is superior to Kant's philosophy so far as life is concerned.
19C.		
Pouchet (1859) It was Prof. Jolly (1859) of the Toulouse Univ., and Musset Ba- stian (1859) who agreed with Pouchet. C. Hernard  1815—1878) He was almost affir- mative, and wrote in his posthumous manuscripts that Pasteur saw only one phase of this sub- ject, and that no orga- nisms woulb exist with- out air. This is what gets at the kernel of a problem that the pre-	L. Pasteur (1822~1895)	In 1859 Pasteur won the epoch-making cont- roversy with Pouchet on this subject in the Academy of France.  The negative theory of this subject has been prominent in the cond- of biology since then.  In this time there were the Cosmozoa theory, and the Panspermia (Preyer, Richeter, Helmholz, and Arrehe- nius), but as these th- eories were lacking in their actual proof, they were obliged to make.
sentday biologists are not aware of.		

Turpin (1832)

He declared that organisms generate themselves out of the dying organisms,

M. Vervorn

(1863-1921)

J. D. Bernal (1954)

A. Oparin (1938)

earth today.

Blum (1953)

eur.

Bernal and Oparin

destart that as train-

.sm will be greatanedor

sly generated on the

Most of the present-

day bioscientists are

the followers of Past-

He affirmed the theory theoretically,

20C.

F. Engels (1820-1895)

He criticized in his "Natural Dialectic" that " offered west too fat in

the fact by this studie

ct, and did not prove why a transition from the dead to the living is absolutely impossible. K. Shiga (1923)

He said that he still had an idea that an organism may occur from an inanimate object, and that he had held this idea for forty years, but that of late, was delighted at the sign of the possibility of spontaneous generation. de Cruif (1941) for Pasteur's theory which may be called mechanism, or formal logic thinking.

C.Bernard and Vervorn, who were both gifted bioscientists, had, evidently, foresight in this subject.

The opponents of the theory in our time are all lacking in both a obtloachteal introduce

with respect of this problem. And so, they gulp down Pasterur theory, and will not try to reexamine it.

For instance, this author published in the learned society in 1954 and in 1958 the affirmative facts of the theory and this author's principle of it, but only a few expressed their affirmative opinions, and the rest kept almost He criticized that Pasteur did not win Pouchet completely, for both of them were right. K.Chishima

(1954, 1958)

In 1954 and in 1958, he pointed out that Pasteur and Oparin, both were incorrect, from his observations and experiments on the basis of the correct principles. In 1958 he published in his monograph that virtues and business and pastences of pastences.

ed.

So far as this author knows, this is the first discovery that has ever been made in Japan and abroad since Pasteur and Pouchet disputed with each other more than one hundred yearsago.

After that, the following Japanese Scientists and theorists published the affirmative results of their experiments or theoretical point of view on this subject. silent.

Therefore, it is not too much to say that seeing that they do not give any response to such a serious suggestion, they are lacking in a scientific conscience. A. Ushiyama, in 1960 T. Gomachi, in 1960 N. Sakurasawa, 1961 K. Saito, in 1961 K. Saito, in 1970 M. Taniguch, in 1961

Analyzing the difference in a mental structure between the proponents and the opponents from ancient times to modern times, we may conclude by saying that in a scientific view of a matter, or in methodology, the former is dynamic, synthetic, and dialectic, while the latter is static, analytical, and formal, as shown in the above table.

## (2) Criticism on the Controversy between Pasteur and Pouchet.

In 1859 the French Academy of Sciences gave a prize contest saying that the Academy would offer a prize to one who could prove whether the Spontancous Generation Theory is true or false through his precise and conclusive experiment.

Among those who applied for this prize contest, there were Pasteur, Pouchet who was then curator of the Museum at Rouen, and Jolly.

Then, Pouchet was already convinced in his voluminous book of seven hundred pages and in his two theses that the spontaneous generation theory is a fact that we cannot possibly deny. And he presented his book and papers on the theory to the French Academy of Sciences in January of 1859. But, as mechanism was as prominent as ever in the domain of science in France, the members of the Academy assumed only a negative attitude towards his book, papers, and experimental results by using a flask

On the 15th of June, when Pasteur and Pouchet were summoned to make an open experiment in the Academy, at first Pouchet insisted on a discussion before entering into the experiment, but it was rejected. And so, he was obliged to walk out of the chamber. On the other hand, Pasteur, as his opponent abandoned his right, exultantly demonstrated by using his well-used flask resembling the neck of a swan that no bacteria are spontaneously generated in the

liquid, sealed off from the air, containing well-sterilized decocted hay-sap in which neither bacilli nor their spores are mixed.

Pasteur, as said by de Cruif, was such a man of strong character as persist his own opinion to the end, and so, he often forced his opponents to be silenced. On the other hand, as he was one of the great scientists that has ever lived in the world, it was natural that the French Academy of Sciences should have accepted by a unanimous vote his triumph in the controversy of him with Pouchet on spontaneous generation, and his successful, open experiment in the Academy.

But, not given in by Pasteur then, Pouchet had continued the most exciting controversy in history of him with Pasteur till 1864, but most of the scientists had come to be subject to the judgment of the French Academy of Sciences in 1860. (As for these full particulars, see the "Basis of Neo-Biology — On the Origin of Life, Cells, and Blood Corpuscles, Vol. 2, pp. 105~212", by K. Chishima, in 1958.)

# (3) Blind Spots of Pasterur's Theory on Spontaneous Generation

Fasteur denied Pouchet's opinion by his ingenious, open experiment in the French Academy of Sciences, the Academy accepted Pasteur's theory by a unanimous vote, and the great controversy between Pasteur and Pouchet on spontaneous generation resulted in Pasteur's triumph.

But, after that, the English medical scientist Bastian produced counter-evidence to Pasteur's theory. He disproved Pasteur by saying that when he sterilized urine by boiling first, then neutralized it by putting a solution of kalium into it, then heated it at 100 C, sealed off from the air, finally put it into the thermostat of 37 C, for seven or twelve hours running, he found that it became turbid, and there appeared bacilli innumerably. It is said that Pasteur examined this process himself, ganined the same result as Bastian's, and was very much perplexed.

But, instead of giving way to Bastian, Pasteur insisted that it was that the spores of bacteria were not annihilated but left alive at 100°C, adding that the urine should be sterilized by dry heat at 180°C for more than 30 minutes, and subjected to disinfection until the cotton plug is scorched.

And, Pasteur did not prove that the spores existed in the urine, and then they developed into bacteria, and those bacteria were proliferated by cell division, but kept on insisting that his theory is always right.

Today, it is a common opinion that when protein, of which a living organism is composed, is heated at 100°C for more than 30 or 60 minutes, it is denaturated by heat, and, as a result, spores or bacteria are annihilated.

If he had had right judgement, perhaps Pasteur must not have thought that he got the better of Pouchet and Bastian in the controversy on spontaneous generation.

This author will not give full particulars of Pasteur's theory here, but will enumerate simply several instances showing how dogmatic and irrational it is in both theory and fact.

- (4) Blind spots of Pasteur's experiment and judgement and blind spots of those modern bioscientists who generally agree to his opinion.
- ① Pasteur's experiment was too short in its duration:

His experiment was sound reasonable in a way under his established condition, indeed, but was too short in its duration.

For, it was for only two or three days that he observed the given fluid after he had sterilized it. If the given fluid had been left as it was then (but supplied of oxygen) for five or ten years, or for a much longer time, bacteria might have been spontaneously generated from it.

Most of the scientists have failed to notice this spot as well as Pasteur.

 Protein in a living organism, if it is heated at 100°C or more, will denaturalize itself or perish.

Pasteur knew that even when the given fluid containing organic matter was sterilized at 100°C for more than 60 minutes intermittently, twice or three times over, sometimes bacteria were spontaneously generated in it. Neverthless, he persisted ideally without proving the existence of spores that it was that there survived some spores which could stand being heated. Moreover, in evidence of his theory he gave us the fact that when the given fluid was ste-

rilized by heat at 180°C, organic matter in it was partly carbonized, or denaturalized, no bacterium was spontaneously generated in it. In this case, he failed to notice that the duration of his observation was comparatively short.

This cannot be any counterevidence against the spontaneous generation theory of a bacterium in the natural state because it was obtained only in the unnatural state.

It is strange that even now, one hundred and eleven later, most of the biologists and medical scientists should not be aware of this blind spot.

(3) If there were to be no air (oxygen), no organism would exist.

Pasteur applied the result of his experiment under the unnatural conditions to a phenomenon under the natural conditions, and generalized it denying all the cases of the spontaneous generation of bacteria without due consideration.

For, the following conditions (a) — (e) are, originally, required so that a bacterium may generate itself spontaneously, and keep on living: (a) proper temperature, (b) water, (c) air or oxygen, (d) nutritive substance or organic matter, (e) passage of a certain time. Pasteur, however, almost neglected the above conditions, and made his experiment.

In the process of his experiment, he shut off air (oxygen), denaturalized nutritive substance (organic matter) by high heat at 180 °C, thus, made worse the conditions required in the generation of life by the unnatural changes.

Furthemore, he neglected that in the generation of life, when it is unnaturally improved by human work, the duration of observation must be long enough, and the season, that is to say, the seasonal and rhythmical changes of temperature, must be well considered. For, he observed the process or development of his experiment for only a few days or a few months at most, and jumped at a conclusion.

It may be said that Pasteur's theory may be right under the unnatural conditions, indeed, but cannot be true under the natural conditions.

It is much to be regretted that there are many bio-scientists in the world who are not aware of this blind spot.

4) Pasteur goes wrong even in theory or methodology:

The reason many bio-scientists have denied spontaneous generation as well

as Pasteur is chiefly that they have not had true methodology but have believed in formal logic. They emphasize the discontinuity of phenomena, stand on the Law of the excluded middle, and believe blindly Virchow's theory, in biology, as an iron rule, saying, "The existing cells and bacteria are proliferated only by cell division". Therefore, they have failed to notice that all natural phenomena, including life, are not discontinuous but continuous.

This is the very mistake that they have made as well as Pasteur, in correct scientific methodology.

Dialectic is the only key to this problem.

Oparin, Professor of the Moscow University, who is well known for his study on the origin of life, supports Pasteur's theory, but that is inconsistent with his own thought. For, he ought to have established his methodology on dialectic.

This author must speak a series of questions and answeres between Oparin and me in 1955 at Nagoya Univ, when he happened to visit this country.

Then, when this author asked him what he thought of spontaneous generation, he positively said to me, "There's no possibility that a bacterium will be spontaneously generated on this earth today". After that, this author, however, has often proved that Oparia's theory is incorrect both theoretically and experimentally. (As for full particulars, see K. Chishima's Monograph in 1957, and his book, "The Foundations of Neo-Biology", vol. 2, pp. 130-140)

(5) No one has ever seen that bacteria are actually proliferated by cell division:

Pasteur, Oparin and the other bio-scientists have not seen, actually, under the microscope that bacteria and their spores intrude into the culture-medium from the outside, and they are reproduced by cell division, and, as a result, putrefaction is brought about.

When they saw bacteria increasing in number in the culture-medium with the passage of a certain time, they only imagined that those countless bacteria were proliferated by cell division of the mother bacteria or the spores which had introduced into the culture-medium. For no one of them have ever shown any decisive evidences of such a process,

It would be impossible for them to prove it. For, this author has often proved in his experiments, as described later, that bacteria are never generated or reproduced by cell division,

No one of the modern bio-scientists has surely seen the process of the increasing in number of hacteria by cell division as well as Pasteur.

## (5) The spontaneous generation theory can be proved on facts.

This author criticized Pasteur's hasty conclusion on spontaneous generation from the four above-mentioned points theoretically, but it is natural that a true theory should be based on facts.

As described later, this, author surely saw with his own eyes through his original experiment the fact that in the process of the putrefaction of blood corpuscles, even when neither bacteria nor spores intrude into blood corpuscles from the outside, the protoplasm of blood corpuscles itself changes into bacteria.

This expresses the fact that spontaneous generation may not be proved by the orthodox methodology most of the modern scientists stand on as well as Pasteur and Oparin, indeed, but can be proved only by such a new methodology as this author stand on in the above instance.

(As for full particulars, see K. Chishima's Monograph in 1958)

Allmost all of the biologists have unilaterally refused the spontaneous generation theory of bacteria since Pasteur did, and also they have been refusing this author's opinion.

This author published his affirmative opinion on spontaneous generation for the first time in 1954, and consolidated the results of his study on spontaneous generation in 1958. Though this author has been pointing out the mistakes of the orthodox theory on spontaneous generation since then, yet no one of the scientists at home and abroad have refuted this author's opinion. No one of the scientists including Oparin have disproved this author's opinion against Oparin's theory, either.

On the contrary, there are a few scientists in this country who have lately published their affirmative opinions on spontaneous generation as described later. But it is much to be regretted that most of the modern scientists still believe blindly Pasteur's theory.

If both Pouchet and Bastian had been aware of the only one of the four blind spots on Pasteur's theory pointed out by this author, they might not have gotten the worse of the epoch-making Controversy with Pasteur in Paris.

And, bacteriology and biology might have been quite different from what they are today.

This author will show you the outline of his controversy with Oparin in the next place.

(6) Blind spots of Oparin's theory on spontaneous generation.

This author will only give the outline of Oparin's theory here as it is given full particulars of in his book called the "Origin of Life", and in this author's Monograph in 1958 (pp. 130~140), including a series of questions and answeres between Oparin and this author.

① Oparin believes that bacteria were scentaneously generated enly once at a certain stage of the evolution of the globe:

He believes that bacteria were spontaneously generated only once at a certain stage of the evolution of the globe, passing through the following stages: inorganic matter — > organic matter — > protein matter — > an organism. And, he suggests that bacteria were spontaneously generated only once at a certain stage of the evolution of the globe eight or ten hundred million years ago, since then they have been reproduced only by cell division, and therefore, no spontaneous generation of a bacterium can be found anywhere on this earth today.

Once, when we had a round-table talk at Nagoya University in this country, he told me the above suggestion, adding that we cannot deny any possibility that bacteria may be spontaneously generated under the limited conditions, but that even if they were to be spontaneously generated on this earth bacteria will soon be preyed upon by the existing Protozoa.

Thus, Oparin persists in supporting Pasteur's theory, but that is not right.

For, it is clear that he is in the wrong from the fact that even when no

Protozoa were to be seen in the blood corpuscles or in the cells, bacteria, a

kind of putrofactive bacteria, were spontaneously generated in the process of this author's original experiment.

Oparin defines life as "protein matter" which can do metabolism.

Oparin defines life as "protein matter" which can do metabolism, but most of the biologists today explain that it is an organism that has the cellular structure, and then it is the life phenomenan that an organism shows.

Even bacteria, whose cells are regarded as the lowest, contain protein, and DNA or RNA. And, as described previously in this book, if the five conditions (described above) required in the spontaneous generation of life, all are well arranged, these matters, protein, DNA, and RNA, will be newly synthesized on this earch today.

This expresses the fact that a transition from a nonliving thing to a living thing is not discontinuous but continuous, and that, when we frankly observe the process of the putrefaction of erythrocytes, there can be seen the spontaneous generation of a bacterium, through the process of a transition from organic matter with no life to a bacterium with life, and then in it there are transitional stages, or a chaotic state, between the living thing and the non living organic matter. As most of the modern bio-scientists believe formal logic, or the Law of the excluded middle, they neglect without due consideration that there exists a middle state in which we are not sure whether a thing is A or B; that is, a chaotic state in which a bacterium appears dimly but gradually out from the interior of organic matter (e.g.a putrefacting erythrocyte).

Indeed, most of the modern bio-scientists may neglect this fact because they believe formal logic, or the Law of the excluded middle, but Oparin ought to be different in opinion from them on this subject because he regards material dialectic as his scientific methodology.

Neverthless, Oparin has failed to notice this fact, but that only means his insufficient understanding of material dialectic, or his selfcontradiction to his own thought.

(3) Most probably, Oparin has never observed under the microscope through his own experiment, "How are bacteria with the cellular element produced or reproduced?"; Oparin once made clear a biochemical process from inorganic matter to complicated organic matter, or to protein matter, in outline, but has never observed under the microscope through his own experiment, "How are bacteria with cellular constitution produced or reproduced?"

He only described an evolution from inorganic matter to protein matter in his study on the origin of life.

Finally, we may say that he did not, or could not, explain exactly the origin of life. For, life consists cheifly of protein matter, and RNA of DNA which are derivatives of protein matter.

Oparin says, "Today, there is no one who believes that monkeys have been evolving into men.":

In a series of questions and answere between Oparin and this author, Oparin said, "Today, there is no one who believes that monkeys have been evolving into men."

Of course, men and monkeys have evolved into what they are today respectively from the same progenitor.

From his above remarks, we can imagine with no difficulty that Oparin helds the preformation theory.

Men are quite different in the process of evolution from bacteria.

Who on earth belives that man or the higher animal may be spontaneously generated?.

This author only persists the fact that spontaneous generation can be found among the unicellular organisms, especially among bacteria, which are called the lowest organisms.

Oparin says in his some paper, "Darwinism is superior to others in that it is convinced of continuity in the natural world", but we can point out his selfcontradiction to his own thought here again.

## (7) Modern bio-scientists are confused in their thinking.

Today, most of the scientists concerned in bacteriology, biology, and medicine generally agree to Oparin's opinion in support of Pasteur's theory against spontaneous generation. Though this author has insisted, since 1954, that Pasteur's and Oparin's theory against the spontaneous generation theory are already brought to an impasse in both theory and fact, and that there are some great mistakes in them, yet they have only kept silence instead of saying either "Yes" or "No" as to this author's opinion.

What does this mean?: they are trying to ignore this author's opinion by keeping silence?, or they have no courage or no confidence to refure it?, or they are not in the least interested in an important matter like this?, or they are dead to a scientific mind, or to conscience.

Perhaps, their attitude will belong to any of these, but, in any case, it is much to be regretted that they are confused in their thinking.

In this country, there are a few scientists who insist on the spontaneous generation theory of a bacterium (See p.254), but although he knows that it is this author's discovery, at first, not his own, some one of them emphasizes had newly discovered it.

This author hopes that scientists will love truth still more, and make their standpoint much clearer, and then that lots of bioscientists will take a decided attitude toward the Eight Principles of this author as well as toward the spontaneous generation theory.

# CHAP. II. K.Chishima's Experimental Results on Spontaneous Generation— - And the Résumé, and Index of his. Papers on it

This author has studied the relations between the origin, and behavior of occysts and merozoites in the feces of chicken, and in the putrefied blood cells within the intestinal contents of chickens with chiken coccidiosis.

In 1954, this author discovered and published that bacteria are spontaneously generated in the erythrocyte falling into decay, and then those bacteria develop into occysts and merozoites, a kind of Protozoa, through or by means

of the A-F-D Process; the A-F-D process represents the Aggregation, Fushon, and Differentiation of bacteria. (See K.Chishima's Monograph in the Research Bulletin of Gifu Univ., No. 3, in 1954)

Since then, this author has tried to make clear this problem by using different kinds of material and methods with his collaborator, and, as a results, found the following facts:

(1) The spontaneous generation of bacteria in the intermittently sterilized potato

Many bacteriologists say that pure potato bacilli can be derived or obtained from the completely sterilized potato which is put in triplicated Petri's shale incubated in the thermostat at 37°C with a small amount of distilled water.

After three or four days, there always appear numerous pure potato bacilli on the surface of the boiled potato. In the case like this, this author found through the microscopic examination that potato bacilli were spontaneously generated in loco and de novo from potato-starch granules themselves as a derivative of starch.

I'erhaps, such a fact, even if it is true, will not be understood by the orthodox bacteriologists. In the case, it is not thought that there is any possibility that the potato will be contaminated by potato bacilli or their spores in the air.

According to this author's examination, it was seen that there were all kinds of transitional phases from starch granules to potato bacilli, clearly, but it was never seen that potato bacilli are proliferated by cell division.

Therefore, we could see that bacteria are newly generated spontaneously from starch granules, using them as a material.

(2) We can see the spontaneous generation of bacili in cow's milk, soyabeans, and others as well as in potatoes.

We can see that even when cow's milk or soyabeans are sterilized by being boiled at 100 °C for 30-60 minutes, and then they are put into the test tude together with a proper water and air filtered with the bacterial filter of Chambeland's type, and kept airtight at the moderate temperature, lactobacilli are produced from the milk through the putrefaction of it, or "natto, bacilli from the

soyabeans through the putrefaction of them, and bacteria of a particular kind, corresponding to the culture medium, such as milk or soyaheans, respectively are spontaneously generated from them, using them as raw materials.

(3) We can see the spontaneous generation of bacteria in the putrefaction of blood cells and cell-fragments.

Once, while studying the phenomenon of the putrefaction of a frog's red blood cells, fortunately this author could see with his own eyes that bacteria were spontaneously generated.

Frogs are easy for us to get as a material, and their red blood cells are much larger than ours or Mammalia's, so it will not be so difficult for any one to see whether bacteria are spontaneously generated or not in the frog's blood. And a close patient observer will see that Pasteur's theory is in the wrong. In observing this, we should prepare for the following tools: a microscope of 600 or 1500 magnifications, cover glasses, slide glasses, a small amount of par-

Fig. 3-1. Spontaneous generation of a large number of putrefactive bacteria in a putrefied erythrocyte. (High power, Oil immersion photo micrograph of a frog's blood). (K.C.)

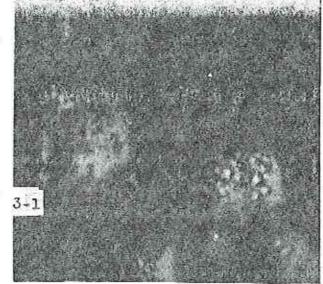


Fig. 3-2. Early stage of putrefaction of two er-

ythrocytes of a frog. Vacuole-like dots appeared spontaneously in the crythrocytes are primordial bacteria. (K.C.)

affin and vaseline, a metal spatula, an alcohol lamp, a thermostat (we may do without it in midsummer.), and a germ-free box. (And, of course, all these tools must be disinfected or sterilized by heat.)

Now, the steps of the procedure will be shown in the following:

We pick a droplet of blood out of the heart of a frog with a glass pipette, then put it on the slide glass but in the whole blood, then cover it with the cover glass, and finally seal the cover glass with an equivalent mixture of sterilized paraffin and vaseline by using a heated metal spatula to prevents the evaporation of the water in the bood. Thus, we can make a specimen.

And then we put this specimen under the microscope, magnify it 800 or 1500 diameters, and fix it within a limited sight after seeing closely if there exist any bacteria in it.

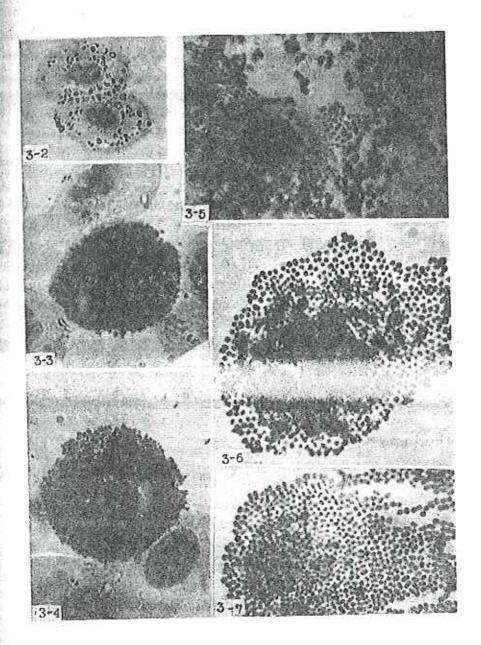
After this, we must observe it for two or three days running. In the summer we can leave it at the room temperature, and observe it.

Especially, when we observe with good care one or a few crythrocytes in the microscopic field for a certain time continuously, we can see that the indefinitely shaped cell-fragments, which are floating in the blood at first, change from a coccus-type into a bacillus-type gradually, and come to move freely in the blood serum.

The spontaneous generation of bacteria is most assuredly proved by the fact that numerous putrefied blood-bacilli make their appearance in the interior of an crythrocyte. Even when neither bacteria nor their spores intrude into the interior of an crythrocyte from the outside, under the room temperature in the summer period there appear at first, some bright vacuole-like circular parts appear in the cytoplasm of an crythrocyte within a week, although the time of their appearance depends upon temperature, and other conditions.

Perhaps, this means that the cytoplasm of an erythrocyte changes into lipoidlike substance. We can see much better the process of such a change of a living erythrocyte by using a phase contrast microscope.

And then, those circular parts change into typical bacilli in a few days, and a nucleus also has the same change. As a result, scores of putrid blood-bacilli are spontaneously generated from an erythrocyte. (Figs. 3-1, 2, 3, 4, 5, 6, 7, 8)



Spontaneous generation of Putrefactive bacteria in the Frog's erythrocytes (K. Chishima '58). Explation of figure:

Fig. 3-2. Two erythrocytes in the whole blood left at the room temperature (in summer). After 24 hours there appeared vacuole like bodies.

Fig. 3-3, 4, 5, 6, 7. And they were then gradually transformed into bacteria. At first, they proceeded from the periphery into the inner cytoplasm and at last changed into the nucleus itself.

There was no evidence of the invading of bacteria (or spores) or cell division.

Sometimes, bacilli resembling the tetanus bacilli with swollen one end, make their apperance in the cytoplasm of an erythrocyte. Similarly, we can see that bacteria are spontaneously generated in the leucocyte as well as in the erythrocyte.

When the whole blood corpuscle is filled with the bacteria which are newly formed, it looks as if they were a bundle of cigaretts and those bacteria are separated one by one from the outmost part of the cluster like a bundle and swim away freely. Each one of the separated bacteria moves vertically and gently at first, then changes his movement from an oblique direction to a horizontal direction, and at last comes to move very rapidly.

(4) No bacillus is proliferated by cell division, or by being longitudinally divided into two parts.

Sometimes, the erythrocyte which became a mass of bacteria by its own putrefaction separates itself into a few or several smaller masses of bacteria.

In such a case, when those bacteria are separated one by one as an individual, and scattered about, it looks as if they were proliferated by cell division, but this never proves that bacteria are proliferated by longitudinal cell division.

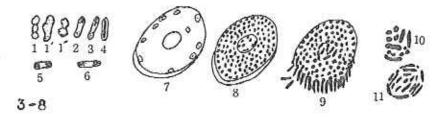
For, this means only that numerous bacteria which had been newly formed at once in the interir of the blood corpuscle were separated one by one as an in dividual, not that one bacterium grew up to be a larger one, and were divided into two parts.

Many orthodox bacteriologists have taught us that bacteria are proliferated

by cell division, or by being divided into two parts, every thirty minutes.

Vernadski says that according to his calculation, if one bacterium goes on being divided into two parts every thirty minutes, even one bacterium of 10<sup>-12</sup> C.C. will cover the whole surface of the globe in thirty-six hours under the best condition. This is, of course, a desk theory.

This author has discussed with many bacteriologists and biologists about this subject, but has never met with those who ever saw that bacteria are proliferated by cell division. Neverthless, they believe it simply because it is written in their Bible, the orthobox text-book.



Schematic figure showing the spontaneous generation from putrefactive frog's blood,

- (1-1') microns or cellular fragments floating in the blood plasm.
- (2~6) transitional phases.
- (7) appearance of vacuole-like bodies in an erythrocyte.
- (8-9) becomes into a mass or a bundle of bacteria. (K. Chishima '58).

Spallanzani, the Italian priest and scientist, who denied the spontaneous generation of bacteria, says that when he was observing one bacterium isolated from a group, he saw that it was divided into two parts, or proliferated by binary division. But, his biography says that he was a dishonest and unreliable man. He often deceived the king to raise his salary, and went on journeys under pretence of preservation of health.

If he had seen that one bacterium was divided into two parts, he might have

misunderstood it as a cell division. But it is only the separation of bacteria from a mass, or a group, of bacteria which were spontaneously generated from organic matter.

If not so, it would be thought that he told a lie against his conscience.

When he was engaged as a professor in the laboratory for biology at Gifu University, this author had once kept taking microphotographs of one bacterium in the putrefied whole blood for twenty four hours running with his collaborator, but never saw that one bacterium is divided into two parts, through the cell division.

The environment was suitable for the proliferation of bacteria, for, in this slidecover method, bacteria increased very greatly in number by using the blood corpuscles, and cellular fragments as a source-material.

No one of the modern bio-scientists, including Pasteur and Oparin, who are against the spontaneous generation theory has seen the actual phase or process of the proliferation of bacteria.

It is a pity that these opponents, however, believe blindly the orthodox cell theory, and will not reexamine if bacteria are spontaneously generated.

(5) The spontaneous generation of bacteria by putrefaction of the blood corpuscle, under the various conditions

Bacteria in the whole blood of a frog, are spontaneously generated in the following order; at first in a micron cytoplasm extruded from the erythrocyte, then in the cell-fragments, then in the leucocyte, and at last in the red blood corpuscle, including its cytoplasm and then its nucleus.

And bacteria appear sooner in the area in the outer area of the well preparation, where the blood corpuscles are scattered, than in the center area where the blood corpuscles are densely aggregated.

We found that when distilled water, boiled water, and serum filtrated by Chamberlan's hacterial filter were added to fresh blood, putrefaction of blood was more rapidly advanced in it than in the fresh whole blood.

## (6) Criticism on the Orthodox view of the thermal resistance of bacteria

This author described previously, in (1), the fact that potato bacilli are spotaneously generated, but Mr. Shiga says from Globig's experiment that red potato bacilli have such a great resistance to heat that they will never die till they are heated at 100°C for six hours, and at 122-123°C for ten minutes, but at 130°C for a moment.

There is no possibility that any bacteria or their spores may exist in such a case. For, if it were to be boiled at 100°C, any protein matter in a living thing would be denaturalized by heat, and then a living thing would die.

The reason potato bacilli are spontaneously generated even in the potato treated at such a high temperature as Globig did, is that the starch granules of the potato change into bacteria, or produce bacteria.

This author can always prove this by his original experiment.

The reason bacilli are spontaneously generated in the potato is never that bacilli or their spores survive in it.

Perhaps Globig did not prove that bacilli or their spores can survive standing high heat, and are proliferated by cell division.

And no one wii be able to prove it, even if he tries to do so.

If one insists on the survival of bacteria or their spores without seeing them, it will be only either imagination or bigotry.

## (7) Characteristics of bacteria depend upon their culture-media

As previously described, the characteristics of bacteria depend upon their culture-media. Namely, when potatoes, milk, and soyabeans are completely sterilized, and free from germs, pure potato bacilli are generated from the potatoes, lactic acid bacilli occur from the milk, and natto bacilli develop from the soyabeans, respectively. And from a frog's, a rabbit's, a mouse's, and a man's crythrocytes, different kinds of putrefactive bacteria are spontaneously generated.

When a piece of meat or a hen's egg putrefies, the putrefactive bacteria which secrete ptomaine toxin develop from the meat or the egg. And, when

the contents of the gastro-intestinal canal putrefy, the bacterial characteristics depend upon their media, the physico-chemical properties of the gastrointestinal contents.

This suggests to us that we should throughly re-examine the orthodox view on the problems of health such as the prevention against infectious diseases, and food conservation.

In viruses and Rickettsia as well as in bacteria, the characteristics of them depend upon their culture media, or upon the physico-chemical properties of the cell in which they make their appearance.

(See K.Chishima's monograph, "Neo-Biology" published in '68, vol. 2, pp.159-179)

(8) Biological transformation from normal protoplasm into pathological protoplasm, pathogenic bacteria and viruses

A macro molecule of protein, of which the protoplasm of a normal cell is composed, is called an elementary body, but this author defines it as a physiological virus" in contrast with a pathogenic virus.

For, this author draws deduction from the principles of his theoretical biomedicine that when, because of the bad environmental conditions in and outside it, a living body decreases its resistance againt injurious factors and, as a result, it becomes a sick body, the protoplasm of the cells changes to a pathological state, and, simultaneously with it, a physiological virus changes into a pathological virus. Therefore, this author believes that most of the infectious discases which are thought to be caused by bacteria or viruses in the orthodox biomedicine, is not due mainly to the infection of bacteria or viruses from the outside, but due mainly to the spontaneous generation of bacteria or viruses. For, as the vitality of a living body gets lower, and the cells, blood, and its body fluid become pathological, bacteria or viruses are spontaneously generated in the blood corpuscles and in the cells or in its body fluid.

We can draw the same conclusion on other various diseases as on the infectious diseases.

Just as, in putrefaction of the erythrocytes and the like, the cells are disintegrated into numerous bacteria, which this author described previously, so, when the cells and blood of a sick body draw to cell death, viruses are newly formed in the cells of it, and then, when the cells die out, they are disintegrated into bacteria by putrefaction.

Finally, the death of an individual means that it is disintegrated into bacteria by putrefaction.

Originally, at the early stage of the generation of life, bacteria are spontaneously generated from organic matter, using it as the mother substance, first, and then, cells are produced through the A-F-D Process of bacteria. Therefore, a living thing is reversely disintegrated into bacteria by death.

When the vitality of a living body suffering from an acute or chronic disease grows weak, and it is hovering between life and death, it will recover if the disease is slight, but if the disease is extremely severe, it will be disintegrated into infinite viruses or bacteria by death.

### (9) The theoretical grounds for the spontaneous generation of viruses

Viruses are the intermediate elements between a living and a nonliving thing, and no one of the present day virologists has given the full explanation about the proliferation of viruses. At present, it is a common opinion that viruses are proliferated only in the living cell, but the way viruses increase in number has not yet been well proved. Some scientist imagines that viruses thrust their sharp ends into the cell, and pour DNA into the cell, but no one of the scientists has proved that viruses intrude into the cell from the outside, and are proliferated by fission.

It would be impossible for them to try to prove it.

According to Heinmets's report in 1948, when he cultured the human influenza B-viruses in the chicken's blood, he surely saw that they adhered to the periphery of the chicken's crythrocyte within two or three minutes at the beginning of culture of them, but he never saw that they intrude into the cell. And, a few minutes latter, he saw that viruses appeared within the crythrocyte, gradually making their figures clearer. This period is generally called the Eclipse Period or the Dark Period. His report goes on to say that eleven minutes later, definite viruses increased greatly in number within the crythrocyte. (See the electromicrophotographs presented to this author by him)

From this fact, we cannot but conclude that as viruses abhere to the

periphery of the crythrocyte, their chemical characteristic (DNA) has some induction on the crythrocyte, and, as a result, the cytoplasm first, and then the nucleus of the crythrocyte, like a chain reaction, change into viruses, or DNA-granules, respectively.

In 1946, Anderson also says that when a bacterium is disintegrated in viruses by bacteriophage, it is never disintegrated according to binary fission. Boshan, the Soviet veterinarian, in 1944, and Moriyama of Japan in 1955 both say that the generation of a virus is due to the autocatalytic reaction of protoplasm.

These opinion are all in favor of the spontaneous generation of a virus advocated by this author.

## CHAP. III. Practical Application of the Spontaneous Generation Theory of Bacteria and Viruses to Health and Medicine

## (1) Infectious diseases and epidemic diseases

The word "infectious disease" is generally used as if it were the synonym of the word "epidemic didease", and since the latter occurs frequently in a certain district and in a certain season, the phenomenon is often called "epidemic". And both are referred to be common to each other in respect that they occur due to the infection of pathogenic microorganisms.

But as previously described, bacteria and viruses are spontaneously generated when organic substances are put under the circumstances which are suitable for the generation of bacteria or viruses, and this phenomenon can be seen not only in the phenomena of the putrefaction of potatoes, cow's milk, the other food, and organic substances, but also in the human body. In the human body, when the body is in low vitality, or the body is suffering from some disease, the symbiotic bacteria (i.e. lact bacillus & bacillus colli) living in the contents of the digestive tract reduce in number, and reversely, the injurious bacteria (i.e. clostridia) increase in number. And these bacteria secrete putrefaction-toxin, and they have harmful effects upon the body.

In the human body, especially when excessive eating and drinking, cooling the abdomen in sleep, and the fatigue or stress of mind and body are repeated or piled up, a pathological change occurs in the gastrointestinal contents, and, as a result, Children's dysentery bacilli (cholera infantum) and dysentery bacilli (amoebae) or typhoid bacilli may be spontaneously generated in the body by using those contents as their culture media, although those contents are not in the least infected with pathogenic bacteria. For, as previously described, this author surely saw that bacteria and Protozoa, which are common in chicken coecidiosis, were spontaneously generated in the intestinal contents or feces of chickens with chicken coecidiosis which is called "chicken dysentery".

Rene Dubos, the famous American bacteriologist, published in 1944, 1955, and 1968 that there is some possibility of a transition from non-pathogenic bacteria to the pathogenic bacteria, but this author presumes that in his case, most probably, a certain change occured in the chemical constitution of the intestinal contents, and, as a result, those bacteria which were adapted to its change were newly formed.

## (II) Reilly's revolutional theory

Reilly, the French doctor of medicine, published in 1956 a revolutional theory, a pathological theory induced by over stimulation of the autonomic nervous system.

According to his report, he succeeded in producing the same pathological change in lung tissue as is seen in miliary tuberculosis by stimulating the branches of the autonomic nervous system branching off into the lung physically with pincette (small pincers) and chemically with bacterial toxin, although the lung was not in the least infected with tubercle bacilli. And also he succeeded in producing the same pathological change in the intestinal mucous membrane as is seen in typhoid or in dysentery only by stimulating the branches of the autonomic nervous system branching off into the gastro-intestine physically and chemically, although the gastrointestine was free from typhoid bacilli or dysentery bacilli.

It is a great shock to orthodox medical scientists that Reilly should have

produced those infectious diseases successfully in his experiment, although the lung and the gastro-intestine were free from pathogenic bacteria.

For the orthodox bacteriologists commonly presume that when a certain epidemic disease occurs very frequently in a certain district in a certain season, it is due to the infection of microoranisms, and being afraid of bacteria, they scatter the disinfectant so as to prevent the infectious disease. But from the results of Reilly's experiment, we should learn that the best way to prevent the infectious diseases is to preserve and strengthen our health rather than scatter the disinfectant, being afraid of bacteria. For when we are in good health, most of the infectious bacilli are sterilized in our bodies by hydrochloric acid (HCL.) which is contained in gastric juice. For instance, there is the well-known experiment. I Prof. Pettenkoffer that he once took the cholera bacilli, but he was not in the least infected with cholera.

Therefore, it is necessary that in order to promote our health and enjoy longevity, we should try to take an adequate quantity and quality of diet to improve the useful symbiotic bacteria in the intestine, or the intestinal symbiotic bacterial flora, rather than he afreid of bacteria.

Most of the diseases which are called "opidemic" do not occur due mainly to the infection of bacteria or viruses, but, as a matter of fact, due to ill health, irregular habits, unseasonable weather, and the other bad circumstances including milicu.

Reilly's finding is not only a revolutional discovery but also a new theory in modern science. And it is, of course, a good illustration of psychosomatic medicine, but this author will preferably infer from his new theory that the physiological function of the lung or the digestive tract was checked by emotional stress, or by sympathicotonia or parasympathicotonia, and, then an abnormal putrefaction was caused in the mucous membrane or in the intestinal contents by the abnormal contraction or dilatation of blood vessels branching off into the lung or into the gastro-intestine, and at last the pathogenic bacteria which were adapted to the lung or to the gastro-intestine were spontaneously generated in situ (in the site).

This author believes firmly that such an inference is possible.

## III. Suppurative inflammation and Septicemia can be explained by the spontaneous generation theory of bacteria.

Pus corpuscles found out in the region of suppurative inflammation are filled with numerous bacilli or cocci. It has been, in general, considered that these microorganisms are engorged by the leucocyte through its phagocytosis.

And those pus corpuscles are said to be the corpses of the leucocytes which fought against bacilli and were defeated by them. But perhaps there is no scientist who has ever observed such a phenomenon actually. For this author discovered a new fact quite different from it by making the observations of the putrefactive phenomenon of the blood cells or the other cells which are dying; that is to say, the protoplasm of the blood cells or the other cells changes into bacilli or cocci in situ (in the site). And in this case, perhaps there is no sign of the proliferation of these microorganisms by binary fission. Moreover, this expresses the fact that this phenomenon corresponds entirely to this author's theory, "the reverse A. F. D. Process" theory.

Septicemia is a disease which is caused by the patrefaction of the blood, and so Septicemia occurs even when no bacillus intrudes into the blood.

For, whenever blood or blood corpuscles change into a pathological state, numerous bacilli always arise spontaneously in the blood by putrefaction, even when no bacillus intrudes into the blood from the outside.

Therefore, it is important that we should usually try to preserve and promote our vitality in order to prevent Suppurative inflammation and Septicemia.

# IV. Tuberculosis, Leprosy, and Malaria: And the spontaneous generation of microorganisms

It is common knowledge in modern medicine that no one will suffer from these diseases, if he is not in the least infected with those pathogenic microorganisms which are adapted to each disease. But this does not agree to this author's theory on the spontaneous generation of microorganisms.

And also it is a well-known fact that the cells in the pathogenic region of tuberculosis or leprosy are filled with tubercle bacilli or bacillus leprac (Hanson's bacilli), and especially, a leprous cell looks as if it were a cigarette case full of cigarettes. But this never shows that bacilli in the leprous cell are proliferated by binary fission, for no one can probably adduce evidence to show that those bacilli intrude into the leprous cell, and they are multiplied in it by binary division.

The crythrocytes of a malarious patient are filled with malaria plasmodia as well. Therefore, like the case of tuberculosis and leprosy, it is imagined in the orthodox medical science that Protozoa intrude into the erythrocyte, and they are multiplied in it by binary fission.

Perhaps there is no one who has ever seen the very actual process that malaria plasmodia intrude into the erythrocyte, and they are multiplied in it by binary fission. So far as this author knows, no one has ever observed such a process actually.

This author can explain this case from his following theoretical bio-medical point of view; malaria plasmodia do not intrude into the crythrocyte, but the constitution of the blood, or milien (internal environment) of blood corpuscles, changes into a pathogenic condition first, then, the blood corpuscles as a result, reverse into protozoa, then the cells degenerate into an early evolutional stage, and at last the cells fall into death. This is the very process that this author calls "the reverse A. F. D. Process".

This author believes firmly that it is quite proper to say that these processes can be all explained by the "reverse A.F.D. Process" theory.

## V. This author's opinion on an infectious disease from his new theoretical biomedical point of view

As above described, most of the infectious diseases are not caused by the pathogenic microorganisms which intrude into the body from the outside, but mainly by the pathogenic microorganisms which are spontaneously generated in the body when the body is in poor health or in low vitality. And there is plenty of evidence to show that those pathogenic microorganisms are spontaneously generated in the human body.

It is true that when the vitality of the body is low, and the power of resistance to disease is weak, one is liable to be attacked with disease, if

pathogenic microorganisms intrude into the body.

The best way for us to prevent these diseases, to preserve and promote our health, and to enjoy longevity is "ki, ketsu, do, no chowa"; that is to say, to keep the harmony of mind, body, and movement ("ki" in Japanese stands for "mind" in English, "ketsu" for "blood" but here "body", "do" for movement or exercise "no" for "of", and "chowa" for "harmony").

To sump up, we may say that pathogenic microorganisms and viruses are not so much the cause of disease as the effect of disease.

# VI. Prevention of putrefaction of foodstuffs and bacterial spontaneous generation

As previously described, the indispensable conditions for bacterial proliferation are as follows: (1) air or oxygen, (2) proper temperature, (3) moisture or water, (4) nutrients-mainly organic substances; but exceptionally inorganic substances only, and (5) enough time to generate bacteria from their culture media according to each physico-chemical nature.

Therefore, we should shut off or isolate foodstuffs from the above (1)-(5) conditions but No. 4 so that we may prevent the putrefaction of foodstuffs and preserve them.

At present, on one hand, there are many kinds of devices for preserving foodstuffs such as antiseptics, additive substances, and artificial colourings with aniline pigment, sometimes with bactericides, but on the other hand, there are many people suffering from public nuisance of foodstuffs, which may be called "food pollution", caused by these processed goods. Moreover, to our regret, there is danger of applying radioactive-isotope to foodstuffs so as to prevent them from putrefying, in near future.

These treatments for foodstuffs may be of great use to preservation of foodstuffs indeed, but they all are injurious to the health. If we keep on taking these artificial foodstuffs for a long time, we will soon develop chronic intoxication, and, as a result, we will be in danger of our life.

Therefore, we have no choice but exclude the above (1)-(5) conditions but No. 4 so that we may preserve foodstuffs safely.

# CHAP. IV. Abstracts from the monographs and original papers published by K.Chishima

- I Index of the Papers on the Third Principle Published by K. Chishima.
- (1) On the Relations between the New-Formation of Occyst and Merozoit in Chick-Coccidiosis and Blood Cells or Bacteria - A Contribution to the Spontaneous Generation Theory, (Research Bulletin of Gifu Univ., No.3.1954.) (in Japanese with an English Résumé) (See pp.265-273) of this volume and the volume 3 of Chishima's Complete works corres.)
- Talking with Prof. Oparin about the Origin of Life, Academio, No.29.1956.
   (in Japanese) (See Chishima's Complete works series vol.8)
- (3) Difference in Opinion between Prof. Oparin and I on the Origin of Life, Soviet Medicine, Na 2, 1956: (in Japanese) (Ibid)
- (4) Criticism on the Controversies among the World Famous Scientists on the Origin of Life, (Basis of Neo-Biology, vol. 2, Origin of Life, Cells, and Blood Cells, pp. 105-140, Origin of a bacterium and a virus, 1958; pp. 142-212) (in Japanese with English résumé).

## II. ENGLISH SUMMARY

of

## Basis of Neo-Biology

## Volume II

The Origin of Life, Cell and Blood Corpuscle--(A separate volume in Japanese, 490 pages, 200 figures)

by

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## Summary and Conclusion

It is said that we are now living in an epoch of atomic energy or in a cosmic age which was brought about in the first half of the twentieth century, by revolutional advance of physical technique.

But we hope and expect that in the forthcoming latter half of our century there would occur not less revolutional discoveries on the principle and practice of life than that of physics. And, as a matter of course, those discoveries should be favourable not only for the promotion of the human happiness but also for the establishment of world peace.

As a matter of fact, some of the leading scientists, namely, Meyer, Bertalanffy, Bernal, Lysenko, Lepeshinskaya and the others have pointed out that the basic priciples of biology are now confronted by a turning point.

In November 1859 appeared Darwin's great book, the "Origin of Species." It shows that the higher forms are evolved from simpler and lower ones. Despite the great value and stimulating character of his theory, Darwin himself, in his day, was unable to find the origin of unicellular microorganism. Hence, on this point, Darwin does not probe a matter of bottom, viz., the origin of the lowest microorganism.

That situation of Darwinism has been continued to the present time. So, according to the modern biological thought, all living beings, even the lowest microorganism, can arise only from others like themselves, so they can not emerge on our Earth at the present time.

In other words, this orthodox view held the conception that even the lowest microorganisms, such as bacteria living at the present day are descendants of pre-existed ones, and they have remained as they were since innumerable years ago, and would remain, as they are, till far off future. As to why some bacteria or amoebas have evolved to higher forms, while some others remain as they were in the geological age, current biology gives us no information whatever.

Consequently, the contemporary biological thought on the origin of life is, in essence, a preformation theory. True biologists, therefore, can not and must not

overlook the contradictory idea between Darwinism (Origin of Species) and the preformation theory as to the origin of life (microorganism and cell).

Hence, this volume was written with the purpose of the re-examination of the two fundamental laws of biology, the laws represented by the following thesis "Omnis vivum e vivo (Pasteur), and "Omnis cellula e cellula (Virchow).

In this volume, then, I have described and discussed, on the subject, from point of view which was secured, mainly, by my own works as to the origin of bacteria, cell and blood corpuscles, and on the related matters. By the way of summary, I should like to state the outline of my opinion.

## (1) Spontaneous generation of bacteria

Ever since Pasteur defeated Pouchet, the negation of spontaneous generation has been accepted by the modern biologists as a firmly established truth, though they can cite no firm evidence under the natural conditions.

However, I have confirmed the following facts, by means of continuous observation under microscope, that some kinds of bacteria can emerge, de novo, in the putrefaction-process of such organic substances as the blood of amphibia and aves, or of several organic substances.

During the putrefaction-process of blood, at first, the minute particles or cellular debris in the blood show transitions into saprogenous bacteria and then a number of bacteria arise within the cytoplasmic extrusion from crythrocyte, and, at last, the bacteria appear within the leucocytes or crythrocytes themselves, notwithstanding the fact that there is no sign of invasion of bacteria from outside into their cytoplasm. In this case, there arise, de novo, many of granules, the bacterial anlage, in the cytoplasm, and then in the degenerating nucleus, and, at last, these blood cells become, in situ, a mass of bacteria. The individual bacterium, then, detaches gradually from that mass, gets free, and then swims away.

The so-called "division of bacillus," due, most probably, to the misunderstanding about the detachment or separation of individual bacterium which emerged, as a mass, in the cell or in the organic substances at the same time.

#### (2) New formation of blood corpuscles.

Virchow's thesis "Omnis cellula e cellula" has been accepted by the majority of

the modern biologists as a fundamental law of biology. But, O. B. Lepeshinskaja ('37-'55) has already published her revolutional finding that the crythroblast or some other cells can arise from living substances (yolk sphere, egg albumen etc.), and I ('49~'58) have also found, independently of Lepeshinskaja's finding, the same fact. The above-described opinion of ours, however, does not imply that we deny entirely the cell division.

Though we can observe, in relatively few cases, the so-called mitotic figure, yet it does not necessarily produce two daughter cells and, moreover, there are many evidences that the cells can arise from organic substances which have no cellular structure. So that it must be obvious to true scientists that the role played by the so-called mitosis, in increasing in number of cells, has been overestimated by cytologists.

## (3) New formation of the sponge cell from an aggregated mass of zoochlorellas

This author found that the sponge cell and amoeboid leucocyte in the fresh water sponge (Spongilla semispongilla Annandale sp.) are formed, de novo, from an aggregated mass of a lot of zoochlorellas, the unicellular green algae. These algae included in the sponge cell, hitherto have been considered it as intracellular symbionts, But, according to my observation, the sponge cell shows neither any sign of phagocytic ingestion of zoochlorelia nor cell division. While these can be seen clear transitions from an aggregated mass of zoochlorellas into a sponge cell, and then, it differentiates into an amoeboid leucocyte. So that the major portion of a sponge is composed of the aggregated or isolated zoochlorellas. It is said that the sponge is "a living hotel". So in my material too, it gives harbour to other many kinds of microorganisms (bacteria, algae, diatoms, ciliates and the others). Therefore, we can say that, so far as, the present material, the fresh water sponge, is concerned, the sponge may be classified rather to plant kingdom than animal.

## (4) Evolution of bacteria through the second coacervation

It has been supposed that every microorganism proliferates and continues its existence by means of cell division. But according to my opinion it is not in all. That is to say, the results of my own observations show that some of saprogenous bacteria, on the surface of foul water or on the putrefying substance, aggregate and agglutinate and then they form a mass, it further differentiates, in accordance with its different circumstances, into a certain kind of fungus, spore, alga, infusoria or amoeba etc. by means of the second coacervation-process (designated by me. It means the new formation of a cell from a mass of lower microorganisms). Some kind of earthworm's blood cell filled with a number of fungi-like inclusion also may be included in the same category.

## (5) Intracellular symbionts and new formation of cells.

It is a well-known fact that the mycetocytes found in a certain kind of insects and other animals or plants include many bacteria or yeasts in their cytoplasm, and these microorganisms are, generally, considered as symbionts.

But, according to my observations described above (3 and 4) the so-called intracellular symbionts can not be considered as mere symbiotic microorganisms, but it may rather be referred to an aggregated mass of microorganisms, and from that mass than arises a new cell element through the second concervation (overcenter), fiscent, organization, and differentiation) of it. No evidence has yet been shown, by any investigators, that these microorganisms had been phagocytized by prexisting phagocyte (mycetocyte).

## (6) New formation of erythrocytes in the digestive tract

According to my opinion the erythrocytes in higher animals are a basal element from which almost all kinds of cells are derived, while there can be found no firm evidence that erythrocytes proliferate in the normal bone marrow (Chishima '53 b, '54 b).

The author agrees with the opinion presented by Duran-Jorda ('47~'51) who claims that the bone marrow of higher animals is not a site of erythropoiesis, but erythrocytes are produced, in situ, within the granular leucocyte in the intestinal wall. And further, I have, found (Chishima '53 b, '55 a) that the nucleated erythrocytes in aves and amphibia show transitions from the cell in lamina propria of the intestinal villi, on the other hand, primordium of non-nucleated mammalian erythrocytes make its appearance, de novo, in a vesicular and large cell located in the lamina propria by means of sporulation-like process. The surface of

intestinal villi, under the well-fed condition, is covered with a layer of digested food (fond monera), the homogeneous layer, which is generally apt to be misunderstood as a degenerating epithelium of villi. But, my experiment results secured by the feeding of colloidal carbon show that the layer, under the normal condition, is not a degenerating one but is a reverse case. In this homogeneous layer then arise, de novo, several numbers of lymphocytoid elements, which transform into the epithelial cells of villi, and further into spindle cells in the frog, or into normoblasts (or globular leucocytes) in the lamina propria of birds and mammals.

#### (7) Erythropoiesis in yolk sack and placenta.

Erythropoiesis in yolk sack (bird) and placenta (mammal) is the same in principle as that in the intestinal canal, though the materials for hemopoiesis is different in each case. Namely, the basic material of the yolk-sack-hemopoiesis is yolk sphere and that of placenta is the maternal blood.

belong, ontogenetically, to the digestive system. From this point of view, the ontogenetical transition of the erythropoietic center from yolk sack or placenta into digestive tract may be considered as a very natural route. My opinion mentioned above further may be substantiated by phylogenetical transition of hemopoietic center. On the contrary, there is no reliable evidence substantiating the theory of intramedullary erythropoiesis. In adition to it, the orthodox view involves a theoretical jumping as to the transition of hemopoietic center.

- (8) In this volume, this the following author described, further problems;
- (i) The transformation from non-pathogenic bacteria into some of pathogenic ones, may be quite within the bounds of possibility.
- Mitochondria, possibly, may regard as a phylogenical or ontogenical vestiges derived from a bacteria-mass from which ancestral cell might be developed.
- (iii) The author laid great stress on the intimate relationship between intracellular symbionts in the digestive canal of insects and new formation of cell.

In conclusion I should like to say that, for the question "Does life arise now, at the present time on our Earth?", "Does cell arise de novo, from some organic

matters having no cellular structure?" I can answer with confidence "Yes, it undoubtedly does." That is to say, under suitable conditions, some of bacteria, protozoa, and blood corpuscles emerge, de novo, from some organic substances with no cellular structure, and there can be shown more surprising facts that some type of cells are derived from an aggregated mass composed of a large number of bacteria or of lower microorganisms including the so-called intracellular symbionts.

My theory described above is so antagonistic to the orthodox view that the present author must expect many oppositions. However, the skeleton of my theory would not be broken by any other investigators.

So far as the origin of bacterium, cell or blood corpuscie is concerned, the adherents of Pasteur's doctrine and of Virchow's view should return, shortly after or in the near future, to the idea of Pouchet and Aristotle.

So bleihe denn die Sonne mir im Rücken!

Der Wassersturz, das Felsenriff durchbrausend,
Ihn schau' ich an mit wachsendem Entzücken.

Von Sturz zu Sturzen wälzt er jetzt in tausend,
Dann aber tausend Strömen sich ergiessend,
Hoch in die Lüft Schaum an Schäume sausend.

Allein wie herrlich, disem Sturm erspriessend,
Wölbt sich des bunten Bogens Wechseldauer,
Bald rein gezeichnet, bald in Luft zerfriessend,
Umher verbreitend duftig kühle Schauer.

Der spiegelt ab das menschliche Bestreben.
Ihm sinne nach, und du begreifst genauer:

Am farbigen Abglanz haben wir das Leben.

-J. W. von Goethe-

## PART IV

THE FOURTH PRINCIPLE: THE NEW-CELL FORMATION THEORY AND ITS PRACTICAL APPLICATION TO HEALTH AND MEDICINE.

CHAP I Relation between Lepeshinskaya's theory and Chishima's opinion.

(1) Outline of Chishima's opinion

The new-cell formation theory in this chapter is common in essence to the other three principles described above.

As previously described, the three principles—the First, the Second, and the Thirb Principle-are very much related with this new-cell formation theory.

The First Principle expresses the fact that all kinds of somatic cells and and germ cells with each typical nucleus are newly formed from the crythrocytes of Mammalia including human beings which are nonnuclested protoplasmic corpuscles and belong to a precellular stage, or to the stage of a moneralike organic substance.

The Second Principle expresses the fact that under the well-fed condition, all kinds of somatic cells and germ cells are newly formed from the erythrocytes of Mammalia which are non-nucleated ones, and from the erythrocytes of birds and lower animals which are nucleated ones, but that under the ill-fed condition, or at an embryonic stage, these fixed cellular elements differentiate reversely into erythrocytes through the "reverse A. F. D. Process".

And the Third Principle expresses the fact that bacteria are spontaneously generated, and then a certain Protozoa are newly formed from putrefactive bacteria through the A.F.D. Process.

It is needless to say that all of these principles in biology are what this author discovered first in the world.

- Lepeshinskaya's discovery on new-cell formation, and this author's studies on it
- O. B. Lepeshinskaya, the Soviet cytologist and haematologist, published her theory on new-cell formation in 1937, prior to this author's publication.

She says in her reports between 1937 and 1956 that she discovered the fact that the embryonic erythrocytes of domestic chicken and amphibian larvae, or a frog's larvae, were newly formed from the yolkspheres of a developing ovum.

It was in 1952 that her first paper on new-cell formation was translated into Japanese by Dr. Kusano and was published on the Japanese Quartery Journal of Biology by Iwanami, the publisher. (See the Japanese Quartery Journal of Biology, "Seibutsu Kagaku", vol. 3, No.4, 1952) Then Dr. Yasugi, editor of the Journal, was kind enough to see her paper and advise this author to publish his opinion on new-cell formation, for Dr. Yasugi had known this author's studies on it.

Thanking Dr. Yasugi for his kind edvice, this author sent his paper to the adition of the dominal vary score. This surfor is very sorry to say that he did not know Lepeshinskaya's discovery till then, but, as for this author, when he was studying the histogenesis of a chick embryo at Kyushu Imeperial University between 1940 and 1950, he often saw that cells were newly formed from the yolkspheres of a chick embryo and from the cell fragments in the blood through the "A. F. D. Process".

In 1947, this author published his new discovery that the primodial germ cells of a chick embryo are newly formed from the erythrocytes of an embryo.

And then this author intended to go on to publish his theory on newcell formation, but he gave up trying so in fear that he should be misunderstood in the orthodox academic circles by publishing one after another a new startling theory that is quite different from the orthodox one.

But, as previously described, Lepeshinskaya's theory was introduced into this country, and this author was advised to publish his theory, so this author was willing to publish his theory on the Japanese Quartery Journal of Biology in 1953. (See the Journal, vol. 4, Na 1, 1953)

This was the first time that this author had ever published his theory on new-cell formation. And it seemed that Lepeshinskaya's and this author's theory both had a fair influence upon the biological and medical societies, then.

Prof. Shigeyasu Amano at Kyoto Imperial University, and president of the Japan Haematological Society in those days, published his opinion against the new-cell formation theory on the same Journal, vol. 4, No. 3, 1953.

Dr. Shichiro Sato at Tokyo University and Prof. Dr. Koen Yoshimatsu at Yamanashi University supported us, but their support was passive.

Then, this author disputed with Prof. Amano on the Journal, vol. 5, No.1, 1953, raising the seven questions as to his opinion, and requested him to reply to those seven questions, but he made not a single reply to them in the long run. (See "the Basis of Neo-Biology" by K. Chishima, vol. 2, pp. 27-pp. 104. This monograph was republished as the first volume of Chishima's complete works series.)

If you read the book "Basis of Neo-Biology" with good care, you will surely see that Prof. Amano and the scientists in this country who stand against the new-cell theory are incorrect in both theory and fact,

- Agreements and differences between Loveshinskbyn's and this author's theory on new-cell formation
- a. Agreements between Lepeshinskaya and this author

As a whole, Lepeshinskaya's and this author's theory are similar to each other, especially as to the following point:

That is to say, cells are prodused from organic substances with no cellular structure such as yolkspheres, egg albumen in the eggs of hens and frogs, and others.

It was in 1936 that Lepeshinskaya discovered this fact and published it bravely, and as for this author, it was in 1952 that he published his theory on new-cell formation. Namely, it was not until her first paper on new-cell formation was introduced into this country in 1952 that this author knew her studies on it. Therefore, this author had been studying it since 1940 without knowing her studies on it.

Her theory is a revolutionary one in opposition to the orthodox cell theory that has been blindly believed since Virchow established it.

This author will pay respect to her on this point.

But this author's theory is rather different from hers in the following points.

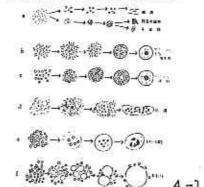
## b. Differences between Lepeshinskaya and this author

The following eleven points are the very facts that most of the scientists including Lepeshinskaya, excepting this author, have ever misunderstood:

Fig. 4 ~ 1. Schematic illustration of the new formation of bacteria, red blood corpuscles, cell, microorganism and fat globule by means of AFD process.

(Aggregation, Fusion and Differentiation)

A-line. Showing new formation of bacteria, mesenchyme



and crythrocyte (both nucleated and non-nucleated) from organic substances.

- B−line. From bacterial mass→amoeba and lower microoganism.
- C-line. From zoochlorellas→a fresh water spongecell.
- D-line. From mycetoamoebas→a slime mold (Myxomycetes.)
  - line. From crythrocytes (non-nucleted or nucleated) -- a Polyanclear giant cell.
- F-line. From crythrocytes→a fat cell or a fat globule.
- (I) Lepeshinskaya does not understand enough the fact that the red blood corpuscles derived from the yolkspheres of hens or frogs, differentiate into other cells, and especially she misses the fact that the red blood corpuscles of adults in Mammalia, whose crythrocytes are non-nucleated ones, differentiate into all the kinds of cells with a nucleus.
- (II) There is some difference between Lepeshinskaya and this author in opinion as to the process of erythrocyte-poiesis from the yolkspheres, egg albumen, and other organic matters in hens or frogs.
- (III) As evidence to show that those newly-formed erythrocytes are cells, Lepeshinskaya gives an explanation that they are proliferated by mitotic cell division, but this author does not think that mitotic cell division is the main factor of the proliferation of cells. For this author thinks that mitotic cell.

division is only a very rare exception.

- (N) Lepeshinskaya does not notice the fact that yolkspheres are produced from the erythrocytes of the mother animal, and that there is a reversible differentiation between the blood corpuscles and the fixed tissue cells.
- (V) Lepeshinskaya does not describe the fact that cells are proliferated through the budding and sporulation-like process of erythrocytes.
- (VI) Lepeshinskaya misses the fact that the haematopoietic center of adults in Mammalia is not the bone marrow but the intestinal villi, and at the embryonal stage of mammals, the cells are newly formed from the mother's blood in the villi of the placenta within the mother's uterus.
- (Vi) Lepeshinskaya misses the fact that the cells of bacteria are spontaneously generated from organic matter by putrefaction.
- (W) Lepeshinskaya does not notice the fact that the germ cells of mammals which are more highly-developed than insects are newly formed through the A. F. D. process of blood corpuscles.
- (E) Lepeshinskaya misses the fact that the sponge cells are newly formed through the A. F. D. process of lower microorganisms. For example, the sponge cells are newly formed from a mass of chlorellas.

Therefore, it may be said from an evolutional point of view that cells are newly formed through the symbiosis of bacteria and other microorganisms and through the AFD process of cellular fragments.

- (X) Lepeshinskaya misses the fact that in the process of new-cell formation, DNA and RNA are produced (synthesized) from protein in the protoplasm of cells.
- (XI) Lepeshinskaya misses the fact that all the cellular elements of cancer cells, of all the cells of inflammatory tissue, and of the cells in wound healing, are newly formed from erythrocytes.

From the above eleven points, you will see that this author studies on new-cell formation are far more extensive than Lepeshinskaya's. And it is needless to say that excepting the new-cell formation theory-the Fourth Principle — of the eight Principles presented by this author the other seven Principles have been all discovered by myself. (See the book "Basis of Neo-Biology" by K. Chishima, vol. 2, pp. 75 — pp. 78, 1958. Or see its revised edition "Chishima's complete works vol. 1)

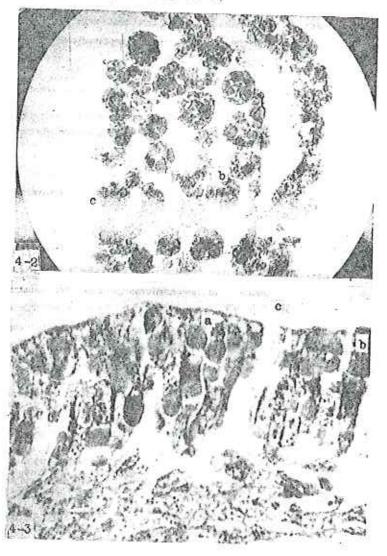


Fig. 4 - 2. New formation of erythrocytes and heart muscular tissue from yolk-spheres in the heart of a newly-hatched tadpole. (K. C.)

armwall of the heart composed of yolk-sphere-mass only, but then they differentiate into heart muscles.

b-aggregated yolk-spheres in the heart.

c...primordium of crythrocytes with a nucleus.

After few days, they develop into normal erythrocytes.

Fig. 4 - 3. Showing the differentiation from yolk-spheres arranged in a line(a) into the columnar cpithelial cell of the intestinal mucous membrane in the young tadpole, in five days after hatching.
c...intestinal cavity.

Fig. 4 - 4. New formation of a mesenchyme cell from yolk-sphere-mass in the frog's embryo. (K.C.)

pmc...previous stage of the mesenchyme cell formation from yolk-shere-mass through the AFDprocess.

my melanin pigment y newyolk-sphere-mass

Fig. 4 - 5. New formation of a sponge cell from zoochlorellamass through the AFD process in the fresh water sponge of the Nagara river (Japan).

Aggregated mass of zoochlorella (a) differentiate into a sponge cell with a nucleus (b).

Fig. 4 - 6. New formation of primordial paramecium (protozoa) (a) from bacteria-mass through the intermediate stage (b) between bacterial-mass and paramecium.

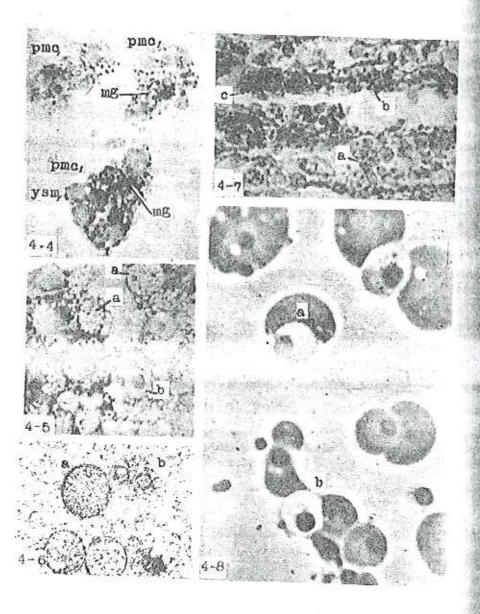
Primordial paramecium then develop into typical paramecium with cillia.(K.C.)

Fig. 4-7. New formation of striated muscular tissue from yolk spheres (standing in a line) in the tadpole's tail. (K.C.)

(a)...yolk-sphere. →(b)...intermediate stage between yolk-spheres and muscle fiber →(c)...begining of newly forming muscle fiber. (K. C.)

Fig. 4 - 8. New formation of a leucocyte from an crythrocyte through the extrusion of its cytoplasm (budding-like process)

a...Single crythrocyte, b...Co-operative extrusion from  $2\sim3$  crythrocytes.



Living crythrocytes under culture. (Phase contrast microphotograph) (K.C.)

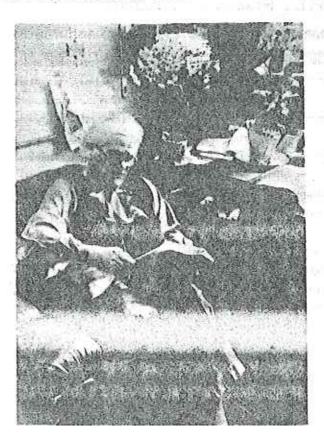


Fig. 4 - 9. O.B. Lepeshinskaya(Academician of U.S.S.R.), the first adovocator of the new-cell-formation theory.

This photograph was presented to this author from her.

## CHAP.II. Practical Application of the New-Cell Formation Theory to Health and Medicine

It has been belived as a golden law in the orthodox biology and medical science that all the cells are proliferated by mitotic cell division.

But, if they now admitted the discovery that cells are newly formed from organic substances with no cell structure, the orthodox biologists and medical scientists would be obliged to reform fundamentally such sciences as embryology, genetics, physiology, pathology, bacteriology, epidemiology, virology, especially cancer research, medicine, biology, ...etc.

Therefore, it seems that they will not admit a new theory on new-cell formation presented by both Lepeshinskaya and this author, being afraid of a revolution of the orthodox sciences.

And also they have published no papers against the new-cell formation theory that they could make us both consent to.

No syrate, it is cortain that the acadesil formation theory will request the orthodox biology and medical science to be reformed fundamentally in both theory and practice.

The new-cell formation theory will be effectively applied to the following cases in modern medical science:

(1) Prevention against and the medical treatment for cancer

This theory will be of great use not only in preventing and treating cancer, but also in trying to find the cause of cancer. (As for the particulars, see the PART 1-III)

(2) Prevention against and the medical treatment for inflammation which is the central problem in the internal medicine

Inflammation arises from the convergence of crythrocytes into the affected part, and then crythrocytes differentiate into the leucocytes and all the cells of inflammatory tissue.

Therefore, it is necessary that we should improve or balance the quality and

quantity of blood in order to prevent the occurrence of inflammation Moreover, under the normal condition blood or crythrocyte is produced in the intestinal villi, or haematopoiesis is performed in the villi, so it will be necessary that we should improve or balance the quality and quantity of food, and then harmonize mind, body, and muscular movement with one another in order to improve or balance the quality and quantity of blood.

(As for the particulars, see PART I -III.)

(3) Prevention against and the medical treatment for infectious diseases

In this case, the new-cell formation theory of hacteria may be effectively applied to the prevention against and the medical treatment for infectious diseases.

For infectious diseases are often caused by the rapid decreasing of vitality of an organism without being infected with pathogenic microorganisms.

(4) Wound hasling which is the fundamental problem in the surgical medicine

Wound healing is performed by the connective tissue cells which arise from non-nucleated red blood corpuscles in Mammalia through the new-cell formation process.

In addition to these cases, the new-cell formation theory will be widely applied to health and sanitation, and eugenics and genetics. (As for the particulars, see PART I - III.)

CHAP. III. Monographs and papers on the new-cell formation theory presented by this author.

## (A) Monographs

(1): In 1958 K.Chishima published the book "Basis of Neo Biology vol. 2", and described the following themes on the new-cell formation in it(1958): (And this monographwas published (revised edition) as a "Chishima's complete works vol. 1. 1972).

- i) General Description and Points in Dispute on New-cell Formation, pp. 27-pp.104
- Relations between New-cell Formation and Intracellular Symbionts, pp. 213-275
- On the Symbionts in the Digestive Canal and the Relations between the Symbionts and the New Formation of cells, and blood corpuscles, pp. 221-300.
- (2): "Revolution of Medical and Biological Sciences" by K.Chishima, (1963) in Japanese.

This monograph also was published (revised edition) as a "Chishima's complete works vol. 3, 1972)

In this monograph, this author also described "On the New-cell Formation and Evolution in Relation to the  $\Lambda$ .F.D process (pp. 5 - 57).

(3) The cleavage of amphibian egg and yolksphere's role played on the increasing in number of embryonic cells.

----Re-examination of the cell-theory----- #

#### Kikuo Chishima

Reprinted from RESEARCH BULLETIN OF THE FACULTY OF AGRICULTURE, GIFU UNIVERSITY No. 6: 268-278 (Jan., 1956)

Résumé

Some investigations were made on the relation between the mechanism of imcreasing in number of blastomeres during the cleavage and on the new-formation of cells from the yolkspheres of developing egg of amphibia, Bufo vulgaris, Rana japonica G, and Rhacophorus reinwardti by means of ordinary sections and of some histochemical techniques.

The results of the investigations may be summarized as fallows:

- (1) The blastomere formation at the early stage of development is performed by the formation of segmentation plane accompanied with melanin granules. But the nuclei of these blastomeres do not show typical nuclear structure and behaviour, c. i., (i) negative Feulgen reaction, (ii) show no typical phases of mitotic division, (iii) each of these nuclei is composed of clear vacuole surrounded by melanin granules which are continuous and mingled with peripheral yolkspheres. Therefore, the writer designates it as a "melaninous primordial nucleus".
- (2) Gastrulation is not an actual invagination of ectodermal cells, but is an invasion of cleavage line accompanied melanin granules. Though there is no cellular structure, at first, then there appear clear transitional phases from yolksperes situated around the melanin (cleavage plane) into the clean its of entoderm and dorso or ventral lip of blastopore. Therefore, it seems probable that the melanin pigment derived from yolkspheres plays an important role in the development or differentiation of embryonic tissues and it seems to bear a certain relation to the organizer.
- (3) There can be found no sound evidence of the orthodox view which interprets small and numerous blastomeres at the blastula stage as a descendant derived, by mitotic division, from a glant blastomere of the morula stage. On the contrary there is the following clear series of transition; scattered yolkspheres→aggregation of certain number of yolkspheres→formation of melanin graules from yolkspheres and yolklysis→appearance of melanin in the yolksphere mass small blastomere with faint basophilic nucleus and with cytoplasm contained yolkspheres (the so-called yolk-cell) → ordinary embryonic cell with a nucle us implied DNA and with cytoplasm contained melanin granules.
- (4) At the early developmental stage of the embryo there can be found, somtimes, the blastomere with double nuclei or lobed nucleus. These blastomeres seem to be at a stage of new-formation of nucleus in the yolksphere-mass, but they may not be a phase of amilosis, since there can be seen no typical phases of amitosis.
- (5) Yolkspheres of developing frog's egg should be considered as a ground substance, from which the embryonic cells may be formed, rather than a nurient

substance for the cell-growth.

The gelatinous layer surrounding the egg surface shows the following series of transitions into ectodermal elements; Gelatin layer > the melanin granules on the egg surface -> yolkspheres -> ectodermal element with melaniferous pri mordialnucleus. The above mentioned process is supported further by the following facts that, (i) the erythrocytes on the surface of growing ovum in adult frog, transform into yolkspheres through melanin pigment-stage, (ii) newly hatched larvae still has a large amount of yolk as much as that of egg at early developmental stage,

- (6) It is inevitable that the results of the present studies should lead to a re-examination of germ-layer theory, which claims that the increase in number of several kinds of embryonic cells is due, entirely, to the mytotic division of respective blastomeres belonging to a certain germ-layer. On the contrary, there can, always, be found sound evidence of new-formation of embryonic cells from yolkspheres.
- (7) The relation between the orthodox view on cleavage and our opinion as to the "new-formation of cell from living substance" was discussed.

#### EXPLANATION OF FIGURES

#### Abbreviations

cn--canal-like prigmordium of

cp--classage plane with melanin

dissersal up of biestopore

dn--double nuclei

ect---ectoderm

ent---entoderm

gd-germinal disk without typical nuclear structure

in---lobed nucleus

mi-tobed interest

mf...mitotic figure

mig...melanin granules

ml---mclanin layer

mm--melanin membrane

nc--new-formation of primordial cell pec--primordial ectodermal cell

proceeding of making and endead of political and making

proce-pric with melanin-nucleus

pinca---mesenchyme cell still having melanin granules

pnd---primordial nucleus with dendrite-like process of melanin granules

so-syncytium of cctoderm

vi---ventral lip of blastopore

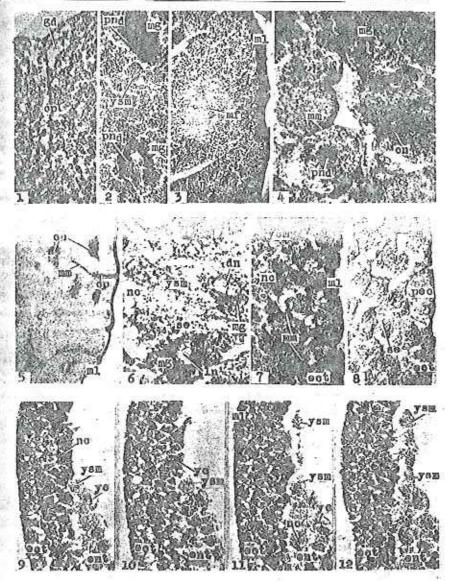
ye...the so-called yolk.cell

yp...yolk plug

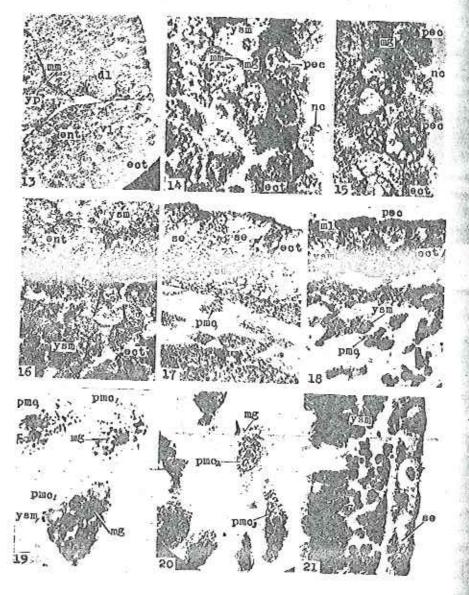
ysm---yolksphere-mass with melanin granules

(1) A Bufo's egg at the 1st cleavage stage: (2) Two primordial nuclei with melanin granules. In the vacuole-like portion of the nucleus contains yolkspheres: (3) Typical mitotic figure in a blastomere of Rana Jap: (4) Blastomeres of a Bufo's embryo at morula stage: (5) Blastomeres of Bufo's embryo at morula stage. Showing a clongated 'tube-like' primordial nucleus with melanin: (6) Blastomere's syncytium of Bufo's embryo at the blastula stage. Showing a double nuclei and a lobed nucleus: (7) Part of ectoderm at the blastula stage of Bufo's embryo. Showing the some of blastomeres with primordial nuclei, while others without nucleus: (8) Part of ectoderm of the somewhat earlier stage than that of figure 7: (7)~(12) Serial sections of part of blastula-wall of Bufo's embryo. Showing the ectodermal layer are composed of primordial cell without ordinal nuclei, while the elements of entodermal area are consisted with yolkspheres or yolk-cell: (13) Region of blastopore of Bufo-embryo at yolk plug stage. Both of dorsal and ventral lip of blastopore still have not segregated into ectoderm

and entodorm. And they are composed of yolksphere-mass only: (14) Ectoderm of a Bufo-embryo previous to 4 days of hatching: (15) A section from the same material as that of figure 14, but is not stained: (16) An area along the blastopore of Bufo-Embryo of before 4 days of hatching. The area show no cell-structure but is composed of yolksphere masses only: (17) Ectodermal syncytium of Bufo-embryo of before 4 days of hatching. Notice there is no ordinary cell,



while major part of it is composed of yolksphere masses: (18) A section from another individual as the some developmental age as that shown in fig. 17: (19) Primordial mesenchyme cells composed of yolkspheres and melanin granules in the lumen between the head epithel and the fore brain of Bufo embryo of before 3 days of hatching: (20) Purther differentiated stage of mesenchyme cell of Bufo-larvae of 1 day (21) Ectodermal syncytium of Bufo-larvae of 1 day.



- (B) The papers in Japanese on the new formation of cells published by K.Chishima.
- On the New-cell Formation through the Cytoplasmic Budding of Erythrocytes, "Kagaku" (Iwanami) vol.20, No.10-11. (1950)
- (2) On the New-cell Formation, and the Differentiatiation and Division of cells, "Seibutsu Kagaku", (Iwanami, Tokyo) vol. 4, No. 1 (1950).
- (3) Criticism on Prof. Amano's Opinion Denying Lepeshinskaya's Revolutionary Cell Theory, "Scibutsu Kagaku" (Iwanami, Tokyo), vol. 5, No. 1 (1950)
- (4) On the Discussions among Biologists on Lepcshinskaya's New Cell Theory, "Kokumin no Kagaku", Feb. (1956)
- (5) On the Some Conflicting Points in the Opinion between Lepeshinskaya and Chishima on the New-Cell Formation, "Soviet Igaku", vol. 4, No. 2. (1956).
- (6) Oparin's Opinion on Lepeshinskaya's New Cell Theory, "Shizen", (Chue-koron-shya, Tokyo)
- (7) On the relation between the increasing in number of embryonic blastmares or cells and the role of yolk-spheres in Amphibian larvae.
  - Reexamination of embryological "germ-layer theory"
    By K. CHISHIMA
  - "Seibutsu kagaku" (Iwanami) vol. 8, No. 3, 1956 : pp.118-125).
- (8) The revised editions of all the papers described above are cellected in "Chishima's Complete Works Series vol. 8.

## PART V

THE FIFTH PRINCIPLE: THE INTESTI-NAL HAMATOPOIETIC THEORY

CHAP. I Contradiction of the Intramedullary
Haematopoietic Theory and Evidence
of the Intestinal Haematopoietic Theory

At present, the intramedullary haematopoietic theory that erythrocytes are produced in the bone marrow of the long bones is referred to be an established theory on hesmatology, in the biological and employed releases. But this author discovered eighteen years ago that the theory goes against the facts and includes much contradiction in it. And this author published his papers in English against the theory between 1953 and 1963. (As for the particulars, See K. Chishima's monographs in 1954, 1956, 1958, 1960, and 1972)

- Blind Spots of the orthodox intramedullary haematopoietic theory, and this author's finding on "intestinal haematopoiesis".
- (I) Under the healthy and well-nourished condition, the bone marrow is filled with fat, no mitotic figure of haemocytoblasts is to be seen in it, and no haemopoiesis is performed in it.

Under the healthy and well-nourished condition, the bone marrow of the long bones in man, mammals, aves, and amphibians is filled mainly with the yellow bone marrow, or fatty tissue.

And a haemocytoblast which has been referred to be a mother-cell of all the

blood corpuscles, hardly shows any mitotic figure. It is generally believed that in the case of an adult, about two million million erythrocytes are produced in his body every day, and they vanish somewhere in his body every day. But, perhaps there is, at present, not a single haematologist in the world who can deny or explain such a contradicted fact.

In 1925 the three American haematologists, Doan, Cunningham, and Sabin, observed and published their experimental results that after fowl and pigeon had been starved out for nine or eleven days, or after they had had excessive bleeding, their bone marrows turned red, and numerous crythrocytes appeared in their bone marrows. After that, they recklessly applied this fact observed only under the ill-fed condition to animals and men under the healthy and well-fed condition, and advocated that crythrocytes are always produced in the hone marrow of the long bones.

As a result, this intramedullary haematopoietic theory has been uncriticallys accepted by most of the haematologists in the world, and it has now become the orthodox theory.

② Intramedullary haematopoiesis may be well explained only by this author's Reverse Dfferentiation Theory

The theory that erythrocytes are produced in the bone marrow of the long bones is not correct because it ignores the fact that there is a reversible differentiation between erythrocytes and fatty tissue or other fixed cellular elements, according to the changes of the nutrient condition.

It may be proved by the following facts that the intramedullary haematopoictic theory is incorrect: (i) the theory ignores that there is a reversible differentiation, (ii) the haemocytoblast which is thought to be the mother of erythrocytes in the normal bone marrow does not show any mitotic figure at all, and (iii) the bone marrow is filled with fat under the well fed condition.

Neverthless, the orthodox haematologists (including Dr. Sabin, et al) applied uncritically the abnormal fact, the reverse differentiation of fat into the blood cells under the starved condition or after a large amount of bleeding, to the normal, well-nourished condition. It is clearly illogical.

Moreover, the orthodox hematoopoietic theory does not agree with the facts.

## (3) The extramedullary haematopoietic theory is incrorrect, too.

According to this author's experimental results, it was found that all sorts of fat, tissues, including the tissues of the viscoral organs, and cells in the body, differentiate reversely into the blood corpuscles under the ill-fed condition and after excessive bleeding.

Hacmatologists who have seen this process, the reverse differentiation of fat, tissues, and cells into the blood corpuscles-designated it "extramedullary haematopoicsis". It is true that numerous erythrocytes can be seen in these areas, but there can never be seen any mitotic figures in the site.

It seems that the orthodox haematologists are unaware of the irrationality of the theory, or they are intentionally disregarding it.

However, this contradiction included in the "extramedullary haematopoietic theory" will be able smoothly to be understood only by this author's theory and it will be verified on the indisputable facts.

## The haematopoietic center is a villus.

The haematopoietic center is closely related with the digestive organs in both phylogeny and ontogeny. It is certain that there are villi in the center, and haematopoiesis is always performed in the villi. On the other hand, there can be found no villi in the bone marrow. And this expresses the fact that the intramedullary haematopoietic theory is in great doubt.

As shown in Fig.5-1-3, at the first stage of ontogeny, the blood corpuscles are newly formed in the villi of the surface of a yolksac from the yolkspheres, and at the following stages, the blood corpuscles of the animals below birds are newly formed in the villi of the intestinal mucous membrane from food moneratigested food substances. But in the case of Mammalia including man, there are a fewer yolkspheres in the egg, so that "yolksac haematopoiesis" is not so actively performed at the first stage of ontogeny, and as a result, at the following stages, the embryonal crythrocytes are newly formed in the villi of the placenta which is made in the interior of the mother's uterus, from the mother's blood corpuscles.

And it is of course that any mitotic figures can never be seen in all

these villi. In spite of this fact, the embryonal blood corpuscles vigorously increase in number.



Fig. 5 - 1. Microphotograph showing this author's new theory that the hacmatopoietic center is in the intestinal villi (K.C.)

A...Digested food substance (food monera) is adhered to the surface of the intestinal villi of a frog.

B.-From(A)newly arise the epithelial cells of a villus(B)through the transitional stage(E) (with no nucleus)

C.-From (B) arise the young erythrocytes and carried by capillary.

1)...intestinal cavity. E. transitional stage.

Fig. 5-2. Longitudinal section of the middle portion of a villus in the goat's small intestine.

a lamina propria cellialis transformed into several erythrocytes they the budding-like or sporulation-like process.

Namely, the epithelial cells of villi are newly formed from the materials such as yolkspheres, the mother's blood, and food monera, while erythrocytes are newly formed from these epithelial cells.

It is natural, from a phylogenetic point of view, that the site in which the cells and crythrocytes from the lower animals to the higher vertebrates are formed should be the coelenteron or the digestive canal belonging to the digestive system.

Therefore, it may be said to be unreasonable, from an embryonic or a phylogenetic point of view, that disregarding these facts, the orthodox haematologists persist that haematopoiesis is performed in the bone marrow which has no direct relation to the digestive system.

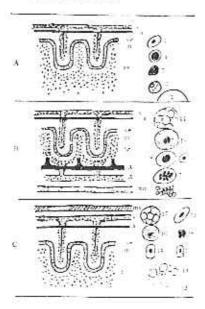


Fig. 5-3. Schematic figure showing the transition of the haematopoietic organ (villus) according to ontogenetical development in the vertebrates including man.

A ... Early embryonal stage.

Haematopoiesis in the yolk-sac-villi. From yolkspheres into blood corpuscles through transitional phases. B ... Embryonal stage in mammals.

Haematoporesis in the villi of the aterus-mucous membrane from the mother's billood corpuseles into embryome blood corpuseles.

C -- From new-horn to adult stage.

Haematonoresis in the intestinal villi. From digested food substance into blood corpuscies.

Abbreviations

V -vein: a cartery: vec-epithel of villus: m-stransitional phase between the material yolk sphere, mother's blood corpor food: y5 volksphere: pcc-mother's blood corp. : A and 8 vertery and vein in the wall of mother's uterus: muscular layer of uterus.

mi muscule layer of intestine! fooligested food substance.

5 The orthodox haematologists have misunderstood the reverse order of the differentiation of cellular elements in the bone macrow.

As shown in Fig. 5-1 - 3, the order of the differentiation of cellular elements in the orthodox intramedullary bacmatopoietic theory is just the opposite of the order idirection, in this author's theory.

For instance, they think that the normoblast, which is called the mother cell of non-nucleated human erythrocytes, is fifty or sixty times as large as an erythrocyte, in volume, and this large erythroblast differentiates into a very much smaller non-nucleated erythrocyte.

But it has yet been proved whether the large nucleus dissolves away or denucleates.

And it may be said to be very wasteful and irrational that only a very much smaller crythrocyte, one fiftieth or one sixtieth of a crythroblast in volume, is produced from a huge crythroblast in a living body which is organized so as to avoid the waste of energy to the utmost.

According to the results of this author's studies on hamatopoiesis, the so-called erythroblast, or the myelohlast, is not the mother cell of an erythrocyte, but it is a resultant from a mass of erythrocytes through the A.F.D.Process under the well fed healthy condition.

Such giant cells as the so-called reticular cells and megakaryocytes are also the very cells that are newly formed from erythrocytes through the A.F.D. Process, synthesizing new nuclei, and with the passage of time, they change ultimately into fat cells and fat tissue, or they change into the yellow bone marrow which is contained in the normal bone marrow, and under the abnormal conditions, such as starvation, and excessive bleeding, the giant cell differentiates reversely into a great number of crythrocytes which are non-nucleated ones.

Therefore, this author has been insisting that direction of the genesis of collular elements in the bone marrow which is shown in the established schematic table should be revised in order that the arrow may be turned toward the opposite direction of it.

6 Peculiarity of the blood vessel system of the bone marrow under the starved conditition

When the bone marrow is under the starved condition, a new blood vessel system arises in the bone marrow, showing its peculiarity.

This evidently expresses the fact that under the normal condition, the blood vessel and the blood cells contained in it degenerate into fat, and then they give rise to the yellow marrow, while under the starved condition, fat tissue diffrentiates reversely into the blood vessel and blood cells. The peculiarity of the blood vessel system of the bone marow under the starved condition also show the reappearance of it from fat tissue.

7 Some hacmatologists think that the bone marrow is the site in which erthrocytes are destroyed

When the non-nucleated crythrocytes of Mammalia differentiate into other kinds of cells through the A.F.D. Process, and these aggregated crythrocytes fuse mutually, they looks as if they were all destroyed. This author calls this state blood monera. Monera is the technical term which Haeckel created, since he thought it of as a sort of protoplasmic mass with no nucleus at the previous stage of cell. At present, the "monera" theory by Haeckel is, indeed, rejected by most of the biologists, but Haeckel's view is quite true. "Blood monera, termed by this author comes under the same category as Haeckel's.

In this "monera"-in an aggregating and fusing mass of erythrocytes-, several nuclei DNA) are synthesized newly, in situ, (or in the site), and then cells are newly formed in it.

Such a phenomenon can be seen not only in the bone marrow but also in all kind of normal tissues. Especially, in the case of the inflammatory area and wound healing, it can be seen more distinctly.

The orthodox intramedullary haematopoietic theory has much contradiction and irrationality in itself.

Finally, this author may draw the conclusion that the orthodox haematologists adhering to the orthodox intramedullary haematopoietic theory have misunderstood the following very important points:

- They disregard the reverse differentiation of crythrocytes, according to the changes of the nutritive conditions of organisms.
- (ii) They misunderstand the meaning of the haematopoietic center (or haematopoietic tissue).
- (iii) They are unaware that mitotic cell proliferation is very rarely in the hone marrow. So it can not be considered that mitosis is not the main mechanism of the production in huge number of crythrocytes every day.
  - iv) They are unaware that the order of the differentiation between the erythrocytes and the marrow elements is just the opposite of the direction that they have believed correct.
  - v) They have neglected that the haematopoietic tissue is a villus at any stage of ontogeny.
- vi. They have overlooked that cells are newly formed through the A. F. D. process.
- vii They have misunderstood that the so-called extramedullary hacmatopointic center is only a site of the process of the reverse differentiation of tissues or fat into the blood cells or crythrocytes:

The most decisive evidence to prove the fault of the orthodox intramedullary haematopoiesis theory.

In Japan there is the case of a DARCMASAN who was unfortunately amputated surgincally his both arms and both legs owing to a wound by war or certain disease in a Cangrene.

According to the orthodox hematology, such a men must inevitably suffer from anaemia, owing to the loss of all the bone marrow of the long bones where erythrocyte's Potesis may be performed.

But, as it is, the man shows no sum of anaemra, but high virality. This author knows the case of a woman who lost her both arms and legs, early in life, suffering from Gangrene, but she lived sixty years and she was mother of two children.

This author knows some other instances resembling this case.

At any rate, this fact is the most decisive evidence to prove the fault of the orthodox erythropoiette theory.

# CHAP. II Practical Application of the Intestinal Haematopoietic Theory to Daily Life

Of the above five principles, the Fifth Principle, the intestinal haemopoletic theory, may be said to be less important than the other four principles that domain of science, indeed, but it may be considered much more important than the other principles in the sphere of its application to daily life.

11 Normal blood -pure and fresh blood is the basal factor by which one's health is preserved and one's life is prolonged. And the digestive organs in which blood is produced are the root of life.

The orthodox haematopoietic theory that haematopoiesis is performed in the bone marrow of the long bones cannot tell us anything about the proper way to produce normal and healthy blood. But, on the other hand, those who know intestinal haematopoiesis and understand the eight principles on life and medicine presented by this author, will realize that blood is the source of life, and the root of life in which blood is produced lies in the digestive system.

The villi in the digestive organs, especially in the intestinal mucous membrane correspond exactly to the roots of a plant absorbing nutrients. And food is the body what soil is to the plant.

Therefore, it is necessary that we should try to improve or balance the quali and quantity of food in order to preserve our health and prolong our life.

And it is also necessary that we should try to improve our eating habit considering the quantity and quality of food to live a hopeful and thankful I excluding every day's mental stress, to take moderate muscular movement, to make the harmony of mind, body, and movement, in order to promote health of the digestive organs.

## (2) Reduced diet, vegetarianism, and chewing the "35 dietary rule

Gluttony, overdrinking, and overeating-especially the overeating of animal protein, animal fat, and white sugar, dilute digestive juice, then bring about the putre-faction of the intestinal contents, then lead to the acidosis of blood, and at last develop bacterial toxin in the intestines. And besides, gluttony, overeating, and overdrinking may be the cause of all sorts of chronic diseases including cancer.

This will be well shown by the fact that the occurrence rate and death rate of cancer both were extremely low at the time of a food shortage during the second World War, but with the favourable turn of the food situation in postwar times, various kinds of diseases has rapidly increased in number, and, as a result, hospitals which were, once, almost empty in wartime are now filled with patients who are suffering from various kinds of diseases including cancer.

And also it has been proved from the results of many experiments that one group of animals forced to reduced their diet, develop slower but live longer than another group of animals allowed to eat their fill.

There is the proverb Too little is rather better than too much", but that is true in this case.

Therefore, it is necessary that we should try to avoid eating much, or getting luxurious in diet, and to eat moderately, or to take a strict diet.

This author would like to advise the sickly or the sick people to carry out strictly the "3 S" diet, or the "3 S" dietary rule: that is to say, "shoshoku", "saishoku", and "soshaku" ("shoohoku" in Japanese stand for reduced diet in English, "saishoku" for vegetarianism, and "soshaku" for chewing). For good chewing helps digestion and absorption, and reduced diet-reducing diet quantity to one-third or one half-is much healthful and economical than eating too much or eating in haste.

The following phrases can be found in the old sayings of Oriental medicine.

"Sokon mokuhi kore shoyaku" (Herbs are a small medicine.)

"Inshoku ifuku kore taiyaku"(food and drink, and clothes are a great medicine.)

"Mi wo osame, kokoro wo osameru, kore yakugen nari"-training mind and body is the source of medicine.

Now this author would like to add to them the phrase "Kagaku-yakuhin wa

kore geyaku nari" (Chemically synthesized new remedies are the lowest medicine.)

## (3) "Danjiki-rycho" - fasting cure-and minus dietetics

Fasting has been performed both in the Orient and in the Occident from ancient times. In Japan "danjiki-ryoho"-fasting cure is widely performed now. Fasting of one or two weeks or fasting of a longer term is often performed in order to train mind, improve constitutions, and treat diseases, having good effect on them.

In modern dictetics, the plus-side of dictetics is too much appraised but on the other hand, the minus-side of dictetics such as fasting, semistarvation, and reduced diet is too little appraised.

Therefore, there are at present, a great number of people in the civilized countries who are in poor health or suffering from various kinds of diseases, owing to overnutrition.

If correctly performed, fasting will have wonderful effect on the prevention against and the cure for such diseases as alimentary disorder, obesity, arteriosclerosis, hypertension, cerebral apoplexy, cancer, heart disease, hepatitis, diabetes, dermatitis, asthma, jaundice, neuritis, epilepsy, various kinds of suppurative inflammation, and other acute or chronic inflammations.

The reason fasting has wonderful effect on the prevention against and the cure for these diseases is that fasting has the functions of excreting noxious waste-matter or toxic substances deposited in the body, of differentiating tissues or cells reversely into the blood corpuscles, of cleaning up and rejuvenizing the alimentary canal or tissues or cells, of annihilating putrefactive bacteria in the intestines, of checking the development of bacterial toxin, and of exterminating parasites and pathogenic bacteria.

Therefore, it is necessary that modern dietetics should be re-examined in this respect, and then the favovrable side of minus dietetics should be reconsidered.

## (4) Nutrition and microbial symbionts in the intestinal canal

It is a cynical and paradoxical fact that mankind—the most highly-evolved animals—can never live without coexisting with microorganisms—the lowest organisms such as lactobacillus, and coli bacillus.

Originally, each of the digestive organs-especially the intestinal canal-has the most primitive nature, and in it a great many useful symbiotic microorganisms, harmful parasites, and putrefactive, or sometimes pathogenic, microorganisms are coexisting with the intestinal contents.

Therefore, man's health and life depend upon whether he can hold the useful symbionts of these intestinal microorganisms successfully or not.

According to the results of this author's studies on cells, the cells of the higher organisms at the first stage of their evolution are composed of the amoebae or paramecia which are spontaneously generated through the A. F. D. process of bacteria, and also the sponge cell of a fresh-water sponge which lives in the River Nagara (in Japan) are composed of scores of zoochlorella (unicellular green algae) which are spontaneously generated through the A.F.D. process of bacteria.

Therefore, cells at their death are disintegrated, or return to, into bacteria through the reverse A. F. D. process, and finally broken up.

Mitochondria in every cell look so much like cocci or bacilli that there are some scientists who say that mitochondria are the vestiges of bacterial symbionts. (Wallin).

This author also supports this theory.

In the intestines of insects, there can be usually found the symbionts such as bacteria, yeast, and Protozoa. These symbionts aid the insects to digest and absorb food, until at last they are absorbed as nutrition of the insects.

The three scientists, Steinhaus ('47:49) Caullery ('52), and Buchner ('53) described the results of their eminent researches that in a certain kind of insects, a mass of symbiotic bacteria which are mixed into the cells of the intestinal wall separate into the body cavity as a bacterial organ, or as a mycetome, and then they become the source of nutrition.

This author and his collaborator once observed the same phenomena in the case of termites (white ants), and we still have the microscopic films of it. Then, we also saw trychonympha campanula, innumerable bacteria and Protozoa there. especially in the intestines of the termites. As for the termites, it is well known that their symbionts are killed when oxygen tension is raised or atomospheric temperature is hightened, and then, the termites, originally having no enzyme that dissolves the cellulose of wood into their food, fall into the state of insufficient nutrition, and die a few days later.

As for the experimental animals and man, Rene Dubos, the famous American bacteriologists, describes this fact accurately in the book "Man Adapting" in 1968. In 1903, Metchnikoff publishes the theory that most of the diseases of old age are caused by toxic products arising from intestinal putrefaction. And he says in his paper that the reason the peasants in Bulgaria and in Southern Russia can enjoy living long is that they take a large amount of milk every day which is acidized by the proliferation of lacto bacillus bulgaricus.

In 1945, the three Denmark scholars O. Jensen, E.Olsen, and T.Geille who were members of the society for the study of longevity in Copen-hagen-published a very interesting report on the results that they obtained by re-examining Metchnikoff's theory.

They say in the report that Metchnikoff's theory that the lactobacilli in milk or y ogkurt which is fermented by lactobacilli are carried to the large intestine, and there they are proliferated by binal division is in the wrong, and, as a matter of fact, the lactobacilli in milk are sterilized, or killed, by hydrochloric acid in the stomach juice, and another lacto bacilli which are quite different from the lactobacilli in yoghurt are proliferated in the large intestine by using milk sugar in milk as the nurient. They conclude that as the latter bacilli produce lactic acid and check the proliferation of putrefactive bacilli(clostridia), the bacterial toxic of putrefactive hacteria is prevented from being produced and absorbed in the int estine, and, as a result, one's health is promoted, and one's long life is maintained According to this author's opinion, the reason one could maintain and promot one's health by taking milk or yoghurt is that lactobacilli are spontaneousl generated in the large intestine by taking milk or yoghurt because the char cteristics of bacteria depend upon the nature of their cultured media-milk ( yoghurt in this case.

Jensen says in his report that cane sugar, if taken in large quantities, is . absorbed in the small intestine, but milk sugar is carried to the large intesti without being absorbed in the small intestine and used as a good culture r dium for lacto bacilli.

And he goes on to say that one can take pharmacopoeial milk sugar interna instead of taking milk in order to maintain and promote one's health.

In ruminant animals, the first stomach is a sort of fermentation chamber,

there protein is synthesized by bacterial fermentation from food (vegetable) which they feed on Therefore, herbivorous animals can produce a large quantity of meat or milk, without eating animal protein.

## (5) The function of coli bacilli

It has never been decided whether coli or coliform bacilli are useful to the human body or harmful.

But a certain German scholar has recently published his studies on the function of coli bacilli saying that some of the coliform bacilli secrete lactic acid, and are very useful to health as well as lactobacilli.

Therefore, we may conclude that lacto bacilli and certain stam of the coli bacilli both are very much alike in characteristic and function, and then they are the very useful bacilli that can hold symbiosis with the human beings,

Hitherto bacteriologists discriminate scores of different strains of lact bacilli and coli bacilli, but according to this author's opinion, these different strains of bacteria are, most probably, due to the difference of their cultural media from which they arise spontaneously.

Since it is said that some of the lactobacilli or coliform bacilli are buried in the cells of the intestinal mucous membrane, we may think that they are absorbed into the large intestine through intracellular digestion.

Anyway, this author does not think that lactobacilli and coliform bacteria are so different in function from each other as they are generally imagined.

## (6) The influence of diet or health condition upon the bacterial flora of the gastrointestinal tract

The bacterial flora of the gastrointestinal tract is often influenced by dietetical composition. Especially, the characteristics and changes of the intestinal bacteria, as previously described, depend upon their culture media, and so there is a great possibility that the physicochemical constitution of the intestinal contents will become either physiological or pathogenic by the influence of diet, drugs, and a man's health condition, or a host's health condition.

Probably, in the case of "physiological", there arise useful symbionts, and in the case of "pathogenic", they change into harmful pathogenic bacterial flora.

In 1968, Rene Dubos suggested that we should think that the non-pathogenic bacteria change into the pathogenic bacteria.

But this author proposes that we should think that the bacterium A does not change into the bacterium B, but another kind of bacterial flora is newly formed by using the intestinal contents (feces) as a culture medium. And this theory will correspond better to the facts than Rene Duhos's theory.

This author also proposes theoretically that we should think that the infectious diseases may break out, beyond expectation, by the spontaneous generation of pathogenic bacterial flora without bacterial infection. For, as the environmental factors become worse, or as mental stress raises, the vitality of an individual becomes lower, and, as a result, there is possibility that the pathogenic bacterial flora is spontaneously generated.

Therefore, instead of fearing bacilli (pathogenic germs), we should try to lay stress on diet and health, and to increase the power of resistance to disease in order that we may prevent the infectious diseases in the digestive system. Most of the biologists and medical scientists generally believe that under the wel-fed condition, one increases the resistance of one's body to the infectious diseases, and destroys the pathogens or slows down the rate of their increasing in number in the body.

But, on the other hand, it is certain that one's health will be promoted, and one's life(.span) will be prolonged by performing the "3 S" dictary rule which this author is now advising people to. And it is of course that the this author stands against the orthodox dictetics, in this case.

In 1968, Rene Dubos says in his book, "However, this theory-the theory that under the well-fed condition, one increases the resistance of one's body to the infectious diseases is not supported on bacterial evidence. For according to the results of the tests with the animals compelled to be infected with the bacillisuch as tubercle bacilli, staphylococci, and Fridlander bacilli, the number of organisms recovered by culture in the blood, the liver, the lung, the spleen, and the kidney was constant within forty-eight hours following the infection, irrespective of diet composition and effect duration. Therefore, it does not seem that poor diets depress the resistance to the infectious diseases by interfering with the bacterial power of organs, or by favouring the multiplication of pathogens, at the early phase of infection."

Rene Dubos goes on to say. "In the case of rats, the inadequate diets such as aminoacid or lysine deficiency depress the activity of the reticuloendothelial system markedly, and then starvation or chronic undernutrition interfers with the harmonious activity of the body indirectly."

Dubos's opinion never conflicts with this author's opinion that one's health will be preserved and promoted by reducing the absolute quantity of the well-balanced diet, or by carrying out strictly the 3 S dietary rule.

## (7) Antibiotic or drugs and intestinal bacterial flora

In 1968, Rene Dubos says, "The administration of antimicrobial drugs often brings about the elimination of lactobacilli, anaerobic bacilli, and bacteroides from the gastrointestinal tract, and the proliferation of clostridia (harmful putrefactives), enterococci, and coliform bacilli. If the animals are fed on pellets, their bacterial flora will return to its pre-penicillin state within a few days or a few weeks at most after the discontinuance of drugs, and, if the animals are fed on the semisynthetic casein diet, it will take their bacterial flora a much longer time to go back to the normal state. In the case of the latter regimen, the animals will fail to overcome the disturbances in intestinal ecology which are caused by pencillin treatment."

It is common knowledge that when chicken or domestic animals are fed on antibiotic, their growth is effectively promoted by it, and also we sometimes see this process in the case of young human adults.

Opinion is divided on this reason, but Rene Dubos says in 1968. There exist many putrefactive bacteria (clostridia) in the intestinal contents of the animals which are slow in growth but when these animals are fed on antibiotic, clostridia in the intestinal contents are reduced, and the growth of these animals is remarkably promoted.

This reason is that putrefactive bacteria secrete toxin, and it promotes catabolism and disturbs aminoacid metabolism."

He goes on to say, "When the germ-free animals or mice are continuously fed on antibiotic, their lymphoid tissue is poorly developed, and their scrum  $\gamma$  globulin level is abnormally low.

Histologically, the intestinal wall of germ-free animals, which is thin and elastic,

is liable to be at an undifferentiated state.

In the case of the caecum, the weight of the caecal contents increases remarkably as well as that of the caecal sack, which occupies 30 to 90 per cent of the abdominal cavity. In fact, it may be said that the enlargement of the caecum is one of the most striking abnormalities resulting from germ-free life in many animals. In the case of germ-free adult guinea pigs, the intestinal mucous membrane still remains incomplete."

It is generally admitted that the animals fed under the germ-free condition are much more susceptible to various forms of stress (stress disease)or bacteria than the animals fed under the normal condition. And also it is well-known that when they are first exposed to the infections diseases experimentally or accidentally, the animals are slow in wound healing, weak in the resistance to the infections diseases, and susceptible to food derivation and nutrition deficiency. Sometimes, the animals (bacteria free) are lethally influenced even by the non-pathogenic bacteria which live in the healthy intestinal contents.

## (8) Environmental pollution-especially the contamination of foodstuffs and blood

With the development of industries, environmental pollution, such as air-pollution, water-pollution, and soil-pollution, arises in the most of the civilized countries, and, as a result, many people are now suffering from various kinds of diseases. The most alarming of all the assaults upon environment by man is the contamination of air, soil, rivers, and seas by harmful, or sometimes lethal, chemicals, and radioactive isotopes fallout. And environmental pollution inevitably results not only in contaminating our foodstuffs and drinking water, but also in injuring our health directly.

At present, many kinds of insecticides are widely used in farms, gardens, and homes by means of sprays, dusts, and aerosol simply because they are very convenient and effective.

But these insecticides are extremely dangerous because they contain harmful, chemical poisons such as organic phosphorite (parathion), organic chloride(D. D. T., B. H. C. etc.), organic mercury compound, lead, and arsenic compound or sometimes contain radioactive isotopes.

These poisons intrude into the blood stream through the mouth, the lung or the skin, and then reach all the tissues and cells.

And, as a result, they often cause infant malformation, cancer, leukemia, hepatitis, and the disturbances of the brain, the nervous system, the kidney, the spleen, the genital organs, and almost all the tissues and organs,

Human being will be destined to perish, or destroy themselves, in near future, if they go on contaminating the earth with these harmful, chemical, physical poisons.

Therefore, it is necessary that we should make every effort to exclude environmental pollution or public hazard, and to restore nature to what it used to be, on a world scale.

And it is also necessary that we should make every effort to reform the present-day society where industry is made too much of, prior to man, towards the natural society where man will take precedence over industry.

Once, this author was ipressed with those two books "Silent Spring" written by Rachel Carson in 1962, and "Man Adapting" by Rene Dubos in 1968.

Now, this author proposes that we, the civilized people, should try to harmonize man with nature, person with person, and mind with body.

As previously mentioned, it is necessary that we should usually try to hold "Ki kelsu no chowa" the harmony of mind, blood (food and living), and movement (sport) with one snother in order that we may maintain our health.

And this author believes firmly that this is the very way that can save us from being suddenly ruined by a nuclear war, and from being gradually declined by environmental pollution.

(9) Leukemia and anaemia are caused by the disturbance of the digestive organs

According to the orthodox haematopoietic theory, erythrocytes are produced in the bone marrow, and lymphocytes are formed in the lymph glands, but that is incorrect because there is no firm evidence for the facts.

On the contrary, according to the results of this author's studies on haematopoiesis, erythrocytes are formed in the villi of the intestinal mucosac of an adult. And lymphocytes and other leucocytes arise from the erythrocytes in most of the tissues. Under the malnutritional condition, leucocytes are derived from fat tissue or other tissues through the reverse differentiation process.

It is reported that those who had been exposed to atomic bombing at Hiroshima or at Nagasaki suffered from haemorrhagic enteritis at first, and then from leukemia.

And it is also reported that the intestinal mucosae of the victims of the atomic bombing were attacked by haemorragic inflammation.

This evidently expresses the fact that at the early stage of these diseases, fixed tissues or cells differentiated reversely into erythrocytes, through the leucocytic phase, because the intestinal mucosae of the victims were disturbed and their villi were destroyed, while the leucocytes of the victims greatly increased in number because the existing erythrocytes differentiated into leucocytes in the process of their aging, and, as a result, both erythrocytes and leucocytes gradually decreased in number, until at last haematopoiesis in their gastro intestinal tracts almost came to a stand still because they got to lack the tissues or cells which were to differentiate reversely into erythrocytes.

Therefore, this author emphasizes that leukemia and anaemia in the victims were never caused by the radioactive destruction of the bone marrow. For, as the bone marrow in a healthy body is fat tissue, all fat in the body must be always disturbed if the bone marrow is destroyed, but such a fact has never been proved by anybody.

On the contrary, it is a well-known fact that the patients who are suffering from leukemia or cancer are liable to accompany not only gastro enteritis but also liver damage.

For, the liver belongs to the digestive system, noxious matter absorbed in the intestines is detained in the liver, and hepatitis is apt to occur.

The cause of anaemia resembles closely that of leukemia, so the disturbance of the digestive organ is common to each other.

This author has not yet heard that the orthodox medical scientists were successful in treating the patients who were suffering from anaemia by giving some treatment or care to their bone marrows.

Even if they give any treatment to the bone marrows of the patients who are suffering from anaemis, they will never succeed in saving them from the

disease because the bone marrow is not the haematopoietic center.

Therefore, it is necessary that we should try to amend the medical treatment for leukemia and anaemia fundamentally.

## (III) Cancer and digestive disturbances

It is said that in the United States, the number of the school children who die of cancer every year is larger than that of the school children who die of any other disease.

Today, many scientists are racking their brains as to the cancerous problem not only in the United States but also in the most of civilized countries, and cancer is connected not only with children but more with adults.

This author does not intend to give his opinions on the whole cancerous problem here, but would like to emphasize that cancer is deeply related to the functional disturbance of the digestive system which is the organs of blood production.

Rachel Carson, the famous American biologist, appeals to public opinion in her best seller "Silent Spring" that to put it in the concrete, especially chemicals which are contained in pesticides, insecticides, and herbicides are extremely dangerous and injurious to the health. And she said, "Warburg, the German biochemist, says that both radiation and chemical carcinogen destroy the respiratory function of normal cells, and then deprive them of their energy." She goes on to say that "those who have contacted with the arsenic of chemical carcinogen are liable to accompany the disorders of the liver, the skin, the gastro-intestinal, nervous system, and malignant tumors, and also domestic animals such as horses, cows, goats, and pigs and wild animals (deer) are liable to be affected by arsenical enteritis, gastric ulcers, and cirrhosis of the liver." This evidently expresses the the fact that like the case of the victims of atomic bombing, chemical carcinogen, attacks, first of all, the digestive organs. Thus, the best way to prvent and seconds.

Thus, the best way to prvent and remedy cancer or anaemia is to promote or recover the function of the digestive system.

## (1) Reversible Differentiation between the Erythrocytes and the Bone Marrow Elements under Normal and Starved Conditions.

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Though many investigations have been given on the intramedullary hemopoiesis and on the genetic relationships of bone marrow elements, the opinions on the following problems have not yet been reached in agreement; (i) the origin and the mode of proliferation of the so called hemocytoblast, (ii) the maturation process of normoblast, especially the denucleation of mammalian normoblast, (iii) origin and fate of yellow bone marrow, (iv) fate of bone marrow elements, (v) genetic relationship between platelets and megakaryocytes, etc..

There are so much discrepancies or uncertainties about the interpretation of the recorded data regarding the problems mentioned above that an investigation on these matters in several vertebrates seems desirable, to make some contribution toward a new genetic system of bone marrow elements. It seems to me that the discrepancies of opinions may due to the following reasons: (i) Complicity of the kinds and arrangement of marrow elements, (ii) uncritical acceptance of the orthodox view, the Virchow's Doctorine (omnis cellula e cellula), and (b) theory of crythrocytopoiesis in normal bone marrow, (iii) deficiency or scarcity of the observation on the living bone marrow under normal conditions, (iv) negligence or confusion about the profound difference of the bone marrow figures between the normal and abnormal materials, (v) overlooking of the differential potencies of the erythrocytes, (vi) deficiency of comparative and phylogenetic studies on the hemopolesis. In previous papers (Chishima '51, '52a, b '53a, b) I have published an opinion regarding the reversible differentiation between the blood cells and yolk sphers, and the differential capacities

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Redaktion der Okajimas Folia Anatomica Japonica Shinjuku, Tokyo, Japan. of erythrocytes in bird. Present work was carried out with special reference to the reversible differential potencies of the crythrocytes in the bone marrow of bird and mammals under normal and starved conditions.

#### Materials and Methods

The observations here reported were made from 1948 to 1953 and were based on the observations of the bone marrow of the femurs, tibias, vertebrae and libs of 5 chick embryos, 8 normal and 8 starved chickens (4-5 days inanition), 5 normal and 4 starved adult fowls (7-21 days inanition), 4 normal and 2 starved rabbits (8 day inanition). 2 adult, normal goats and 1 underfed goat, 5 normal and 5 starved frogs (5-17 days inanition), 2 normal and 2 starved dogs, (10-12 days inanition) 2 starved cats (10-12 days inanition). For histological study of the bone marrow, bones were cut at both ends, fixed in 10% neutral formalin solution or Bouin's fluid. Decalcified bone with marrow or bone marrow only, sectioned serially in paraffin. The sections in 5-8μ thick were stained with hematoxylin and cosin. For the comparison, observations were also made on the imprinting bone marrow preparations stained with Giemsa's solution, and on the bone marrow culture (slide-cover glass method) without addition of any other artificial medium, and in some cases it was stained supravitally (Sabin and Sugiyama's method) with janus green and neutral red,

In the certain instances, vital staining of marrow were employed with Japanese Colloidal carbon ink (Bokujyu) diluted with about 2 times volume of physiological salt solution then it was pasteurized and filtered. This colloidal carbon were injected into wing vein of adult hen (single dose of 5-10 cc), into the heart of anethetized yound chickens (single dose of 2-3 cc), or into ear vein of adult rabbit (single dose of 8-15 cc). And at the certain intervals after the injections the animals were killed and stained bone marrow sections were made.

### Observations

(A) Origin of the small lymphoid elements in the bone marrow of chick embryos, chickens and adult fowls under normal condition.

In the stained sections of the bone marrow in chickens and adult fowls there can be seen many lymphocytoid areas. But these areas have no typical "germ center" at where it has been supposed that the lymphoid elements showed active mitotic proliferation. It is also noteworthy fact that the mitotic figure of "hemocytoblast" (small lymphoid elements) in the normal bone marrow of fowls is hard to find, while they show transitions from erythrocytes located in the venous sinusoid. That is to say, erythrocyte →polychromatic spherocyte with eccentric nucleus, decrease in amount of cytoplasm and eventually transform into small lymphoid elements (Meta-lymphocytes). (Fig. 1) This transition is also demonstrable in vitro (marrow culture) within 48 hours at room temperature. The so-called venous sinusoid of the marrow has been generally considered as a dilated venous capillary which is lined by continuous layer of endothelial cells. However, according to my careful observations the so-called venous sinusoid of marrow are only blood space which are unlined, in main part, by endothelium, and is continuous, on the one hand, with arteriole, and, on the other hand, with the tissue spaces of marrow. Even if certain parts of the sinusoid is covered with few endothelial cells which show clear transition from erythrocytes adhered and flattened on the periphery of the spaces. It was found that in the marrow stained vitally with colloidal carbon, the carbon particles often be seen in the cellular spaces. The spacial volume of the venous sinusoid is extraordinarily larger (60-70 times or more) than that of arteries. From this and the result of the vital staining with colloidal carbon it seems most probable that the blood current of the venous sinusoid has stagnated or already has stopped at certain area.

The Spherocyte (sphere erythrocyte) and lymphocytes, even if, show oscillating movement, in vitro but show no translocomotive capacity. Therefore, the elements in the lymphoid area can not be considered as that they have been gathered together by their own locomotion. Moreover, it is common, that the lymphoid areas are continuous to the venous sinusoid, and there can be seen the transition between erythrocytes and lymphoid elements. This transitional phase are demonstrable not only in the stained sections but also in the imprinting preparations and in the bone marrow culture. Thus the writer can not be escaped from the conclusion that the most of, if not all, lymphoid elements (the "meta-lymphocytes" designated by present writer) in the normal bone marrow are a derivative of erythrocytes. And it should be discriminated from the "pro-lymphocytes" which arise in depleted marrow only.

The connected type of lymphoid elements. On the imprinting preparations of the bone marrow of 17-19 day chick embryos, there

can be seen a special type of cell, "the connected type of two lymphoid elements". (Fig. 3) This type of nuclei might have been referred to, by some preivious workers, as an amitotic division of indifferent hemocytoblast. But it may not be the case, because the one half of the connected or constricted nucleus stains deeper and smaller in size than the other half. And the lighter staining half show transition from the extruded cytoplasm from erythrocyte and, the darker staining half show transition from the nucleus of erythrocyte. The lighter half, then, increase in size and show further transition into cytoplasmic portion of the cosinophilic granular leukocyte, while deeper staining nuclear half show transition into small lymphocyte resembling to the so-called extruding (denucleation) nucleus or into a eccentrically located light basophilic polynuclear or polymorph nuclear part of the granulocyte. These differential phases of the connected type are also be seen in that of chickens and adult fowls.

Budding type of erythrocytes in the marrow in the imprinting preparations, I have also observed another curious connected type of erythrocytes with myeloid elements. This type seems to be a kind of the connect types, but it may rather suitable to designate as a "budding type". The "Budding type" is composed of one (single budding type) or more of erythrocytes sticked tightly (Mutual B. t.) with its concaved side, on the surface of a granulocyte or of a promyelocyte. (Fig. 1, 4)

In the wet preparation of the bone marrow this element moves passively here and there as an unit cell when the suspension of the marrow are agitated artificially.

The budding phenomena, the extrusion of the cytoplasmic portion of erythrocyte through the invisible minute hole of the cell wall observable on the culture of the marrow, or of whole blood. The erythrocyte changes its form, at first, into a concaved, bell shape of which surface show oscillation movement and then extrude a very clear thin hyaline-line substance containing minute microns through the cell wall of the hollow side. This phenomena can be recognized by thoughtful observation with common light microscope, however, the use of phase contrast microscope is the better. This phenomena, perhaps, belongs to the same category of the "pinocytosis" designated by Lewis ('31) or "potocytosis" designated by Zollinger ('48) even though, both of the investigators have been described neither on that of erythrocyte nor on the new cell formation from extruded substance. That may have been due to the fact that they had used an artificial

cultural medium. On the stained imprinting preparations. The extruded substance derived from the co-operative extrusion of cytoplasmic contents of two or more erythrocytes show successive transitions into a large neutrophilic or cosinophilic granulocyte which is often covered tightly with flattened or crescent shaped erythrocytes. In this case minute microns contained in the extruded substance increase in size through their coalescence (coacervation), then they show transitions into typical granules of myeloid series. (Fig. 1)

The following order of the staining capacity of granules will be demonstrated on the section or in vttro; netrophile → eosinophile → basophile → polychromatic granules.

It is not seldom to find an myeloid element in which contains granules with different staining capacity,

(B) Origin of the small lymphoid elements in the normal bone marrow of frogs.

Small lymphoid elements in the frogs marrow also show transition from erythrocyte through the same manner as that of the fowls. (Fig. 4) I have observed an interesting fact that a drop of frog's blood mounted under a cover glass and then the cover slip was pressed by figer tip, from which stained smear preparation was made. From examination of that preparation, it was revealed that the most erythrocytes have been destructed and naked nuclei of erythrocytes showed close resemblance to small lymphocytes. From this fact it is undeniable that a certain part of the so-called lymphoid element on the smearing of marrow or blood of oviparous vertebrate animals may be originated to the extruded nucleus from erythrocytes by mechanical action of the smearing.

(C) Origin of small lymphoid elements in the normal bone marrow of mammals.

In the stained sections of the bone marrow of well fed rabbits, goats, and guinea-pigs the small lymphoid elements are also very abundant in the venous sinusoid and the stroma. Sections give histological support for the view that the capillary system of mammalian marrow is also an open type as in the bird.

The lymphoid elements in the mammalian marrow also show no reliable evidence that all of them proliferate homogenetically through mitosis or amitosis, while there is certain evidence that they arise de novo from erythrocytes in situ through the following two modes;

The first mode, individual erythrocyte in the venous sinusoid transform into polychromatic spherocyte and then it acquires basophilic staining capacity and eventualy transforms into a small or micro lymphocyte. (Fig. 2) The second mode takes place at the area where the erythrocytes are aggregated as a mass. (Figs. 2, 5, 8) By their fusion, these erythrocytes become to a eosinophilic homogeneous masses varying in size according to the difference of the amount of erythrocytes composed of these masses. The writer designates these mass as "F E monera" (Fused Erythrocyte-Monera). "F E Monera" would have been referred to, by previous workers, as a mass of destructed or hemolysed erythrocytes or as a hemophage (or Macrophage) which has engorged the crythrocytes. It is important fact that the F E monera show no sign of its natural extinction, on the contrary, it show very startling behaviour, the new cell formation in it through the following process (coacervation).

In the F E monera, at first, arises various numbers of vacuoles, probably lipoidal in nature. Then basophilic granules take its appearance at inside or periphery of the vacuoles. These basochromatin increase in number and in size and eventually coalescence into pyknotic round nuclei corresponding in shape and number to that of the vacuoles.

The lymphoid elements (Meta-lymphocytes) produced are not necessarily uniform in size, probably according to the amounts of erythrocytes contributed to their formation.

In the goat, erythrocyte is especially small (3-4 $\mu$  in diameter), however, the newly arised lymphocytoid nucleus is almost equal in size with the other mammals used, therefore, it is probable that a lymphocytoid element of goat may be arised from several erythrocytes' fusion, and even that of other mammals used, also, often may be arose from two or more of erythrocytes.

Accordance with the new synthesis of basochromatin substance the F E monera gradually descrease its eosinophilic staining capacity and a part of it then becomes to neutrophile or faint basophile substance surrounding the newly formed nuclei. But in some case the newly formed nuclei are provided with eosinophilic cytoplasm. Such elements are correspond to the so-called orthchromatic normoblasts, but there is no evidence that these elements differentiate into crythrocytes in the normal bone marrow. The new formation of meta-lymphocytes or so-called "normoblasts" from F E monera recognizable on the both the imprinting preparations and sections of the bone marrow (Fig. 2) (D) Monocyte and neutrophile leukocyte in the bone marrow of bird and mammals.

The questions as to the origin and the fate of monocyte has not yet been solved. The stained sections and imprinting preparations of the marrow gave histological support for the view that there can not be drew a sharp discriminative-line between the so-called monoblast and the small lymphocyte (meta-lymphocyte) arose from the F E monera through coacervation process. In the other words, monocyte seems to be nothing but a differentiated product of a large meta-lymphocyte, though, it varies in size within considerable extent. The so-called non-granular series of the myeloid elements seems to be a transitional stage from meta-lymphocytes into granulocytic series.

It can be said that the marrow element having a dark staining nucleus and non-granular cytoplasm belongs to the early developmental stage of the myeloid elements. As the element grows further the nucleus becomes vesicular, decrease its staining capacity and give rise to cosmophilic and then basophilic granules in its cytoplasm. (Fig. 1-2)

However, it should not be overlooked that cytoplasmic granules in the marrow elements or lipoidal globules suspended in the marrow liquid can clearly be seen on the wet and the imprinting preparation, but on the stained sections a considerable parts of them are dissolved away. Moreover, on the smear, usually be seen neutrophilic or faint basophilic substances having no definite cellular structure and each of which is surrounded by the F E monera or by erythrocytic debris. It seems probably correct to look upon these substance as a preceding stage of promyelocyte. These substances, then, show transitions into neutrophilic or basophilic myelocytes through promyelocyte phase. It has been believed that the three types of myelocytes, the heterophile, eosinophile and basophile, cannot be transformed into another type of myelocytes. However, according to the present studies there is no clear distinction among these three kinds of elements. That is, in one element often contains granules with different staining capacities. Furthermore, in chick's marrow culture (stained supravitally) I have observed that the certain cytoplasmic granule changed its staining capacity from janus green to neutral red, and there were granules stained intermediately. And some granules showed a polarity of staining capacity, viz., the one end of a granule stained with neutral red, while the opposite end with neutral red. Such a transition of staining capacity of granules is also demonstrable on the smear and sectioned preparations.

From these facts the writer cannot accepts with polyphyletic view

on the hemopoiesis, on the contrary, though there are remained some unsolved problems as to the detail of genetic relationships of myeloid elements, it may be concluded that the circulating blood cells especially erythrocytes play a very important rôle as a stem cell (in bird) or a material from which the bone marrow elements are formed de novo (in mammals).

(E) Origin of the macrophage,

In general, macrophage stored carbon particles are found at the periphery of the venous sinusoid or in interstices of the bone marrow injected with colloidal carbon. However, there can hardly be seen the evidence of its mitotic proliferation or of the preexistence of the parent cell of the macrophage. While sections give the evidence of the transition from an aggregated erythrocytes' mass of chick or F E monera of mammals into a macrophage. Macrophage at a transitional phase often contains intact erythrocytes, debris of crythrocyte and carbon particles. (Fig. 1-2) It is not uncommon that the precursor of macrophage, the F E monera, often contains small lymphocyte or other leukocytes originated to the circulating blood.

It was also revealed that the syncytium of small lymphoid elements shows transitions, on the one hand, from F E monera, and, on the other hand, into macrophage. Macrophage often hypertrophied to form a giant cell containing several nuclei.

This type of macrophage probably produced by the fusion of blood cells irritated by the injected carbon particles,

From the facts described above macrophages in bird and mammals can not be referred to a independent cell lineage but they are nothing but a irritated, fused and hypertrophied type of the so-called reticular endothelial cells derived from erythrocytes or from other blood cells.

(F) Polynuclear giant cell in the chicken marrow.

It is a generally accepted opinion that there is no megakaryocyte or polynuclear giant cell in chicken marrow. But, in the imprinting or sections of marrow of chicken embryos (18-21 day incubation) or young chicken there can be found polynuclear giant cells with several or more nuclei. (Fig. 6) And these nuclei stains in light basophile and vesicular in nature, and often show the sign of their degeneration.

The cytoplasm, sometimes, contains erythrocytic debris, lymphoid elements, or granulocytes at the peripheral part of cytoplasm. The polynuclear giant cell in chicken show no difference in essential points from the mammalian megakaryocyte, in the staining capacity of the nucleus and cytoplasm. Thus it is highly probable that the element

is homologous with mammalian megakaryocyte. There is no evidence of the mitotic or amitotic proliferation of the element, and there could be found no one of specific stem cell of the elements. While it show clear transition from an aggregated and fused mass of erythrocytes of which nucleus, of course, show transition into individual nucleus of the giant cell. Sometimes two of the nuclei in the element are closely arranged by and show an appearance as if they are resulted by a mitotic division of a nucleus. But it may not be a resultant of amitosis, since it lacks a series of the typical amitotic phases, on the contrary, these two nuclei show different staining capacity showing transition from the "connected or budding type of crythrocyte" derived from a connection of a extruded cytoplasm of crythrocyte and the residual crythrocyte,

(G) Megakaryocyte in mammals,

From the results of careful observations of the imprinting or sections of bone marrow of the mammals used it was revealed that megakaryocyte can be traced to a mass of blood cells, the F E monera. Megakaryocyte was usually located extravascularly, however, sometimes, it appear in intravascularly. (Fig. 5, 8) Megakaryoblasts in stained marrow sections were often provided with a peripheral layer resembling in staining capacity and structure to the degenerating arterial wall. In this case, the megakaryoblast shows clear transition from agglutinated blood cells (F E monera) included in collapsed vessel. In general, nucleus of megakaryoblast is polynucleatic, viz., it appears as a syncytium of aggregated small lymphoid elements, and the cytoplasm of it is acidphilic at the most early stage of the development. It is apt to misunderstanding that these nuclear feature of megakaryoblast is a mitotic or amitotic division. As the megakaryoblast developes its nuclei transform into a dark staining polymorphnucleus embedded in a polychromatic cytoplasm which then becomes to a light basophilic cytoplasm containg granules. It is not surprising that the new cellular element, the megakaryocyte, taken its appearance from F E monera through coacervation process if we would drop out of Virchow's idea and would accept truthfully with the facts.

Platelets formation and megakaryocyte in the mammals. Though it is a dominant opinion that the blood platelets are megakaryocytic origin, there could not be found the reliable evidence of platelets formation by means of pinched off of the pseudopod-like processes of megakaryocyte. Though it is true that there can be seen rarely a few excrescences on the megakaryocyte, but its frequency seems too

few to supply the tremendous numbers of platelets found in the circulation. Moreover, these excrescence perhaps be originated to the degenerated crythrocyte (or extruded substance from erythrocyte), because the transitions between these two elements are demonstrable, (Fig. 8) Thrombocyte (spindle cell) in oviparous vertebrates also show neither the evidence of their polynuclear giant cell origin nor of the evidence that they are homologue with mammalian blood platelets, The spindle cell show transition, on the one hand, from the "prolymphocyte and, on the other hand, into erythrocytes. (Fig. 1)

(H) Fate of bone marrow elements and the origin of the yellow bone marrow.

It seems to be a most curious fact that, notwithstanding the red marrow in the diaphysis of long bone in adult animals is replaced by fatty marrow, the fate or function of the several kinds of myeloid elements, and its relations to the fatty marrow formation have been remained unsettled. Therefore the thoughtful re-examination on the matter seems to be a most important key to the solution of the question about hemopoietic views. From the present studies it was confirmed that the so-called fat cells (it seems rather suitable to designate as a fatty tissus or fat drop) in the normal marrow show transitions, not only, from granular myeloid elements but also from blood cells through their fatty degeneration. Under the well nurished conditions of animals the bone marrow seems to be a most favorable site where the cellular elements fall into fatty degeneration.

On the marrow sections the fully developed granules contained in cosinophilic or basophilic granulocyte series (including megakaryocytes) show transitions into minute fat droplets and then the nuclei also show their fatty degeneration (fatty vacuole). The most usual process of fatty degeneration of marrow elements is the passing through the granulocyte series, but it is not uncommon that erythrocytes located at the periphery of fat drop show their fatty degeneration directly or through lymphocytoid stage. And then the small fat drops produced by the manner mentioned above, and the fat cells and fat drops fuse together with others, and eventually a single giant fat drop (40-50 $\mu$  in diameter) is being formed. The so-called fat cell with a eccentrically located nucleus is nothing but a transitional stage from avian bone marrow elements or from mammalian granulocyte having eccentric nucleus into fat drop.

It is common, that a giant fat drop is covered tightly with several or more of crescent shaped and flattened fibroblast-like elements. However, there could be seen least evidence of that these nuclei of fibroblasts-like elements are the nuclei which have been survived science early stage of the fat cell. While these fibroblast-like elements often show the transition on the one hand, from erythrocytes through the coacervation process, and on the other hand, into fatty degeneration contributing to the enlargement of the fat drop.

I have observed the process of the fatty degeneration of the erythrocytes in chicks and rabbits in vitro by the aid of a bone marrow culture (slide-cover glass method) without any medium, but in certain cases, supravital staining method introduced by Sabin and Sugiyama was also employed. At certain intervals after the culture, the smear preparations were made and examined. Better result were obtained from the culture without addition of any artificial medium or of supra vital dyes. After 24 hours, the most parts of chicken erythrocytes were transformed into spherocytes, and, in their cytoplasm, several spherical and vacuole-like minute globules have appeared. At first these globules did not stain supra vitally with neutral red, but then become to be stained with it. These vacuoles increase in size and become the granules corresponding to the eosinophilic or basophilic granules of granulocytes. After 4-5 days culture the granules become stainable with Sudam III. Eventually, the nucleus becomes vesicular and granules also takes its appear in it. In the bone marrow of the well fed animals all kinds of the mycloid elements including polynuclear giant cell, megakaryocyte and macrophage show their de-differentiation into fatty tissue (yellow bone marrow). (Figs. 1, 2, 5, 8, 9) From the above mentioned facts, I can not escape from the conclusion that the erythropoiesis does not takes place in the bone marrow under well fed normal conditions, on the contrary, blood cells, especially erythrocytes give rise to all kinds of the marrow elements, and the marrow elements located in the diaphysis of the long bone eventually fall into fatty degeneration producing yellow bone marrow. However, some parts of the blood cells contribute to the bone formation, but as to this problem I will report in another paper.

(I) Erythropoiesis, the reverse differentiation of the yellow bone marrow under inanition.

Studies on the hemopolesis in the bone marrow of the birds (domestic fowls), the mammals (rabbits, dogs, goats, cats and guineapigs) and of the amphibia (frogs) under starved conditions have been carried out.

So far as the depleted bone marrows by starvation are concerned

the results of the present studies support, in the gross, the orthodox view regarding erythropoicsis, even though, the orthodox view does not agree in some essential point with the results of the present studies. It is true, as has been recognized, that the bone marrow cavity of the diaphysis of the long bone in the well fed adult animals is filled with yellow bone marrow, while in the depleted marrow by starvation, that the area is replaced by red bone marrow. The mechanism by which this replacement takes place is not yet solved. However, from the results of the present studies it was revealed that the decreasing in the mount of the yellow bone marrow (fatty tissue) in starved animals does not due to the dissolve away of fat as has been supposed. While the marrow fat cell (or drop) shows transition into a cloudy and foamy substance with light eosinophilic or polychromatic staining capacity. I have designated the substance as a "fat monera". (Figs. 11-13) The fat monera then shows transition into the elements of red bone marrow through the following series of transitional phases. At first, the fat monera is equal in size and in shape to the giant fat drop but then its peripheral region acquires a light basophilic staining capacity at where then arise de novo and spontaneously many of mesenchymatous elements with foamy, syncytial cytoplasm. (Figs. 1, 2, 11-13, 19) Characteristic feature of these elements can be seen more conspicuously in detail on the imprinting preparations than the sections. They may correspond to the so-called "hemocytoblast with foamy cytoplasm". And then they transform into small lymphocytoid elements (pro-lymphocytes designated by mc) through rounding up of the mesenchymatous elements. Thus, the fat moneral descreases in size from its periphery as the new cell formation has been proceed toward the inner region of the monera. However, sometimes the process takes place at once both of the periphery and inner region of the fat monera, consequently it appears as if a polynuclear giant cell with several or more nuclei. (Fig. 12) However, cellular elements in the monera further increase in number by the reverse differentiation (re-differentiation) from fat monera through coaccervation process, but there is no evidence of mitotic or amitotic proliferation of them. At the same time, the lymphocytoid elements (hemocytoblasts) transform into basophilic and then into orthochromatic normoblasts. Thus the reverse differentiation from a giant fat drop into a sphere mass composed of 50 to 60 or more of the normoblasts or erythrocytes is established. (Figs. 10, 19) The writer designates this process as "Re-differentiation of Blood cells from Fat monera by

Sporulation and Budding ". (R B F process,) since this process resembles closely with the process of spore formation in sporozoa and with the proliferation by budding in lower microorganisms. The "R B F process" is, in general, common to the vertebrates used in present studies, but the maturation process from a mammalian normoblast into non-nucleated erythrocytes is differs markedly from that of birds having the nucleated erythrocytes. It is a noteworthy fact that the avian lymphocytoid hemocytoblast, at the early stage of the R B F process, arises in a connected type as if it is a reappearing of the connected type or the budding type of erythrocyte described before. It seems that this connected type may have been misunderstood by some workers as a amitotic figure of the hemocytoblast. But, most probably, it is not a true amitosis or a mitosis because the connected two neuclear halfs differ in staining ability and in size, namely, the one half is somewhat larger and stain lighter than another one. (Fig. 1) And the former is somewhat granular in structure and then shows transition into a avian orthochromatic normoblast which may corresponds to eosinophilic granulocyte in the normal bone marrow because it contains eosinophilic granules in its cytoplasm though these granules are smaller in size and less in number than the typical cosinophile found in normal marrow. At the same time the dark staining another half becomes to a small lymphocytoid element and is connected with a granulocyte-like normoblast so that it appears as if it is the so-called nuclear extrusion of the normoblast. (Figs. 11, 12) These connected type cells can be seen on the both of imprinting and sections, but they occur more frequently in the former case. This may due to the fact that some of the connected type cells may be arose from the cytoplasm-extrusion of erythrocyte" The writer, however, could not be found a criterion to distinguishes those two kinds of connected types. A granulocytic normoblast with two nuclei (sometimes one or three) show transition into one or two erythrocyte and the lymphocytoid elements connected with normoblast also show transition into erythrocyte through orthochromatic normoblast stage. (Fig. 1) While mammalian orthochromatic normoblasts with one nucleus (but sometimes with polynuclei or polymorphnucleus) differ in size, namely the smallest one is equal in diameter to erythrocyte, middle sized is 2-3 times larger, and the largest one is 4 times or more larger in diameter than that of erythrocyte. Thus usually the volume of a middle sized normoblast may be estimated in gross as about 6-9 times larger in volume than an erythrocytes. (Fig. 11) Such a large normoblast by no means show

transition into one erythrocyte though it has been supposed by previous workers. On the contrary, as has been pointed out by Boström ('48) there is clear evidence that one normoblast usually give rise to several or more of non-nucleated erythrocytes. The maturation process of the normoblast at first takes place by diffusion of nuclear substance into the cytoplasm accompanying with somewhat swelling of the both of cytoplasm and nucleus and then they transforms into a light eosinophilic cloudy monera-like substance having no longer any nuclear structure by unknown physico-chemical process. It is the most striking phenomena that in such a monera-like substance, especially at the peripheral region, arises de novo several erythrocytes as if they are budding off from the cytoplasm of normoblast, and further the process proceed toward the inner region of the substance by means of sporulation and coacervation. (Figs. 11, 14, 15, 19) This process resembles closely the R B F process though it is smaller in scale than latter, However, the normoblasts does not always show individuality but more or less syncytial in nature, therefore, an erythrocytic mass derived from a fused normoblasts-monera is often composed of several scores or more of erythrocytes. Of course, a small sized normoblast gives rise to only 2 to 3 erythrocytes. It is not uncommon that the non-nuclear erythrocytes directly arise de novo in the fat monera without passing through the normoblast stage. Mammalian erythrocytes arose by the above mentioned modes, at first, are spherical in shape measuring in diameter about 3-4 µ, then they become to discoidal, probably due to the mutual pressure. (Fig. 14) Besides the erythrocyte-formation from the fat monera there have been observed certain evidences of the reverse differentiation of normoblast from the bone marrow elements including megakaryocyte, myelocyte series, eosinophilic granulocyte, monocyte, lymphocytoid element (mcta-lymphocyte) and others. (Figs. 1, 2) When myeloid elements, which had not yet been fallen into fatty degeneration under well fed conditions, were subjected to starvation the reverse differentiation of them into the normoblast or erythrocytes may possibly take place. Even the elements of the collapsed arteries in the bone marrow show the reverse differentiation into normoblast. (Fig. 18)

A special type of cell was found on the imprinting preparations and sections of the cock's bone marrow depleted by starvation for 14 to 21 days long. The structural details of the cell are more conspicuous in imprinting than the sections. In the imprinting, the cells resembles to the basophile myelocytes measuring 16-20µ in diameter, and each of them contain in its cytoplasm 1-3 spherocytes or their primordium,

(Figs. 16, 17) And a well developed spherocyte is sphere in shape measuring 5-8μ in diameter and a nucleus staining in light blue is surrounded by orange yellow colored cytoplasm. Therefore, it may be referred to, by general hematologists, as a crythrophagocyte. But the cell, the so-called phagocyte, has not own nucleus.

Moreover, the cell show transition from a fused mass derived from the erythrocytes and their cytoplasm extruded. The writer designated it as "erythromyelocyte". Erythromyelocyte never been found in the normal bone marrow but was found only in the adult fowl's marrow depleted by prolonged starvation.

As has been described in previous chapter, under normal nutritional conditions the derivatives from "budding type of erythrocyte" and "connected type of erythrocyte with the marrow element" are eventually de-differentiate into fatty degeneration. While the differential process of the elements of depleted bone marrow is entirely reverse in direction. And further, it was revealed that there is no marked difference between the blood picture on the smear prepartion of peripheral blood of the depleted animals and that of the normal animals.

From these facts it may not be unreasonable to consider the "erythromyclocyte" as a transitional phase of re-differentiation (reverse differentiation) from a myclocytic element derived from erythrocyte into crythrocytes under prolonged starvation. Vascular system of the bone marrow under prolonged starvation falls into so marked confusion that there can hardly be seen a typical or intact artery or a venous sinusoid. While there can clearly be seen transition from the elements of collasped arterial wall into normoblast and then into erythrocytes. (Fig. 18) The so-called typical venous sinusoids provided with a endothelial layer already have disappeared, and instead of them, here and there are large blood pool filled with erythrocytes. Behaviours of the marrow elements in the starved frog is essentially the same as that in the fowl.

#### Discussion.

(1) Origin and the fate of lymphoid element in the normal bone marrow in the birds and mammals. As I have been described in the foregoing chapter there is neither evidence of mitotic proliferation of the mesenchymal (or lymphocytoid) hemocytoblasts nor of the crythrocytopoiesis in the normal bone marrow. But the most widely accepted opinion as to the intramedullary hemopoiesis is based mainly upon the results of the observations on the depleted marrow by starvation for 9-10 days (Doan, Cunningham and Sabin, '25; Jordan '35) or by large amount of bleeding, or on anemic bone marrow (many workers).

It seems unreasonable that the results obtained from such abnormal materials has long been applicated uncritically to that of the normal condition. As I have pointed out (Chishima '52b) the direction of differentiation between the elements of tissues and blood cells becomes to entirely reverse under the influence of nutritional conditions. I think, negligence or overlooking of this fundamental fact may necessarily brings confusion about the views of hemopoiesis. And furthermore, if we would not drop out of adherent to the orthodox view as to the origin and the mode of proliferation of the hemocytoblast, we should not be able to escape from confusion of the opinions regarding hemopolesis in bone marrow.

Direction of differentiation of bone marrow elements under pathological conditions, such as anemia, several kinds of chronic diseases, underfed condition, and after the large amount of bleeding may brings a result the same as that of starved condition. Because all of these abnormal conditions may bring eventually the so-called depleted bone marrow. From the view point of the unitarian theory (Jordan '39 et al) the small lymphoid elements in the marrow are true lymphocytes, while the dualist (Downey and Sundberg '39 et al) looks upon them as myeloblasts or micromyeloblasts. This controversy of opinion may be solved, in some extent, by my hypothesis that there are two kinds of lymphoid elements, one is the "meta-lymphocytes" which are a derivatives of erythrocytes and are found usually in normal bone marrow, though it can not be denied that a certain amount of them possibly be carried into the depleted bone marrow via circulating blood, while the "pro-lymphocytes" (correspond to the so-called hemocytoblasts) which are a precoursor or parent cells of erythrocytes or other blood cells, and they are found in depleted marrow, but not in the normal marrow,

Meta-lymphocytes in the normal bone marrow show no evidence of their differentiation into erythrocytes, on the contrary, they show clear evidence of differentiation into marrow elements. As has been pointed out by Joffey ('50), tremendous numbers of lymphocytes daily leave the peripheral blood, though it is not known where these lymphocytes are going. The following hypothesis have been presented by previous authors to, explain the disappearance of lymphocytes;

(i) migration into intestinal lumen (Bunting and Huston '21.) (ii) presence of lymphocytes in the intestinal lumen is only a postnatal change (Stenguist '34), (iii) to be returned into lymphatic tissue (Sjöval '36), (iv) the view (iii) explains only the small percentage of lymphocytes leaving the blood (Joffey and Drinker '39), (v) transform into myeloid elements (Jordan and Speidel '23) (vi) in avian bone marrow lymphocyte with multiple differential capacities differentiate into erythrocytes, granulocytes, monocytes and thrombocytes, (Jordan '36), (vii) in the Tunicata lymphocytes give rise not only to the various blood cells but also to all other cell types as well, (George '39), (viii) into macrophage, (Ajema '29), (ix) into large lymphocyte, histiocyte and plasma cell etc., (Maximow '28) (x) injected lymphocytes labelled with 3.6 diamino 10-methylacridinium chlorid transform into myelocytes and from which further into granulocytes, (Farr '51). Farr ('51) says "the writer is in agreement with the conception of the pluripotentiality of the lymphocytes as advanced by Dominici ('01), Maximow ('09), Weidenreich ('11), Dantschakoff ('16), Jolly ('23), Latta ('24) Lang ('26) and Bloom ('37)". (xi) I have also published the opinion that the lymphocytes with multiple potencies differentiate into the almost all of the fixed elements in birds, amphibian and mammals. I can not agree with the theories i, ii, and iii, of which detail I will publish in another paper. The view from (iv) to (x) support the present view. From these facts the view maintained by most dualists that the small lymphocytes after having filfilled their hypothetical functional activities in every part or tissue of the body are doomed for destruction should be requested to reexamined. Thus the many controversial opinions as to the origin and the fate of small lymphoid elements in several kinds of vertebrates may be explained smoothly by my hypothesis that the meta-lymphocyte in normal nutritional condition is a first step of the differential process from erythrocytes into not only the myeloid elements but also into other fixed elements, while the pro-lymphocytes (hemocytoblasts) in the depleted marrow are arose from the fatty tissue and mycloid elements by the reverse differentiation.

(2) Origin of the macrophage. Keys ('15) observed that the endothelium of venous sinusoid of the healthy fowl usually ingest the red corpuscles, therefore, he has designated it as hemophage. Bueno ('47) also found that the macrophages (perfectly identical with mononuclearcytes) in the guinea pig infected with Brucella showed marked phagocytic activity and their cytoplasm has contained red corpuscles as well as particles and granules of hemosiderin. These opinions support in parts my opinion that the macrophage is derived from fused blood cells (especially erythrocytes) irritated by foreign substances. Some workers believe that the new macrophage arise only from mitotic division of preexisting macrophage. Maximow and Bloom ('50) describe that the macrophage arise by phagocytic activity of the cells having mesenchymal potencies in myeloid tissues, from primitive reticular cells, and from the hypertrophy and development of lymphocytes and monocytes, but in parts, by homogenetic proliferation. Chevremont (quated by Maximow and Bloom '50) believes that macrophages do not constitute a specific cell lineage; they rather represent a functional transformation of many different types of cells under the influence of cholin. These opinions also support, in parts, my opinion.

(3) Origin of the Megakaryocyte. As Fuente ('49) has pointed out, the origin of megakaryocyte is largely controversial, and it has been traced almost all of types of blood cells and the data are at hand to support each theory, neverthless, proofs to establish one hypothesis are not so conclusive as to exclude the others. That is to say, various workers have been considered that the megakaryocyte is originated to the growth or hypertrophy of; i) small lymphocyte (Howell 1890), ii) hemocytoblast (Lapidari '29, Rothermel '30, Kingsley '34 '37, Potter and Ward '40), iii) Polyblastic histiocyte (Fontana '29), iv) mycloblast (Downey, Palmer and Powell '30, Howell and Donahue '37), v) megakaryoblast (Fuente '49). However these elements which has been referred to be the stem cells of megakaryocyte correspond to the different developmental stage of mesenchymal element or prolymphocyte derived from crythrocyte, therefore, in a certain sense, they agree with my opinion. It is strange, however, that there is no one who has pointed out the formation of megakaryocyte through the fusion of elements derived from erythrocytes.

As Marinone ('52) has shown, the mitotic figure of mcgakaryocyte can hardly be seen. Recently, Hartoroft and Ridout ('51) found that "the megakaryocytes in cirrhotic rats were located both intra and extravascularly in bone marrow, spleen and lymphnode. In the remainder of the tissues the megakaryocytes were intravascularly only". Furthermore, Smith and Butcher ('52) has recently published that the large nucleus of a megakaryocyte conforms to the contour of the space it occupied the splenic pulp, and a tortuous "naked nucleus" conforms to the shape of the capillary loop of a glomerulus.

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These observations also support, in parts, my conception that, in some case, megakaryocytes may be arose from collapsed blood vessels and its contents.

(4) Origin of the blood platelets and its relation to the megakaryocyte. (i) Mammalian blood platelets. Since Wright claimed in 1906 that the megakaryocytes of bone marrow gave rise to platelets by fragmentation or budding off of its cytoplasm. One by one, the leading histologists and hematologists of the world have come to accept his view. Even recent time Gridwood ('49) and Fuente ('49) accepted with Wright's view but the conclusion of both of them are based upon the observations on the smear preparations. Austin ('39) said, "some workers (Rohr and Koller '36) believe that there is positive correlation between the number of megakaryocytes in the bone marrow and that of circulating platelets but such correlation has not always been found (Nickerson and Sunderland, '37)". Wislocki, Bunting and Dempsey ('47) believed that "the lipoidal particles, mitochondria and the bodies (tinged with supravitally with neutral red) contained in the blood platelets are similar to those found in the cytoplasm of megakaryocytes, therefore, Wright's view was reconfirmed". His logic appears as if be correct, but it conflicts with my view that the most of platelets in the blood film are the derivative of cytoplasm-extrusion of erythrocytes and the megakaryocytes in bone marrow are the derivative of erythrocytes. Therefore, it does not follow that because both megakaryocyte and platelets contain the similar substance, not necessarily megakaryocyte give rise to the all blood platelets. The historical review on the origin of blood platelets was described in detail by Tocantins ('48). I have also published an opinion regarding the origin and function of the platelets (Chishima, '51) in that paper I have discussed on the opinions presented by Hayem, Schmidt, Lowit, Bremer, Wlassov and others, though their opinions have been discarded as classic ones, but seems to be very suggestive. Petri ('26) and Cincinaci ('28) (quated by Potter and Ward '40) denied the relationship between the platelets production and megakaryocytic activity, as had been claimed by Wright and Bunting. My opinion agree with the opinion of Petri and Cincinaci, because Wright's view does not substantiated quantitatively. From the evidences mentioned above, it may be quite possible that the most part of circulating platelets are erythrocytic origin but not megakaryocytic,

(ii) Thrombocytes (spindle cells) in lower vertebrates. Deetzen('01), Deckhuysen ('01), and Koppsch ('01) (quated by Tocantins

'48) considered the thrombocytes in invertebrates and oviparous vertebrates as homologous to the mammalian platelets. While, Jordan ('40) says "As first demonstrated by Wright ('10) the thrombocytes of amphibian blood are homologous to the megakaryocytes of mammals, both arise from hemoblasts (lymphocytes). The writer can not be agree with his opinion, but rather agree with the following view, though it is a classic one, that the spindle cells are premature erythrocytes (Luzet, Marquis Neumann and Hayem).

(5) Origin of the yellow bone marrow and its relation to the fate of the myeloid elements under normal nutritional conditions. Regarding the origin of the fat cell, the following, controversial opinions have been presented by the previous observers; that the fat cell derived from, i) connective tissue cell, lymphatic cell and reticular cell (Ganifini '32 quated by Chang '40), ii) Macrophage, (Chang '40), iii) Granulocyte (Brines and Johnson 49), iv) primitive reticular cell, lymphocyte and macrophage (Smith et al. '52', v) fibroblast (preadipose cell) (Clark and Clark '40, quated by Smith et al '52), Controversy of these opinions mentioned above may be solved smoothly by my view that all of the mesenchyme cell, small lymphocyte, connective tissue cell (it is nothing but a flattened lymphocyte), fibroblast and reticular cell (intermediate stage between mesenchyme and lymphocyte), and macrophage do not belong to the genetically different cell lineage, but are crythrocytic origin differing only in their developmental phases, and cellular environments where they are located,

Chang ('40) has shown that, in the specimens of the bone marrow of rabbit injected subcutaneously with benzol and olive oil the newly formed fat cells as for as the macrophages are seen, contain hemosiderin formed by destruction of erythrocytes caused by drugs, The hemosiderin in the cytoplasm of the fat cells was by drugs. The hemosiderin in the cytoplasm of the fat cells was imterpleted by him to means that the fat cells have just come through the stage of being macrophage, at which stage this substance had phagocytosed. His finding almost entirely agree with my view, though he has overlooked that the macrophage arise from fused blood cells (not by phagocytosis) and, under and the normal conditions, all marrow elements fall, eventually, into fat cells andthen into the fat drop without having cellular structure. Some authors have already been noticed the possibility of the direct fatty degeneration from granules of granulocyte (Metzner quated by Chang '40; Brines and Johnson '49), or from protein granules (Metzner 1890, quated by Chang '40). This view supports

my opinion that the fatty degeneration of marrow elements usually preceded by a granulocyte stage.

Recentry, Hartoroft and Ridout ('51) found a very interesting and suggestive facts that the ceroid globules (prefatty substance) in fatty cyst in liver of rat fed on cholin deficient diet, frequently, resembled erythrocytes in size and shape, and there is clear evidence to suggest the possibility of transformation from erythrocytes into ceroid substance in vivo and in vitro. Fawcett ('52) observed that the rat's brown adipose tissue received rich blood supply. Pigon ('49) describes that the vacuoles in the amphibian erythrocytes are built up of lipoids with protein. These facts also suggest the possibility of my view, the erythrocytic origin of adipose cells.

Erythrocytopoiesis in the bone marrow, the reversible differentiation from yellow bone marrow and from other bone marrow elements into blood cells under starved conditions. As have already been described, by the auther there is no reliable evidence that the erythrocytopoiesis in the depleted marrow due mainly to the mitotic proliferation of the hemocytoblasts. In order to solve the matter, we must be pursued the behaviour of fatty tissue, which may be the very thing holding the key to solve the question.

Auguste ('51) states "Embryonic fat cells, once differentiated, are said to be unable to lose their fat, become generalized mesenchyme, or redifferentiate as blood cells" Even if this conception has already discarded, the conception involve deep significance. Jaquees ('36) says "Experimental studies of peritesticular fat lobules in the cavy leads to the conclusion that the fat cell is neither a highly differentiated cell, incapable of metamorphosis, nor a fibroblast with accumulated fat, but is a special histiocyte, normally or physiologically blocked by fat substance which prevents the cell from manifesting its histiocyte character...The essential characteristic of histiocytes can, however, be revealed experimentally (by inanition etc.)... A dedifferentiation of the cells takes place, and the fat is reabsorbed by the increasing protoplasm. The cells then begin to store trypan blue, to mobilize, and to transform to histiocytes (usually), sometimes to indifferent mesenchyme cells, to monocytes, or to fibroblasts". Present writer agree with him excepting some parts of his opinion that "the fat cell is not a highly differentiated cell". In my opinion, fat cell, especially, fat drop having no cellular structure is an end product of differentiation of several kinds of cells, though it has re-differential potencies into mesenchyme cells. Rutledge and Latta (quated by Chang '40) showed that the fat cells

in rat (injection of trypan blue into the peritoneal cavity) had lost their fat content and were transformed into the cells resembling the macrophage which took dye like other macrophages. About this conception, Chang ('40) says "they did not support macrophage as the origin of fat cells but, the reverse the possibility of the transformation of fat cells into macrophages. It is not improbable that fat cell return to their original form of macrophages by losing the fat content." Hartoroft and Sellero ('52) also reported the following noteworthy facts regarding the dissolution of fat, "the treatment of cholin-deficient precirrhotic or cirrhotic rat with lipotropic factors for period up to 3 months bringing about dissolution and eventually disappearance of nearly all pathologic fatty cysts encountered in this condition. After cholin is restored to the diet of such animals, intracellular lipid can be demonstrated within the cytoplasm in the walls of the fatty cysts. This is associated with a decrease in the lipid found within the lumina of the cysts. After the lumina of fatty cyst have been emptied by any of mechanism the cells in the cyst wall re-assume the appearance of normal parenchyma and after passing through a stage in which they exhibit rosettes re-form in the usual cord or plate pattern of liver".

The photomicrographs (Fig. 1-9) illustrated in their paper seems to me as if the mural cells surrounding the fatty cysts are showing transitions from "fatty-monera" through mesenchyme or small lymphocytoid cell stage by redifferential process of fatty tissue. Lepeshinskaya ('37-'50) published a very important idea and claimed courageously, that the new hemocytoblasts are formed de nove from the living substance (Yolk sphere) in the incubating hen's egg.

Above mentioned facts presented by many authors seems in favour of my hypothesis, the reversible differentiation between fatty tissue and blood cells.

Furthermore, I (Chishima '52b, '53b) have also expressed a new theory that the hemocytoblasts arise de novo from yolk sphere (in chick embryo), from placental "blood monera" (in mammalian embryo), and from the "food monera" on the wall of the digestive tract (in postnatal stage of both the bird and the mammals). It is said that about a trillion red cells wear out and remove from circulation each day in healthy man. An equal number of them are formed in bone marrow, from hemocytoblasts by its mitotic proliferation and maturation, and enter the blood stream to replace these removed (Haden '46). However, the orthodox view lack the firm evidence of i) surviving of the tremendous number of mesenchmal cells in the bone marrow or in

other site of the body, ii) mitotic proliferation of the hemocytoblasts, iii) maturation from one mammalian normoblast into one non-nucleated erythrocyte, iv) identity of the differential process of both the elements in normal bone marrow and that of the depleted marrow. v) site and manner of wearing away of the tremendous number of erythrocytes. Doan et al ('25) Jordan and Johnson ('35) and Jordan ('36, '38, '39) studied on the erythropoiesis in the depleted avian bone marrow by starvation for 9-10 days. And they and their followers applied the results as it is to the bone marrow under normal nutritional conditions. But it goes without saying that such view is illogical one, Many workers observed the maturation process from normoblast into erythroblast in vitro (Astaldi and Tolentino '48, Frieschi and Astaldi '48, Rusjuxyak et al. '47, Heleny '51, and Basaserja ('49). However, all of these observations were based upon the pathological bone marrow or on the marrow diluted by artificial medium. Therefore the results differ markedly from that of normal condition,

Erythrocytes may achieve their ripening in the circulation as Nijet ('49) has shown. Granick ('49) states the red cell maturation, and its relationship to the R N A content of the erythrocytic series, But his interpretation based entirely upon the view regarding hemopoiesis introduced by Doan et al. ('25). Therefore it can be said that his view can applicable to that of abnormal bone marrow. Kabelitz's ('52) view (that the megaloblasts are irreversible) contradicts to my opinion. Yamazaki ('48) claimed that in pathological marrow of rabbit differential process is mycloblast→promyelocyte→erythroblast. This view is in agreement with my opinion so far as pathological condition is concerned. Schleicher ('45) and Schwind ('50) denied the megaloblast conception of Doan et al. ('25) and said that the megaloblasts are found in pathologic bone marrow only. John ('36) says that "the erythrocytes of herring's larvae (Amphibia) arise from a syncytial sponge-work which fills most of the cavity of the heart by means of budding off of megaloblasts which then multiply and become erythrocytes". If his material was of underfed or starved conditions his view may be true, but if not so, his view may be entirely reverse in direction to the fact that I have observed on the frog's heart under normal or starved conditions. Doan et al ('25) concluded that the erythrocytes in depleted marrow of pigeons are derived from endothelial cells of intersinusoidal marrow capillaries. But Maximow ('27), Turnbull ('36) and Jordan ('37) asserted that crythropoiesis in marrow takes place extravascularly. Though his finding has not been gained the wide acceptance, Jordan ('32) had published a very suggestive opinion that the larger lymphocytes or lymphoid hemocytoblasts generally contain one or more nuclei. This cell may divide and the daughter cells assume characteristic more nearly like those of typical lymphocytes; or the "hemocytoblasts" may change directly into the more typical lymphocyte of the larger group of lymphocyte. These lymphocyte become transformed into crythrocyte by the elaboration of hemoglobin. His view agrees, in main parts, with the present studies on the depleted marrow of fowl. But according to my observations the "large, reticular and polynuclear hemocytoblasts" may correspond to the derivative from the fatty monera or to the young stage of "crythromyclocyte". It is a strange fact that the mechanism of denucleation of mammalian normoblast is still unsettled.

Some investigators believe intracellular nuclear disintegration (Naegeli '31 Leiter '44), while the others (Shilling, '38) keep the nuclear extrusion theory (quated by Boström '48).

As I have pointed out in foregoing chapter the nuclear diffusion theory may be true, on the contrary, the adherents of extrusion theory, most probably, have been misinterpreted the "connected type of granular normoblast with small lymphoid cell in fowl" or the "connected type of small normoblast with non-nucleated crythrocyte in mammal" because the small lymphoid cell or small normoblast show no evidence of its extrusion process but rather show evidence of the cytoplasmic budding off and of the transformation from the nuclear substance into the cytoplasmic substance,

Recently, Boström ('48) published a very interesting hypothesis regarding the erythropoiesis. According to her "Budding hypothesis" one mammalian erythroblast (normoblast) can form several erythrocytes through the budding off of protoplasm from normoblast. My hypothesis agrees in main parts with her theory in the following points; i) the erythroblasts of the marrow are not sufficient for the enormous amount of erythrocytes required each day if, as according to the denucleation theories, one erythroblast can only form one erythrocyte, ii) it has been impossible to explain what becomes of all the extruded nuclei, iii) unharmonious in size between normoblast and non-nucleated erythrocyte. Her opinion has attacked the blind spot of the orthodox view as to the hemopoiesis. However, it seems very regrettable that her hypothesis based mainly upon the abnormal bone marrow (Pernicious anemia or after hemorrhage).

According my observations mammalian normoblast gives rise to

several crythrocytes by not only "budding" but also by "sporulation" of it. If normal bone marrow is not the site of erythropoiesis as I have been claimed, a question might arise, "Where is the site of erythropoiesis under normal conditions?" The question may be solved by the hypothesis of Duran-Jorda ('47-'50, '51) and of the writers view (Chishima,'52b) that the crythropoicsis in healthy fowls and the mammals takes place at the wall of digestive tract. However, as to the detail of this problem I will publish in the another paper. There have been published many papers on the extramedulary hemopolesis in several tissues (Krumbhaar,'49, Plum,'47 and many others). However, it can be said, I believe, that if these studies on the so-called "extramedullary hemopoiesis" were based upon the materials under abnormal or malnutritional conditions, it may be true, but if the materials used were normal, may be referred to a misunderstanding of the differential process from blood cells (especially erythrocytes) into fixed elements composing several tissues.

#### Summary

Differentiation, de-differentiation and re-differentiation of the bone marrow elements including the blood cells and yellow marrow of oviparous animals (chick embryos, chicken and adult fowls) and mammals (rabbit, goats, dogs, cats and guinea-pigs) under well fed and starved conditions were studied by means of examination on the imprinting, sections and culture of the bone marrow. The results obtained are summarized as follows.

- (A) Differentiation from blood cells into the bone marrow elements under normal conditions.
- (1) Erythrocytes in the marrow of the oviparous animals often show transition into small lymphoid elements (meta-lymphocyte) through spherocyte stage, while the mammalian erythrocytes generally form a fused mass ("Erythrocyte-monera) in which small lymphoid elements arise de novo through the "sporulation and coacervation process" (new synthesis of chromatin substance in the F E monera).
- (2) Mammalian "meta-lymphocytes" are not always equal in size owing to the amounts of crythrocytes contributed to their formation.
- (3) Mitotic figure of the "meta-lymphocytes" in the marrow is hard to find, while the "meta-lymphocytes" show the evidence of further differentiation into monocytes, promyelocytes or into myelocytes. Therefore, the "meta-lymphocytes" should be discriminated from

"pro-lymphocyte" which is a stem cell of erythrocyte and are found in the depleted bone marrow only.

- (4) Isolated erythrocytes in the marrow often extrude its cytoplasm and the both the extruded portion and the residual portion transform into two connected lymphocytes resembling to an amitotic figure of a lymphocyte. This type (connected or budding type of cell) is seen in the marrow film of chick embryos and young chickens. The extruded portion of the erythrocyte show transition into eosinophilic granulocyte. However, in bird and especially in mammals, two or several erythrocytes extrude co-operatively their cytoplasmic content and form a neutrophilic granulocyte. And those erythrocytes eventually contribute themselves for the myeloid element formation,
- (5) The neutrophilic granulocyte then transform into eosinophilic and then into basophilic granular myeloid element. There can be drew no sharp distinctive line among the three kinds (neutro, acido, and basophile) of granulocytic series, or even between non-granular and granular myeloid elements.
- (6) There is no firm evidence that the so-called macrophage belongs to a specific cell lineage, but it seems most probable that it is a derivative from fused blood cells irritated by foreign substance induced into the blood.
- (7) Polynuclear giant cells in chicken marrow and megakaryocytes in mammalian bone marrow also have no special stem cell, but are the derivative from fused blood cells. Mammalian blood platelets hardly show the evidence of their megakaryocytic origin, but show the transition from the extruded cytoplasm or debris of erythrocyte.
- (8) Yellow bone marrow composed of fat cells and fatty drops having no cellular structure is a resultant from fatty degeneration of granular myeloid elements including macrophage and megakaryocyte, and sometimes, from that of erythrocytes or non-granular myeloid elements.
- (9) Capillary system, including venous sinusoid in the bone marrow, are, in general, open type, and it is not uncommon that there can be found collapsed or degenerating arteries.
- (B) Erythropoicsis, the reverse differentiation from the yellow bone marrow into blood cells under starved conditions.
- (10) Under inanition or malnutrition, the fatty tissue in the bone marrow decreases in amount, however, it may not due to the dissolve away of it. While the fat drop transform into a neutrophilic or polychromatic cloudy substance ("fat monera") in which arise de

novo several scores of mesenchymatous hemocytoblasts, which show further transitions into basophilic normoblasts, and then into orthochromatic normoblasts.

- (11) Avian orthochromatic normoblasts with somewhat granulocytic nature maturates usually into a nucleated erythrocyte. However, mammalian normoblast is, in general, several times larger in volume than the erythrocyte, so that one normoblast gives rise to several or more of non-nucleated sphere erythrocytes. During the maturation of normoblast, the nucleus swells and diffuses into the cytoplasm and transforms into acidophilic cytoplasm, from which emerges spontaneously several erythrocytes by "budding" (at periphery) and by sporulation (at interior part) of the cytoplasm.
- (12) A characteristic cell, "crythromyelocytes" were found in the depleted bone marrow of cocks under prolonged starvation. The cell resembles the promyelocyte but it contain 1-3 spherocytes or its primordium. These elements may be considered as a transitional form of the reverse differentiation from the myeloid element into crythrocytes under starved condition.
- (13) Not only the yellow bone marrow but also the marrow elements show reverse differentiation into normoblasts, eosinophilic granulocyte or directly into crythrocytes.

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#### Explanation of Plates

#### Abbreviations

Ber, budding of erythrocyte; Bmeg, hemocytoblast formation from megakaryocyte by sporulation and budding off of megakaryocyte; Bnor, budding of normoblast; Ce, the so-called nucleus of fat cell; Da, degenerating artery: Dnor, dissolution of normoblastic nuclei; Er, crythrocytes; ExE, erythrocyte extruding its cytoplasmic content; Exg, neutrophilic granular leukocyte formed by cytoplasm-extrusion of erythrocytes; F, fat tissue; Fer, fusion of crythrocytes; Fmg, megakaryocyte formation by fusion of crythrocyte; Fmn, fat-monera; Myc, myelocyte; Res, residual body of crythrocyte which have already extruded its cytoplasm; Spo, new formation of hemocytoblasts in the fat-monera by the sporulation;

Plate I

Fig. 1. Schematic illustration of the reversible differentiation between the crythrocytes and the bone marrow elements in the domestic fowl under normal and starved conditions. 1. erythrocyte; 2. Spherocyte; 3. Meta-lymphocyte; 4. Promyelocyte; 5. Polychromatic myelocyte; 6. connected type of small lymphoid elements found in the bone marrow of chick embryo; 7. eosinophilic granulocyte connecting with meta-lymphocyte; 8. Plasmacytoid promyelocytes; 9. budding (extrusion of cytoplasm) of erythrocyte; 10, new formation of monoblast by mutual-cytoplasm-extrusion from erythrocytes; 11. monocyte; 12. granulocyte formation by mutual-cytoplasm-extrusion from erythrocytes; 13. granular leukocyte; 14, polynuclear giant cell in the chick embryo and young chick; 15, macrophage; 16, connective tissue cell; 17. giant fat drop (yellow bone marrow); 18. fat monera; 19.

#### Reversible Differentiation between Bone Marrow and Erythrocytes

new formation of mesenchymatous cell in the fat monera; 20. hemocytoblast; 21, polychromatic crythrocyte; 22. connected hemocytoblasts (pro-lymphocyte (left) connected with somewhat granular hemocytoblast (right)); 23. eosinophilic granulocyte connecting with lymphoid element (pro-lymphocyte); 24, 25, 26, transformation from connected type (23) into spindle cell-like pro-crythrocytes (26); 27, hinucleated eosinophilic granulocyte connecting with pro-lymphocyte; 28, transitional phase; 29, eosinophilic granulocyte connecting with pro-lymphocyte; 30, transitional phase; 31, spindle cell-like pro-rythrocytes F, agglutination and fusion of crythrocytes; SC, several kinds of cells in the bone marrow.

Fig. 2. Schematic illustration of the reversible differentiation between the erythrocytes and bone marrow elements in the mammals under normal and starved conditions.

1. non-nucleated erythrocyte; 2. spherocyte; 3. polychromatic spherocyte; 4. spherocyte with somewhat basophilic nature; 5. small "pro-lymphocyte"; 6. the so-called orthochromatic or basochromatic normoblast; 7. promyelocyte; 8. cytoplasmic extrusion of erythrocyte; 9. transitional phase; 10. cooperative cytoplasm-extrusion of erythrocyte; 11. monoblast; 12. monocyte; 13. basophilic myelocyte; 14. cooperative cytoplasm extrusion of erythrocytes; 15. neutrophilic or eosinophilic granulocyte; 16. megakaryocyte; 17. polychromatic myelocyte; 18. macrophage; 19. budding or elongation of erythrocyte; 20. connective tissue cell; 21. (at drop. (yellow bone marrow); 22. (at monera; 23. sphere erythrocyte; 24. mesenchymatous hemocytoblast; 25-29. small lymphoid, monocytoid, large sized, polymorph, and polynuclear basophilic normoblast; 30. orthochromatic normoblast; 31. diffusion of normoblastic nucleus; 32. dissolution of nuclear substance in normoblast and new formation of spherocytes by budding and sporulation; 33. freed spherocytes; F, F E monera (agglutinated crythrocytes); SC, Several kinds of cells in the bone marrow.

Plate II. Pigs. 3-6, 8 and 9 are normal bone marrow and fig. 7 is depleted marrow

Fig. 3. Six pairs of connected type of small lymphoid elements derived from crythrocytes are shown. Imprinting from femur bone marrow of a chick embryo at 18 days incubation. Glemsa's stain. × 400

Fig. 4. Neutrophilic leukocyte formation from erythrocyte by means of cytoplasm extrusion (budding process). Imprinting from femur bone marrow of a frog. Giemsa's stain. ×800

Fig. 5. Bone marrow section from a rabbit's femur, showing megakaryocyte formation by fusion of erythrocytes, and fat drop formation by fusion and degeneration of myeloid elements. H. E. Stain. ×800

Fig. 6. A polynuclear giant cell in the bone marrow of a chick embryo at 18 days incubation. Imprinting preparation. Giemsa's stain. ×1000

Fig. 7. Formation of neutrophilic granulocyte by means of cytoplasm extrusion from erythrocytes in the bone marrow of a chick under 4 days starvation.

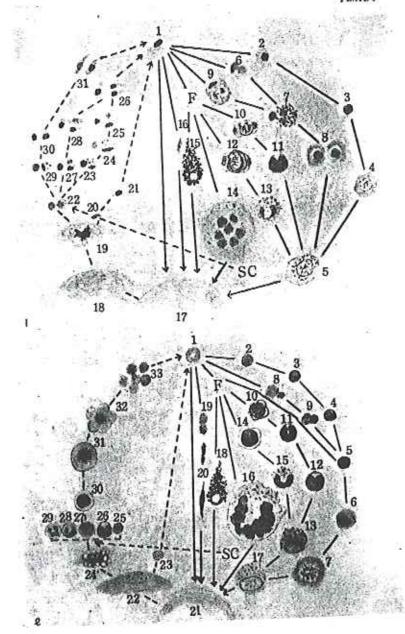
Fig. 8. Femur bone marrow from rabbit, showing megakaryocyte formation through the fusing of erythrocytes and myeloid elements, and showing the fat drop formation through fatty degeneration of myeloid elements. H. E. stain. ×800

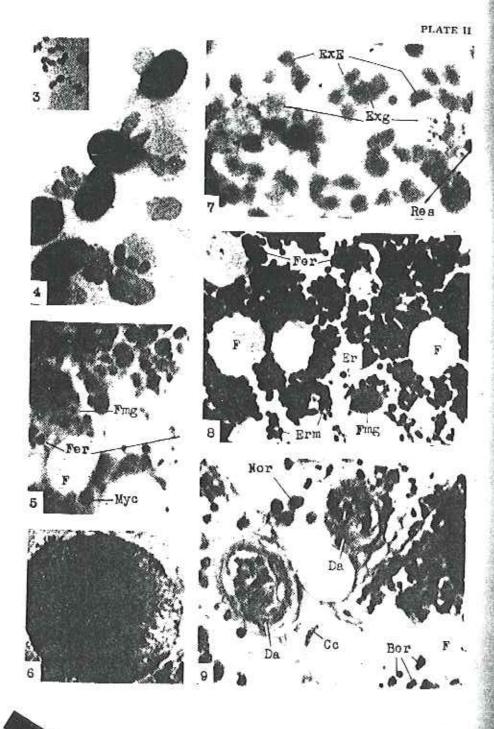
Fig. 9. Two degenerating arteries and several fat drops are shown. Degenerating marrow elements and erythrocytes in the process of fusing to form fat drops, and two fat drops (lower left) are at stage just preceding fusion. The same preparation as the fig. 8. ×1000.

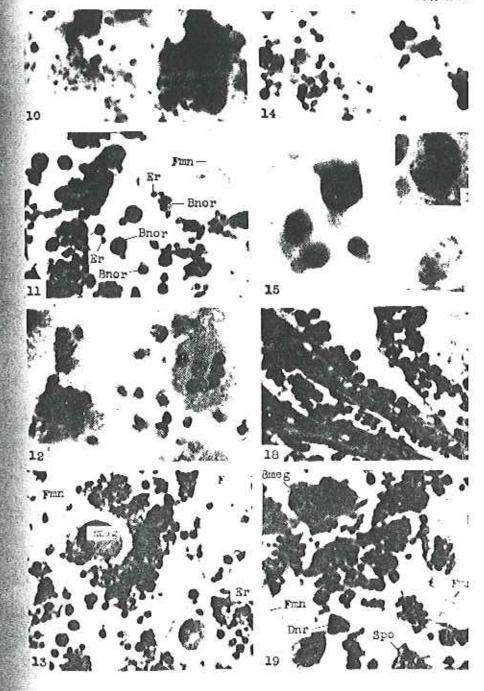
Plate III. Bone marrow figures under starved conditions (Fig. 10-13, 18, and 19 are sections stained with H.E.)

Fig. 10. Section of bone marrow from a chick starved for 4 days, showing crythrocytic masses which resemble the fat drops in shape and size. H. E. stain. × 800

- Fig. 11. Budding off of erythrocytes from normoblasts, and fat monera derived from fat drop are shown. Section of femur from a cat under 12 days starvation. ×800
- Fig. 12. Marrow section from a chick under 4 days starvation, showing the new formation of crythroblasts in the fat moneras, and there can be seen transition from hemocytoblasts in the fat moneras into crythrocytes. ×800
- Fig. 13. Femur's marrow from a dog under 9 days starvation, showing the reverse differentiation of normoblast from fat monera and megakaryocyte. ×800
- Fig. 14. Smear preparation of fixed bone marrow from a cat under 12 days starvation. Direct arising de noto of erythrocytes and normoblasts from fat monera, and erythrocytes formation by budding and sporulation of normoblasts. ×800
  - Fig. 15. Higher magnification of a part of Fig. 14. ×1600
- Fig. 16 and 17. Marrow imprinting from a adult cock under 21 days starvation, showing a "spherocyte contains mycloid element" ("erythromyclocyte") one of which (Fig. 16) contains two spherocytes and a primordium of spherocyte, and the another (Fig. 17) contains one spherocyte. × 1200
- Fig. 18. Bone marrow section of femur from a dog under 10 days starvation, showing reverse differentiation from the elements of the wall of collapsed artery into normoblasts.
- Fig. 19. Bone marrow section of femur from a cat under 12 days starvation, showing reverse differentiation from megakaryocyte and fat monera into normoblasts. ×800







# CHAP. III Monographs and Papers on the "Intestinal Haematopoietic Theory" published by this Author

#### (A) Monographs

- (1) Reaxamination of the orthodox intramedullary haematopoietic theory. Reversible differentiation theory of blood cells-(In Japanese with English resumé) (Igaku-shoin, Tokyo, 1954)
  (This monograph's revised edition is collected in "Chishima's Complete Works Vol. 4)
- (2) Basis of Neo-Biology Vol. 2-Origin of Life, cell and Blood Corpuscle. 1958. PP. 319~380. (Meibundo Co.) (This monograph also was republished as "Chishima's Complete Works Vol. 1)

#### (B) Papers

- 1953- The Reversible Differentiation between the Erythrocytes and the Bone Marrow Elements or Bone under the Normal or Starved Conditions, Okajima's Folia Anat., 25, 3, pp. 119-148 (Original Paper)
- (2) 1954- The Haematopoietic Problem and Modern Medicine or Biology. The haematopoietic problem will inevitably require a revolution of the basic principles of modern medicine and biology, Ijiköron, No. 1975 (paper)
- (3) 1960— A Series of Talks about a New Haematopoietic Theory by K. Chishima with the Haematologists who visited Japan from America, Soviet, and Denmark, Kagaku Shinbun, No. 856-857.

# PART VI

THE SIXTH PRINCIPLE: REVOLUTION OF GENETICS - K.CHISHIMA'S THEORY THAT GERM CELLS ARE DERIVED FROM ERYTH. ROCYTES

- [A] The Relations between the Revolution of Genetics and the Origin of Germ Cells
- (1) Promising Genetics and Despairing Genetics

At present, two different kinds of genetics are sharply opposed to each other. One is the orthodox genetics which is called "Mendel-Morganism", and the other "Lysenkoism" T.D.Lysenko (1898-), the Soviet geneticist, advanced. The former claims that the hereditaryalterations or mutations are "indefinite", and presumes that such alterations cannot be predicted as a matter of principle, or that such alterations cannot be influenced by environmental conditions, such as, natural, social, and educational circumstances.

Such a hereditary doctrine is a fatalistic and despairing idea. For, this theory suggests that if his hereditary disposition is not good, a man cannot transmit any better hereditary disposition to his posterity than his own one, or that he cannot make his hereditary composition any better, even if he makes efforts to improve his environment, such as, natural, social, and educational circumstances.

To put it strongly, the orthodox genetics says that it is impossible or despairing that we try to improve our hereditary disposition.

Therefore, this author says that the orthodox genetics is a fatalistic and despairing one. On the contrary, the latter suggests that it is possible for us to make our hereditary disposition any better on Michurinism I.V. Michurin(1854-1935) advanced. Michurin asserts, "It is possible, with man's intervention, to force any form of animals or plants to be changed more quickly,

and more freely in a direction desirable to man. There opens before man a broad field of activity of the greatest value to him." Michurin and his follower Lysenko reject flatly the fundamental principle of Mendel-Morganism that hereditary is completely indendent of the plant's or animal's environmental conditions of living.

Lysenkoism asserts that the alteration of hereditary characters in organisms or in their separate organs may not be always, or fully, transmitted to the offspring but changed germs in newly-generated organisms always occur only as a result of changes in the body of the parent organisms under the direct or indirect influence of the environmental conditions of living.

Therefore, hereditary changes in organisms and their complexity increase in accordance with the accumulation of new characters and properties acquired the organisms in their successive generations. Thus, Lysenkoism may be called a promising genetics.

These two theories on heredity are, at present, sharply opposed to each other as described above, while the believers in the orthodox genetics are predominant in numbers,

However, this author ventures to say that there can be found in Mendel-Morganism a lot of spots that are thought to be incorrect methodologically and virtually.

Therefore, this author will offer the following suggestions to the Mendel-Morganists.

#### (2) Suggestions to the Mendel-Morganists

It is natural that the Mendel-Morganists should admire G, J. Mendel and T. H. Morgan for their precursory achievements on genetics, but it is regrettable that many of them are still clinging to the ghost of Mendel or the remains of the old Mendelian doctrine which has already fulfilled its mission in modern science.

The orthodox genetics the chromosome theory of heredity-asserts as follows;

 Genes or hereditary substances localized in the chromosome are completely independent of environmental changes, and never generated de nova.

- ii) Germ cells are immortal, and independent of somatic cells genetically.
- iii) Hereditary alterations are produced only by sexual breeding or indefinite mutation which is completely independent of the changes of natural environment.

However, it is clear that such orthodox Morganism is a static conception dwelling still on the Preformation theory or the Pre-Darwinian thought. For, the three following fundamental discoveries going against the leading idea of Morganism were recently published:

The first is the proof of the inheritance of acquired characters which was discovered by I. W. Michurin, T. D. Lysenko, and K. Chishima who also proved it from his theoretical point of view.

The second is the verification of the new-formation of cells from living or organic substances, such as yolkspheres, egg albumen, and others, which was discovered by O. B. Lepeshinskaya & her cooperators (between 1937-51) and K. Chishima (in 1950, 53, 56, 58, 63).

The third is the finding that germ cells-sperms and ova are produced through differentiation or dedifferentiation-from the somatic cells, or from the erythrocytes in Mammalia including man, Aves, the reptiles, amphibia, fish, insects, and others, which was discovered by K. Chishima (in 1948, 51, 52, 54, 55, 57).

iv) The fourth is the reversible differentiation between the blood cells and almost all kinds of fixed cells including germ cells, yolkspheres, fat tissue, the bone marrow, bones, and others, which was discovered by K.Chishima (in 1953, 54, 55, 60, 63, 68).

However many of the orthodox Morganists may try to reject, or take no notice of, or treat with silent contempt, these new findings on the facts, they are all evident facts, and beyond question.

Preferably, it is necessary that they should reform the orthodex genetics fundamntally, just as the larva of a certain insect attains to an adult stage through metamorphosis (hystiolysis solution of tissues and recontsructive histogenesis). Namely, the present state of Mendel-Morganism is just like

the eve of metamorphosis, or just like that of the replacement of the Ptolemaic system by the Copernican theory.

In this case, the immortal saying of J.W.von Goethe "Stirb und Werde" may deserve the deepest contemplation to the present conservative Morganists.

The above mentioned opinion can be also seen in this author's monograph which was published in 1958, but this author believes firmly that the opinion is never incorrect as yet.

v) Molecular biology leads us to chaos, too,

With the development of molecular biology, the biochemical analysis of DNA (Deoxyribo Nucleic Acid) which hereditary substances or genes are composed of has made remarkable progress, and so some scientists talk exaggeratedly as if the mystery of genetics (or its essential qualities) is going to be solved by means of the chemical analysis of DNA. However, so long as these scientists believe in the orthodox genetics as ever, and have a bias toward analysis, they will go away from the essential qualities of genetics against their will. And such an attitude will keep one genetics from the other farther off, and then lead us to chaos.

# (3) The Two Opposing Theories on Genetics and K.Chishima's Finding—the Germ-cell Origin Theory on Genetics-

This author will give here the essentials of his criticism on the two opposing theories and of his germ-cell origin theory on genetics. (As for the particulars, see K.Chishima's book already published in 1957.)

i) The orthodox genetics is the successor to Weismannism-the continuation theory of germ plasm. It asserts that germ cells are entirely independent of somatic cells, and continue their hereditary substances eternally through mitotic cell division and nuclear division. But this conception is fundamentally incorrect, for germ cells are, in fact, derived from somatic cells (erythrocytes) through the A.F.D. process of the nonnucleated red blood corpuscles of Mammalia or the A.F.D. process of the nucleated erythrocytes of Aves, Reptilia, and other lower animals.

Therefore, it is necessary that the orthodox genetics should be reformed fundamentally and immediately.

ii) Germ cells are derived from the red blood corpuscles which are a kind of somatic cells (in Aves, the reptiles and other lower animals) or pre-cellular element (non-nucleated red. bl. corp.) (in mammals).

From this fact, it may be well understood that sometimes, brothers and sisters who must have inherited the same hereditary substances from the same parents are quite different from each other in shape and character. Namely, in the case of man, as sperms and ova are formed from the red blood corpuscles about a month before fertilization takes place, the constitution of germ cells is very much influenced by the conditions of the parents' health, food, medicine, and chemical compound which the parents took in, or by mental stress, and environmental conditions.

Thus, the mother is so much influenced by her material and mental life environment or environment in the womb during a ten-month embryonic stage that it is possible that sometimes, the elder brother and the younger brother have no resembrance to each other. This phenomenon is simply called "individual variation" or "fluctuation variation" in the orthodox genetics, but the reason it occurs is not in the least elucidated. On the other hand, the theory of the derivation of germ cells from erythrocytes had not been known to Lysenko before it was discovered by K.Chishima, but Lysenkoism may be greatly supported or backed up by this finding of K.Chishima's, since it asserts that there is possibility that germ cells may be changed under the influence of environmental conditions.

Lysenkoism may be also supported by the new-formation theory of cells from organic substances, which was discovered by O.B.Lepeshinskaya, the famous Soviet cytologist. Of course, Lepeshinskaya as well as Lysenko had not known of the theory of "the derivation of germ cells from erythrocytes" before K. Chishima published it. Anyway, Mendel-Morganists who believe in the orthodox genetics may be dealt a fatal blow by this finding of K.Chishima's-the theory of the derivation of germ cells from somatic cells(blood corpuscles).

# (4) The Irrationality of Chromosome Genetics

In the orthodox genetics, it is asserted that there is no course or mechanism through which the variations of somatic cells acquired by environmental changes may be transmitted to germ cells. And also it is thought that the somatic cell and the germ cell both are irrelevant to, or independent of, each other, and then that hereditary substances are localized only in a chromosome.

Moreover, in the orthodox genetics, even the chromosome map is drawn as a map composed mainly of giant chromosomes in the salivary gland of Drosophila.

But, in fact, the salivary-gland cells of insects have no direct relation to hereditary, but preferably it is even more probable that they may degenerate shortly into saliva. Therefore, it is a great irony that the chromosome map in which genes are drawn in a line on the chromosomes looks so much like the homunculus theory in the age of the preformation theory.

There is a theory that sex determination is made by the number of chromosomes or the morphological difference of them, but this is not true because the shape and the number of chromosomes can be individually changed in the same species by the concentration sorts and the temparature of fixative solution used in making the preparations.

The orthodox theory asserts that hereditary substances are localized only in a chromosome, but preferably the presumption that they are not localized only in a chromosome but included in the constitution of the whole of protoplasm seems to be even more rational. For, as a matter of fact, there are those scientists in the world who do not agree even on the chromosome number of man.

For instance, some say that the chromosome number of man belongs to Type XO, and others say that it belongs to Type XY.

The following table shows the difference in research results between the twelve prominent biologists who made a study of the chromosome number of domestic fowl between 1908 and 1942.

#### RESEARCH RESULTS ON THE CHROMOSOME NUMBER OF DOMESTIC FOWL

Published Year	Investigator	Chromosome Number In Germ Cells	Chromosome Number In Somatic Cells
1908	Sonnenbrodt	8-12 (about 12)	
1909	Guyer	\$ 17	
1910	,	\$ 18	\$ 18
n.	Lecaillon	♀ 24 ?	우 24
1923	Crew	32	
"	Reush	3 about 12	
11	Stevens	\$ 36−38	
1924	Shiwago	\$ 32	
1926	Hance	1070 000-0	\$ 35 − 36
1927	Akkeringa	32 ?	34-44
1930	Suzuki	\$ 74 4 73	
1942	Oguma	\$78 977	

As shown in the above table, the chromosome number of domestic fowl still remains indefinite. For instance, the chromosome number of domestic fowl was 17 (3) in 1909 but 78 (3) in 1942. The reason the chromosome number of domestic fowl rapidly increased from 17 to 78 for only thirty-three years may be that the researchers gradually became more proficient in their art, not that such a rapid increase was brought about by some hereditary factor.

Of course, the chromosome number of man still remains indefinite. For instance, in Japan it has been said that the chromosome number of a man is 47, while that of a woman is 48, and so man belongs to Type XO. But, on the other hand, in America it has been asserted that the chromosome number of man is 48 both in a man and in a woman, and so man belongs to Type XY. Thus, a wise scientist will not believe in the theory that a sex

is determined by the number of chromosomes and the morphological difference of them. Therefore, this author insists that probable errors should be always added to the determined number, especially when more than scores of chromosomes can be measured. Neverthless, the orthodox geneticists who stick to determinism try to determine formally the strict and fixed number of chromosomes in organisms according to their species, but that is true neither in fact nor in theory.

According to this author's opinion, the sexual difference of the numbers or shapes of chromosomes is not cause of sex determination but only the result or in parallel with sex.

#### (5) Sex Reversal and Chromosome Genetics

Sex reversal can be seen in various kinds of animals. This may be well shown in the five following examples:

i) The sex reversal of Bonnellia viridis, the marine lower invertebrate:

This is a well-known fact since it was discovered by Baltzer in 1935.

ii) The sex reversal of a domestic hen:

This is also a well-known fact. It is the fact that when the ovary of a domestic hen was surgically cut off from her, the sexgland rudiment on her right side developed into a functional testis, and then spermatogenesis was done in it. And then the hen that changed into the cock was successful in copulating and fertilizing another hen, and, as a result, from the fertilized eggs chickens were hatched.

#### iii) The sex reversal of an oyster:

According to the discovery of prof. Amemiya, the Japanese biologist, in 1931, oysters are always the female ones so long as they live in the seawater warm and abundant in food, but they change into the male ones when they are transferred into the seawater cold and poor in food. And then when they are replaced into the warm and nutritious seawater the male oysters reverse into the female again.

#### iv) The sex reversal of a killifish:

70 --

In 1955, prof. T.Yamamoto, the Japanese biologist, found the fact that killifish hatched as males change into the female ones once that they are given the food in which female sex hormone is mixed, and reversely the female killifish change into the male ones when they are given the food with male sex hormone.

v) Sometimes, sex reversal can be seen in black porgies & "funegai" (shell).

Although the orthodox geneticists know all the above-mentioned facts on sex reversal, they are very bigoted to explain those facts according to Mendel-Morganism.

But there is no one of the orthodox geneticits who has been successful in establishing the fact that an individual is adapted to its living environmental changes immediately after its birth. Sex reversal is, sometimes, done according to its living environmental changes, and, as a result, the chromosome number of an individual or its sex-chromosome increases or decreases corresponding to the acquired sex. Clearly this fact is antagonistic to the orthodox theory.

Therefore, sex in organisms cannot, or should not, be divided into male and female strictly and fixedly, but preferably sex should be considered . plastic and elastic, sometimes reversible.

As shown in the above-mentioned examples, there exists a neutral sex or an intersex, and sometimes, in man an intersex between a man and a woman can be seen. For instance Goldsmith was once successful in forming the intersex of a moth experimentally, while in the natural world there exists a bird with male feather on one side of the body and female feather on the other side.

This is well known as an example of gynandromorphism.

Moreover, as for the evolution of sex, it has gradually evolved from asexuality to sexuality. For instance, the lowest microorganisms are asexual, then tapeworms or snails at a little more highly-developed stage are hermaphroditic, then, as for Mollusca, some of them are bisexual-monoecism, or some of them are distinctly differentiated into the male and the femaledioecism, and at last insects or vertebrates at an even more highly-developed stage are separated into the male and the female-dioecism However, in the world of the higher animals, sex reversal or intersex can be seen on rare occasions?

This may prove the fact that "sex" contains something asexual or hermaphrod-

itic latently.

Life phenomena are originally elastic or labile. Therefore, so long as the orthodox geneticists try to explain sex deterministically in conformity with formal logic, they must repeat the illogical and conflicting explanation as to such problems as sex reversal and sex differentiation.

This author does not reject any experimental facts presented by the orthodox geneticists, but cannot agree with them on the principle of the orthodox genetics. For, it is inconsistent with the facts, and then falls into self-contradiction logically, as described above.

## (6) Environment and Heredity: Inheritance of acquired characters

The focus of the dispute between the orthodox genteicists and the Lysenkoists on heredity lies in the inheritance of acquired characters. In other words, it is the question whether acquired characters will be inherited or not. And the orthodox geneticists deny it, while the Lysenkoists affirm it.

In 1953, in his book "The Situation in Biological Science", Lysenko says, "I shall now conclude. Thus, comrades, as regards the theoretical line in biology, Soviet biologists hold the Michurin Principles. The Weismannists and their followers, who deny the heritability of acquired characters, are not worth dwelling on at too great length. The future belongs to Michurin." He goes to say in it, "The Michurin trend in biology is a materialist trend because it does not separate heredity from the living body and the conditions of its life. There is no living body-without heredity, and there is no heredity without a living body. The living body and its conditions of life are inseparable. Deprive an organism of its conditions of life and the living body will die. The Morganists, however, maintain that heredity is isolated, something apart from the mortal living body, from what we call the soma.

The Michurinists say that the inheritance of acquired characters is possible and necessary.

This principle has once more been fully confirmed by the abundant factual material evidences in plants and animals." Lysenko gives abundant data on this problem, such as the "nutritive hybrid" method-the grafting hybrid method, the vernalization method of wheat by treating it at the lower temperature, the grafting of a rabbit's ovary, the egg albumen exchange in incubating the hen's egg, etc. It is true that some of his experimental data may still leave the door open to disputes, but Michurinism and his opinion concerning the possibility of the inheritance of acquired characters modified by environmental changes are quite correct from a theoretical point of view. Moreover, his opinion will be supported by this author's finding that germ celle are derived from somatic cells, or red blood corpuscles which should be influenced by environmental factors or by milieu.

#### (7) Blood and Heredity

From antient times, the word "blood" has been used as a synonym of heredity in every country of the world, as if by common consent. If we try consulting the dictionaries, we shall be able to find the following words in them with case:

Chi (Japanese), blood (English), Blut (German), sang (French), Pkobd (Russian), Sanguis (Latin), Blod (Swedish), Sangre (Spanish), Khrag (Tibetan), Sangue (Italian), Sangue (Portuguese), Kan (Turkish), rakta or rudhira (Sanskrit), etc.

All these words mean, beside circulating blood, "family line", "strain", "parental heritage", "lineage," "the essence of life," etc.

And also the following words and phrases may prove the fact that the word "blood" has been used as a synonym of heredity:

"Blood is thicker than water", "blood will tell", "kinship between parent and offspring", "half blood strain", "prince (princess) of blood", "blue blood" "blood brother", etc.

From these words and phrases, we can know that ancient sages were wise enough to see through the intimate relationships between blood and heredity intuitively. But the orthodox geneticists conclude that blood plays only the role of supplying nutrient for germ cells or embryos, and don't think that there is any direct connection between blood and heredity. As for this respect, this author thinks that they should follow the example of ancient sages with modesty.

The word "Chisuji" in Japanese for lineage (strain or family parentage in English) has been widely used in Japan, but it originally means a blood vessel. We can see the deep insight of Japanese into blood in the word "Chisuji", although it is far-fetched. For instance, if we observe the microscopic preparation of an amphibian's ovary, we can see very clearly that crythrocytes in the blood vessel of the ovum are newly formed by means of the A.F.D. process (Aggregation, Fusion, and Differentiation), as shown incolor plate Fig. ) In other words it is blood or a blood vessel (chisuji) that connects offspring with parent And then the fact that ancient sages had an insight into can be now proved scientifically through such an observation.

#### (8) Orthodox Genetics and Formal Logic

The orthodox genetics may be unscientific and incorrect so long as it is based on formal logic. The opposition of the two genetics is, in essence, attributed to the difference in viewpoint or in philosophy (scientific methodology) between both of them. The orthodox geneticists think of formal logic as a standard of judgement, and try to explicate the results of their studies on the "law of the excluded middle". Namely, they try to distinguish two phenomena into A and B strictly or rigidly, not admitting that there exists the intermediate between A and B. Therefore, they are liable to make unnatural explanations that are contrary to the facts. For instance, they think that the things which are opposed to each other, such as germ cells and somatic cells, chromosomes and cytoplasm, dominant and recessive, environment and heredity, are not related to, and independent of, each other.

But, all matter and phenomena in nature, especially life phenomena including heredity, are continuous. All things under the sun are set in motion and flow, but they transmigrate dialectically. Therefore, from such a philosophical point of view, it is presumed that there exists the transforming domain of gray between black and white, and the very things on such a vague borderline should be attached more importance to. For instance, in heredity the relations between environment and an organism are interactive. When the somatic cells (erythrocytes) transform themselves into germ cells, the cells that can be temporally seen on the borderline are neither somatic cells nor germ cells, but they are the very intermediate cells between somatic cells and germ cells.

They always pass such an intermediate phase,

On the contrary, the orthobox biologists and geneticists have quite neglected such an obscure transforming phase. Fortunately, this author has studied especially such a borderline in life phenomena, so that he could find the blind spots of the orthodox genetics.

# [B] Criticism on Orthodox Genetics; and a list of papers and monographs already published by K.Chishima

 1932: The Inheritance of Acquired Characters should be Affirmed (in Japanese) (cited in the book "Essence of Zootechnical Science" by K.Chishima, pp.216-220, Meibundo, Tokyo)

This is the first essay in Japan that was published against the orthodox genetics.

(2)1950 - 51: Problems on the Inheritance of Acquired Characters (in Japanese) (published on the journal "Biological science", 2-4 & 3-2, Iwanami, Tokyo)

- (3) 1956: The New Theory on the Relationships between Blood and Germ cells (in Japanese). (published on the journal "Academia-Japan." No.28)
- (4) 1957: Basis of Neo-Biology-Genetics, Embryology, and Evolution in relation to the Origin of Germ cells by K.Chishima, vol. 1, pp.1~ 467.
  (published in Japanese with English Suggestions, Meibundo, Tokyo)

In this monograph, this author publishes his opinion on the erythrocytic origin of ova and spermatozoa in Insects, Amphibia, Reptilia, Aves, and Mammalia. And then he deals with the orthodox opinions on genetics and embryology, Weismannism, the theory of the continuity of germ plasm through mitotic cell division, and all other opinions on the orthodox principles.

His criticism on the orthodox genetics is described in detail through 1~462 pages in this monograph. This author concludes by saying that the orthodox view on embryology and genetics should be fundamentally re-examined exactly by seeing this author's new theory that germ cells are derived from somatic cells through the differentiation of crythrocytes.

(5) 1957: Criticism on the Controversy between Mendel-Morganists and Lysenkoists-Inconsistency between embryology and orthodox genetics, and its unification. -Criticism on orthodox genetics based on the mitotic cell division theory, (in Japanese).

(Published in the book "Basis of Neo-Biology" by K.Chishima, Genetics, Embryology, and Evolution in relation to the Origin of Germ cells, vol. 1, pp. 1-462, Meibundo, Tokyo).

In these monographs, this author treats of the above-described problems in detail.

(6) 1966 : Lysenkoism Is Not a Fanciful Theory (in Japanese) (published on the paper "Nihon Kagaku Shinbun (Japan Science Newspaper), Oct. 7, 1966, and reprinted on the Journal "Mind. Body, and Life," vol. 4, No.4, pp.1-7, 1967) (Seimei to Kiketsu)

Many of the orthodox geneticists have published their opinions against Lysenkoism in the newspapers and journals, and, as if by common consent, they say in them that Lysenkoism is a fanciful and erroneous theory. But this author thinks that their comments are not true. For, this author has found far more mistakes in the orthodox genetics than in Lysenkoism.

This author once criticized them in a paper from his new theoretical point of view on the relationships between the origin of germ cells and heredity. Then, in the same paper, Dr.H.Kihara, President of the Japan Imperial Institute of Genetics, Dr.T.Komai, the famous geneticist in Japan and Honorary Professor of Kyoto Univ., and Dr.H.Tsuge, Professor of Hosei Univ., published their opinions on Lysenkoism in relation to this author's, opinion. Of these three scholars, Dr.Kihara and Dr.Komai, who are the authorities of genetics in Japan, both denied Lysenkoism, but they avoided commenting on this author's opinion without knowing why. This may clearly express the fact that they could not find out any proofs of denying the facts and theory presented by this author. On the other hand, Dr.Tsuge, the progressive biologist in Japan, adopted of both Lysenkoism and this author's opinion.

# [C] Practical Application of the Sixth Principle to Health and Medical Science

 The cause of almost all diseases may be attributed to the bad environmental conditions, not to hereditary disposition

Many of the laymen and specialists in medicine believe firmly that almost all diseases, such as cancer, tuberculosis, heart diseases, hypertension, neurosis, gastric ulcer, malformed children, etc., often result from hereditary disposition.

But, as a matter of fact, most of these diseases or abnormality are caused by the bad environment influence (conditions) soon after one's birth or during the period of pregnancy. It is often said that the cause of such diseases as mental diseases (psychosis), optic abnormality (colour blindness, strabismus, etc.), the malformation of the joint (or bone) of one's fingers or toes are attributed to hereditary disposition.

Such a tendency can be certainly seen in these diseases, but it cannot be seen so often. But people are generally apt to misunderstand that even the diseases or malformation which are not thought to be hereditary are all attributed to hereditary disposition. The orthodox geneticists should bear a part of the responsibility for this prejudice. For, when they investigate the relationships between parent and offspring chiefly according to statistical data, they are liable to decide hastily that all diseases are transmitted from parent to offspring without condition, if they chance to find that some members of the same family hold the same disease or the same malformation. And then some of the orthodox geneticists say, "Ilabits are inherited, too," But it would be premature for them to think so. For, if the same family repeat to eat the same food and to hold the same mode of living every day, they all will come to look like one another in constitution, mentality, behavious, and even in facial features (physiognomy).

The reason they all will come to do so is that a mode of living, a practice, and other environmental conditions are all the same. Therefore, if the same family happen to live together under the same bad mode of living and the same bad conditions of environment, naturally the same disease or the same disturbance will occur among them, or among the parents and their children.

Neverthelss, most of the orthedox geneticists explicate that it is due to hereditary transmission, but that is not proper. For, it is not so easy as generally thought to discriminate between hereditary disposition and "a posteriori" characters-acquired characters. Heredity and environmental modification are an indivisible entity, and then the characteristics of an organism are, as a whole, composed of both what used to be inherited and what has been acquired.

(2) The characteristics of a child are influenced by the interior environment of the mother's womb during the period of pregnancy.

Generally, people are apt to think that the characteristics a child holds immediately after his birth are all hereditary, but it is necessary that they should know that all is not so, or that all is not as said in the orthodox genetics.

The orthodox geneticists think that genetic characteristics are already determined when an ovum is fertilized with a spermatozoon, and then that hereditary substances are the genes localized in the chromosomes of germ cells.

But, it is clear that an embryonic life in the interior of the womb after fertilization is an inner environment. Therefore, even if a newly-born child has a disease or abnormality, we should not easily jump at a conclusion that the cause of his disease or abnormality is attributed entirely to here—ditary disposition.

Neverthless, laymen are, in general, liable to think that his disease or abnormality is a hereditary disease or a hereditary deformity. This author gives here an instance of environmental influence, It is the case of "pheco-

nelia" children. It is the case that some of the women who had habitually used thalidomide pills since the first or second month of their pregnancy gave birth to "pheconelia" children who have no arms or no legs or too short arms or too short legs. The number of these "pheconelia" children amounts to about 6000 in West Germany, and about 1000 in England and in Japan, respectively. The reason these "pheconelia" children were born is not that they were hereditary monstrosity, but clearly that the young cells of a sensitive embryo, especially those of the nervous and blood vessel system, were very narcotically affected by an anesthetic contained in the thalidomide pills through the mother's blood, and, as a result, the growth of these children's arms and legs were deadly suppressed. Therefore, the cause of such diseases as leukemia, polio, a weak-minded child, a yellow baby, and others, which can be often seen among the children, may be attributed not to the congenial diseases, but to the food or chemical substances the mother takes in during the period of pregnancy, the mother's mode of living, and the influence of unnatural and unhealthy "milieu" (inner environment).

# (3) The cause of almost all chronic and regressive diseases may be also attributed to bad environment.

Most of the chronic disturbances of the internal organs, such as the heart, the kidney, the liver, and others, may also result from environmental pollution, such as air-pollution, water-pollution, soil-pollution, radio active isotopes—pollution and foodstuff-pollution.

At present, not a few people are suffering from environmental pollution in the most highly-civilized countries. To put it in the concrete, environmental pollution is often caused by soot and smoke from the factories, waste gas from the motorcars, waste matters from the factories, waste disposal or radioisotopes from the experiments of atomic explosions and the atomic power plants, the scatter of insecticides or herbicides, foodstuffs or drinks artificially coloured, harmful chemical-additions, and others. Even the foodstuffs treated with radial ray are about to be sold.

Thus, natural environment-air, river, sea, and land-which surrounds us is gradually contaminated by such harmful chemical and physical-substances, and, as a result, the globe is now changing into an uninhabitable land.

This also arises from the one-sided development of modern civilization or modern industry which has priority of economy to life, taking no account of it.

Originally, since man has endured all trials of nature for more than several hundred thousands years, he ought to have been sound in mind and body.

Therefore, if only natural environmet is reformed in a better condition, it is possible that man will enjoy better health and longer life, but, on the contrary, if modern civilization is too much biased toward matter and economy as it is today, it is certain that the health and life of man, especially those of the civilized men, will be gradually undermined, the regressive, chronic diseases including cancer will increase still more in number, even the hereditary disposition of man will be pathologic, and at last man will follow the road to ruin himself.

Therefore, now is the time when we should reconsider this material civilization essentially and seriously, and then make all efforts to restore fresh nature. It is necessary that we should realize that we are now facing the most important turning point of modern civilization.

## (4) Personality or individual character depends more upon environmental conditions than upon hereditary disposition.

Generally, people are liable to think that the character of a man is inherited chiefly from his parents, but, as a matter of fact, it depends more upon postnatal environmental conditions, especially more upon home education at an early age, than upon hereditary disposition. People often say "They are brothers, but they are not in the least similar to each other in character", but this may express the fact that the character of a man depends so much upon environmental condititions.

As for this respect, there are lots of cases that brothers are makedly dissimilar to each other in face and physical build, while the orthodox geneticists are a loss how to explain it because the hereditary substances of brothers should be the same according to their theory. Consequently, they are obliged to define it as an "individual variation" under the pressure of necessity, and then they assert that it is quite different from mutation, and has no connection with heredity. The technical term "mutation", however, is also a very ambiguous expression as treated of in the latter chapter.

Talking of infant education, this author introduces here the following anecdote of Darwin:

Once, when Darwin was asked by the next-door woman with a baby in her arms, "When should we start to educate our child?" he said, "How many months have passed since your child was born?" She answered, "Six months", and he said to her, "It is already six months late to do so".

If this author is in his place, he will answer to her, "In a broad sense, it is too late to start to educate your child after he was born. More accurately, you should begin to educate your child a month before you were pregnant with child, or when germ cells are newly formed from the red blood corpuscles."

For, a child depends so much on the interior environment of the womb during the period of pregnancy as described above. For instance, in a tenmonth pregnant mother, the healthy development in mind and body of a developing emdryo is very much controlled by her mental and physical mode of living.

In the Orient, the necessity of prenatal education has been urged from ancient times, but that is never incorrect in comparison with the presentday true science.

Especially, the character of a child is very much influenced by education, training, and discipline at a very early stage in postnatal life.

Good and strong will is also cultivated chiefly in the period from the cradle to the kindergarten. There is the common saying "Children are what their parents make them", but this is exactly correct.

The character of a man surely depends even more upon the discipline and environmental conditions upon than hereditary disposition. In Japan, there is

the proverb "Uji yori sodachi (Better is breeding than birth)", but this may express well the relationships between a man and environment.

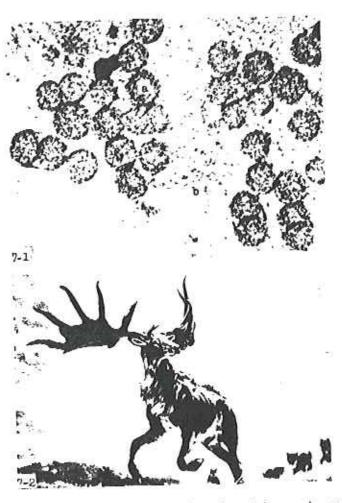


Fig. 7-1. New-formation of Paramecium from bacterial mass by means of AFI) process (Aggregation, Fusion of Differentiation, a-early stage of paramecium, b-bacteria.) (K. Chishima.)

Fig. 7-2. Irish EIK. This species became extinct, and remains only as a fossil, owing to the unbalanced over-growth of their weapon, the antler.

### PART VII

# THE SEVENTH PRINCIPLE : BLIND SPOTS OF EVOLUTIONISM AND CRITICISM ON IT

- (A) Criticism on Evolutionism and its Application
- Darwin's achievements in biology are epochmaking, but they involve some blind spots in themselves, and leave room for criticism.

In 1859, Charles R. Darwin (1809-1882) published his famous work \*On the Origin of Species by means of Natural Selection\*. In 1958, a centenary of Darwinism, as you know, was largely held in every part of the world, but so far as this author knows, there was no biologist who had ever pointed out or criticized any blind spots involved in Darwinsim. It is true that evolutionism discovered by Darwin is exactly epochmaking and extremely excellent, but it cannot be completely independent of the trend of the times, the scientific level of the times, and the social status of the then scientists who supported it, although it is above the common run.

Therefore, it may be said that even Darwinism involves some blind spots in it, especially from a new bjological point of view. In 1958, from this point of view, this author published the article "My Impressions of the Centenary of Evolutionism" in the journal "Academia" No. 34 in Japanese.

It is a correct and a great thing that Darwinism positively proved in its basic principle that organisms evolve and change gradually from simple to complicated ones with the transition of time and space, but we cannot lose sight of the blind spots Darwin held himself, and then the static points of view his followers have established, deviating from the basic principle of Darwinism.

Therefore, it is very important that we should rectify the distortion of evolutionism, since it is the basic and leading principle to biological science today.

Next, this author will give the outline of his criticism on evolutionism brie-

fly. (As for the particulars, see the book "Basis of Neo-Biology" written by 1 K. Chishima, vol. 1, 1957. The revised edition of this monograph is collected in "Chishima's Complete works vol. 2, 1971".)

- (2) Blind spots of Darwin and his followers Conception .
- 1) Evolutionism runs into a blind alley ahead of amoebae.

In his book "On the Origin of Species by means of Natural Selection", Darwin says, "It is impossible for us to explain the origin of life, or the origin of amoebae and bacteria", and he gave up explaining it, but this attitude of his may be inconsistent with the spirit of evolutionism. For, since mankind has evolved from the lower unicellular organism, such as an amoeba or a bacterium quite different from him, to what he is today, evolutionism will be lacking in consistence, unless the evolution of mankind from the lower and simpler organism than an amoeba or a bacterium to what he is today is sufficiently elucidated by evolutionism itself.

In 1936, Aleksandr I. Oparin (1894———) published his famous book "The Origin of Life," and he explains in it that life is generated through the following stages of evolution:

inorganic matter → organic matter → complex organic matter → protein → a unicellular microorganism

He says that life is spontaneously generated, only he makes it a proviso that this process of evolution or spontaneous generation was made only once at a certain evolutional stage of the globe more than eight or ten hundred million years ago. And most of the modern biologists conclude by saying that evolutionism is consistent in Alpha and Omega by this opinion of Oparin's.

But, it is a wonder that though there is a big illogical mistake in his theory no one of the modern biologists have noticed it. For, assuming that the higher organism or mankind has evolved from an amoebae or a bacterium that appeared first on the earth more than eight or ten hundred million years ago to what it is today, it will be easily supposed that amoebae or bacteria that can be widely seen on this earth today have continued to exist as they were at primitive stage by means of cell devison without evolution for more than eight

or ten hundred million. Consequently, if they persist in such an assumption, evolutionism on organisms will not be able to get rid of the contradiction that evolutionism involves non-evolutionism in itself.

As described in the foregoing chapter, it is impossible to assume that amoebae or bacteria have continued to exist by means of cell division without evolution for more than eight or ten hundred million years. For, today we can collect no evidence that they have continued to exist by means of cell division. Preferably, as this author advances, bacteria that can be widely seen today were spontaneously generated from organic matter on the earth very lately.

Therefore, the present-day evolutionism will not be logical and conclusive enough to break such a blind alley until it is reformed according to this author's opinion on the facts and theory.

#### The five-step advancement of evolutionsism and evolutionsism tomorrow

As mentioned above, Darwin's evolutionism is confined to the range from a unicellular organism to mankind, but it may be said to be the first step that man ever attempted to explain the facts of evolution in organisms on scientific methodology. And it may be said to be the first of the greatest findings that man had in the nineteenth century. But it is necessary that the sphere of evolutionism should be enlarged more widely and studied more thoroughly because it is not perfect. As a matter of fact, many scientists have tried to do so down to this day.

This author will give here the outline of thier achievements in evolutionism briefly, believing firmly that true evolutionism tomorrow will be produced by the exhaustive study of evolutionism today.

- The outline of the five-step advancement of evolutionism and its advocators
- (1) The first step of evolutionism and its advocators.

The first step is the theory of the following evolution from true energy to an atom:

True energy (ultra elementary particles) → through the A.F.D. process (condensation by centripetal spiral movemet) → elementary particles → through the A.F.D. process → an atom

Notes (1) true energy...lt is an ultra-elementary particle with no mass and no charge, such as photon, neutrino, and what is called ether.

(2) elementary particles. They are the particles, each of which is an indivisible entity of matter and energy, such as an electron, proton, etc.

The advocators of this theory are some of the ideologists, religionists, and theoretical physicists. This author published the same paper as this theory in 1970.

As for the evolution of atoms, the periodic table of atoms that Dmitri I. Mendeleev (1834~1907) discovered expresses a periodic evolution of atoms, and this finding of his has made a great contribution to the development of science. Recently, C. Louis Kervran (1962), the French theoretical physicist, published a unique theory "on the transmutation of atoms in the hody of organisms or in the natural world". (translated into Japanes by, G. Ohsawa, 1962).

(2) The second step is as follows:

Inorganic matter → organic matter → complex organic matter (protein body)

- - A. I. Oparin (1894~ ) and others

3 The third step is as follows:

Organic matter -- a unicellular microorganism and a cell (New-formation theory of cell)

- O. B. Lepeshinskaya (1937-1957) and K. Chishima (1954-

4) The fourth step is as follows:

Unicellular microorganisms → the higher plants and animals including human begings (The so-called evolutionism and its outriders)

> J. B. P. A. M. Lamark (1744-1829), J. W. Goethe (1749-1832), C. R. Darwin (1809-1882), A. R. Wallace (1823-1913)

The fifth step is as follows:

The fifth step is the application of evolutionism to the fate of mankind, the earth, the solar system, and the whole universe. Of course, this is the step that should be studied in future.

 Darwin and his followers lay too much stress upon the one side of the "struggle for existence", making light of the important role of "symbiosis",

"Natural selection" has been generally approved of as an important factor of evolution, but this theory has a slight bias toward mechanism. As you know, Darwin was deeply impressed with the book "An Essay on the Principle of Population" written by T. R. Malthus (1766~1834), and taking suggestions from it, he consolidated the thought of the "struggle for existence". He was not unaware that mutual aid or symbiosis, as well as the struggle for existence, can be seen in the organic world, but he laid too much stress on the latter, making light of the former.

Friedrich Engels (1820-1895) and Trofim Lysenko (1898-) both criticized this point strictly. In 1953, Lysenko says, "Many are still not clear about Darwin's error in transferring into his teaching" Malthus's preposterous reactionary ideas on population". The true scientist cannot and must not overlook the erroneous aspects of Darwin's teaching", quoting the following phrase of Engels:

"The entire Darwinian teaching on the struggle for existence merely transfers from society to the realm of living nature like Hobbes's Neverthless, the successors to Darwin and most of the modern biologists have further developed the idea "the struggle for existence" into the idea "The stronger prey upon the weaker". Devout Darwin, however, might have little expected that such an idea results from his thought "the struggle for existence".

At present, it seems that the idea "The weak fall a prey to the strong" gives the warmongers in contemporary society a specious pretence. This may express well a tragic aspect that has been brought about by the distortion of true Darwinism and the misunderstanding of evolutionism. Today, in spite of this fact, the conservative biologists insist that the law of the struggle for existence is the main factor of evolution in organisms including human beings.

And also it seems that most of the laymen believe in the law of the struggle for existence. Therefore, there are still limited wars here and there in the world, and there are various kinds of social troubles around us, as though the law of the struggle for existence were an eternal truth.

#### 4) P.A.Kropotkin's view - "Mutual Aid"

Perhaps no one had definitely affirmed that the main factor of evolution lies in "mutual aid", not in the "struggle for existence", until P. A. Kropotkin 184; ~1921), the Russian anarchist and geographer, did so. It was in 1902 that he published his famous work "Mutual Aid", but he says in it, "The paper "On the Law of Mutual Aid", which was delivered at a Russian Congess of Naturalists in January of 1880 by Prof. Kessler, the well-known Russian zoologist and then Dean of St. Petersburg University, struck me as if it had thrown a new light on the whole subject. Prof. Kessler's idea was that besides the law of "Mutual struggle", there is in Nature the law of "Mutual Aid", which, for the success of the struggle of life, especially for the progressive evolution of species, is far more important than the law of mutual contest. This suggestion, which was, in reality, nothing but a further development of the ideas expressed by Darwin himself in the "Descent of Man", seemed to me so correct and of signed an importance that since I became acquainted with it in 1883, I began

to collect materials for further developing the idea, which Prof. Kessler had only sketched cursorily in his lecture, but had not lived to develop. He died in 1881 ....... I consequently directed my chief attention to establishing, first of all, the importance of the "Mutual Aid" factor of evolution, leaving to the ulterior researches the task of discovering the origin of the "Mutual Aid" instinct in Nature".

And also he cites the following episode from "Goethe's Remark":

"If its generality could only be demonstrated" — did not escape the naturalist's genius so manifest in Goethe. When Eckermann once told to Goethe —it was in 1827— that two little wren-fledgelings, which had run away from him, were found by him next day in the nest of robin redbreasts (Rotkehlchen), which fed the little ones together with their own youngsters, Goethe grew quite excited about this fact. He saw in it a confirmation of his pantheistic views, and said, "If it be true that this feeding of a stranger goes through all Nature as something having the character of a general law, then many an enigma will be solved". He returned to this matter on the next day, and most earnestly entreated Eckermann (who was, as is know, a zoologist) to make a special study of the subject, adding that he would surely come "to quite invaluable treasures of results". (Gespräche, edition of 1948, vol. 3, pp. 219—221)

Unfortunately, Eckermann could never make a special study of the subject, but then he might have been inspired by Goethe's remark, on mutual aid among animals.

A.P. Kropotkin arranged a large amount of results of his studies in mutual aid, including some impressions of his journeys in Eastern Siberia and North Manchuria, and concluded as follows:

"In the animal world, we have seen that the vast majority of species live in societies, and that they find in association the best arms for the struggle for life understood, of course, in its Darwinian sense — not as a struggle for the sheer means of existence but as a struggle against all natural conditions unfavourable to the species.

The animal species, in which individual struggle has been reduced to its narrowest limits, and the practice of mutual aid has attained the greatest development, are invariably the most numerous, the most prosperous, and the most open to further progress.

The mutual protection which is obtained in this case, the possibility of attaining old age and of accumulating experience, the higher intellectual development, and the further growth of social habits, secure the maintenance of the species, its extension, and its further progressive evolution. The unsocial species, on the contrary, are doomed to decay.

As for man, we found him living in clans and tribes at the very dawn of the stone age; We saw a wide series of social institutions developed already in the lower savage stage, in the clan and the the tribe; and we found that the earliest tribal customs and habits gave to mankind the embryo of all the institutions which made later on the leading aspects of further progress .....

In the practice of mutual aid, which we can retrace to the earliest beginnings of evolution, we thus find the positive and undoubted origin of our ethical conceptions; and we can affirm that in the ethical progress of man, mutual support -not mutual struggle-has the leading part. In the wide extension, even at the present time, we also see the best guarantee of a still evolution of our race.

The views of Kessler and Kropotkin which were described above are both right. All living things originally have both sides of the struggle for existence and mutual aid. Of course, it is beyond question that mutual aid is far more important than the struggle for existence, as compared with each other in importance.

#### Symbiosis and the A.F.D. process as a basic factor of evolution

Kropotkin elaborately observed and investigated the fact that mutual aid can be widely seen in the animal kingdom, and then he referred to mankind, but he was not aware of mutual aid in the world of microorganism.

So he says as follows :

"Mutual aid is found even amidst the lowest animals, and we must be

prepared to learn some day, from the students of microscopical pondlife, unconscious mutual support, even from the life of microorganisms.

The truth of his prophecy was proved later on by this author's finding that symbiosis or the A.F.D. process is the main factor of evolution. This author found it out separately from the thought of Kropotkin, but, in the end, this author's agrees to his opinion in respect that mutual aid is the basic principle of evolution. As mentioned above in chap. I-V, the lowest unicellular microorganisms, such as bacteria, amoebae, paramecia or eels composed of multicellular organisms, are spontaneously generated by means of the A.F.D. process (Aggregation, Fusion, and Differentiation of organic materials or the lowest microorganisms).

For convenience's sake, the A.F.D. process may be classified into two kinds of type. One is the first type of the A.F.D. process, and the other the second type,

#### 6) The first type of the A.F.D. process

The first type of the A.F.D. process is, in principle, quite alike the coacervation process in colloid chemistry. However, the coacervation is a chemical term applied to the phenomenon, that is, the aggregation and fusion of minute particles in colloidal solution, through the process of which a coacervate (a minute liquid droplet) is formed in colloidal solution.

A.l. Oparin referred to this phenomenon, and regarded it as the first step of the origin of life on the earth, but this technical term may be applied even to inorganic colloidal solution. Namely, the A.F.D. process designated by this author may be applied to the new formation of bacteria from organic matter, of non-nucleated red blood corpuscles in mammals including man, or of nucleated crythrocytes in other lower vertebrates from digested intestinal monera, and of embryonic mesenchyme cells from yolkspheres or from non-nucleated red blood corpuscles. (As for the particulars, see chap. I-V).

In short, the cells or the unicellular microorganisms that are the small unit of life are formed by means of the first type of the A.F.D. process, and then they are differentiated and evolved into the higher complicated organisms that are the larger unit of life, by means of the aggregation and fusion of the organic elements that are the lower and more minute unit of life.

Therefore, this process stands against the law of the struggle for existence or the law of the junggle in Darwism, while it stands for mutual aid, and corresponds to the primitive type of mutual aid that Kropotkin advanced.

And also this process expresses the fact that the smaller particles peacefully harmonize with each other, unite with each other, and finally develop into organisms at the higher grade. In other words, this process—the first type of the A.F.D. process—may be said to be the basic rule of the development of life at the earliest stage that Kropotkin could not explain in his time.

#### 7) The second type of the A.F.D. process (symbiosis)

As mentioned in Chap. VII (the new formation of cells), this is not only the A.F.D. process at the higher stage than the first type of the A.F.D. process, but also the process that the cells or the unicellular microorganims already formed repeats Aggregation, Fusion, and Differentian. For instance, it is a well-known fact among biologists that in zoochlorella and Zooxanthella-unicellular algae that are regularly seen in the cytoplasm of various Protozoa (amoebae, viridis, etc.) and in the tissue of invertebrates belonging to different groups (Sponge, Coelentrates, Rotifera, Mollusca, Annelida, and others), both of them are generally considered the intracellular symbionts because the former look like a green body, and the latter yellow. But according to this author's studies in fiesh-water sponges subsisting in the River Nagara in Japan, it is confirmed that coloured Zoochlorella are never the symbionts.

For, this author has confirmed the fact that in this case, sponge cells do not cat Zoochlorella as a phagocyte, but Zoochlorella themselves aggregate into, the mass and develop into sponge cells by means of the A.F.D. process. Therefore, it may be presumed that Zoochlorella and Zooxanthella seen in the cells of many other Protozoa and animals are generated by means of the same process, or by means of the second type of the A.F.D. process. Zoochlorella and Zooxanthella, which are generally thought to be the intracellular symbionts, do not continue to keep the same structure and colour indefinitely, but, with the

passage of the time, they change their physico-chemical properties gradually, until at last a sponge cell-with one nucleus, one cytoplasm, and one protoplasmic membrane is newly formed from scores of those chlorellas.

Namely, cells are spontaneously generated, which this author has often confirmed. The reason those algae belonging to the plant kingdom subsist in the cytoplasm of animal cells is not that they are phagocytosed by the amoebae or the other animal cells that are regarbed as phagocytes, but that some of those chlorella aggregate, fuse together in a group, and finally evolve into a cell, through their own efforts (ability). This may prove the fact that there exists, in reality, the evolution from a plant to an animal on this earth. Since none of the modern biologists have yet noticed it, this fact may be taken for heterodox by those scientists who believe firmly the orthodox cell theory, but, as for such a fact, many other similar examples can be, in reality, seen on this earth.

Therefore, this author is convinced that the time will come soon when the truth of this author's opion will be understood.

The most important meaning this process involves is that some of the cells that are the smallest unit of life aggregate, fuse together in a group, and develop into something at the higher stage, or into the larger unit of life.

This author has often confirmed that amoebae or paramecia are spontaneously generated in the surface of the water containing organic matter by means of the A. F.D. process of bacteria. As described in Chap. V (Intestinal haematopoiesis theory), symbiotic bacteria, yeast, and sometimes even Protozoa are often found in the cell of the intestinal mucous membrane widely seen in the insects and other higher animals including human beings, but the orthodox scientists refer it to the symbiosis between animals and microorganisms, while this author believes firmly that this is also an example showing that the cell of the intestinal mucous membrane is newly formed from a mass of bacteria by means of the A.F.D. process of bacteria and organic matters.

If a conscientious scientist re-examinines this fact, it will be definitely proved by him that this author's view is correct.

#### 8) The higher type of the A.F.D. process.

The A.F.D. process is the very basic rule that can explain definitely the evolution of an organism as well as that of a cell. In other words, the A.F. D. process is also the basic rule of ontogeny that shows the following process:

cells → tissue → an organ → a system → an organism (individual)

The most highly-developed man cannot live without being in symbiosis with the lowest microorganisms (intestinal symbionts). Furthermore, the A.F.D. process is also the basic rule of the mutual aid and symbiotic communication between the intraspecies and the interspecies in mankind and the other animal and plant kingdom. The "Struggle fur existence" or the "law of the junggle" is only the rule that holds good at most for the stage of the beasts of prey in evolution. Therefore, the present-day civilized people who have both intelligence and wisdom at all should abandon very soon the wrong rule of evolution that only holds good at most for the stage of wild animals, and acknowledge the truth of the A.F. D. process this author advances. Thus, the time is now coming when they should do so.

There is the western proverb "United we stand, divided we fall", but that is true. Next, this author will present that the A.F.D. process is the principle of development, growth, and prosperity, and on the contrary, the reverse A.F.D. process is the way to degrowth, decline and to death.

#### 9) The gap between the orthodox genetics and modern embryology: the mutation theory and evolution

The orthodox genetics originally belongs to the category of the preformation theory that all the characters of an organism are previously determined by the genes localized in chromosomes, while modern embryology and evolutionism both belong to the category of epigenesis that all the characters of an organism are not determined previously, but they develop gradually with the development of an individual. Thus, there lies across a deep gap between the orthodox genetics and modern embryology or evolutionism. Of course, it is beyond question that the preformation theory is nothing but an anachronism, for not only such a static thinking disagrees to true logical argument, but also it conflicts with the facts.

Originally, any of the three sciences embryology, genetics, and evolutionism is the science that makes a special study of the development of organisms, and these three sciences have an intimate connection with one another, so that they ought to be consistent with one another on the unified principle.

Mutation has been referred to be an important factor of evolution, but this technical term "mutation" in the orthodox genetics is a very enigmatic one. For, it seems that this technical term is one-sidedly exploited by the orthodox geneticists in order that they fool us by using it as the magic of a term as if they could make us understood what is incomprehensible.

Essentially, the term "mutation" is generally used in modern biology as the following meaning that a mutation arises suddenly from unknown cause, irrespective of environment and living conditions and almost all of the generated mutants are morbid or abnormal, deformity individuals, which are referred to be unfit for survival. And the frequency of mutation is generally said to be very rare.

The characteristic of an organism consists in its adaptability to various kinds of environmental conditions. But, the orthodox geneticists regard mutation as an important factor of evolution in organisms, although it is, in essence, abnormal and independent of adaptation. Therefore, it is natural that their thought should be suspected as a misconception by the biologists and physiologists who are aware that the characteristic of an organism lies in its adaptability to environment.

The biologists who take a mechanistic point of view are liable to attribute the main factor of evolution in organisms to accidental chance, independent of environmental conditions, but that is in the wrong. For, it is more logical or reasonable that we suppose that, as for the characteristic of mind and body in man, man has been adapted to environmental conditions for a long time, while he has gradually accumulated the characters acquired in his adaptation to environmental conditions, and then he has gradually transmitted the acquired characters to his offspring through the long evolutional process.

If one denies the presumption that man has been adapted to environmental changes for a long time, while he has gradually evolved into what he is today, repeating the innumerable generations, one will be blamed for one's judgement being too short-sighted and then it seems as if one concluded by observing a short hand of the clock for only a short time that the hand is immovable, or as if one concluded by observing a part of the arc in a large circle that the part is a straight-line.

Most of the present-day biologists deny Haeckel's law-the recapitulation theory, but that is also in the wrong. For, their judgement is too short-sighted. (As for the particulars, see the book "Basis of Neo-Biology" by K.Chishima, vol. II

Biologists and evolutionists should not be simple tecnical workers in order that they may understand the evolution of life correctly, and establish true evolutionism.

Furthermore, they should have true philosophy or true methodology in order that they may see the whole widely through the framework of time and space and will have good and synthetic judgement. For, evolutionism was once founded on data (facts) correctly, but it is now distorted partially, that is to say, there are many things that have lost the chain of continuity for a long time. Therefore, it is much to be desired that true, scientific methodology will be established as soon as possible.

This author ventures to say by your allowance that the orthodox evolutionists seem to have been lacking in such methodology. For, they have hardly paid attention to it because the orthodox genetics has been predominant. (As for the particulars, see Chap. VII)

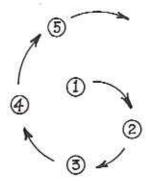
Therefore, as described above, evolutionism today has not only a lot of blind spots but also some contradictions that may be called "antievolutionistic." It is true that some of the scientists who have been described above pointed out some blind spots, but, so far as this author knows, there is no other scientist in the world who has pointed out more blind spots than this author.

#### 10) The spiral tendency of evolution, especially in mentality

In general, the trend of evolution is apt to be considered a straight-line, but that is in the wrong. For, it is, in fact, shown as a wavy curve or a spiral line according to this author's studies in evolution. (As for the particulars, see K.Chishim's monograph "Revolution of Medical & Biological Sciences", pp.5-59, 1963)

This author deals here chiefly with such problems as peace vs. war, symbiosis vs. the struggle for existence or the law of the junggle, and so on, from a historical and mental-evolutional point of view on mankind, and indicates them schematically. The reason this author deals with such problems here is that Darwinism has originally the tendency to make much of the material and physical side of evolution, neglecting the mental side of it.

The Schematic Illustration of the Spiral Tendency of Evolution in Mankind (Special Reference to the Turning Point of the Human Spirit)



Explanation of Fig. 7-3

- (1) The age of the most primitive life (bacteria and Protozoa): In this age, the main factor of the development, growth, and evolution of life was symbiosis and the A.F.D.process(mutual aid).
- (2) The stone age: the savage age or the times of clans (tribes).
  In this age, there may have been sometimes, quarrels or battles among tribes, but mutual aid was principally promoted among them.

- (3) The medieval ages: the times of the establishment of the states.
- (4) Modern ages: From the medieval ages to modern ages, war and peace were alternately repeated among states.
- (3) The present age:

  In the present age, war and peace are alternately repeated as well as in the foregoing ages (3), (4), but the aspect and scale of wars in the present age has so remarkably changed that if by any chance an all-out war should break out, not only all living things on the earth but also even the earth itself will be on the brink of ruin or destruction.

Thus, the reason we, mankind, are still confronted with the menace of wars is that we have been too much absorbed in developing scientific technique, neglecting to develop spiritual culture. Now, we live in the so-called atomic age, and we have atomic bombs and then biological chemical weapons for wars, while, as for our moral civilization, we still remain in the same stage as that of the wild animals or the beasts of prey. In other words, we are still influenced by the misconception that the law of the struggle for existence or the law of the junggle is a natural one in the social life of mankind as well as in the world of wild animals.

It is much to be regretted that there are too many who reconcile themselves to the misconception that a war is the destiny of mankind without noticing the contradiction that material civilization, especially scientific technique, lies in the atomic age, while spiritual civilization lies in the wild-animal age.

Therefore, the biologists and evolutionists who have popularized the erroneous Darwinian thought of the struggle for existence should feel no small responsibility for this matter.

Thus, we should realize that one of the most important mistakes those evolutionists have made is the exaggeration of the thought "the struggle for existence", and then that the idea "The strong prey upon the weak" can be applied only to the world of wild animals, not to mankind who is endowed with intelligence and wisdom.

Namely, we should realize that instead of the law of the struggle for existence, mankind has long lived on the basic principle of "symbiosis", "mutual aid", and the "A.F.D. process", keeping the harmony and balance of man and nature, man and man.

In fin de siecle, or in the end of the twentieth century, we are confronted with the three difficult problems to be solved.

The first is the problem of wars. We are still exposed to the danger of wars.

Whatever excuse may be made for it, a war is not only a crime but also a vice, evidently.

The aspect and scale of wars have so more changed in the present day than in the past that if by any chance a total war should happen, all mankind will be on the brink of ruin or destruction. Therefore, we should make every effort to avoid going to war, and then to renounce war.

Now, we should not act the folly of "Irish elk" that were all extinct in the past because they overgrew their own horns (weapon) in order to use for the struggle for existence.

The second is the problem of environmental pollution. This is the very problem that has been brought about by the development of industry. A war destroys our life directly and rapidly, while environmental pollution destroys our life indirectly and gradually.

The third is the problem of moral decadance. This results from the fact that one is descending to an economic animal that pursues only one's own profits without paying any attention to another man's profits or even to another man's life.

Thus, wars and various kinds of environmental pollution arise from this tendency of the preference of economy or matter to life or spirit.

Therefore, we should reform this attitude of the preference of economy immediately. If not so, mankind will be inevitably led into ruin or destruction from this moral aspect. Now, it is necessary that we should know the true rules of nature, and realize intelligent wisdom in order to get rid of these three dangers and then to make the world more peaceful and more prosperous.

- (B) Index of K.Chishima's Works: Articles, Monographs, and Essays on Criticism on Evolutionism
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- 1957: On the Contradiction of the Orthodox Genetics against True Evolutionism, Basis of Neo-Biology, vol.1, pp.379-416. Meibundo, Tokyo, in Japanese
  - : Relationships between Hereditary and Evolution, and K.Chishima's Theory-the Recapitulation of Protoplasmic Post Record or Protoplasmic Memory, ibid pp. 417-444.
  - Disputation on the Inheritance of Acquired Characters and its Relation with Evolutionism, ibid pp. 303-348.
- 1963: On the Spiral Tendency of Evolution, K.Chishima's Monograph "Revolution of Modern Medical & Biological Sciences, pp.5-59, Kobun-sha, Tokyo, in Japanese
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- 1971: World Peace: The way to establish one family of all mankind on the earth Its basic principle Bio Dialectic (Atarashiki Ningengaku; pub, by Chikyuikka Nippon Iinkai: pp. 201 227) (In Japanese)