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An Approach to the Nature of Qi in TCM–Qi and Bioenergy

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1. Introduction

Traditional Chinese medicine (TCM), has been practiced for more than five thousand years, is a complete ancient medical system that takes a deep understanding of the laws and patterns of nature and applies them to the human body. TCM believes that the human body is a microcosm of the Universal macrocosm. Therefore, humans must follow the laws of the Universe to achieve harmony and total health. Even today TCM practitioners use these essential theories to understand, diagnose and treat health problems. In TCM, "harmony" is the ultimate goal. So, when nature's Qi undergoes change as it does seasonally, a person's internal Qi will respond automatically. If, for any reason, it can't make a smooth transition to the energy of the next season, TCM understands that illness will result. Often Western Complementary and Alternative Medicine (CAM) practitioners and their patients or clients derive their understanding of TCM from acupuncture. However, acupuncture is only one of the major treatment modalities of this comprehensive medical system based on the understanding of Qi or vital energy. These major treatment modalities are Qigong, herbal therapy, acupuncture, foods for healing and Chinese psychology.

Meridians, or channels, are invisible pathways through which Qi flows that form an energy network that connects all parts of the body, and the body to the universe. The ancient medical text 'The Yellow Emperor's Inner Canon (Nei Jing)' states: "The function of the channel (meridian) is to transport the Qi and blood, and circulate yin and yang to nourish the body". The energy practice of Qigong, with its postures and movements, also affects the flow of Qi. The energy pathways and the Organ Systems they link provide TCM with a framework for identifying the root cause of health problems and the diagnoses to heal them. Meridians work by regulating the energy functions of the body and keeping it in harmony. If Qi stagnates for too long in any meridian, it can become blocked and eventually turn into matter, setting the stage for conditions that can create a physical mass. TCM Meridian Theory states: "As long as Qi flows freely through the meridians and the Organs work in harmony, the body can avoid disease".

The study of Qi phenomena may help bridge some of the apparent difference between Western and Eastern culture. Several years ago, I was lucky to notice that some scientists contributed novel experimental works on Qi, and subsequently, the papers by Ohnishi *et al.*(2005) (Ohnishi first attended the school of Nishino Breathing Method in Tokyo over 10 years ago, and 3 years later, the collaboration with Mr Nishino started in order to find a

scientific basis for Qi) stimulated the philosophical discussion by Flowers (2006). As Flowers beautifully described, in the Christian West, God was the center of everything as opposed to Qi being the center of everything in the East. Qi may be another name of 'life', Qi may represent the entity of life itself (Ohnishi *et al.*, 2007). Then, the understanding of Qi may shed light on other aspects of biological sciences. These articles prompted us to write this chapter covering the nature of Qi as well as its philosophical aspects and the significance in the modern civilization because the true foundation of TCM is Qi.

2. The history and concept of Qi

2.1 Qi in China

Qi (in Chinese, equivalent to Ki in Japanese) has been used as a healing technique in China for 4000 years. In Japan, Qi has been known to have a healing effect at least for 1500 years (Ohnishi *et al.*, 2007). The origin of the character of Qi was traced back to 3500 years ago. Confucius (who lived approximately 2500 years ago), taught moral and ethical behavior. In his *Analects*, the character of Qi appeared in four locations. It expressed the concept related to breathe, food and vitality. Taoism, which was founded by Lao-Tze (who was believed to have lived around the time of Confucius or 100 years later), have had more influence on Qi and Qigong. In the book '*Zhuangzi*', which compiled the thoughts of Lao-Tze in the third century BC, the character of Qi appeared 39 times. What it explained was: 'Qi exists throughout the universe. When it assembles, it appears as a human life. When it disassembles, the human will dies. Therefore, do not worry about life and death. Live naturally and freely as you are'. The concepts of Qi, Yin/Yang and meridians formed the foundation of Chinese medicine.

A central medical classic, *The Yellow Emperor's Inner Canon* teaches us: 'It is from, calm, indifference, emptiness, and nondesiring that true Qi arises. If the spirit is harboured inside, whence can illness arise? When the will is at rest and wishes little, when the heart is at peace and fears nothing, when the body labours but does not tire, then Qi flows smoothly from these states, each part follows its desires, and the whole gets everything it seeks'. The Chinese philosopher, Mencius (372–289 BC) described Qi in terms of moral energy, related to human excellence. This reinforces the argument that Qi is contextual, fluid in nature and not a fixed entity.

Qi is pronounced "chee". You may see it spelled "Chi" or even "Ki" in Japanese, but they all carry the same meaning. What is meant by Qi? The concept of Qi is based on the ancient Chinese initial understanding of natural phenomena. That is, Qi is the most basic substance of which the world is comprised. Everything in the universe results from the movements and changes of Qi. Man depends on nature for his production and growth and must observe the common laws of the world. As everything in the world comes from the interaction of Heaven Qi and Earth Qi, man must breathe to absorb Heaven Qi and eat to absorb Earth Qi. Qi was originally a philosophic concept. The ancient Chinese philosophy holds that Qi is the most basic substance constituting the world. This concept was introduced into TCM and became one of its characteristics. Accordingly, TCM also believes that Qi is the most fundamental substance in the construction of the human body and in the maintenance of its life activities. After a comprehensive survey of the statements on Qi in TCM documents, we have come to the conclusion that the meaning of Qi in TCM has two aspects. One refers to the vital substances comprising the human body and maintaining its life activities. The other

refers to the physiological functions of viscera and bowels, channels and collaterals. For example, clean Qi, turbid Qi, and the Qi of water and food (food essence) are substantial Qi, while the Qi of the heart, liver, spleen, kidney, stomach, and the Qi of the channels and collaterals are functional Qi. In TCM, Qi is considered to be the force that animates and informs all things. In the human body, Qi flows through meridians, or energy pathways. Qi is the most basic substances that constitute the human body and maintain its functional activities. Generally speaking, Qi is an essential substance that is full of vigor and flows fast. Qi is attributed to Yang, because it is mobile and functions to move and warm. In this sense, Qi is also named Yang Qi.

2.2 Qi in other countries

Qi, that which defies definition, is the key concept in Eastern medicine, Eastern philosophy, as well as in martial arts (Yuasa, 1993). It naturally follows that Qi is an important element in complementary and alternative medicine (CAM). Many authors have presented work on the effects and nature of Qi (Chang, 2003; Lee, 2003; Chen, 2004; Olalde, 2005; Hankey and McCrum, 2006; Shinnick, 2006; Weze *et al.*, 2007; Abbott *et al.*, 2007). For the pre-modern Chinese, Qi comprised both yin and yang, with duality and interdependence in operation. In this thinking, to narrowly define Qi is considered unnecessary. The workings of nature were explained as the workings of Qi. Qi was all encompassing. Humans were subject to the workings of Qi as well as being agents of Qi, every person being so in different ways and at different times. Still, we can not precisely describe Qi. We cannot objectively say 'Look! This is Qi'. When Western people talk about Qi in terms of the healing arts, Qi seems to be understood as 'vitality' or 'life-energy'. For those who are studying Chinese medicine, Qi is presented as being a substance flowing in our body along the 'meridians'. In the view of martial artists, Qi is a source of spiritual strength for winning. When an Eastern philosopher defines Qi, it is a function of life, which permeates through the life of an individual and the life of the universe. Physicists see it as a new kind of 'energy', and still, brain physiologists approach it as 'information' or 'entropy' (Ohnishi and Ohnishi, 2009a). Thermographical studies demonstrated that skin temperature was raised by 3–4°C when exposed to Qi emitted from Qigong healers (Machi, 1993). When Qi was received from Nishino, instructors of his school or from students who practice for many years, a warm sensation was felt. This again supports the idea that Qi has an infrared radiation component (Ohnishi *et al.*, 2007). Depending upon one's profession, discipline and necessity, Qi is understood differently, this looks like reports from many blind persons touching different parts of an elephant.

Qi has energy and entropy aspects. While it is often described in the West as energy, or vital energy, Qi is the energy of the body, of the meridians, of food, of the universe. The term Qi carries a deeper meaning. Qi has two aspects: one is energy, power, or force; the other is conscious intelligence or information. Many believe Qi is an 'energy'. However, it is interesting to note that there is a subtle difference in understanding between the Chinese and the Japanese. The former seems to believe that it is a 'substance' or 'matter' flowing in and through our bodies, and that it can be emitted from the body of a Qigong healer. In contrast, the Japanese considers that it is a form of energy. An interesting concept was published by Shinagawa's group that treats Qi as a form of 'information' (Shinagawa, 1990). Flowers considers Qi as being about 'relationships and patterning'. These concepts are another way of describing 'information'. The most interesting practice in Nishino Breathing Method (NBM) is called the Taiki-practice (a method developed by Kozo Nishino, the

founder of the NBM, to develop the level of individual's Qi through the Qi communication between an instructor and a student). Through the study on the Taiki-practice, Ohnishi *et al.* (2006) raised the possibility that Qi-energy may carry information, and that the information is in a form of 'entropy'. If Qi consists of simple energy, then, Qi effects might be mimicked by an instrument. However, if Qi involves entropy, it may be difficult to artificially reproduce the entire Qi effect.

China has, in recent decades, spent an inordinate amount of resources on experiments to determine the existence and nature of Qi. China is easing up on this research for lack of concrete breakthroughs. But the quest to define Qi continues, with there being no breakthroughs that we know of. Whether someone in China or anywhere has the Holy Grail hidden from view I cannot say, but in the report by Ohnishi, it is claimed that the effects of Qi energy can be measured. The question is also posed of what Qi actually is. Qi acts as Subtle Energy? We have still not defined Qi.

3. The formation of Qi

Qi of the human body comes from the combination of three kinds of Qi, Primordial Qi inherited from parents, the fresh air inhaled by the Lung and the refined food Essence transformed by the Spleen. Primordial Qi is derived from the Congenital Essence of the parents and is the primary substance to produce an embryo. So it forms the basis of the human body and its life activities. Without Congenital Essence, there can be no human body. After birth, the congenital Essence is stored in the Kidney to promote development and to control the reproductive activity of the human body. The refined food Essence is generated by the food which is taken in after birth and is distributed all over the body to produce nutrients and Qi and Blood under the action of the Spleen and Stomach. Fresh air is inhaled by the Lung after birth and is the main source of Qi of the human body.

From the process of formation of Qi, we can see that Qi of the human body is closely related to the functional activities of the Kidney, the Spleen and Stomach, and the Lung, in addition to the congenital constitution, food and nutrients, and the environment. Only when these organs function properly can the Qi of the body flourish. Conversely, dysfunction of any of these organs will influence the formation of Qi and the physiological function of Qi. For example, dysfunction of the Lung will weaken respiration, leading to failure of fresh air to be inhaled and the turbid Qi of the body to be exhaled, with the resultant inadequate formation of Qi. The transformation and transportation of the Spleen and Stomach play a particular role in the formation of Qi, for man relies on the nutrients transformed and transported by the Spleen and Stomach for his life after birth. On one hand, the Spleen sends up nutrients to the Lung to be dispersed, on the other hand, it sends down nutrients to the Kidney to supplement Kidney Essence. So, hypofunctioning of the Spleen and Stomach influences all three elementary substances that produce Qi.

4. The functions of Qi

Generally speaking, different kinds of Qi have different functions. Qi of the human body serves several vital functions within the body. When imbalances arise, they are seen as disruptions in the functions of Qi. A prolapse, for example, is seen as a disruption in the ability of Qi to provide the raising and stabilizing function on a particular organ. The main functions of Qi within the body are listed below:

4.1 Promoting function

Qi is a sort of essence full of vitality. It can promote the growth and development of the human body, promote the physiological functions of each viscera, bowel, channel, collateral, tissue and organ and speed up the formation and circulation of blood and the metabolism of body fluid as well. For example, if the above functions are weakened as a result of the deficiency of Qi (vital energy), the following will occur: late and slow growth and development of the human body or senilism; weakened functions of viscera and bowels, channels and collaterals, tissues and other organs; insufficient blood formation or stagnation in blood vessels; and disturbance in the metabolism of body fluid. After birth, the Genuine Qi generated from Kidney Essence determines the growth and development of the human body. After middle age, Genuine Qi gradually declines, so a person grows old. If his Genuine Qi is deficient, a person's development will be poor.

The physiological functions of viscera and bowels and Channels and Collaterals of the human body all depend on the pushing of Qi as well as the nourishing of Blood. The vigor and the ascending, descending, exit and entry movements of Qi play a very important role in promoting the functional activities of viscera and bowels and Channels and Collaterals. Therefore, when Qi is deficient, hypofunctioning of viscera and bowels will ensue. For instance, deficient Lung Qi often leads to feeble breathing, a lower voice, lassitude, weak pulse, etc. Qi also promotes the generation, distribution and discharge of the Blood and Body Fluids. As Yin substances, Blood and Body Fluids depend on Qi's activities to be generated. In other words, generation of these substances relies on the activities of Qi of the Spleen and the Stomach, the Lung and the Kidney. Besides, Qi is a vigorous substance, so it can activate the flow of Blood and Body Fluids, as well as transform them into various secretions and excretions. For this reason, Qi Deficiency often leads to an impeded flow of Blood or stagnation of Blood, or retention of Body Fluids in the body, which, in turn, causes Phlegm or edema.

In TCM theory, blood and Qi are inseparable. Blood is the "mother" of Qi; it carries Qi and also provides nutrients for its movement. In turn, Qi is the "commander" of the blood. This means that Qi is the force that makes blood flow throughout the body. Losing too much blood causes an overall Qi deficiency. When there is a Qi deficiency, the body cannot function properly.

4.2 Warming function

Qi, as a Yang substance, is rich in heat, which can warm viscera and bowels, Channels, skin, and muscles and tendons, to maintain normal body temperature and the normal functional activities of these organs and tissues. Qi helps to control homeostasis and provides warmth for the body. Yellow Emperor's Inner Canon says: "Qi has a warming action". Qi is the main source of the heat needed by the human body. The body keeps its constant temperature mainly through the warming action of its Qi. Motion produces heat, so the heat carried by Qi is in fact, a result of the constant movement of Qi, and the body temperature is maintained by the constant movement of Qi. In addition, Qi's warming function contributes to the movement of Blood and Body Fluids. The warming effect of Qi is an imperative condition for the free flow of Blood and Body Fluids within the body.

Pathologically, disorders of Qi in its warming function are mainly manifested as two kinds: one is a cold manifestation due to Deficiency of Qi, which results mostly from the deficient

Qi failing to produce adequate Heat to warm the body, marked by aversion to cold and a desire for warmth, cold limbs, lower body temperature and sluggish flow of Blood and Body Fluids. A deficiency of Qi can cause lowered body temperature, intolerance to cold and cold limbs. The other is the manifestation of Heat due to stagnation of Qi, which is usually caused by sluggish flow of Qi in a local area.

4.3 Defending function

The defensive ability of the body results from the combined action of a number of physiological functions, of which the function of Qi plays a particularly important role. The defensive effect of Qi mainly indicates that Qi can defend the body from external pathogens. The defending action of Qi is shown in two aspects. One is to guard the surface of the skin against the exopathogen. The other is to combat the invading exopathogen so as to ward it off. Defensive Qi functions to protect the body surface, and control the opening and closing of the pores, so it can prevent the invasion of external pathogens. If the defensive function of Qi is deficient, the resistance of the body against the invasion of these factors will be weakened, and as a result, susceptibility to such diseases as the common cold is likely to occur. When the defending function of Qi is normal, the exopathogen has difficulty in invading the body. When the defending function of Qi becomes weaker, when the ability of the human body to fight the exopathogen is lowered, the body is easily invaded and diseases are caused. And what is more, these diseases are hard to cure.

4.4 Consolidating and governing function

By "consolidating and governing action", we mean that Qi holds organs in their place, keeps Blood in the vessels, governs the removal of fluids. Qi can keep blood flowing within the vessels; control and adjust the secretion and excretion of sweat, urine and saliva, and prevent the body fluid from escaping; consolidate and store sperm and prevent emission and premature ejaculation; hold the organs so as to prevent them from descending. A decrease in the above functions of Qi may cause various kinds of hemorrhage, spontaneous perspiration, polyuria, salivation, spermatorrhea, premature ejaculation, prolapse of the stomach, kidney and uterus. When Qi is deficient, Yin Fluids will be profusely lost. For example, failure of Qi to control Blood will cause various kinds of bleeding; inability of Qi to control Body Fluids will cause spontaneous sweating or profuse sweating, incontinence of urine or profuse urine; and failure of Qi to control emission will cause nocturnal emission, premature ejaculation, or seminal emission. The controlling effect of Qi and the pushing effect of Qi are opposite and supplement each other. On one hand, Qi promotes the distribution and discharge of Blood and Body Fluids; on the other hand, Qi controls the flow of these Yin substances to prevent their unnecessary loss. Only when these two opposite aspects are harmonized can the normal flow and discharge of the Yin substances and the metabolism of Blood and water be maintained.

4.5 Promoting metabolism and transformation

This refers to various conversions occurring along with the movement of Qi. It includes the changes of Qi during its movement and the generation and metabolism of Essence, Blood and Body Fluids and their transformation. "Qi hua" is a specific term in the science of TCM. It refers, in general, to various kinds of changes taking place in the body under the action of Qi. Specifically, it refers to the metabolism of fundamental substances, Qi, blood and body

fluid, and the transformations which can occur between them. For example, Qi, blood and body fluid are formed in the following manner: ingested food is changed into food essence, and food essence is, in turn, transformed into Qi, blood or body fluid, and these can then be changed into any one of the others according to the physiological need of the body. All these are the specific manifestations of the action of the activity of Qi. The dysfunction of Qi in performing its action will affect the whole metabolism of the body. That is to say, it will affect the digestion, absorption, transformation and transportation of food: the formation, movement and transformation of Qi, blood and body fluid; and the excretion of feces, urine and sweat; thus causing various symptoms associated with abnormal metabolism. In short, the process in which Qi performs its functions is the process in which the substances in the body are metabolized, and in which the substances and energy are transformed. Qi assists in the formation and transformations within the body, for example the transformation of food into Qi and Blood. Qi is the foundation of all movement and growth in the body.

Although the above mentioned five functions of Qi differ from each other, they are all based on the basic property of Qi and enjoy close cooperation and mutual support.

5. The movement of Qi

As a whole, Qi in the cosmos takes two patterns of existence, diffused Qi and coagulated Qi. The former is more vigorous, cannot be detected directly and exists everywhere. The latter is manifested as various kinds of things that can be seen or that have certain shapes. In order to survive, coagulated Qi must communicate with diffused Qi and its generation as well as its ending results from movement of the diffused Qi. The movement of Qi is called Mechanism of Qi, which can be generalized as four aspects: ascending, descending, exiting and entering movements, which are based on directions. Ascending refers to the movement from below; descending, from above; exiting, from the interior; and entering from the exterior.

The various functions of Qi are all performed by its movement. The physiological function of viscera and bowels is often reflected on their Qi's ascent, descent, exit and entry movements. Qi flows throughout the whole body because of its strength and vigor. Although the activities of the human body are multiple, they can all be summarized as these four aspects. For example, the dispersing effect of the Lung is a manifestation of the exit and ascent of Qi, while its descending effect is a manifestation of the descending and entering movements of Qi. These movements of Qi are vital to life. Once they stop, life comes to an end. The four movements of Qi have to be kept in harmony. Only in this way can the physiological functions of the human body remain normal in TCM, the physiological state in which the four basic movements of Qi are coordinated and balanced is called "harmonious functional activities of Qi".

Qi has four main states of disharmonies: Qi deficiency, Qi stagnation, sinking Qi and rebellious Qi. These disharmonies may affect many parts of the body at once or within a particular meridian, organ or area. Deficiency of Qi, for example, may affect the Lungs with symptoms of shortness of breath, the Stomach/Spleen with symptoms such as poor appetite and the body in general with symptoms of fatigue and weakness. The ascent, descent, exit and entry movements of Qi are of prime importance in human life. The Kidney Essence, the food Essence transported and transformed by the Spleen and Stomach and the fresh air inhaled by the Lung, will not be distributed over the body to perform their physiological functions if they do not make ascent, descent, entry and exit movements.

6. The classification of Qi

As the most basic substance that constitutes the world, Qi can be used to name everything in the world, so it is hard to classify it. However, Qi mentioned here is something concrete. Qi of the human body also has two patterns of existence. The coagulated Qi is manifested as various visible or structural components of the body, such as viscera, body figure, sense organs, Blood, Body Fluids and Essence; the diffused Qi is manifested as the Qi that flows in the body, but takes no certain form, such as Primordial Qi, Pectoral Qi, Nutritive Qi and Defensive Qi that is classified according to its distribution, origin, and function.

6.1 Primordial Qi (yuan Qi)

Primordial Qi is also called "Inborn Qi", "Primary Qi" or "genuine Qi". It is the most important and fundamental of all, originates from the congenital essence (the innate essence stored in the kidney). But it also depends on the supplement and nourishment of the acquired essence developed in the spleen and stomach. It is received from heaven and combined with food essence to nourish the body. It commences from "the vital gate", the portion between the two kidneys, passes the triple warmer and circulates throughout the body. It goes inward to the five viscera and six bowels and outward to the superficial layer of the body. It goes everywhere and acts on all parts of the body. The primordial Qi has the functions of both activating growth and development and promoting the functional activities of all the viscera and bowels, channels and collaterals, tissues and other organs. Therefore, it is the motivating power of the vital activities of the human body. If Primordial Qi is deficient due to a congenital defect or improper feeding after birth, the functional activities of the whole body will become weakened.

6.2 Pectoral Qi (zong Qi)

Pectoral Qi is also termed Great Qi, it accumulates in the thorax where Qi of the whole body converges. So the thorax is also known as "the sea of Qi". Pectoral Qi is a combination of the fresh air inhaled by the lung and the food essence derived by the spleen and stomach from water and grain. It is stored in the chest and poured into the channels of the heart and lung just as Miraculous Pivot (Lingshu), says: "It goes out of the lung and circulates through the larynx and pharynx. This is the reason why it exits when being exhaled and enters when being inhaled." The book Classified Canon compiled by Zhang Jiebin in 1624 A.D. says: "It goes down to the elixir field to be stored, and fills the Point Qijie of the yangming Channel from which it continues to go downward to the feet." Pectoral Qi has two main functions. One is that it flows through the respiratory tract to promote the respiratory movement of the lung and is involved in the loudness or softness of voice and words. The other is that it fills the heart channel to promote and adjust its beat, and to promote and adjust the circulation of blood and Qi. It also exerts an influence on the warmth and activities of the limbs. In short, it has the function of nourishing the lung and the heart, thus promoting respiration and blood circulation.

Generally speaking, when Pectoral Qi is sufficient, the pulse will be moderate and forceful, and the Heart will beat rhythmically and evenly. If Pectoral Qi is deficient, the pulse will be swift, irregular, feeble or scattered. Pectoral Qi is usually considered a link connecting the functional activities of the Heart and those of the Lung. In the clinic, Deficiency of Pectoral

Qi in most cases indicates Deficiency of Lung Qi leading to Deficiency of Heart Qi and ensuing Blood Stasis. For example, when a patient suffering from chronic bronchitis develops pulmonary Heart disease, which is marked by shortness of breath, a low voice, palpitation, a purplish face, running or intermittent pulse, etc., he or she can be diagnosed as having deficient Pectoral Qi.

6.3 Nutritive Qi (ying Qi)

Nutritive Qi refers to the Qi circulating within the blood vessels and having a nourishing function. As it flows through the vessels with blood, it has such a close relationship with the latter that TCM often mentions them in a combined way "nourishing blood". In TCM, Blood consists mainly of two parts: Nutritive Qi and Body Fluids. Compared with defensive Qi, nourishing Qi belongs to yin, so it is also called "nourishing yin". Nutritive Qi comes mainly from the food essence transformed and transported by the spleen and stomach. After its formation, Nutritive Qi is sent to the Channels to flow in the order of the Twelve Regular Channels. This is why a chapter on Arthralgia-Syndrome of Plain Questions (Suwen) says: "What is nutritive Qi? It is actually the essence Qi transformed from food and water". Nutritive Qi originates from the middle warmer and enters the channels by way of the lung. It circulates throughout the body along one after another of the fourteen channels. The main functions of Nutritive Qi are to generate Blood and to nourish the whole body. That is, it flows into the channels through the lung and becomes a component of blood, and nourish the whole body for the physiological activities of all the viscera and bowels, channels and collaterals, tissues and other organs. Plain Questions says: "Nutritive Qi secretes its fluid, which enters the channels and turns into blood, thus nourishing the four extremities, the five viscera and the six bowels".

6.4 Defensive Qi (wei Qi)

Defensive Qi is the Qi moving outside the conduits and having protective functions. Compared with nourishing Qi, it belongs to yang, so it is also known as "defensive yang", it also comes from the food essence transformed and transported by the spleen and stomach. It is characterized by braveness in defence. That is why a chapter on Arthralgia-Syndrome of Plain Questions says: "Defensive Qi is a brave kind, which is produced by food and water." The distribution of Defensive Qi has two features: the flow following Nutritive Qi and free flow. The former indicates that Defensive Qi also goes along the Twelve Regular Channels, while the latter indicates that Qi is distributed all over the body. Defensive Qi circulates not within but outside the channels. Being vaporized to the diaphragm and scattered in the chest and abdomen, it travels between the skin and flesh. In spite of circulating outside the channels, it still leans against the channels when moving. Defensive Qi has three functions. The first is guarding the surface of the body against exopathogen. The second is keeping a relatively constant body temperature by controlling the opening and closing of the muscular striae and adjusting the excretion of sweat due to its permeation to the muscular striae. The third is nourishing the viscera, bowels, muscles, skin and hair. When defensive Qi is insufficient, the defending function of the human body is weakened, the exopathogen invades the body easily, and the disease is hard to cure. Abnormal circulation of defensive Qi may cause sleep disorders. When defensive Qi is deficient, spontaneous sweating will occur.

Nutritive Qi and defensive Qi have the same source. The former circulates within the channels, has the nourishing function and belongs to yin, whereas the latter circulates outside the channels, has the function of guarding the exterior of the body and belongs to yang. Only when they coordinate with each other can the opening and closing of the pores be kept normal, the body temperature constant, and the defending ability strong.

7. Modern investigations on Qi

In China, Qi has been known for 4000 years. In Japanese literature, the documentation of Qi goes back 1500 years. This is not limited to the East. In the West, Biblical literature suggests that curing sickness by extending a hand was practiced by a gifted individual. Since then, thousands of accounts have been published, and millions of people have talked about Qi-energy. Practical, clinical, philosophical and scientific studies on Qi have been actively reported in journals of complementary and alternative medicine (CAM). However, no reasonable mechanism, which can be examined or refuted from the scientific point of view, has been presented (Ohnishi and Ohnishi, 2009b).

Scientific investigations of Qi started about 30 years ago, but we still know very little and have so much to learn. Flowers (2006) mentioned that the speed of Qi investigation seems to have slowed down in recent years. Now the question comes as to what is the nature of Qi? As to the nature of Qi, Chinese and Japanese scientists have already reported that it involves infrared radiation. It was also reported that other forms of energy may be involved in Qi which include electromagnetic waves, electrostatic energy, magnetic energy, sound waves and so on (Kiang, 1978; Yuasa, 1993; Machi, 1993; Shinagawa, 1990). However, in the study of Qi, one difficult problem encountered. Namely, Qi can't be measured quantitatively with modern technology now (Ohnishi and Ohnishi, 2009a). We do not even know the qualitative nature of Qi yet, not to mention quantitative methods of measuring it. One of the pitfalls in the study on Qi is obviously that there seems to be no 'scientific' objective measure to evaluate its 'quantity'. Thus, the concept of Qi would be as important and effective, and also as difficult to quantify, as the concept of 'stress'.

7.1 The effects of Qi-therapy on health

External Qi-therapy (QT) is a process by which Qi is transmitted from a Qi master to another person for the purpose of preventing and curing disease, as well as protecting and improving health through regulation of mind and body. This may be a very useful intervention. Research studies have shown that QT is effective for relief of pain, relaxation of stress states and increasing immunity (Lee *et al.*, 2001a-c). Several studies attempted to reveal a specific effect of external Qi by modern biochemical and immunological methods (Chien *et al.*, 1991; Fukushima *et al.*, 2001; Lee *et al.*, 2001a and b; Shah *et al.*, 1999). Chien *et al.* (1991) reported that facilitating Qi from a Qigong masters increased the rate of cell growth and DNA synthesis. Lee *et al.* (2001a and b) reported psychoneuroimmunological effects of *in vivo* QT on humans and stimulatory effect on natural killer (NK) cell activity *in vitro* by emitted Qi. QT has an acute stimulatory effect on neutrophil superoxide generation (Lee, 2003). The studies show that Qi positively affect human innate immunity.

TCM considers chronic fatigue to reflect a disharmony and depletion in the supply of Qi, with blockage, stagnation, imbalance or change in the pattern or organization of Qi resulting in disease (Shin, 2002; Xing, 1987). Disruption to Qi manifests in symptoms such as pain,

fatigue and mood disturbances. TCM practitioners consider that chronic fatigue reflects a disharmony and depletion in the supply of Qi in the body. Qigong is one of the traditional complementary interventions used to strengthen Qi through self-practice, and to manage the state of Qi to prevent and cure disease. Qigong seems to improve factors related to chronic fatigue such as sleep, pain, mental attitude and general mobility after 3 and 6 months. Qigong's positive effects indicate that it represents a potentially safe method of treatment for chronic fatigued patients (Mike Craske, 2009).

People attempt to find the mechanism behind the healing effects of Qi. Why do students of NBM continue to attend the class (many of them once a week, but some of them more often) for 10 or even 15 years? Because they feel healthier, or because they have a more youthful feeling than before. Through their study, students were shown to have higher immune activity and lower stress levels (Kimura *et al.*, 2005). Some students overcame cancer themselves by attending the class almost everyday to lift their Qi level. This experience may be related to *in vitro* results that Qi inhibited the growth of cancer cells (Ohnishi *et al.*, 2005). As to the anti-aging effect of NBM, Mr Nishino has long proposed that Qi may stimulate mitochondria to become more active, and thus, to provide more energy to the cells. Ohnishi *et al.* (2006) demonstrated that in isolated rat liver mitochondria, the respiratory control ratio was protected from deterioration by Qi, and lipid peroxidation was inhibited by Qi. These results suggest that Qi may inhibit apoptosis of the cells in our body, thereby inhibiting aging. Some students were shown to have higher bone density than their age- and gender-matched contemporaries who do not practice NBM (Nishino, 2006). Through *in vitro* tests, Ohnishi *et al.* found that Qi may be beneficial in preventing osteoporosis (Ohnishi *et al.*, 2007). They are accumulating data on health-related benefits of NBM, and also, trying to correlate this with the molecular and cellular mechanisms of Qi effects.

7.2 The effects of Bu-Zhong-Yi-Qi-Tang on health

TCM, with its long history of clinical practice, occupies an important place among the "alternative medicine" that has been gaining attention in recent years. Because of the general mildness in nature and the emphasis on relief, balance and harmonization rather than forceful suppression, a good many Chinese medicines are particularly suited for the frail, the elderly, the very young and those already weakened by diseases. Bu-Zhong-Yi-Qi-Tang, a basic prescription as an Qi tonic (Chinese medical concept: Bu-Qi) and a general health tonic, also one of the typical formulae in Japanese Kampo which is prescribed for people with the Qi deficient conditions in order to enhance their Qi (Terasawa, 2004; Li, 1992; Kawakita and Nomoto, 1998), composed of Astragali radix, Ginseng radix, Atractylodis rhizoma, Glycyrrhizae radix, Angelicae sinensis, Aurantii pericarpium, Cimicifugae rhizoma and Bupleurum radix, has been prescribed for the alleviation of fatigue and depressed vitality as well as the improvement of gastroenteric circulation (Shih *et al.*, 2000). It has been reported to possess anti-tumor (Ito and Shimura, 1985), anti-bacterial (Li *et al.*, 1992), anti-nociceptive and anti-depressive activities (Koshikawa *et al.*, 1998), and to have some effects on impairment of hematopoietic organs (Ikeda *et al.*, 1990), stress incontinence (Murakami, 1988) and male infertility (Ishikawa *et al.*, 1992), to reduce the extent of radiation-induced apoptosis and protect the jejunal crypt (Chai *et al.*, 2009) and improve health status in general but slows down or partially reverses aging in particular (Shih *et al.*, 2000).

7.3 The effects of Qi on health

Qi is the concept of the state of the mind/body as a whole. It is thus not a 'subjective' state, which can only be known introspectively. From the clinical experience, the Qi deficiency state is diagnosed very 'objectively': those with 'Qi deficiency' are weak in voice, have no 'strength' in their eyes and their posture is poor. In this sense, Qi is a very objective entity. It is not an abstract and subjective entity like soul or spirit. Practitioners of TCM can judge a patient's Qi state by just glancing at their skin condition. Those people healthy in mind-body, or with good Qi, have bright and 'full' skin. Though difficult to quantify, these are 'objective'. Qi can be approached 'objectively'. There is thus a definite possibility that we can elaborate on the concept of Qi as an objective 'scientific' term. It is a basic East Asian 'philosophy' of health/disease that those with a good Qi state are highly immune to diseases (Kobayashi and Ishii, 2005). It is very nice to see that Western clinical researchers such as Irwin have undertaken the challenge to tackle this difficult problem of Qi or mind-body unity. Now is an exciting era, when for the first time it has become possible for a western psychiatrist and an Eastern dermatologist to work together towards reconciling this fundamental difference between the medicines of the East and the West.

In Asia, the use of Qi in enhancing one's vitality and improving health is employed even today. For example, Qigong therapies are popular in China as Qi-therapies are in Japan. More recently, similar healing techniques were known in Europe as the working of mesmerism or hypnosis. Unfortunately, these techniques are not well accepted as a branch of today's main-stream sciences, especially in the Western hemisphere. Many people consider them as folk medicine. Some people believe that they are 'supernatural' and 'parapsychological' phenomena. In fact, Qi is neither a paranormal nor para-psychological phenomenon but is a normal phenomenon. Since it is a normal phenomenon, Qi can be studied by modern scientific methodology. Only a limited number of investigators have been studying them as the object of scientific, medical investigation for the past 30 years.

In the past 30 years, many Chinese scientists regarded 'Qi' as a real substance flowing in our body, which can be represented by mass. On the contrary, most Japanese scientists treated 'Qi' as energy, except for Shinagawa who considered it to be information. Although neither Qi itself nor the mechanism of its effects is understandable or explicable within any paradigm of modern medical science, its effects on the human body are apparent and some studies have been tried to find the underlying mechanism with laboratory experiments (Ohnishi, 2007).

Ohnishi *et al.* are demonstrating that so-called 'Qi-energy' is a natural phenomenon, and therefore, it can be analyzed by rigorous scientific and objective investigations. A 'breathing method' was developed by a Japanese leading Qi-expert, Kozo Nishino. Since 'breathing' is directly related to oxygen respiration, he has long proposed that mitochondria may play a key role in maintaining vitality and health (Nishino, 1997;2004). This led them to undertake the project to explore a possible relationship between Qi-energy and mitochondrial function (Ohnishi *et al.*, 2006). Kozo Nishino has hypothesized for many years that the breathing method would increase oxygen delivery in the body, activate cell metabolism including mitochondrial function, thereby bringing us tangible health benefits (Kimura *et al.*, 2005; Ohnishi *et al.*, 2005). Recently, Ohnishi *et al.* found that his Qi protected isolated rat liver mitochondria from heat-induced deterioration, possibly by reducing the production of reactive oxygen species (ROS). The protection of mitochondria and the reduction of ROS

generation would produce more energy from the nutrients and would result in healthier cells and organs. The protection of mitochondria from adverse effects of ROS would reduce the likelihood of premature apoptosis, and therefore would contribute to the longevity of the practitioners. His prediction that mitochondria would play key roles in maintaining health and longevity seems to be supported by these experiments (Ohnishi *et al.*, 2006).

Isolated rat liver mitochondria are a well-established model for studying biophysical and biochemical aspects of energy metabolism. The simplest marker for the integrity and intactness of mitochondria is a respiratory control ratio (RCR, which is the ratio between State-3 and State-4 respiration) (Chance and Williams, 1955). Ohnishi *et al.* measured the RCR and analyzed the degree of lipid peroxidation in the mitochondria by measuring the amount of TBARS (thiobarbituric acid reactive substances). Using this model, they found that a heat treatment (incubation at 39°C for 10 min) decreased the RCR by about 60%. While the Qi-energy emitted from the fingers of Nishino could inhibit the decrease. They also attempted to find the mechanism for the Qi-effect. After the early work by Boveris and Cadenas (1975), ROS has been recognized as an important factor to damage mitochondrial functions. In order to test whether Qi-energy could reduce the ROS production, they measured the amount of mitochondrial lipid peroxidation after the heat treatment using a well-known assay technique for TBARS. Lipid peroxidation was increased during the heat deterioration, suggesting that mitochondria were exposed to oxidative stress. Lipid peroxidation is known to damage the mitochondrial membrane. However, lipid peroxidation was inhibited by Qi-energy, and the mitochondrial integrity was preserved.

From the standpoint of health and longevity, their results may have the following significance: (i) Qi-energy may protect mitochondria from oxidative injury. If the same reaction takes place in the practitioners' body, then mitochondria may produce more energy, and therefore, it has beneficial effects on cellular metabolism. (ii) Mitochondria are known to play key roles in apoptosis of many cell types. If cytochrome c and other apoptosis-inducing factors (AIF) are released from mitochondria, they activate a series of cascade reactions to cause apoptotic cell death (Green and Reed, 1998; Narita *et al.*, 1998; Susin *et al.*, 1999; Lorenzo *et al.*, 1999; Shimizu *et al.*, 1999). Although apoptosis is a fundamental feature of almost all animal cells and it is indispensable for the normal development of tissues, organs and immune systems (Jacobson *et al.*, 1997), excessive apoptosis could cause diseases (Thompson, 1995). Therefore, protecting mitochondrial integrity would help prevent cytochrome c release, thereby inhibiting inappropriate apoptosis from taking place. In conclusion, Qi-energy maintains mitochondrial membrane integrity during the heat deterioration process. Mitochondria are constantly exposed to the danger of ROS-induced oxidative injury. The effect of Qi seems to be related to the inhibition of oxidative injury on mitochondrial membranes caused by ROS. Therefore, Qi would have a beneficial effect on protecting mitochondria; thus, it would maintain efficient cellular metabolism and decrease the chance of unnecessary apoptosis.

'Qi-energy', which can be enhanced through the practice of Nishino Breathing Method (NBM), was reported to have beneficial health effects. It has been known for 20 years that the practitioners of Qi experienced beneficial health effects (Yumi, 2005). It was shown that the practice increased immune activity and decreased the stress level of the practitioners (Kimura *et al.*, 2005). From the collaboration with Master Nishino, Ohnishi *et al.* showed that 'Qi' is not a paranormal or parapsychological phenomenon, but a natural phenomenon. An interesting observation from the standpoint of CAM was that the Qi-energy, which inhibits

cell division of cultured cancer cells (Ohnishi *et al.*, 2005) or protects isolated mitochondria from oxidative injury, was the same as that which could move other individuals in the Taiki-practice (Ohnishi and Ohnishi, 2006). This suggests that the training gained from the Taiki-practice may produce beneficial health effects. This is the reason why they are studying the mechanism behind the Taiki-practice.

Ohnishi *et al.* explain the philosophical and psychological background of Qi, emphasize that the unique aspects of Eastern philosophy are 'non-linearity' and 'holistic' approach and then present physics aspect of Qi. Their experiments demonstrated that a 'Qi-beam' carries 'entropy' (or information), which is different from 'energy' (Ohnishi and Ohnishi, 2009a). We believe that the human will uncover the secret of Qi in the near future with the rapid development of modern life science.

8. The significance of studying Qi

The difference between the cultures in the West and the East may be described by the difference between 'linear philosophy' and 'nonlinear philosophy'. Since Qi phenomena are essentially nonlinear, a straightforward application of linear philosophy may not be effective in its study. We hope that the study of Qi phenomena may help bridge some of the apparent difference between Western and Eastern culture. As Flowers mentioned, in the Christian West, God was the center of everything as opposed to Qi being the center of everything in the East. Qi may be another name of 'life'. As Flowers beautifully described, Qi may represent the entity of life itself (Flowers, 2006). Then, the understanding of Qi may shed light on other aspects of biological sciences. We hope that the study of Qi might help to unite more aspects of Eastern and Western philosophy.

Understanding of Qi will help bridge Western and Eastern viewpoints, According to Eastern thought, the universe has 'life' and the function of 'life' is represented by Qi. Qi flows and circulates throughout the universe and through each human being. Qi is a non-linear phenomenon, and therefore, it can function as an essential element of life and the universe (both of which are non-linear). If Western people could understand Qi more, they would incorporate holistic Eastern philosophy into their own philosophical system. Then, mind and body, as well as life and its environment, will be viewed as a unified entity, and the world would finally become a better place to live.

The concept of Qi would be of great value towards this direction, as it is understood as a kind of 'energy' of mind/body as a whole. If, therefore, there was some concrete method to enhance (strengthen) Qi, it would become one of the cornerstones of holistic medicine of the future. Thus, from the medical point of view, Qi can be seen as the totality of the body's healing systems or defense mechanisms which include the immune system as their essential part. Qi has both energy and entropy (information) aspects. The practice of breathing to enhance the Qi level may in-essence help to restore the original ability of human beings. Therefore, it may contribute to improve our health, wellness and life itself.

Qi phenomenon seems to be characteristic to the nonlinear nature of life. If so, the study of Qi may help deepen our understanding on our life and the universe itself. Since Qi is related to our life activity, the understanding of Qi would contribute to the elucidation of the beautiful nature of life itself. Further development and understanding of Qi may help round out our belief in technology-oriented modern science which lacks humanistic aspects. This may help to transform the 'Century of Death' to the 'Century of Life'. The 19th century was the age of the 'industrial revolution' which was symbolized by an invention of a steam

engine. The 20th century is the age of 'nuclear energy'. Then, what would make the 21st century more humanistic so that history might regard it as a century of life? The pursuit of studies on Qi might be a positive step. In conclusion, Qi phenomenon is not paranormal. It is a normal and real phenomenon and can be the object of rigorous scientific study. If the question is posed, 'Why do you study Qi?' We will answer, as a famous mountain climber once said, 'Because it is there!' We believe that further analysis of Qi may open up a new horizon in life science.

9. The comparisons between Qi and bioenergy

Qi, an important category in the ancient Chinese philosophy, is a simple understanding of natural phenomena. According to ancient Chinese philosopher, Qi is the most basic material that constitute the world, the everything in the universe were produced by the motion of Qi, and it is roughly similar to the concept material of Western philosophy. The theory of Qi in ancient philosophy was introduced into the medical field, the basic theory of Qi in traditional Chinese medicine (TCM) was formed, i.e., the concept of Qi in TCM was established during the mutual penetration between the materialist philosophy and medicine in ancient China, it is a concept of material. In TCM, Qi is constantly in motion, is the subtle substance with a strong vitality which constitute the human body and maintain the activities of human life, is one of the most basic material, it is also known as the "essence Qi". When the concept Qi in TCM was used to discuss the human body, it often has the meaning of both life material and physiological functions. Therefore, Qi in TCM is one of the most important basic concepts. Bioenergetics research in life sciences have played an important role, Mitchell's chemiosmotic theory earned the 1978 Nobel Prize in Chemistry, as the coupling between electron transport in the respiratory chain and adenosine diphosphate (ADP) phosphorylation which is caused by electrochemical gradient of protons between internal and external mitochondrial membrane was expounded; Nobel Prize in Chemistry in 1997 was awarded academician PD Boyer in the U.S. Academy of Sciences for elucidating generation mechanism of adenosine triphosphate (ATP)—the most important energy molecules. The work was closely related to the energy production and consumption which is required for life activities, and the binding-changes and rotation-catalytic mechanism of ATP synthase was proposed. ATP synthase is the smallest molecular motor in the world. In this paper, the relationship between Qi and bioenergy was approached to.

9.1 The generation of Qi and ATP

9.1.1 The generation of Qi

Qi in TCM, constitute the body and maintain life activities, has the following three sources and is a combination of them. (i). Congenital essence: This essence, which is born before the body, is the basic material of life, is intrinsic from the parents. (ii). Acquired essence: is acquired from the diet to obtain nutrients from the transportation and transformation through the spleen and stomach, that is, the essence of water and food. (iii). The clear air in the nature: the fresh air inhaled through the breathing exercise of lungs.

From the generation process of Qi, Qi depends on the normal function of the organs and tissues of the body, but the physiological functions of the viscera kidney, spleen and stomach, lungs are closely related to it. The lung, being the dominator of Qi, operates the Qi of the whole body; spleen and stomach, being the acquired foundation, their function of

transformation and transport is particularly important in the Qi generation process; kidney, being the source of Qi generation and the congenital foundation, store the essence of life which includes congenital and acquired essence. For example, Qi, blood and body fluid are formed in the following manner: ingested food is changed into food essence, and food essence is, in turn, transformed into Qi, blood or body fluid, and these can then be changed into any one of the others according to the physiological need of the body. The waste from the eaten food and the products produced in the course of metabolism are changed, separately, into feces, urine and sweat which are ready to be removed from the body.

The Qi in the human body is different in classification and formation. But, generally speaking, it has no more than two sources. One is the innate vital substance one inherits from one's parents before birth. The other is the food essence and fresh air one receives from air, water and food in the natural world. The materials obtained in the two ways above have to be processed and transformed by the viscera and bowels before becoming the Qi of the human body. The process for Qi to be formed is as follows: The innate vital substance acted on by the kidney comes out of the gate of life (the portion between the two kidneys) and goes up to the middle warmer. There it combines with the food essence coming from the spleen and continues upwards until it combines with the fresh air inhaled by the lung. The food essence transformed and transported by the Spleen must be sent up to the Lung to combine with fresh air to produce the nutrients necessary for man's life activities. Finally it turns into Qi. It is easy to see from the above that the Qi of the human body is formed through the joint work of the kidney, the spleen, the stomach and the lung in combining the innate vital substance taken from one's parents, the food essence received from water and food, and the fresh air obtained from nature.

9.1.2 The generation of ATP

The major function of mitochondria is the generation of ATP, the energy currency of the cell, by oxidative phosphorylation. Essential mechanisms of energy production, signaling, biosynthesis and apoptosis are contained within mitochondria, and their orchestration plays a determinant role in cell physiology (Benard *et al.*, 2006; Bailey *et al.*, 2005). Since mitochondria generate between 80% and 90% of all ATP produced in the cell, the rest of the energy was provided from anaerobic glycolysis and the conversion of creatine phosphate (PCr) by creatine kinase (CK) (Papa, 1996; Radda *et al.*, 1995), it is understandable that in tissues like the cardiac muscle and liver (each hepatocyte contains 1000–2000 mitochondria) these organelles occupy 20–30% of the cell volume, having mitochondrial function, or dysfunction, a critical role in the performance of these tissues (Smith *et al.*, 2008; Yang *et al.*, 2010). An adult needs about 3000 kcal, or 400 mol ATP (about 200 kg) every day. Mitochondrial oxidative phosphorylation (OXPHOS) enzymes including 5 oligomeric protein complex, i.e. complex I (NADH dehydrogenase), complex II (succinate ubiquinone reductase), complex III (cytochrome c reductase), complex IV (cytochrome c oxidase, COX) and complex V (H⁺-ATP synthase). Complex I and II capture electrons from the reduced coenzyme I (NADH) and succinate respectively, and transfer them to coenzyme Q (CoQ), CoQ is oxidized by complex III and IV. These complexes (except complex II) are coupled electron flow to proton pump and to ensure that the generated proton driving force was used by complex V to form ATP from ADP and phosphate (Pi) coupling reaction, each complex is composed by different subunits, and complex I, II, III and IV contain several redox active prosthetic groups (Papa, 1996).

Bio-energy materials - ATP generation process in modern medicine is as follows: ATP, the "Universal Currency" of bioenergy in the cell, is a direct provider of energy required for the body, provide efficient energy for any endergonic reactions. Therefore, life is basically dependent on the activities of ADP -ATP cycle. There are two types of ATP-generating mechanisms: substrate level phosphorylation in the original fermentation pathway and photophosphorylation and OXPHOS that use electron transport system in the evolutionary pathways. The efficiency for generating ATP of the latter is about 20 times compare to the former, the key reasons for high efficiency in photophosphorylation and OXPHOS system depend on the proton pumps and ATP synthase in biomembrane, for example, ATP synthase catalyze endergonic reaction by binding the protons that accumulated in one side of the membrane: $\text{ADP} + \text{Pi (phosphate)} \rightarrow \text{ATP}$. Then, proton pump coupled with the electron transport system to generate energy.

Now, let's look at the overview of the mitochondrial ATP production. Mitochondria are intracellular organelles mainly devoted to energy production. From the point of the main generation process of bio-energy substance-ATP, at first, the three major nutrients carbohydrates, lipids and proteins are decomposed into the simple sugars, fatty acids and amino acids respectively by different enzymes in the body. Then pyruvate was generated from glucose by glycolysis, acetyl coenzyme A (CoA) was then formed from pyruvate through the pyruvate dehydrogenase complex, acetyl-CoA, can also be generated in mitochondria from fatty acids by β -oxidation, then enter the Krebs cycle, and the 20 kinds of standard amino acids that make up proteins can be decomposed in the body to generate acetyl-CoA, oxaloacetate, fumarate, succinyl-CoA and α -ketoglutaric acid and other substances to enter the citric acid cycle. The hydrogens stripped off in the Krebs cycle were accepted by nicotinamide adenine dinucleotide (NAD⁺) or flavin adenine dinucleotide (FAD) to enter in the respiratory chain of inner mitochondrial membrane through a series of electron carriers (low potential to high potential), the electrons were finally transported to oxygen accompanied by the phosphorylation of ADP to generate ATP.

The following describes the basic processes occurring in a typical normal cell, using glucose as a major source of energy. The breakdown of glucose into water and CO₂ includes two steps, namely, glycolysis (the anaerobic phase) taking place in the cytoplasm, and OXPHOS (the aerobic phase) occurring in the mitochondria. Of the total yield of 38 ATP per mole of glucose, two are produced in the glycolysis process and 36 during the OXPHOS. It is important to note that oxygen availability in the mitochondrion is a critical factor for the normal ATP production in the cell. Glycolysis depends on the entrance of glucose from the capillary into the cell via the glucose transporter. The end product of glycolysis, pyruvate, is transported into the mitochondria by a specific carrier protein. The pyruvate is transformed, in the matrix of the mitochondria, into acetyl coenzyme A that activates the tricarboxylic acid (TCA) cycle. In the mitochondria, the TCA cycle generates NADH which enters the electron transport chain (ETC) leading to the OXPHOS that generates ATP (Mayevsky, 2009).

The mitochondrial respiratory chain consists of four enzyme complexes (complexes I-IV), and two mobile carriers (coenzyme Q and cytochrome c) along which the electrons liberated by the oxidation of NADH and FADH₂ are passed, and ultimately transferred to molecular oxygen. This respiratory process generates the electrochemical gradient of protons used by the F₁F₀ ATP synthase (i.e., complex V) to phosphorylate ADP and produce ATP. Briefly, nutrients such as glucose, amino acids and fatty acids are transformed by intermediary metabolism into their reduced equivalents (NADH, H⁺ or FADH₂), which are further

oxidized by the mitochondrion to generate ATP. Mitochondria of normal tissues typically oxidize combinations of these energy substrates (fatty acids, the glycolysis end product pyruvate and amino acids) to establish the electrochemical gradient of protons ($\Delta\mu\text{H}^+$) used by the F_1F_0 -ATP synthase to produce ATP (Benard *et al.*, 2010). In this regard, mitochondria play a pivotal role by producing almost all the cellular energy (Freyre-Fonseca *et al.*, 2011). It is quite evident that the generation of ATP requires both acquired essence – the essence of water and food (which can be regarded as decomposition products of the three major nutrients – monosaccharides, fatty acids and amino acids) and the clear Qi in the nature - the fresh air (mainly oxygen, around 90% oxygen inhaled by the body was consumed by the process of ATP production through mitochondrial electron transport), mitochondria are also needed. But modern biochemical research show that human mitochondria are maternally inherited, that is, mitochondria of everyone are from the mother genetically, and this can be called the congenital essence. Therefore, the Qi and ATP have common sources.

9.2 The functions of Qi and bioenergy

Generally speaking, Qi of the human body has five functions: promoting, warming, defending, consolidating and governing, promoting metabolism and transformation, these functions of Qi are consistent with those of energy metabolism. All cells in the body depend on a continuous supply of ATP in order to perform their different physiological and biochemical activities (Mayevsky, 2009). In modern medicine, all the physiological activities of the body are dependent on bio-energy source (ATP) generated by substance metabolism (including oxygen metabolism), various forms of physiological functions can be played by ATP through different effectors to maintain all life activities. Large amounts of ATP are used in muscle contraction, nerve impulse conduction, compound biosynthesis or other biological processes (Benard *et al.*, 2010).

Qi is a vigorous substance that flows fast in the human body. So it promotes the growth and development of the body, the movement, distribution and discharge of Blood and Body Fluids, and the physiological functional activities of viscera and bowels, channel, collateral, tissue and organ. Qi, as a Yang substance, heat source of the body, is rich in heat, which can warm viscera and bowels, channels, skin, and muscles and tendons, to maintain normal body temperature and the normal functional activities of these organs and tissues. This Qi function is of important to physiological significance of the human body. "Qi hua" is a specific term in the science of TCM. It refers, in general, to various kinds of changes taking place in the body under the action of Qi. Specifically, it refers to the metabolism of fundamental substances, Qi, blood and body fluid, and the transformations which can occur between them, it is actually material conversion and energy conversion process. Although the above mentioned five functions of Qi differ from each other, they enjoy close cooperation and mutual support. Qi is the foundation of all movement and growth in the body.

According to TCM, "if Qi gets together, it will result to the birth; if Qi is harmonious, then the human body is healthy; if Qi is disordered, the human will be sick; if Qi is depleted, the human will die." According to the modern life science, energy metabolism is the center for life activity, if the energy metabolism is normal, the body can carry out normal vital activities, If no bio-energy is supplied for the body, the life activities cease immediately. Therefore, Qi and bioenergy have identical functions.

10. The effects of QIHM and QRHM on energy metabolism—An experimental perspective

ABSTRACT Aims: TCM practitioners usually compose prescriptions made up of Qi-invigorating herbal medicines (QIHM) or Qi-flow regulating herbal medicines (QRHM) for Qi system diseases, and have accumulated abundant clinical experience for a long time. To approach to the nature of Qi in TCM from bioenergetics, the effects of QIHM (ginseng, astragalus root, pilose asiabell root, white atractylodes rhizome) and QRHM (immature bitter orange, magnolia bark, green tangerine and lindera root) on oxidative phosphorylation (OXPHOS), bioenergy level and creatine kinase activities were investigated.

Methods: QIHM and QRHM were administered by oral gavage daily for 10 days. Mice liver mitochondria were isolated by differential centrifugation. The effects of QIHM and QRHM on energy metabolism were studied from the production, regulation, and storage of bioenergy. Mitochondrial OXPHOS curve was determined by Clark oxygen electrode method. The levels of adenosine triphosphate (ATP), adenosine diphosphate (ADP) and adenosine monophosphate (AMP) in liver cells were determined by reversed-phase high performance liquid chromatography (RP-HPLC), adenylate energy charge (AEC), total adenylate pool (TAP) were calculated. The creatine kinase (CK) activities in mice skeletal muscle were determined by a commercial monitoring kit. The regularity of action of QIHM and QRHM were analyzed and concluded.

Results: Ginseng and astragalus root can decrease oxygen consuming rate and respiratory control ratio (RCR) of liver mitochondria obviously, we consider this is appearance of lowering standard metabolic rate and is a kind of protective adaptation. QRHM can increase P/O ratio and RCR. Both QIHM and QRHM can stimulate activity of CK significantly in the storage of energy, and QRHM is stronger than QIHM. But it is worth notice that all the four QIHM can increase levels of ATP, AEC and TAP; on the contrary, all the four QRHM can decrease levels of ATP, AEC and TAP in liver cells. In a word, QIHM and QRHM increase and decrease bioenergy level of liver cells respectively *in vivo*. Therefore, Qi is closely related to bioenergy.

Conclusion: Qi and bioenergy have common sources and identical functions. QIHM and QRHM are able to improve and decrease the energy state of the body respectively. Qi and bioenergy have general characteristics in many aspects. The experiments provide scientific evidence for Qi in TCM is bioenergy.

Key words: Qi; bioenergy; Adenosine triphosphate; qi-invigorating herbal medicine; qi-regulating herbal medicine.

According to TCM theory, Qi (vital energy) refers to a kind of refined nutritive substance within the body. Qi is one of the most basic, the most important, and the most complicated concept in TCM. We propose a hypothesis that Qi is closely related to bioenergy according to the ancient concept of Qi and modern bioenergetics. TCM practitioners usually compose prescriptions made up of Qi-invigorating herbal medicines (QIHM) or Qi-flow regulating herbal medicines (QRHM) for Qi system diseases, and have accumulated abundant clinical experience for a long time. QIHM is a kind of herbal medicines which can invigorate Qi and treat syndromes of Qi deficiency, they have the effects of invigorating Qi, promoting the production of body fluid and tonifying the spleen and lung etc. QRHM is a kind of herbal medicines which can induce the flow of Qi, regulate the Qi system diseases and treat the

syndromes of stagnation of Qi or rebellious Qi etc. They can activate Qi to reduce pain, depress upward-reverse flow of Qi, break the stagnant Qi to remove masses etc. QIHM and QRHM have similar nature and attributive channels, but their flavours are different significantly. QIHM taste sweet while QRHM taste acrid-bitter, and their compositions are also different. Although Qi of TCM is similar to the concept of modern medical bioenergy in some aspects, the energy nature of Qi still lacks convincing evidence. Therefore, we take it as our basic point to approach the characteristics of QIHM and QRHM on energy metabolism. We have approached the rules of QIHM and QRHM from the production (oxidative phosphorylation), storage (creatine kinase activity) and regulation (adenylate energy charge) of bioenergy (ATP). Since there is no direct detection method on Qi, the widely used QIHM (ginseng, astragalus root, pilose asiabell root, white atractylodes rhizome) and QRHM (immature bitter orange, magnolia bark, green tangerine and lindera root) were selected to study the effect on energy metabolism to approach to the nature of Qi in TCM.

Sasang constitutional medicine (SCM) is a unique traditional Korean therapeutic alternative form of medicine. In both SCM and TCM theories, Qi is the most essential element, the 'driving force' that constitutes the body and maintains the activities of life, visceral functions and metabolism. In a generalized scope, the essence of Qi in SCM can be compared with that of energy in modern physiology. The metabolic process in physiology provides energy, kinetic and potential energies, whereas metabolism in SCM produces and regulates Qi. Since catabolism breaks own complex molecules into simple ones and releases kinetic energy, this pathway can be compared with the process of consuming Qi in SCM. Similarly, anabolism, which links together simple molecules to form more complex molecules and stores potential energy, is comparable with the process of producing and storing Qi in SCM. In terms of interior-exterior exchange, the process of taking up raw materials from the external environment to produce Qi in SCM (function of the spleen) corresponds to the process of digestion and absorption of food and water and inhaling air in physiology (Kim and Pham, 2009). To approach to the nature of Qi in TCM from bioenergetics, the effects of QIHM and QRHM on oxidative phosphorylation (OXPHOS), bioenergy level and creatine kinase (CK) activities were investigated.

Materials and methods

Animals and materials

Male Kunming mice (Grade II, Certificate No 2002-5), weighing 22 ± 2.0 g each, were purchased from Experimental Animal Center, Dalian University. All mice were cared for according to the Guiding Principles in the Care and Use of Animals. The experiment was approved by Medical College Council on Animal Care Committee of Dalian University (China) in accordance with NIH guidelines (NIH, 2002). Rodent laboratory chow and tap water were available *ad libitum* during the period. Spherisorb C₁₈ reversed-phase chromatographic column (4.6 mm×250 mm, 5 μm particle size) was produced by Dalian Institute of Chemistry and Physics, Chinese Academy of Sciences. Adenosine triphosphate (ATP), adenosine diphosphate (ADP), adenosine monophosphate (AMP), 2-Thiobarbituric acid (TBA), and 1,1,3,3-tetraethoxypropane (TEP) were from Sigma Chemical (St Louis, MO, USA). N-2-Hydroxyethylpiperazine-N'-2-ethane sulfonic acid (HEPES) was from Merck (Darmstadt, Germany). Coomassie Brilliant Blue G-250 (CBBG-250) was purchased from Fluka (Buchs SG, Switzerland). Bovine serum albumin (BSA) was from Boehringer Mannheim Corp. (Indianapolis, IN, USA). Tris(hydroxymethyl)aminomethane (Tris) was from Gibco BRL

(Grand Island, NY, USA). A commercial creatine kinase monitoring kit [N-acetyl-L-cysteine(NAC)-activated] was from Beijing Zhongsheng High-Tech Bioengineering Company (Beijing, China). All other chemicals and solvents used in the study were of analytical grade made in China. Ginseng, astragalus root, pilose asiabell root, white atractylodes rhizome, immature bitter orange, magnolia bark, green tangerine and lindera root, are *Panax ginseng* C.A. Mey (Tongrentang red ginseng), *Astragalus membranaceus* (Fisch.) Bge.var. *mongholicus* (Bge.) Hsiao, *Codonopsis pilosula* (Franch.) Nannf, *Atractylodes macrocephala* Koidz, *Citrus aurantium* L, *Magnolia officinalis* Rehd et Wils, *Citrus reticulate* Blanco and *Lindera aggregate* (Sims) Kosterm respectively, were purchased from Beijing Tongrentang Drugstore, and identified by professor Li Jiashi at Beijing University of Traditional Chinese Medicine.

Preparation of the aqueous extracts of QIHM and QRHM

Powdered dry ginseng, astragalus root, pilose asiabell root, white atractylodes rhizome, immature bitter orange, magnolia bark, green tangerine and lindera root were immersed in distilled water (the ratio of the drug and distilled water was 1:10) for 0.5 hour and extracted thrice with distilled water for 0.5 hour each in a boiling water bath. The filtrate was collected after filtration with gauze, mixed and condensed to 0.2 g crude drug/ml.

Animal groups

Mice in each QIHM and QRHM group (n=10) were administered respective aqueous extracts (4 g crude drug/kg/day) by oral gavage and mice in the control group received an equivalent volume of normal saline for 10 days, there are nine groups all together. All the mice were maintained with free access to food and drinking water.

Isolation of liver mitochondria

Mitochondria were isolated by differential centrifugation using a modified version of the protocol of Michele *et al.* (1992). Mice were dislocated and their livers were removed immediately and placed in an ice-cold isolation medium (containing 0.25 M sucrose, 0.5 mM EDTA and 3 mM HEPES, pH 7.4). Livers were homogenized with a motor-driven Teflon pestle in wet ice at 0°C. Following homogenization, samples were centrifuged at 1,000 g for 10 min. This, and all other centrifugation steps, used a Beckman JA-25.50 rotor and Beckman J₂-MC centrifuge at 4°C. Supernatants were removed and centrifuge at 12,000 g for 10 min. The pellets were washed twice in the isolation medium, and respun at 12,000 g. Following the final wash, mitochondria were resuspended in the same medium. Protein determinations were carried out using Bradford (1976) method.

Measurement of oxidative phosphorylation curve of liver mitochondria

Respiratory control ratio (RCR) of liver mitochondria was measured using the method described by Estabrook (1967). Oxygen consumption was measured at 30°C in a closed, stirred, and thermostatted glass vessel equipped with a Clark-type oxygen electrode in 2.0 ml respiration buffer. The respiration buffer (pH 7.4) consisted of sucrose 225 mM, EDTA 1 mM, MgCl₂ 5 mM, KCl 15 mM, KH₂PO₄ 15 mM, Tris 50 mM, L-glutamic acid 5 mM, DL-malate 10 mM, and mitochondrial protein 5 g/L. Respiratory state 3 (S₃) was the oxygen (O₂) consumption by mitochondria in the presence of substrate after the addition of 0.25 mM adenosine diphosphate (ADP, ADP is a potent stimulator of mitochondrial respiration). Respiratory state 4 (S₄) was the oxygen consumption when all the ADP has been phosphorylated. S₃ and S₄ can be calculated according to the oxidative phosphorylation

(OXPHOS) curve. Respiration rates were expressed in nanomoles atom O per minute per milligram of protein. RCR was the ratio of S_3 to S_4 respiration. P/O ratio is the number of ADP molecules phosphorylated per oxygen atom reduced.

Determination of creatine kinase activity

Mice were killed via dislocation, and skeletal muscle from the hind leg was rapidly removed, weighed and made into 1% homogenates with normal saline at 0°C. 2.0 ml homogenate was centrifuged at 2,000 g for 5 min, 100 μ l supernatant was added to 900 μ l normal saline and mixed, 10 μ l of which was used for determination of creatine kinase (CK) activity. CK activity was measured by using a commercial CK monitoring kit [N-acetyl-L-cysteine(NAC)-activated], following the manufacturer's protocol.

Measurement of ATP, ADP, and AMP in liver cells by HPLC

Mice were killed via dislocation, and livers were rapidly removed, weighed and made into 10% homogenates with normal saline at 0°C, 1 ml of ice-cold 0.3 M perchloric acid was added to 1 ml of 10% liver homogenates that were kept on ice for an additional 5 min. Harvested materials were centrifuged at 15,000 g at 4°C for 10 min. The supernatant was neutralized with 80 μ l of 3 M KOH, and tubes were kept on ice for an additional 30 min. The resulting precipitate was removed by centrifugation, and the supernatant was stored at -80°C until it was analyzed. 10 μ l of neutralized cell extract was used for determination of ATP, ADP, and AMP in liver cells, which was carried out by gradient RP-HPLC (reversed-phase high performance liquid chromatography) with ultraviolet detector at room temperature and with mobile phase at a rate of 0.8 ml/min. Mobile phases used for the gradient system were buffer A (0.05 M KH_2PO_4 - K_2HPO_4 , pH 6.0) and buffer B, consisting of buffer A plus 10% methanol (*v/v*). All buffers and solutions used for HPLC analysis were filtered and degassed through a 0.45 μ m filter. Gradient elution procedure: buffer A was used as mobile phase between 0 and 3 min, buffer A was changed from 100% to 0% and buffer B from 0% to 100% between 3 and 6 min, buffer B was mobile phase between 6 and 9 min, buffer A was the mobile phase after 9 min, all the running time was 12 min, the detection wavelength was set at 254 nm. ATP, ADP and AMP quantitation in liver cells was calculated by computing the peak area of them, identification and quantitative measurements of nucleotides were carried out by the injection of standard solutions of nucleotides with known concentrations. Standard curves were plotted for individual compounds and were used to determine the contents of ATP, ADP, and AMP in each sample. Total adenylate pool (TAP) and adenylate energy charge (AEC) were calculated by the following formulas respectively: $\text{TAP} = [\text{ATP}] + [\text{ADP}] + [\text{AMP}]$, $\text{AEC} = ([\text{ATP}] + 0.5[\text{ADP}])/\text{TAP}$. AEC represents a linear measure of the metabolic energy stored in the adenine nucleotide system.

Statistical analysis

Data were expressed as means \pm SD and statistical differences between groups were analyzed by Student's *t* test which was performed using SPSS 16.0 statistical software (SPSS Inc., Chicago, Illinois, USA). The probability (*P*) values <0.05 were considered to be statistically significant.

Results

The effects of QIHM and QRHM on OXPHOS of liver mitochondria

The liver is known to be the hub of the metabolism; it plays a major role in controlling glucose storage and flux. It is also known that, during heat stress, both lipids and

carbohydrate stores can be mobilized for energy generation to attenuate the stress response (Manoli *et al.*, 2007). In addition, many biochemical studies have been performed using mitochondria from liver cells. The rate of ATP synthesis and oxygen consumption (respiratory state 3) driven by complex I substrates, the respiratory control ratio (RCR) and P/O ratio were reduced in liver mitochondria by ginseng and astragalus root, but there were no significant effect on state 4 ($P > 0.05$) (Table 1). It showed that the efficiency of ATP production via ADP phosphorylation was decreased. In perfectly coupled mitochondria, there would be no proton leak across the inner mitochondrial membrane, and the entire gradient generated by the respiratory chain would be used to generate ATP (Boudina and Dale Abel, 2006). Control of oxidative phosphorylation (OXPHOS) allows a cell to produce only the precise amount of ATP required to sustain its activities. Recall that under normal circumstances, electron transport and ATP synthesis are tightly coupled. The value of P/O ratio (the number of molecules of Pi consumed for each oxygen atom reduced to H₂O) reflects the degree of coupling observed between electron transport and ATP synthesis (Mckee and Mckee, 1999). Oxygen consumption increase dramatically when ADP is supplied. The control of aerobic respiration by ADP is referred to as respiratory control. Substrate oxidation accelerates only when an increase in the concentration of ADP signals that the ATP pool needs to be replenished. This regulation matches the rates of phosphorylation of ADP and of cellular oxidations via glycolysis, the citric acid cycle, and the electron-transport chain to the requirement for ATP (Horton, *et al.*, 2002).

Ginseng and astragalus root can decrease oxygen consuming rate and RCR of liver mitochondria obviously, I consider this is appearance of lowering standard metabolic rate and is a kind of protective adaptation. Qi deficiency patients need nutritional supplements, adequate rest, and should reduce energy consumption, ginseng and astragalus root can just achieve this goal, while the effect of other QIHM is not obvious. All the four QRHM can increase RCR and P/O ratio (Table 1).

The effects of QIHM and QRHM on creatine kinase activities

Although ATP is the instantaneous donor of bio-energy in the body, it can not be stored, but phosphocreatine (PCr) can. Among the energy metabolism enzymes in the muscle cells, creatine kinase (CK, EC 2.7.3.2) plays a significant role in energy homeostasis. CK is distributed in skeletal muscle, heart, brain and other tissues and catalyzes the reversible conversion from ATP and creatine (Cr) to ADP and phosphocreatine (PCr, high energy phosphate able to supply ATP on demand) (Zhao *et al.*, 2007; Brancaccio *et al.*, 2007). CK performs a pivotal physiological role in high energy consuming tissues, by acting as an energy buffering and transport system between the sites of ATP production and consumption by ATPases (Bessman and Geiger, 1981). Creatine kinase rapidly provides ATP to highly energy-demanding processes, the rate of transfer of the phosphoryl group from PCr to ADP by CK is greater than the maximum rate of ATP generation by OXPHOS, and this ensures rapid resynthesis of ATP (Wallimann *et al.*, 1998). High tissue CK activity, whether constitutive, induced, or both, may rather directly enhance contractile responses by enhancing cellular energy and contractile reserve (Brewster *et al.*, 2007). Greater CK activity could bind more ADP and increase the rate of the conversion of ADP to ATP, which could reduce the relative levels of local ADP at the contractile proteins (Clark, 1994). CK enhances ATP buffer capacity. We believe that high CK activity may be quite beneficial for rapid and dynamic energy demand. Thus, increased CK activity in muscle tissue might lead to hyperdynamic activity. Both QIHM and QRHM can stimulate activity of CK significantly in the storage of energy, and QRHM is stronger than QIHM (Table 1).

Group	State 3 (nmol /min/mg) ^d	State 4 (nmol /min/mg) ^d	RCR	P/O	CK (U/μg) ^e
Control	83±11	19.4±2.6	4.2±0.6	2.61±0.28	2.25±0.28
<i>Panax ginseng</i>	66±11 ^b	18.3±1.9	3.6±0.4 ^a	2.21±0.30 ^b	2.58±0.26 ^a
<i>Astragalus membranaceus</i>	68±13 ^a	18.0±2.5	3.7±0.4 ^a	2.32±0.24 ^a	2.60±0.29 ^a
<i>Codonopsis pilosula</i>	80±15	18.3±2.2	4.3±0.6	2.66±0.26	2.59±0.29 ^a
<i>Atractylodes macrocephala</i>	81±14	19.1±1.8	4.2±0.7	2.60±0.28	2.63±0.32 ^a
<i>Citrus aurantium</i>	91±10	18.5±2.9	4.9±0.4 ^b	2.89±0.27 ^a	3.32±0.27 ^b
<i>Magnolia officinalis</i>	99±13 ^b	19.0±2.1	5.1±0.5 ^b	2.92±0.34 ^a	3.20±0.44 ^b
<i>Citrus reticulata</i>	96±12 ^a	19.3±2.2	4.9±0.6 ^a	2.88±0.22 ^a	3.09±0.49 ^b
<i>Lindera aggregate</i>	86±16	16.6±2.3 ^a	5.2±0.7 ^b	2.93±0.31 ^a	3.23±0.35 ^b

^d nanomole O₂ per minute per milligram protein (nmol O₂ min⁻¹ mg protein⁻¹). ^e Unit of CK activity per microgram protein (U μg protein⁻¹). ^a P < 0.05 vs Control. ^b P < 0.01 vs Control.

Table 1. Effects of QIHM and QRHM on respiratory function of liver mitochondria and CK activities *in vivo* (n=10, mean ± standard deviation).

The effects of QIHM and QRHM on energy state of mice hepatocyte in vivo

Adenylate energy charge (AEC) is a sign parameter of cellular energy state (the higher [ATP], the larger the AEC, the higher [AMP], the smaller the AEC), when the tissue's ATP level increased, the pathway for generating ATP would be inhibited; When ATP levels drop due to over consumption of energy by the body, the pathway for generating ATP would be stimulated. AEC represents a linear measure of the metabolic energy stored in the adenine nucleotide system. AEC remained at a fairly narrow range of changes, just like pH value in the cells, energy charge also has a buffering effect, AEC of the most cells fluctuate in the 0.8-0.95 range. Ginseng is commonly known as a high-level herb for tonifying Qi, according to our former study, *Panax ginseng* polysaccharide could increase levels of ATP, TAP and AEC in liver cells under chronic hypoxia condition, therefore, improving energy status, protect mitochondria by inhibiting mitochondrial swelling (Li *et al.*, 2009). It is worth notice that all the four QIHM can increase levels of ATP, AEC and TAP, the effect of ginseng is the most potent; on the contrary, all the four QRHM can decrease levels of ATP, AEC and TAP in liver cells. All the four QIHM can't affect the levels of ADP and AMP; while all the four QRHM can decrease levels of ADP, and increase levels of AMP in liver cells. In a word, QIHM and QRHM increase and decrease bioenergy level of liver cells respectively *in vivo*. Therefore, Qi is closely related to bioenergy. This result shows that the decreased energy state of the body can be improved by taking QIHM and the effect of QRHM is contrary to that of QIHM. Therefore, the effects on energy regulation of two types of Qi system drugs are different (Table 2).

The similarities and differences in natures, tastes, channel tropism and compositions

Qi is an important concept in physiology and pathology of TCM, directed towards the two main therapeutic principles of Qi—qi-invigoration and qi-flow regulation are self-evidently extreme important. The two therapeutic principles are closely related, complementary and

two-way adjustable, and difficult to substitute by others. If they are used properly, they will play an important clinical role in overcoming various difficult diseases. Since there is no direct detection method on Qi, the widely used QIHM (ginseng, astragalus root, pilose asiabell root, white atractylodes rhizome) and QRHM (immature bitter orange, magnolia bark, green tangerine and lindera root) were selected to study the effect on energy metabolism to approach to the nature of Qi in TCM, Comparison of the regulatory role of QIHM and QRHM are summarized as follows.

Group	ATP/ (mmol ·L ⁻¹)	ADP/ (mmol ·L ⁻¹)	AMP/ (mmol ·L ⁻¹)	TAP/ (mmol ·L ⁻¹)	AEC
Control	1.02±0.28	0.78±0.20	0.09±0.07	1.89±0.33	0.745±0.021
<i>Panax ginseng</i>	1.41±0.36 ^a	0.86±0.24	0.07±0.05	2.34±0.46 ^a	0.786±0.031 ^b
<i>Astragalus membranaceus</i>	1.36±0.31 ^a	0.84±0.23	0.11±0.05	2.31±0.38 ^a	0.770±0.026 ^a
<i>Codonopsis pilosula</i>	1.33±0.22 ^a	0.85±0.25	0.12±0.08	2.30±0.32 ^a	0.763±0.015 ^a
<i>Atractylodes macrocephala</i>	1.25±0.19 ^a	0.81±0.26	0.10±0.06	2.16±0.28	0.764±0.016 ^a
<i>Citrus aurantium</i>	0.70±0.26 ^a	0.53±0.14 ^b	0.25±0.12 ^b	1.48±0.27 ^b	0.651±0.024 ^b
<i>Magnolia officinalis</i>	0.71±0.23 ^a	0.61±0.13 ^a	0.19±0.09 ^a	1.51±0.23 ^b	0.673±0.033 ^b
<i>Citrus reticulata</i>	0.75±0.25 ^a	0.49±0.14 ^b	0.27±0.12 ^b	1.51±0.26 ^a	0.660±0.028 ^b
<i>Lindera aggregate</i>	0.61±0.22 ^b	0.47±0.16 ^b	0.29±0.13 ^b	1.37±0.21 ^b	0.618±0.027 ^b

All values are mean±SD (n=10). ^aP <0.05, ^bP <0.01 versus Control group. Each value expressed in mmol·L⁻¹ (ATP, ADP, AMP, TAP) or as a ratio (AEC). ATP: adenosine triphosphate; ADP: adenosine diphosphate; AMP: adenosine monophosphate; TAP: total adenylate pool; AEC: adenylate energy charge

Table 2. The effects of QIHM and QRHM on energy status of mice hepatocytes *in vivo* (n=10, mean ± standard deviation).

The channel tropism of QIHM and QRHM are all the spleen, lung and stomach channel, this shows that they have common target sites in the body. The natures of QIHM are mild or warm, and QRHM are warm, the properties of the two kinds of medicines are similar. QIHM are sweet taste, medicines with sweet taste have the effects of invigoration, normalizing the function of the stomach and spleen, and buffering emergency, etc. they are usually used for tonifying deficiency, easing the pain, and harmonizing the property of different drugs, they are mostly moist and good at nourishing and moistening dryness evil. QRHM are bitter and/or hot tastes, medicines with bitter taste have the effects of purgation and drying the wetness evil etc. medicines with hot taste have the effects of dispersing, promoting the circulation of qi and blood. Therefore, QIHM and QRHM have obviously different effects due to the different tastes. All the QIHM contain more water-soluble carbohydrate due to the sweet taste, and almost all QRHM don't contain or contain less water-soluble carbohydrate composition, most of them contain volatile components (Zheng *et al.*, 1998). Therefore, QIHM and QRHM have obviously different components due to the different tastes (Table 3).

Effects	Items	QIHM	QRHM
Same or similarities	1. channel tropism	spleen, lung and stomach	spleen, lung and stomach
	2. natures	mild or warm	warm
	3. CK activity	increase	increase
Cross effects	1. RCR	decrease or no effect	no effect or increase
	2. oxygen consumption rate	decrease or no effect	no effect or increase
Differences	1. tastes	sweet	bitter and/or hot
	2. compositions	more carbohydrate	volatile components
	3. bioenergy level	increase	decrease

Table 3. Comparisons of the regularity between QIHM and QRHM

11. Conclusion

Qi, is the most basic, the most important and the most nebulous concept, and can be called the biggest enigma in TCM. Research on the nature of Qi in TCM has important theoretical and clinical significance. By analyzing and concluding generation process and function of Qi and bio-energy (ATP), and the effects of Qi-invigorating herbal medicines (QIHM) and Qi-regulating herbal medicines (QRHM) on energy metabolism, the following conclusions can be drawn: Qi and bioenergy have common source and identical functions. Regulation on energy metabolism by QIHM and QRHM showed significant differences due to the different chemical compositions and flavors, QIHM and QRHM are able to improve and decrease the energy state of the body respectively. QIHM invigorate "Qi" through increased intracellular ATP level; and QRHM regulate "Qi" by reducing intracellular ATP levels. Thus, there are many common natures between Qi and bio-energy. Studies on the nature of Qi in TCM should be carried out in other areas of life science due to the wide implications for Qi. With the rapid development of modern life science, we believe that mankind will reveal the truth of the enigma in the near future, it would be better for clinical services.

Without having a scientific model, we cannot advance the research. A future step in Qi research would be to set up effective model to assess Qi effect and identify the effect of Qi on energy metabolism which plays the central role in life activities. If such a model is found, then, the next task might be to find the mechanism of how Qi act. We have a long way to go, but at least, we now have a model which is based upon biochemical pharmacology. With this, we can advance our search to understand the mechanisms of Qi-related phenomena and Qi-healing processes, which have been known for 4000 years.

12. References

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During the recent years, traditional Chinese medicine (TCM) has attracted the attention of researchers all over the world. It is looked upon not only as a bright pearl, but also a treasure house of ancient Chinese culture. Nowadays, TCM has become a subject area with high potential and the possibility for original innovation. This book titled *Recent Advances in Theories and Practice of Chinese Medicine* provides an authoritative and cutting-edge insight into TCM research, including its basic theories, diagnostic approach, current clinical applications, latest advances, and more. It discusses many often neglected important issues, such as the theory of TCM property, and how to carry out TCM research in the direction of TCM property theory using modern scientific technology. The authors of this book comprise an international group of recognized researchers who possess abundant clinical knowledge and research background due to their years of practicing TCM. Hopefully, this book will help our readers gain a deeper understanding of the unique characteristics of Chinese medicine.

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