2009
VOLUME 23
NUMBER 2

BIOGENIC AMINES

INTERNATIONAL JOURNAL OF STRESS AND NEUROPROTECTION

ISSN 0168-8561

Biogenic Amines Vol. 23, issue 2 (2009), pp. 53–74
BIA230209A01

Human Specific Intractable Immune Diseases – The Hypothesis and Case Presentation to Disclose the Causes and the Cures

Submitted: May 5, 2009 • *Accepted*: June 15, 2009

Katsunari NISHIHARA, DMSC, DMD

1. President of Japanese Association for Therapeutics of Immunediseases
2. President of NISHIHARA INSTITUTE, Hara Bldg. 3F, 6-2-5, Roppongi, Minato-ku, Tokyo, Japan.

Key Words: Intractable immune diseases; intracellular infection; deterioration and mutation of mitochondria; autoimmune diseases; opportunistic infection; non pathogenic common enteromicrobes; diagnosis ex-juvantibus

Summary.
Human specific intractable immune diseases are generally accepted as autoimmune diseases in modern medicine, i.e. self-and-not-self immunology, in which leukocytes are recognized mistakenly as not-self and revolt against their own cells with their MHC (HLA). The causes of these immune diseases have not yet been disclosed, even though they are commonplace in today's civilized life-style. The authors have confirmed from clinical research that cooling the gut by just 1° from 37°, intracellular infection of leukocytes occur via M-cells in Peyer's patch, which develop into granulocytes. Granulocytes contaminated with numerous bacteria circulate in the whole body disseminating bacteria into various organ cells resulting intracellular infection of these organs. The authors hypothesize that these intractable immune diseases are not autoimmune diseases but severe cases of formally accepted opportunistic infections, which are caused by intracellular infection of own common nonpathogenic enteromicrobes. Contaminated granulocytes from pus of periodontitis, sputa of lung diseases, or sedimentation of urine of nephritis, in which vivid numerous moving bacteria can be observed, are verified by highly magnified (×3000) light microscope. These intracellular infections deteriorate as well

as mutate mitochondria, and result in functional disturbances of specialized organ, which look like immune diseases. With this hypothesis, the authors developed therapeutic methods by means of preventing intracellular infection as well as activating mitochondria, and applied these curative methods for various patients having been diagnosed as immune diseases in authorized hospitals. With the successfully cured cases presented here, the hypotheses of the authors are verified as diagnosis ex-juvantibus.

This paper was presented at the 35th Annual Meeting of the Japan Society for Clinical Immunology held on the 19th Oct. 2007 in Osaka.

1. NONPATHOGENIC INTRACELLULAR INFECTIONS IN MODERN LIFE STYLE

Medical sciences have overcome contagious and infectious diseases with antiserums and vaccines, as well as infectious diseases by pathogenic microbes, including surgical infections, with antibiotics, and vaccines. However, we have not yet disclosed the unified systemic body mechanism as a multiorgan creature, the evolutionary mechanism of the vertebrates, the immune mechanism, nor the unified control system of 60 trillion cells. In this situation, human specific intractable immune diseases are increasing in developed countries only.

Human specific immune diseases are generally accepted as autoimmune diseases and recognized as maladies with intractable inflammation, granulation tissue or granuloma of unknown causes with functional disturbance without any established cure (Nishihara 2007b).

Self-and-not-self immunology has been established to solve the mechanism of immunotolerance by LeDouarin (Le Douarin 1982), which is very important for organ transplantation but not to treat immune diseases and infectious diseases.

In self-and-not-self immunology, intractable immune diseases are explained as follows: In the normal mammal immune system, no antibodies are generated by leukocytes against self-tissue cells. In some malady conditions, however, the normal immune system is disturbed, and diseased self-tissue cells with inflammation are recognized mistakenly as not-self by degenerated leukocytes and the leukocytes generate antibodies against their own malady inflammatory self tissue cells, by means of degeneration namely revolt leukocyte MHC (HLA). They call this as autoimmune disease.

However the author is skeptical about the above explanation. How can leukocytes discern self or not-self? Through extensive clinical examination of such cases, the author, a stomatologist, disclosed that the leukocytes of those patients were infected and contaminated intracellularly by entero-viruses, mycoplasma and entero-bacteria. They are non pathogenic common enteromicrobes from Waldeyer's lymphadenoid or GALT (gut associated lymphoid tissue), i.e. Peyer's patch, by mouth breathing or by cooling the gut by cold food. Thereafter, contaminated leukocytes disseminate them into various tissue or organ cells, resulting in intracellular infection by nonpathogenic enteromicrobes. The authors also detected deformed leukocytes contaminated by nonpathogenic enteromicrobes by TEM observation (Nishihara 2007a; Selye 1937a). The self-and-not-self immunologists seem to overlook such opportunistic intracellular infections.

Consequently, the authors have supposed that intractable immune diseases are not autoimmune diseases, but chronic opportunistic infections in the case of adult patients, or autotoxic diseases in the case of children, which became common about 40 years ago at the emergence of modern lifestyles and electric appliances.

These severely contaminated cells display no auto antigen as autoimmunity, but induce very weak antibody such as CRP, antinuclear antigen, anti-phospholipid antigen or IgE, and the healthy leukocytes attack these contaminated cells with MHA (HLA), which looks like healthy leukocytes attacking self-tissue or organ cells because of overlooking intracellular infection.

These intracellularly infected leukocytes and epithelial cells can be easily observed in pus of periodontitis or sputa of lung diseases by highly magnified (×3000) light microscope or TEM.

About 40 years ago not only opportunistic infections and autotoxic diseases in slight cases but also intractable granulomatous infectious diseases were often observed. The former symptoms were well known to closely resemble chronic colds and the latter corresponding diseases were sarcoidosis, histiocytosis, granulomatosis, and lymphoma (Nishihara 2007a; Nishihara 2007b).

The authors hypothesize that human-specific intractable immune diseases are severe cases of opportunistic infections or autotoxic diseases caused by intracellular infection of common nonpathogenic entero-bacteria and/or entero-viruses as a result of life-style changes. The authors also hypothesize that by intracellular infection of common entero-bacteria and/or entero-viruses mitochondrial deterioration and mutation in cytoplasma takes place. The authors verified the intracellular infections of common enterobacteria observing the

leukocytes as well as epithelial cells obtained from sedimentation of sputa of lung diseases or urine of nephrosis using highly magnified (×3000 monitor) light microscope or TEM. With this hypothesis and understanding, the author established the mitochondria activating therapeutic method to cure those diseases by means of prevention and recovery from intracellular infections in conjugation with nose breathing during sleep as well as warming the gut, recovering bone rest time by laying down, moderate eating and drinking with optimal mastication, treating periodontitis, optimal exposure to sunshine by sun bathing, and by administering suitable bifidus factors, effective anti-viral agents, as well as antibiotics. As, in most of the cases, the patients who had been diagnosed with intractable immune diseases in authorized hospitals showed evident recovery by these curative methods. By the complete cures of intractable immune diseases, their hypothesis is verified as diagnosis ex-juvantibus, i.e., diagnosis based on the results of treatment.

2. CRITICAL ROLE OF MITOCHONDRIA IN OUR BODY

The life of higher animals has both acceptors of energy, i.e. gravity, atmospheric pressure, temperature, light and sound waves, and acceptors of substance with mass, e.g. nutrients and oxygen. The former are sensory organs and the latter are visceral intestinal organs. All stimuli affecting the creature, e.g. physico-chemical, nutrition, toxins, bacteria, parasites, and psychological stresses, are transmitted through the thalamus into the hypothalamus by means of the neuromuscular as well as the cardiovascular system. These stimuli are transmitted to the frontal lobe of the hypophysis. They are then converted into hormones cytokine, and growth factor, which are the direct control system of intracellular respiration of mitochondria in 60 trillion cells. This is the hypophysis-systemic hormone system. Representative of these hormones are adrenocorticotropic hormones which control the secretion of minerals and glycol-corticotropic hormones.

All cells in creatures having 800–3000 mitochondria are directly controlled with hormones, cytokines, and growth factors. Mitochondria supply energy substances for metabolism, development, growth, remodeling, and proliferation. All specific functions of specially differentiated cells are carried out by their mitochondria (Lehninger 1964). Without mitochondria no cells except erythrocytes in vertebrates can live. Common entero-bacteria, mycoplasma and viruses without pathogenicity are easily parasitic in various organ cells intracellularly in some conditions, which bring about the deterioration and mutation of mitochondria and their functional disturbances (Nishihara 2008a; Nishihara 2008b).

3. CASE STUDY WITH THE PRESCRIPTION OF MITOCHONDRIA ACTIVATING METHODS (MAM)

Case reports are presented of the following 28 patients (see photos on the following pages) who have been diagnosed as autoimmune diseases in authorized hospital and have been completely treated and cured by the author's **Mitochondria Activating Methods** (**MAM**). It should be particularly remarked that no case was treated with steroid hormones during author's MAM.

For these methods, five kinds of devices for best breathing were prescribed;

1) Best-breathing exercise to correct and rectify trilateral biomechanical habitual behavior namely mouth breathing, unilateral mastication, and poor sleeping posture as well as short sleeping;
2) Energy control by avoiding cold drinks and food and not cooling the skin;
3) Normalizing the gut with bifidus factors;
4) Activating mitochondria with nutrition;
5) Administering of antibiotics or anti-viral agents for intracellular infection.

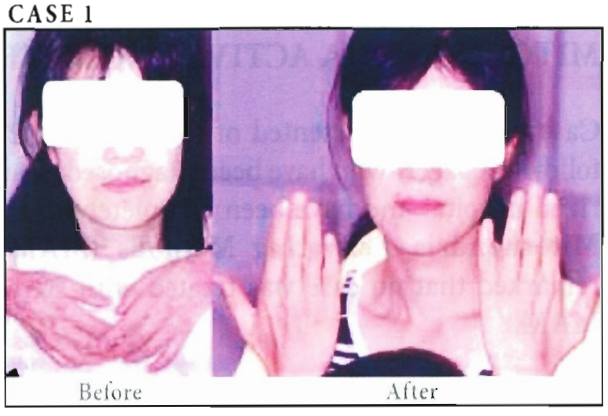
4. DISCUSSIONS

The authors have successfully developed hybrid-type artificial bone marrow chambers as well as artificial dental roots by applying biomechanical stimuli to sintered hydroxyapatite and won the Original Prize Award of in the 32nd annual congress of the Japanese Association for Artificial Organs in 1994. Using them, the authors have clarified that evolution occurs according to the biomechanical functions of the animal in response to gravitational forces. They have also developed an experimental evolutionary study method that applies trilateral research, integrating morphology, molecular biology and molecular genetics, with biomechanics. From these studies the authors verified Lamarck's Use and Disuse Theory. Following that, they carried out research on the basic construction of Mammalia from the viewpoint of the Gravity Evolutionary Theory. Thereafter, they disclosed the riddles of development of bone marrow hemopoiesis as well as the immune system and published several papers concerning them (Nishihara & Tanaka 1996; Nishihara 1997; Nishihara 1999; Nishihara 2000; Nishihara 2001; Nishihara 2003a; Major & Delp 1956; Nishihara 2003b). The life of higher animals has both acceptors of energy, and acceptors of substance with mass, e.g., nutrients and oxygen.

CASES PRESENTATION

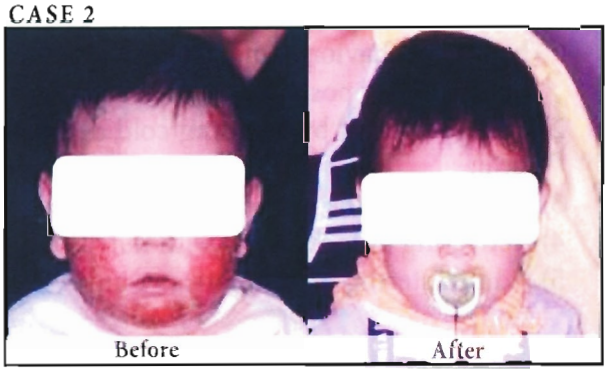
CASE(1) 38-year-old mother with ulcerative colitis concomitant with glaucoma and atopic dermatitis, has been cured by MAM with bifidus factors conjugated with a vaginal douche.

CASE 1



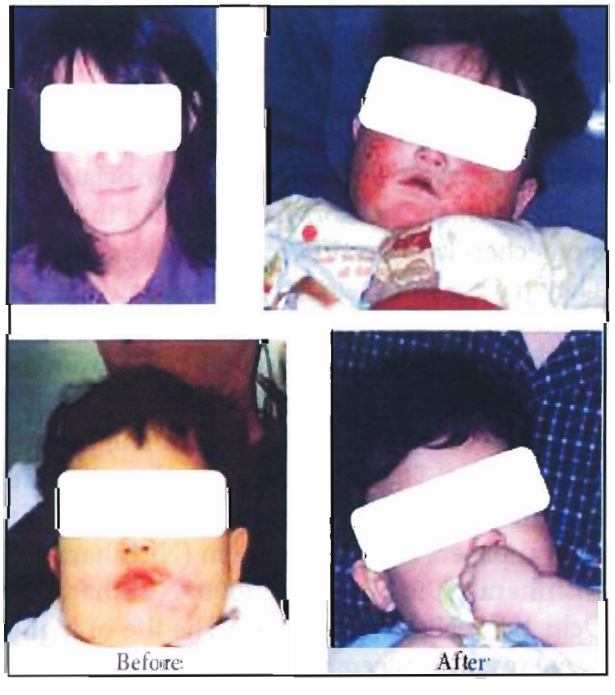
CASE(2) Her son, an 8-month-old infant with atopic dermatitis caused by contaminated mother's breast milk, has been cured by means of the complete treatment of his mother's immune disease.

CASE 2

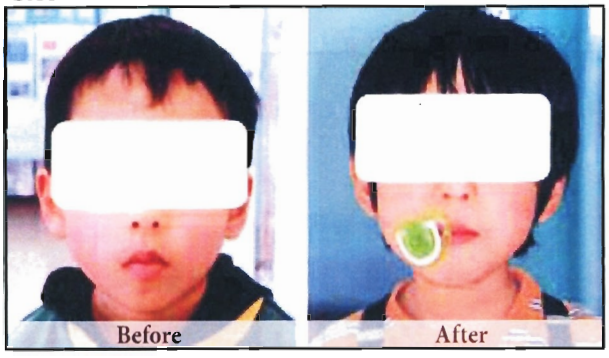


CASE(3) Atopic dermatitis caused by mother's breast milk who has severe atopic dermatitis, has been cured by 42°C powdered milk (right side, under). When milk is under 37°C, eczema around the mouth occurs (left side, under).

CASE 3

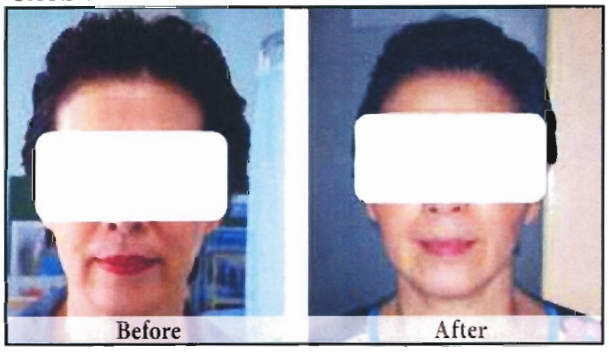


CASE 4



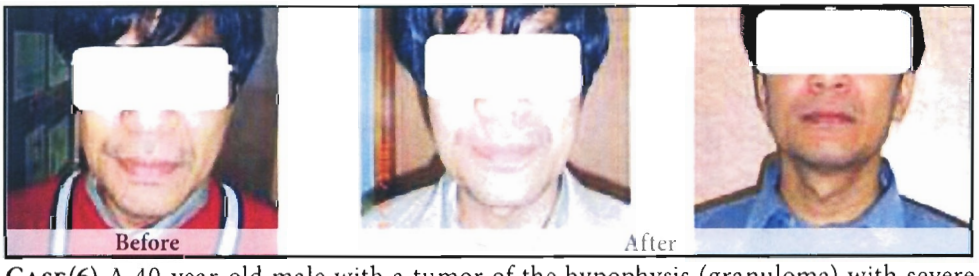
Case(4) 5-year-old boy with epilepsy of which a probable cause was too early feeding of raw shrimp, has been completely cured by MAM with a pacifier.

CASE 5



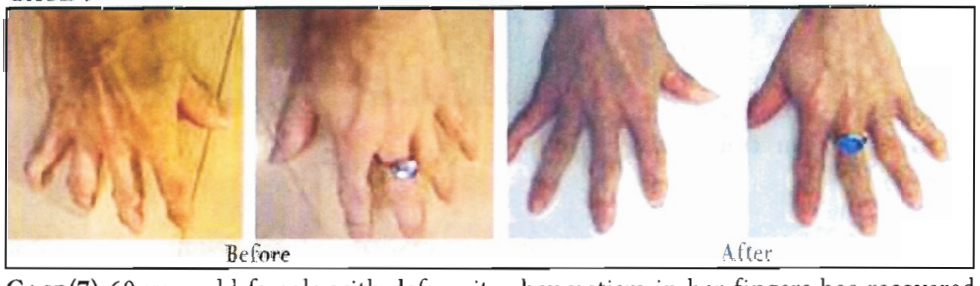
Case(5) 55-year-old female with a tumor of the suprarenal gland (granuloma) concomitant with pustulosis. Palmaris et plantaris has been completely for 3 years cured by MAM with bifidus factor

CASE 6



Case(6) A 40-year-old male with a tumor of the hypophysis (granuloma) with severe headache has been cured completely and disappeared by x-ray CT scan by MAM with bifidus factor and antibiotics for 6 months.

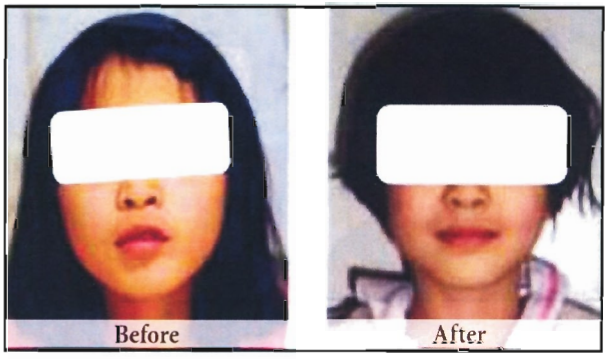
CASE 7



Case(7) 60-year-old female with deformity rheumatism in her fingers has recovered markedly by MAM with bifidus factors.

CASE(8) Eight years old girl, who has been in university hospital to tread acute nephritis. As she did not want to have steroid puls therapy, visited us with hematourine. In urine sedimentation leukocytes with vivid moving bacteria were observed case(8), lower. After several day's treatment with bifidus factor and antibiotics, leukocytes with vivid bacteria diminished in urine sedimentation. After that she recovered by MAM.

CASE 8



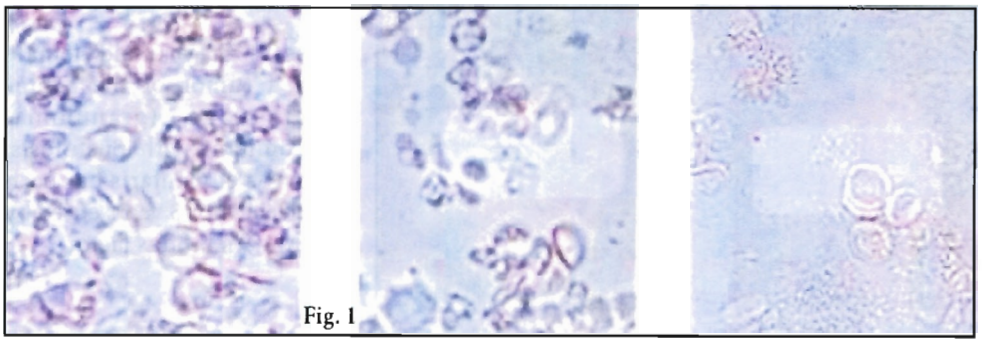
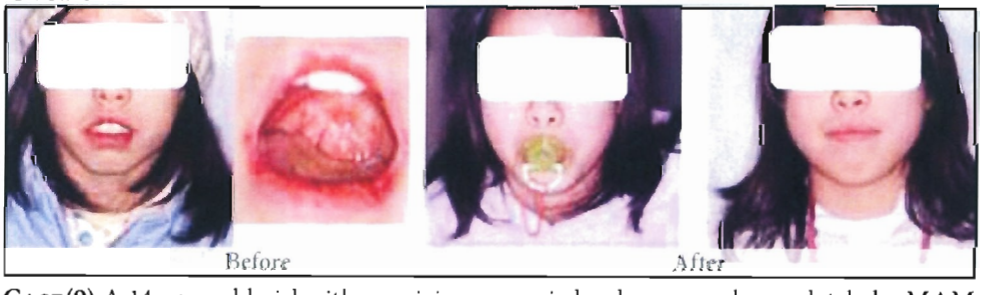


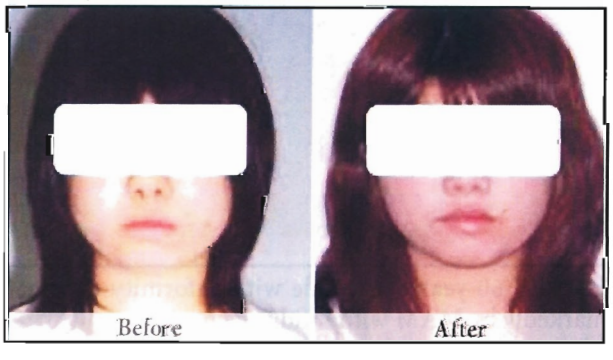
Fig. 1

CASE 9



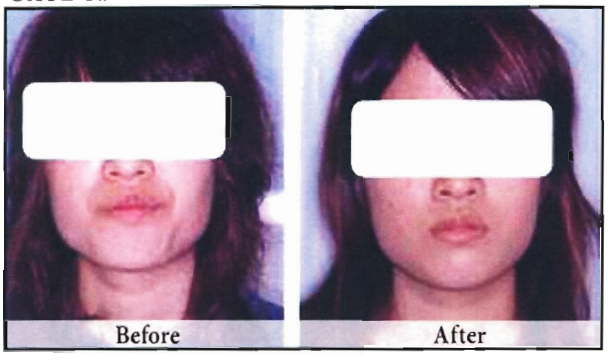
CASE(9) A 14-year-old girl with pernicious anemia has been cured completely by MAM with pacifier.

CASE 10



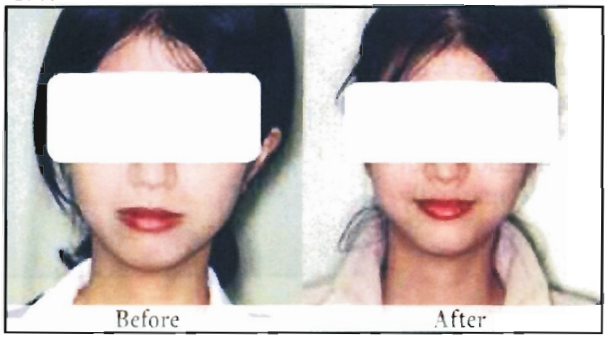
CASE(10) 15-year-old girl with uveitis has been completely cured by MAM;

CASE 11



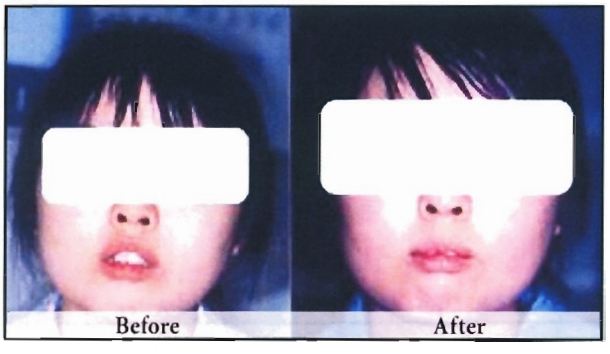
Case(11) 17-year-old girl with nephrosis (IgA nephrosis) has been completely cured by MAM.

CASE 12



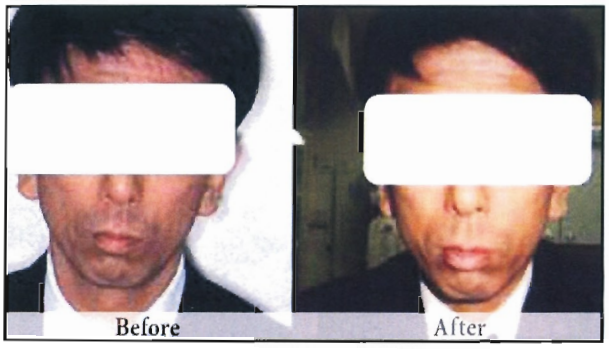
Case(12) and **Case(13)** 18-year-old girl as well as 26-year-old woman with a child, suffering from ulcerative colitis have been completely cured by MAM with bifidus factor.

CASE 13



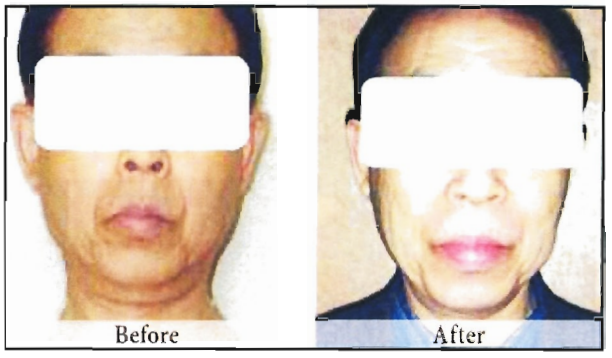
Case(12) and **Case(13)** 18-year-old girl as well as 26-year-old woman with a child, suffering from ulcerative colitis have been completely cured by MAM with bifidus factor.

CASE 14

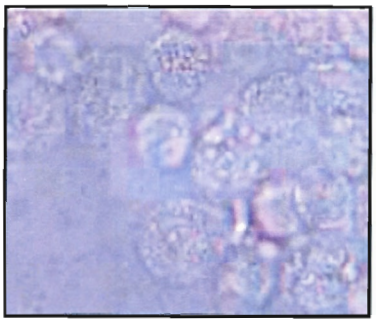


Case(14) Retinopathy, 43-year-old patient with atopic dermatitis, who had become blind 13 years ago has been cured and his sight recovered by means of MAM. He had played American football and rugby with severe atopic dermatitis and mouth breathing. His retina was contaminated by enterobacteria and retinitis, resembling atopic dermatitis in subcutaneous tissue.

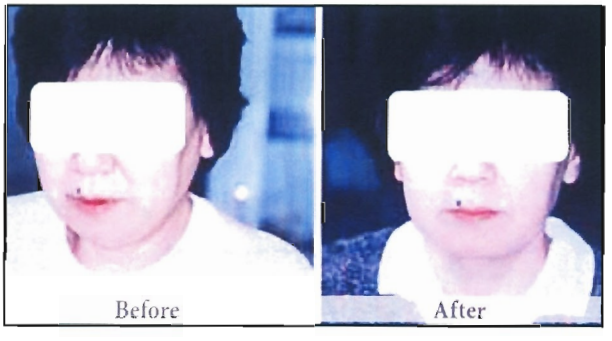
CASE 15



Case(15) 68-year-old male suffering from hypertension, cardiac hypertrophy and angina pectoris with severe periodontitis, who denied to accept operation of stent insertion into his coronal arteries. Arrythmia was so severe that local anesthesia with adrenalin could not be used. Heart and periodontitis were treated by prescription of bifidus factors, antibiotics and antiviral agents. Severe arrythmia was recovered by MAM and local anesthesia could be used for periodontal treatment. Leukocytes with vivid moving bacteria in pus from periodontal pockets were observed **(Case 15 lower)**. After complete treatment of periodontitis by operation with local anesthesia, cardiac diseases have markedly recovered.

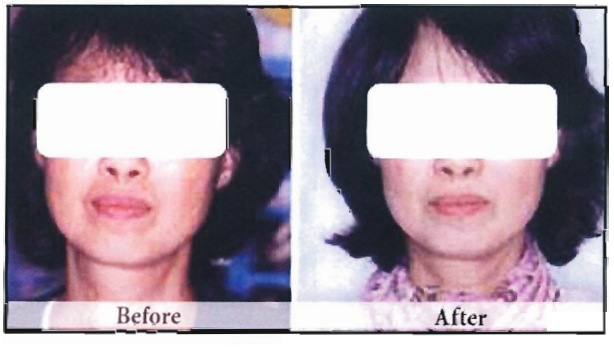


CASE 16



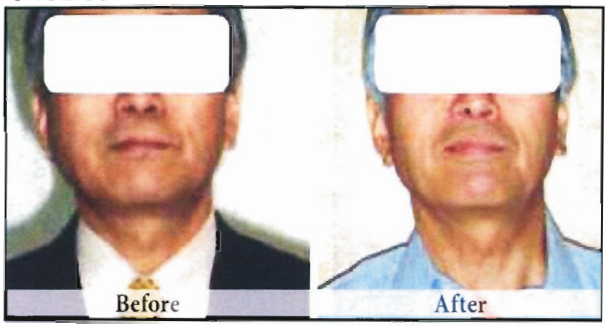
Case(16) 56-year-old female with fibromyalgia with half of her sight lost, and who was unable to walk, recovered her walking ability. The disease progress was stopped by MAM.

CASE 17



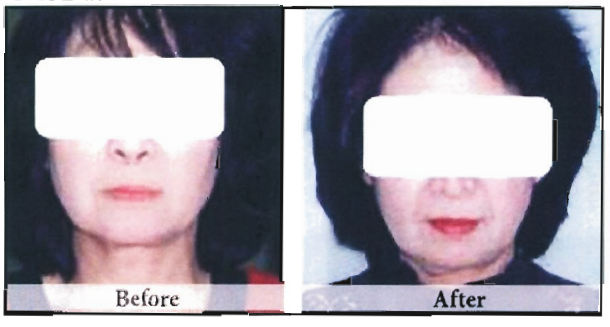
Case(17) 51-year-old female with spinal cerebellar degeneration has been markedly recovered by MAM.

CASE 18



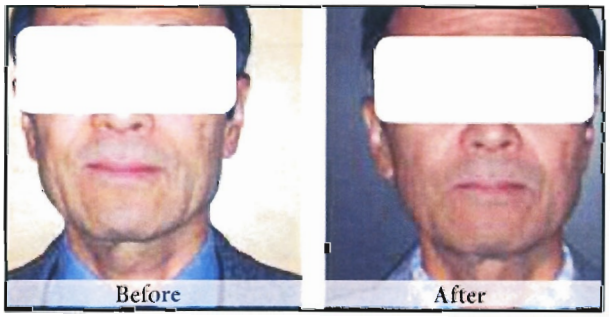
Case(18) 58-year-old male suffering from dysacousis and otitis media, who could not be cured by otologist, has recovered completely by MAM.

CASE 19



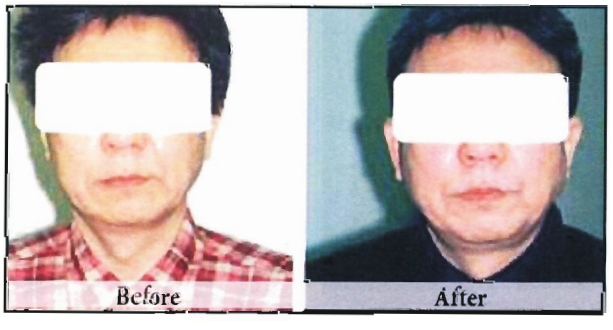
Case(19) 58-year-old female musician, who badly suffered from arthritis and bronchitic asthma since 24 years of age, has recovered completely by MAM.

CASE 20



Case(20) 66-year-old male with myasthenia and polymyositis, who could not stand up and walk, has improved completely by MAM.

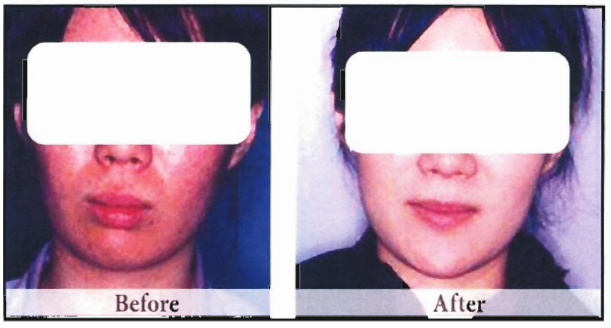
CASE 21



Case(21) 56-year-old male with interstitial pneumonitis and severe bronchitis, who was unable to work two weeks per month, has recovered completely by MAM.

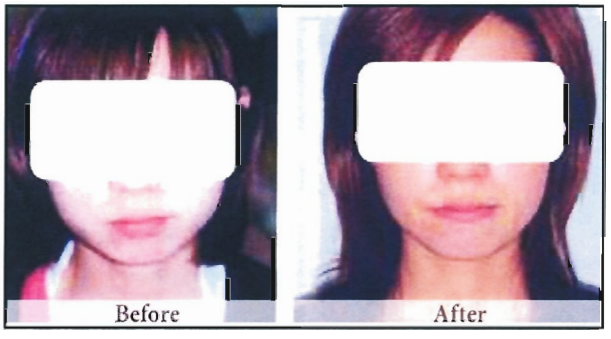
CASE 22

Case(22) 18-year-old female with atopic dermatitis has recovered completely by MAM with bifidus factor.



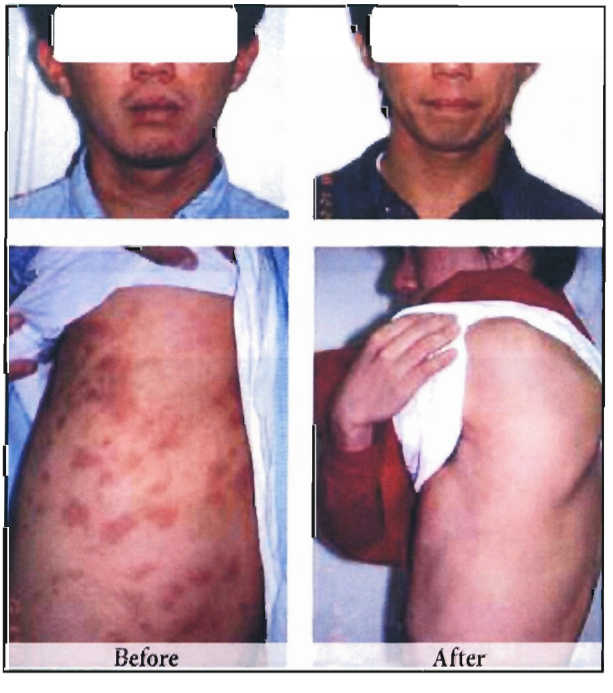
CASE 23

Case(23) 20-year-old female with dermatitis and chronic fatigue with high-level antinuclear antibodies, has recovered completely by MAM with bifidus factor.

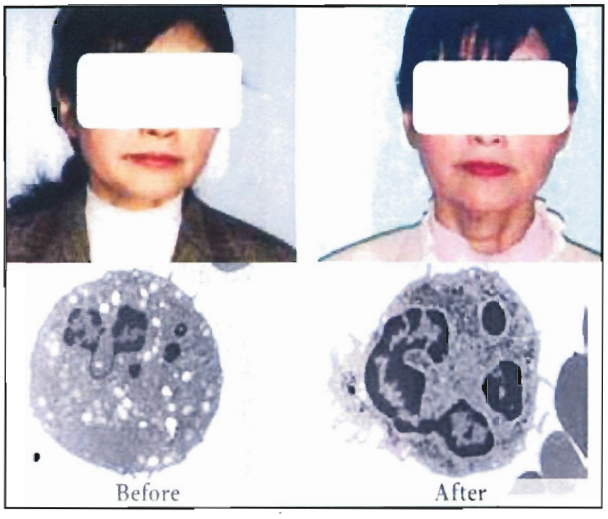


CASE 24

Case(24) 20-year-old male with, severe dermatitis and tonsillitis caused by a cytomegalovirus infection has recovered completely by MAM.

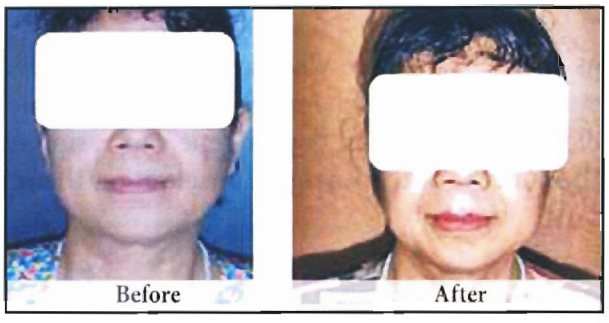


CASE 25



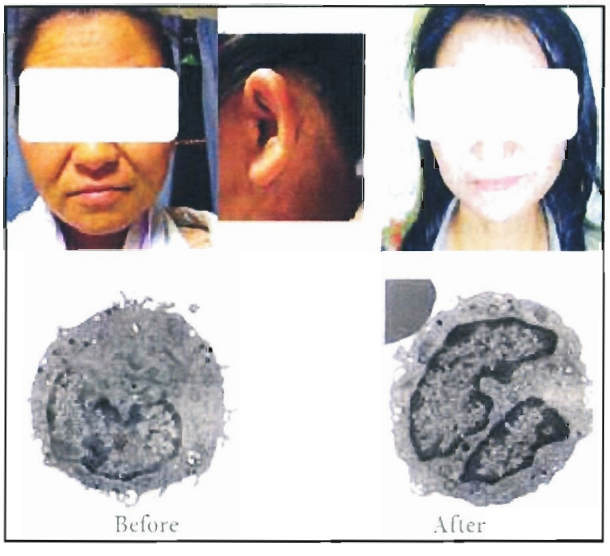
Case(25) 63-year-old female with C-type hepatitis having leukocytes with vacuole mitochondria by TEM has recovered completely by MAM with bifidus factor.

CASE 26



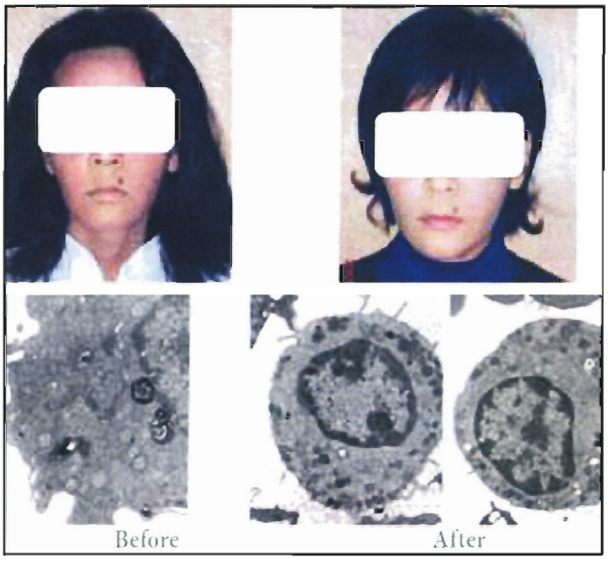
Case(26) 64-year-old female with mydriasis has recovered completely by MAM with bifidus factor.

CASE 27



Case(27) 28-year-old female with atopic dermatitis has recovered after 3 months treatment of MAM with bifidus as well as with a virginal douche and antibiotics administration.

CASE 28



Case(28) 35-year-old female with severe atopic dermatitis concomitant with extrapyramidal tract syndrome has recovered by MAM with bifidus factor and antiviral agents.

The former are sensory organs and the latter are visceral intestinal organs. All stimuli affecting the creature, e.g., physicochemical, nutrition, toxins, bacteria, parasites, and psychological stresses, can trigger gene expression in mitochondria or nuclei from the concept of the Energy Conservation theory (Caneva 1993).

1) Mechanism of intracellular infections:

Viral diseases occur essentially intracellular infection.
However bacterial infection occur extra, inter- or intracellularly.

Since humans first started cooking approximately one million years ago, the inside of our mouth has been excellent culture medium for enterobacteria, because of nutrient debris of cooked food. And in our gut, there exist tremendous aerobic as well as anaerobic enterobacteria and enterovirus. It is those bacteria and virus that are absorbed through Waldeyer's lympho-adenoid tissue cooled by mouth breathing as well as through GALT cooled by cold drinks and ice cream.

The intracellular infections are verified by microscopic observation of leukocytes in pus from periodontitis or epithelial cells obtained from sedimentation of sputa of lung diseases, or urine of nephrosis, (Case8, 11, 15). Contaminated and normal breast milk were microscopically observed and compared. (***Fig. 1***). Leukocytes with vivid moving bacteria in pus from dental apical cyst are observed (***Fig. 2***), which resembles contaminated leukocytes in urine or pus out of periodontal pockets.

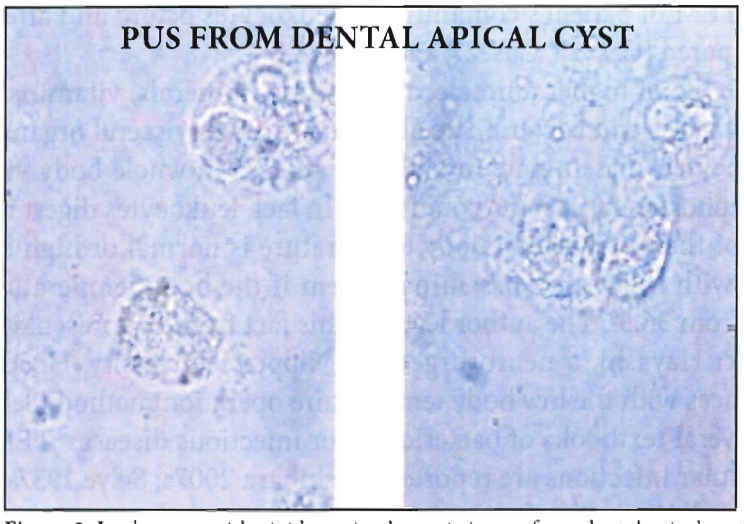


Figure 2. Leukocytes with vivid moving bacteria in pus from dental apical cyst resemble contaminated leukocytes in urine or pus from periodontal pockets.

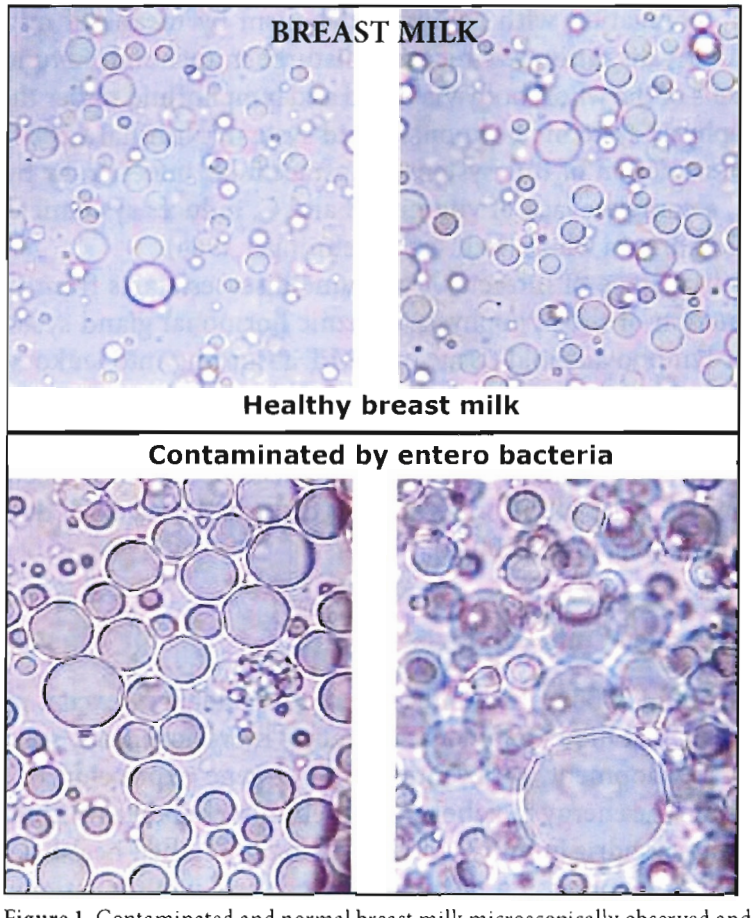


Figure 1. Contaminated and normal breast milk microscopically observed and compared (healthy breast milk above, contaminated breast milk below).

The TEM of patient's contaminated leukocytes before and after treatment are compared (Case25, Case27, and Case28).

In the life of higher animals, all nutrition, minerals, vitamins, oxygen, as well as viruses and bacteria, are absorbed through visceral organs into blood or leukocytes, disseminate into almost all cells in whole body via the blood and lymphostream in some conditions. In fact, leukocytes digest bacteria and get rid of them only when body temperature is normal or high enough, but coexist with them and disseminate them if the body temperature falls one degree from 36.5°. The author learned this fact from the presentation of Prof. Nariyuki Hayashi, a neurosurgeon at Nippon University. Hospital, on his experiences with the low body temperature operation method (Selye 1937b).

In several textbooks of bacteriology or infectious diseases ,TEM photos of intracellular infections are reported (Nishihara 2007a; Selye 1937a).

Multicellular animals live under sunlight and the gravitational energy of the earth and the moon, and incorporate substances with mass via the gut. Using both energy and substances with mass, creatures remodel themselves in conjugation with energy metabolism by means of mitochondria. Intracellularly disseminated microbes disturbe mitochondrial functions in 60 trillion cells of the whole body via blood and lymphofluid under the control of the hypophysis-systemic hormonal gland system (Nishihara 2004; Nishihara 2005). Dysfunction of this system by intracellular infection or by malnutrition, e.g., a complete lack of vitamins B and C, induces systemic dysfunction of mitochondria in whole body cells (Lehninger 1964).

The initial stage of intractable immune diseases starts from intracellular contamination of the hypophysis-systemic hormonal gland system through Waldeyer lympho adenoid tissue or GALT absorbing into leukocytes enterobacteria or viruses by cooling the gut. After that, dysfunction in secreting the adrenocrticotropic hormone could take place, and intra-cellular infection over all cells in whole body may occur. If intracellular infection occurs in some organs, the function of the organ's cells is disturbed because of dysfunction of mitochondria (Nishihara 2004a).

2) Essential role of mitochondria

There are 800 ~ 3000 mitochondria in an individual cell except erythrocytes in mammals. All life phenomena, including morphogenesis, specialized cell function, development, differentiation, and gene expression of completely depend upon the energy metabolism of their mitochondria. Without vivid and healthy mitochondria humans could never maintain their health. Complexion, color, looks and expression of the face, vigor and vitality, fatigue, tiredness,

and exhaustion, all of these body states indicate mitochondrial conditions and possible intracellular infection (Nishihara et al. 1994).

Therefore it is natural that our important organs loose their functions and sometimes cause fatal failures, when their mitochondria are deteriorated by intracellular infection of common enteromicrobes: heart attack is a dysfunction of mitochondria in cardiac muscle cells, dementia is a dysfunction of mitochondria in neurons in the cortex of the cerebrum (Nishihara 2008a; Nishihara 2008b), and nephritis is a bacterial infection resulting in a dysfunction of mitochondria in the glomerulus cells and mesangium cells.

Characteristic functions of the specially differentiated cells are carried out through their specific activties of mitochondria (Lehninger 1964). E.g., in neurons, metabolism of monoamine, a neurotransmitter is carried out in mitochondria. As well, mitochondria in cortext cells in epinephron synthesize mineral and glycocorticosteroid hormones (Lehninger 1964).

About 40 years ago, the author carried out experiments to disclose major causes of mitochondrial mutation using yeast, administering several kinds of antibiotics, which disturbed protein synthesis (Nishihara 2004a). Results revealed that only in disturbance of cytoplasmic protein synthesis with cycloheximid, i.e. antibiotics for eukaryote, mitochondrial mutation took place, but that in case of disturbance of mitochondrial protein synthesis mitochondria stopped respiration without any mutation. Therefore it is reasonable that mitochondrial mutation occurs, when intracellular infection by numerous microbes disturbs cytoplasmic protein synthesis.

3) Energy metabolism and the function of mitochondria

In the life sciences of today, especially in molecular biology and the study of the phenomena of life, energy is completely overlooked, while in organisms, gene expression can be triggered by energy just like a catalyst in a chemical reaction (Caneva 1993).

Immune diseases are due to a hindrance of cellular renewal or remodeling which is carried out concomitant with the energy metabolism of mitochondria. The causes of most immune diseases are a deterioration of the mitochondrial function by various energies as well as intracellular infections by enormous bacteria or viruses, i.e. parasites (Lehninger 1964; Nishihara 2004a). At the cellular level, all immune disease are induced by the deterioration of mitochondrial function.

The causes of mitochondrial functional disturbances are categorized by the following five items: 1) inadequate energy, 2) malnutrition, 3) toxins, 4) infections by pathogenic microbes, and 5) intracellular infection by common enteromicrobes.

From the view point of cellular energy metabolism, humans have the following improper habitual behaviors: 1) breathing through the mouth, 2) cooling the gut with cold drinks and foods, 3) workaholism without sufficient bone rest, 4) infant feeding of solid foods containing protein instead of breast feeding, 5) lack of natural solar light in rooms, and 6) excessive drinking and eating with poor oral hygiene or with movable teeth caused by periodontal disease.

In particular, mouth breathing and cooling the gut induce intracellular infection over whole body cells. As a result of low body temperature as well as a lack of bone rest, the mitochondria of hemopoietic cells loose their vitality. Breathing through the mouth as well as cooling the gut allow leukocytes infected with parasitic entero-bacteria, which are disseminated into various organ cells (Nishihara 2003a; Major & Delp 1956; Nishihara 2003b; Tache 1989). Thereafter, intracellular infection takes place, and, as a consequence, the metabolism of mitochondria in various organ cells is disturbed and their functions deteriorate.

4) Intracellular infection of the specially diffentiated cells

In the human body, there are various cells in several different evolutionary stages. Leukocytes correspond to the stage of protozoa, and, therefore, they can penetrate through small pit holes of blood or lymphovessels with amoeboid movement. More significantly they can invade even into cerebral liquor and a fetus through placenta. Thus the infected leukocyte gives rise to further intracellular infection of organ cells or tissue cells by non-pathogenic enteroviruses or -bacteria, and mycoplasma.

In the central nervous system the major nutritional circulatory system is lympho-fluid and there exists a blood brain barrier. However, this barrier can only restrict erythrocytes, and cannot exclude leukocytes. Contaminated leukocytes with enterobacteria in Waldeyer's ring move in cervical lymphovessel to lymphnode easily, then enter to brain through arteria carotis interna, and penetrate into cerebral liquor through amoeboid movement passing blood vessel into tissue fluid.

Then contaminated bacteria are disseminated in neurons of cellebrum as well as of the limbic system, thus cerebritis easily take place. Migraines or depression, hallucinations and senility also take place. These systemic immune diseases are induced by aerobic or anaerobic intracellular parasitic microbials, which are disseminated by leukocytes. These aerobic microbials consume oxygen in specialized functioning cells of organs and the anaerobics consume intracellular nutrition, causing the mitochondria to lose their specially differentiated functions.

It is expected that through mitochondrial activation intracellularly infected bacteria or viruses may be digested.

5) Symptoms of so-called auto immune diseases is that of intracellular infection of common enteromicrobes

The author disclosed so-called 'autoimmune diseases' cases to be the intracellular infection (I.I.) in specific cells and organs resulting functional deterioration of mitochondria as follows:

Glaucoma is a symptom of I.I. in ciliary cells. Mydriasis occurs by I.I. of the pupil. Exceeding bleeding after delivery occurs by I.I. of bone marrow hemopoietic nests, resulting disturbance of synthesis of the XII blood coagulation factor. Atopic dermatitis takes place by I.I. of enterobacteria or viruses in subcutaneous tissue cells. Tumors of suprarenal glands and hypophysis are symptoms of granuloma of I.I. of respective gland cells. Chronic fatigues with antinuclear antibodies are caused by tremendous I.I. by enterobacteria in whole body cells. Following that, mitochondria in whole cells deteriorate.

Amyotrophic lateral sclerosis and spiral cerebella degeneration are a symptom of I.I. of spinal cord and cerebral or cerebella neurons concomitant with skeletal muscle cells. Epilepsy is caused by I.I. in neurons in the neocortex by enteromicrobes. Neurons and muscles develop concomitantly, and notably neurons develop for muscles. Therefore, if some involuntary movement or convulsion occurs, disorder of cerebral neurons namelyI.I. inevitably takes place.

Depression occurs by I.I. of neurons in visceral brain namely the limbic system, which control visceral smooth muscles. Ulcerative colitis and Chron's disease take place by I.I. of endodermal epithelial cells as well as subepithelial mesenchymal cells with enteromicrobes of the throat or intestines through contaminated leukocytes. Asthma and bronchitis as well as interstitial pneumonia take place by I.I. of epithelial and subepithelial cells in pharynx, bronx, and lungs. Deformity rheumatism is a symptom of I.I. with viruses of cartilage cells in synovial joint. Diabetes mellitus and pancreatitis take place by I.I. of Langerhans islet's cells or pancreas gland cells.

Viral infections such as cytomegalovirus, C-type hepatitis can be cured by administration bifidus factors or antiviral agents, and can be detected by TEM of leukocytes at the same time.

Myasthenia gravis takes place due to severe I.I. of thymus via tonsillitis by mouth breathing through contaminated leukocytes. Often dermatitis occurs concomitantly by same enteromicrobes of thymus infection through contaminated leukocytes, which disseminate into skeletal muscle cells as well as subcutaneous tissue cells inducing severe I.I. of these cells.

6) Selye's general adaptation syndrome

Circa 40 years ago, these slight immune maladies were called opportunistic infections or autotoxic diseases. Afterwards, these infectious diseases disappeared and severe intractable immune diseases appeared instead. The causes of these immune diseases are unknown, but accepted to be non-infectious allergic reactions or inflammations induced by stresses (energy). However, without infection no disease occurs. In any kind of diseases there are inevitable infections of microbes, of even nonpathogenic or common enteromicrobes just like opportunistic infections. Self-and-not-self immunologists have overlooked these intracellular infections of common non-pathogenic entero microbes.

Selye's theory, proposed in 1936, stated that mammalians have reactions to the secretion of not only adrenalin from the suprarenal glands medulla, but also adrenocortico hormone from the hypophysis–suprarenal glands hormonal system, to prevent any disorder of the organism under adverse stimuli, physical, mental or emotional, internal or external, such as bacterial infection, fatigue, starvation, cold, blows, noise, chemical and pharmacological agents, impressions, and restlessness which tend to disturb homeostasis (Nishihara 2004; Nishihara 2005). If these compensating reactions are inadequate or inappropriate, they may lead to maladies. Selye called these adverse stimuli "stressors", and proposed the concept of Selye's syndrome, namely the general adaptation syndrome.

He stated that the general adaptation syndrome is the sum of all non-specific, systemic reactions of the body, which occur after long, continued exposure to stress. The alarm reaction is sum of all non-specific systemic phenomena elicited by sudden exposure to stimuli to which the organism is quantitatively or qualitatively not adapted. Selye discovered that humans fall ill not only by bacterial infection or inappropriate nutrition, fatigue or starvation, but also by energy, such as cold or noise.

He proposed that inflammatous maladies induced by stress or allergy can be treated by corticosteroid hormones. However he prohibited to administer steroid hormones to infectious inflammations by bacteria or viruses, because the target organelles of corticosteroid hormones are mitochondria (Lehninger 1964). They promote oxidative phosphorylation of mitochondria to generate energy substance of ATP, but are almost not effective for infection of microbes but promote inflammatious reaction. Therefore, steroid hormone therapeutics is contraindication for infectious inflammation. Selye's stress theory is just half the story because of his overlooking intracellular infection of the cells in the organism. As immune diseases take place by intracellular infection of

common enteromicrobes, administration of steroid hormones is a contra-indication.

7) Real truth behind the 'revolting' story

Against common entero bacteria, our body never yields effective antibodies. However severely intracellularly contaminated cells are just like chimera cell of cytoplasmic nucleus with tremendous numbers of bacterial nucleic acids. These bacteria absorbed in cells have their own DNA, and they stimulate and transform cell membrane structure, which may eventually display nucleic acid antigen on its surface. It is against these chimera nucleic acid antigens that leukocytes yield very weak antibodies such as the anti-nuclear antibody, anti-phospholipid antibody, anti-cardiolipin antibody, CRP (c-reactive protein), IgE, etc. As these antibodies are targeted and designed against chimera nucleic acid antigen on the surface of cell membranes, they cannot destroy cells. Therefore, they attack against cell membranes in vain and bring about no curative effect for intracellular-infection by numerous common entero-bacteria and viruses. Only through mitochondrial activation intracellularly infected bacteria or virus are digested.

Observing these fruitless attacks, the "self-and-not-self" immunologists and those who are unaware of intracellular infection by bacteria or viruses may claim that leukocytes are revolting and attacking against their own healthy cells. But the life phenomena are purely electric reactions in water-soluble colloid, therefore it should be very simple and there is no place to speak of revolt or rebellion.

CONCLUSION

In conclusion, the authors have disclosed that the causes of human-specific intractable immune diseases are the result of mitochondrial deterioration or mutation due to intracellular infection of tremendous numbers of common enteromicrobes. With this understanding, the authors have developed the therapeutics of mitochondria activating methods to prevent and to cure intractable immune diseases by means of recovering intracellular infections.

REFERENCES

1 Caneva KL (1993). Robert Mayer and the Conservation of Energy. Princeton Univ. Press
2 Le Douarin N (1982). The Neural Crest. Cambridge Univ. Press.
3 Lehninger L (1964). The Miochondrion. Benjamin Inc, New York. pp. 56-104.
4 Nishihara K et al (1994). Development of hybrid type artificial bone marrow using sintered hydroxyaptite. *Bio-Medical Materials and Engineering* **4**(1): 61-65,
5 Nishihara K, Tanaka J (1996). Successful inducement of hybrid type artificial bone marrow using bioceramics in various vertebrates. *Bioceramics*. **9:** 69-72.
6 Nishihara K (1997). Development of hybrid-type artificial immune organ by means of experimental evolutionary research method using bioceramics. Tissue Engineering for Therapeutic Use 1. Amsterdam: Ikeda Y and Yamaoka Y (eds). pp. 39-50.
7 Nishihara K (1999). Evidence of biomechanics-evolutionary theory by using bioceramics, Bioceramics, Vol. 12. Ohgushi H, Hastings GW (editors). pp. 253-256.
8 Nishihara K (2000). Evidence-Based Evolutionary Research and Development of the Practical Phylogenetics: Verification of the Gravity-corresponding Evolutionary Law by Means of Biomaterials. Faenza, Italy. Ceramics, Cells and Tissues. pp. 167-172.
9 Nishihara K (2001). Verification of the Gravity Action in the Development of Bone Marrow Hemopoiesis During Terrestrialization. Ceramics, Cells and Tissues. pp. 277-288.
10 Nishihara K (2003a). Differentiation into Hemopoietic Cells from Mesenchymal Cells in Porous Ceramic Bone Marrow Chamber Surface in Vivo by Means of Hydrodynamics, Ceramics, Cells and Tissues, Faenza, Italy. pp. 157-162.
11 Major RH and Delp MH (1956). Physical Diagnosis. WB Saunders.
12 Nishihara K (2003b). Verification of use and disuse theory of Lamarck in vertebrates using biomaterials, *Biogenic Amines* **18**(1): 1-17.
13 Nishihara K (2004a). Research on the evolution and development of autonomic nervous system. *Biogenic Amines* **18**(2): 95-106.
14 Nishihara K (2004). Establishment of a new concept of the immune system, disclosure of causes, and development of the therapeutic system of immune diseases. *Biogenic Amines* **18**(2): 79-93.
15 Nishihara K (2005). Trilateral research on neural system and biogenic amines: Disclosure of the major causes and mechanisms of human characteristic neurocerebromuscular (psychosomatic) disorders. *Biogenic Amines* **19**(3): 197-208.
16 Nishihara K (2006). Disclosure of Mechanisms of the Mammalian Life System and Selye's Stress Theory, *Biogenic Amines* **20**(5-6):171-184.
17 Nishihara K (2007a). Disclosure of causes of human-specific intractable immune diseases – Mitochondrial deterioration due to intracellular infections. *Biogenic Amines* **21**(1-2):23-41.
18 Nishihara K (2007b). Disclosure of causes of human-specific intractable immune diseases by means of bio-energy resonance. Detection of mitochondrial deterioration due to intracellular infections using Bi-Digital O-ring Test, Faenza, Italy, 2007.
19 Nishihara K (2008a). Development of Therapeutics for Human-specific Intractable Immune Diseases by Means of Bio-energy Resonance - Remedy of Mitochondrial Deterioration Due to Intracellular Infections Using Bi-Digital O-Ring Test. *Biogenic Amines* **22**(1-2): 75-84.
20 Nishihara K (2008b). Disclosure of Major Causes of Mitochondrial Mutation by means of Molecular Biology Part1. *Biogenic Amines* **22**(4-5): 99-114.
21 Selye H (1937a). Studies on adaptation. *Endocrinology*. **21**(2): 169-188.
22 Selye H (1937b). The significance of the adrenals for adaptation. *Science* **85**: 247–248.
23 Tache Y, Morley JE, Brown MR (Eds) (1989). Neuropeptides and Stress. Springer Verlag, New York.

http://node.nel.edu