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Yang/Qi Invigoration : An Herbal Therapy For Chronic Fatigue Syndrome With Yang Deficiency?

Prof. Ko Kam-Ming
The Hong Kong University of Science & Technology

The Assessment Result Of Exercise On Fall Efficacy Among Community-dwelling Elders

Dr. Cynthia Wu
The Hong Kong Polytechnic University

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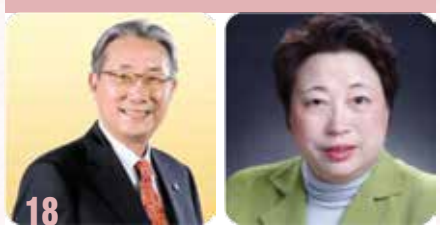

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A Word from the Editor in Chief

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Dear Readers,

Wish you and your love ones Happy and Healthy 2015!

Thank you for your continued interest in our "Asia Health Care Journal", the team is really excited for the coming issue. We bring in healthcare professional from different fields to share with their experience. Topics covered "An Herbal Therapy For Chronic Fatigue Syndrome With Yang Deficiency" by Prof. Ko, "The Impact Of Exercise On Fall Efficacy Among Community-dwelling Elders" by Dr. Cynthia Wu, "FDA Commissioner's Fellowship" by Tehyen Chu. We also have the medical device commercialization process sharing by Kenny Pang, and the "5 Steps To a Successful Product Launch"by Calvin and Jainam.

Hope you enjoy the reading and contact us if you are interested in sharing your healthcare related research. ■

Prof. Jack Wong
Asia Regulatory Professional Association

The Asia Regulatory Professional Association (ARPA) is an organization of healthcare regulatory affairs professionals in Asia. ARPA aims to raise the standard and social recognition of regulatory professionals as part of healthcare team.

Details of ARPA can be found in
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Values of Asia Regulatory Professional Association (ARPA)

To uphold and enhance standards among regulatory affairs professionals in Asia and to encourage the creation of better educated regulatory teams in the area, regardless of the background and regulatory situation of their countries. A new body, the Asia Regulatory Professional Association (ARPA), was established in 2010 with more than 3,500 members today.

Structure

ARPA strives to be neutral. There is a good balance of key individuals from different countries as well as from academic and regulatory bodies.
The ARPA chairman is Dr. Saleh S. Al-Tayyar from Saudi FDA and co-chairman is Madam Liu Li-Ling from Taiwan FDA. Dr. Saleh and Madam Liu are also the chairman and co-chairman in Asia Harmonisation Working Party (AHWP) to help avoiding duplication with relevant work that is ongoing within that organization which aims to work towards greater harmonization in medical device regulations in Asia.
Prof. Rosanna Peeling is our advisor (ex-WHO staff, now working in London University).

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Research expertise: Antioxidant mechanism(s) of Chinese tonic herbs with focus on the regulation of cellular glutathione redox status; Pharmacological basis of Yang/Qi-invigoration in Chinese medicine

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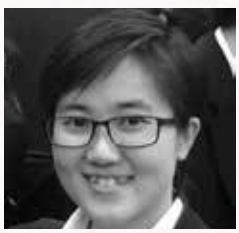

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Yang/Qi Invigoration : An Herbal Therapy For Chronic Fatigue Syndrome With Yang Deficiency?

Abstract

According to traditional Chinese medicine (TCM) theory, Yang and Qi are driving forces of biological activities in the human body. Based on the crucial role of the mitochondrion in energy metabolism, we propose an extended view of Yang and Qi in the context of mitochondrion-driven cellular and body function. It is of interest that the clinical manifestations of Yang/Qi deficiencies in TCM resemble those of chronic fatigue syndrome in Western medicine, which is pathologically associated with mitochondrial dysfunction. By virtue of their ability to enhance mitochondrial function and its regulation, Yang- and Qi-invigorating tonic herbs, such as Cistanches Herba and Schisandrae Fructus, may therefore prove to be beneficial in the treatment of chronic fatigue syndrome with Yang deficiency.

Concepts of Yang and Qi in traditional Chinese medicine

Traditional Chinese medicine (TCM) views the human body as an organic entity, consisting of an assembly of various organs that function in a mutually inter-dependent manner [1]. "Yin/Yang Theory" is a conceptual framework of TCM. According to Yin/Yang theory, the universe is a result of a unity of opposing forces, namely, Yin and Yang. The dynamic equilibrium between Yin and Yang determines the status/phase of a given object [2]. With this philosophical concept, TCM classifies body structures,

explains clinical symptoms and guides treatment of diseases on the basis of the Yin/Yang Theory [3]. Vital substances (namely, essence, Qi, blood and body fluid) are fundamental to life and provide the material and functional basis of the human body [1]. According to Yin/Yang Theory, functional activities of the body (such as Qi) are classified as Yang, while the material basis (such as essence, blood and body fluids) of vital functions belongs to Yin [4].

TCM theory states that the interaction between Yin and Yang generates Qi. Qi refers to the refined and nutritive substances flowing in the body as well as the functional status of organs and tissues. Within this framework, the complete deprivation of Qi signifies death in TCM [5]. To provide vital energy for supporting life activities, Qi flows through the meridians and nourishes the organs. With regard to the role of Qi in modulating physiological functions, Qi can be sub-categorized into three functionally-related types, namely primordial Qi, pectoral Qi and normal Qi, with the latter being sub-divided into nutritive Qi and defensive Qi (Fig. 1) [5]. In essence, primordial Qi, which is also known as "congenital essence of the kidney" is inherited from parents, and is responsible for stimulating growth and development, as well as invigorating the vital activities of organs in the body, i.e. it is Yang in nature. Pectoral Qi is comprised of the "natural air" inhaled by the lungs and the "grain Qi" transformed from food and water by the spleen and stomach, i.e. it is Yin in nature. The principal actions of pectoral Qi are to facilitate gas exchange in the lungs and regulate blood circulation in the heart as well as its rate of beating. Primordial Qi combines with pectoral Qi to form normal Qi (also called Zheng Qi in Chinese), which circulates in the body for supporting various body functions. The interrelationship between primordial Qi and pectoral Qi is consistent with the notion that Qi (or normal Qi) arises from an interaction between Yin and Yang. Normal Qi (generally referred to as Qi hereafter) manifests as two functions, namely nutritive Qi and defensive Qi. While nutritive Qi nourishes the internal organs to sustain the physiological functions of the body, defensive Qi protects the body against disease-causing internal (inflammation and cancer) and external (bacteria and viruses) factors.

Biochemical and physiological basis of Qi function

Over the past decades, the mitochondrion has been considered to be a central co-ordinator of life and death in cells by virtue of its regulatory role in both bio-energetics and programmed cell death [6]. According to TCM theory, the depletion of Qi is casually linked to death. In this regard, the concept of Qi in TCM is consistent with the vital role of mitochondria in determining life and death within the conceptual framework of Western medicine.

The mitochondrion is the "power house" of the cell, where the aerobic metabolism of fuel molecules takes place. In aerobic metabolism, acetyl-CoA, which is formed from glucose via glycolysis and oxidative decarboxylation of pyruvate, enters the Krebs cycle occurring in the mitochondrial matrix. Acetyl CoA is ultimately oxidized to carbon dioxide, with the concomitant production of the high energy reducing equivalents, NADH and FADH2. Both NADH and FADH2 then donate their high energy electrons to the mitochondrial electron transport chain that generates a proton gradient across the mitochondrial inner membrane. By utilizing the electrochemical potential energy stored in this proton gradient, ATP synthase synthesizes ATP from ADP. ATP, a molecule with high phosphoryl transfer potential (i.e. potential energy), energizes a number of endergonic reactions in the cell, particularly those supporting vital activities. During the mitochondrial electron transport process, reactive oxygen species (ROS) are unavoidably produced from the leakage of electrons, particularly from complex I and III. The excessive production of ROS from mitochondria, under conditions of high respiratory activity and/or in the presence of threats to homeostasis, results in an increase in oxidative stress. Under conditions of severe oxidative stress, mitochondrial permeability transition pores open, with the subsequent non-specific release of pro-apoptotic factors (e.g. cytochrome c and apoptosis-inducing factor), leading to caspase-dependent and caspase-independent cell death [7]. With regard to the regulation of bio-energetics and cell death, the mitochondrion can be considered as the functional unit of Qi. This postulation may explain the relatively short lifespan of erythrocytes which do not have mitochondria.

Primordial Qi, which is the primary driving force of human life in the context of TCM, can be functionally related to the pumping action of the heart that maintains the circulation of the blood throughout the body (Fig. 1). Recently, by adopting the concept of "resonance", Wang et al. have proposed a novel model for explaining how a pumping heart can propel the circulation of blood throughout the body [8,9]. In essence, the arterial system and various organs in the body are connected by branches of arterial blood vessels. The rhythmic contraction of the heart causes vibrations in the arteries, and the potential energy stored in elastic walls of these blood vessels will subsequently be transmitted through the blood stream. It is hypothesized that the pumping action of the heart can provide the arterial system with a series of harmonic frequencies of oscillations that can be transmitted to various target organs. If the natural frequency of the target organ synchronizes with one of these harmonic frequencies, the resultant resonance will facilitate the entry of blood into the organ. Despite the fact that this "resonance" model has not been generally accepted in Western medicine, it paints a picture describing how primordial Qi may work by driving the circulation of blood or Qi throughout the body. Pectoral Qi results from the combination of inhaled fresh air and ingested food "essence" (i.e. essential nutrients). The digested and subsequently absorbed nutrients are first transported to the liver for assimilation. Accordingly, the function of pectoral Qi may be related to the assimilation of ingested nutrients.

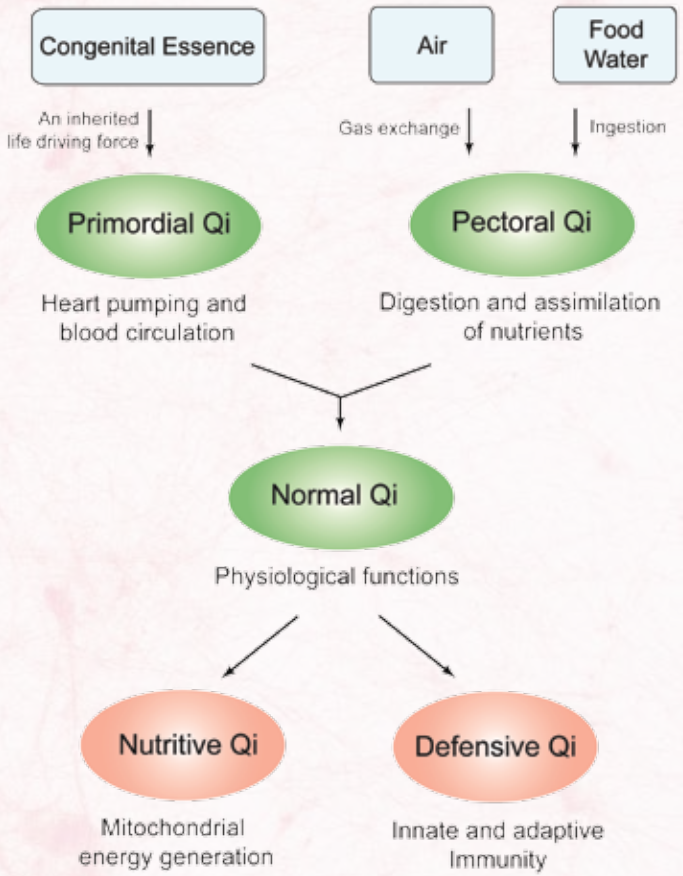

Fig.1. Biochemical and physiological basis of Qi function

Primordial Qi (Yang) interacts with pectoral Qi (Yin) to form the normal Qi, which is comprised of nutritive Qi and defensive Qi. Nutritive Qi is responsible for nourishing visceral organs. In this regard, nutritive Qi may be related to the efficiency of tissues/cells to generate energy from nutrients, i.e. the efficiency of mitochondria to generate ATP using fuel molecules (Fig.1). This postulation is strengthened by the earlier notion that the mitochondrion is regarded as the cell origin of Qi (energy). In this regard, nutritive Qi may also be Yang in nature. Defensive Qi is responsible for protecting the body against disease-causing internal and external factors. In the face of pathogen invasion, the innate immune response is elicited, during which phagocytic cells (macrophages and neutrophils) migrate to the site of invasion and engulf the invading pathogen. The engulfed pathogen is then engulfed by ROS/lysozymal vesicles inside phagocytes and is thereby degraded. The "respiratory burst" involves the NADPH oxidase-catalyzed generation of ROS in phagocytic cells. According to TCM theory, bone (marrow), blood and body fluid, which are enriched with immune cells, are classified as Yin, suggesting that defensive Qi may be Yin in nature. Recently, age-related deterioration of immunity ("immunosenescence") was found to be associated with oxidative stress [10], and immunosenescence is closely related to the aging process [11]. In this connection, the involvement of immunosenescence in aging is consistent with the TCM theory which states that the substantial depletion of Qi is the primary cause of aging. To safeguard immunosenescence caused by oxidative stress, immune cells are equipped with an antioxidant defense system, which is composed of free radical scavengers and antioxidant enzymes. The fortification of antioxidant defense can therefore enhance immune function and thereby indirectly invigorate the defensive Qi.

'Yang/Qi deficiency" disease: chronic fatigue syndrome

Given the causal relationship between Yang and Qi, we adopted the term "Yang/Qi" in the subsequent discussion on chronic fatigue syndrome (CFS). According to TCM theory, Yang/Qi are the driving forces of biological activities in the human body. Deficiencies in Yang/Qi display a high prevalence in the "fatigue syndrome" in humans [12]. While Yang-invigoration involves the enhancement of body function and energy metabolism in various organs, Yang deficiency is characterized by decreased metabolic activities, as evidenced, for example, by a reduction in body temperature [13]. A recent metabonomic study has shown that a severe impairment in both glucose and lipid metabolism was observed in a rat model of hydrocortisone-induced kidney 'Yang deficiency' [14], which reflects a deficiency of nutritive Qi in TCM. An impaired mitochondrial functional capacity, as evidenced by reduced urinary levels of creatinine (a product of phosphocreatinine breakdown) and citrate (an important metabolic intermediated in the Krebs cycle), were also found in animals with kidney 'Yang deficiency' [15]. The use of 1H nuclear mass resonance spectrometry and partial least squares discriminant analysis in patients suffering from Yang deficiency syndrome revealed that blood lipid parameters, the ratio of low density lipoproteins to very low density lipoproteins, lactic acid and sugars, which are fuel molecules or metabolites of energy metabolism, were found to be unbalanced and/or abnormal [16], indicative of a dysregulation of mitochondrial energy metabolism.

Interestingly, CFS in Western medicine partially resembles the Yang/Qi deficiency-induced fatigue syndrome in TCM [17]. Unlike fatigue, which is a transient, a common self-limiting symptom, CFS is an illness characterized by a persistent (or relapsing) debilitating and clinically unexplained fatigue that leads to a substantial impairment in functional status and subsequent personal and economic morbidity [18]. Patients suffering from CFS exhibit a profound disabling fatigue for at least 6 months, which is accompanied by numerous rheumatological, infectious and neuropsychiatric symptoms [18]. CFS is a heterogeneous syndrome, for which there appears to be a genetic predisposition, characterized by a variety of pathophysiological features including neuro-endocrine abnormalities, increased susceptibility to infections, obesity and chronic stress. Despite the diversity of these pathophysiological anomalies, mitochondrial dysfunction has been shown to be crucially involved in the development of CFS. Studies focusing on CFS-induced changes in gene expression demonstrated a differential expression pattern of mitochondria-related genes and a decrease in mitochondrial metabolic processing in CFS patients (Fig. 2) [19]. It was also found that the structural integrity of mitochondria in skeletal muscle was disrupted, which was likely related to the reduction in the energy level of patients suffering from CFS [20,21]. Cross-sectional studies using a magnetic resonance technique also identified distinctive and reproducible muscle and cardiac biogenetic abnormalities in CFS patients [22], which is a manifestation of Yang deficiency in TCM. Patients suffering from CFS displayed a marked increase in intramuscular acidosis in response to repeated exercise when compared with non-fatigued controls, suggesting an increased reliance on anaerobic metabolism as a result of the reduced mitochondrial oxidative phosphorylation capacity [23]. In addition, a clinical study investigating the association between CFS and mitochondrial function proposed that as a heterogeneous syndrome, CFS is not necessarily associated with the impairment of mitochondrial integrity, but rather with a deficit in mitochondrial functional capacity, as evaluated by the amount of cellular magnesium-complexed ATP, the capacity of mitochondrial oxidative phosphorylation and the efficiency of ADP/ATP-exchange between mitochondria and cytosol (Fig.2). The findings demonstrated a significant correlation between the degree of mitochondrial dysfunction and the severity of CFS.21 However, some symptoms of CFS resemble the manifestation of Yin deficiency, such as an increased sweating [24], a low grade fever [25] and a dryness of mucous membrane [26]. In addition, the dysfunction of immune system (defensive Qi, i.e. Yin in nature) was found to be associated with CFS [27,28]. We hereby propose that CFS can be divided into 2 sub-categories in terms of clinical symptoms: Yang-deficient type with mitochondrial dysfunction (c.f. nutritive Qi) and Yin-deficient type with immune/body fluid regulatory dysfunction (c.f. protective Qi).

A growing body of evidence has suggested the involvement of mitochondrial dysfunction in the pathogenesis of CFS with Yang/Qi deficiency. In this connection, physical exercise, which was shown to improve oxidative capacity of skeletal muscle in patients with mitochondrial myopathy [29], is being proposed as a treatment for CFS [30]. Clinical studies have revealed that graded exercise therapy and cognitive behavioral therapy produced beneficial effects in patients with CFS [31,32]. Based on a body of clinical evidence, Van Cauwenbergh et al. have summarized practice guidelines of exercise intervention for CFS patients [30]. However, Kindlon reported harmful side effects associated with the graded exercise therapy and cognitive behavioral therapy in some CFS patients [33]. Presumably, the inability of the graded exercise therapy and cognitive behavioral therapy to ameliorate the symptoms of some CFS patients may be due to the existence of Yang-deficient and Yin-deficient types of CFS. Whether or not exercise intervention is the panacea for Yang-deficient type of CFS clearly requires more extensive clinical investigation.

Yang- and Qi-invigorating herbs and mitochondrial function

In the realm of TCM, a pathological condition is caused by an imbalance of Yin/Yang status in the body. A prescription with tonic herb(s) can help to restore the balance of Yin and Yang and achieve a healthy condition. Tonic herbs are generally classified into four categories on the basis of their health-promoting actions, namely 'Yang-invigorating', 'Qi-invigorating', 'Yin-nourishing' and 'blood-enriching' herbs (Table 1). The 'Qi-invigorating' and 'blood-enriching' herbs possess Yang and Yin characteristics, respectively. With the notion that Yang and Qi are related to mitochondrial energy metabolism in the body, the prescription of Yang-invigorating and Qi-invigorating herbs was found to enhance mitochondrial ATP generation [34], which may be beneficial to patients with CFS of Yang-deficient type. Consistently, Yin-nourishing herbs were found to produce an im-

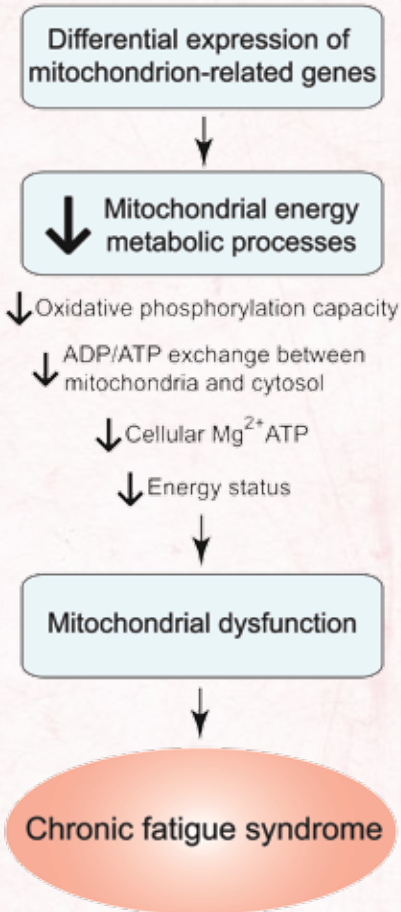

Fig.2. A hypothesis of mitochondrial dysfunction-mediated chronic fatigue syndrome

Yang-invigorating	Qi-invigorating
Eucommiae Cortex	Schisandrae Frutus
Psoraleae Fructus	Ziziphi Fructus
Cistanches Herba	Astragali Radix
Cynomorii Herba	Codonopsis Radix
Epimedii Herba	Fici Radix
Dipsaci Radix	Ginseng Radix
Morindae Radix	Glycyrrhizae Radix
Cibotii Rhizoma	Pseudostellariae Radix
Drynariae Rhizoma	Quinquefolii Radix
Cuscutae Semen	Atractylodis Rhizoma
	Dioscoreae Rhizoma

Yin-nourishing	Bood-enriching
Ligustri Fructus	Lycii Fructus
Dendrobii Herba	Mori Fructus
Ecliptae Herba	Testa Dolichoris
Asparagi Radix	Loranthi Ramulus
Ophiopogonis Radix	Angelicae Radix
Oryzae Radix	Polygoni Radix
Polygonati Rhizoma	Rehmanniae Paraparata Radix
Prinsepiae Semen	Polygonati Rhizoma
	Sesami Semen

Table 1. Different categories of Chinese tonic herbs

munomodulatory effects, presumably invigorating the defensive Qi (Yin) [35]. Recent studies have compared the effectiveness of various Yang-invigorating herbs in increasing mitochondrial ATP generation capacity (ATP-GC) in H9c2 cardiomyocytes in vitro and in rat hearts ex vivo. Cistanches Herba was found to increase the ATP-GC in H9c2 cardiomyocytes and in rat hearts, with the extent of stimulation being most potent among all tested Yang-invigorating herbs. Among Qi-invigorating herbs, Schisandrae Fructus has been shown to confer cellular/tissue protection against oxidative stress in rodent brain, heart, liver and skin tissues via the enhancement of mitochondrial antioxidant status [36]. In this regard, we sought to review the pharmacological actions of two commonly prescribed Yang- and Qi-invigorating herbs in relation to their beneficial effects on mitochondrial function.

Cistanches Herba, one of the 'Yang-invigorating' tonic herbs, was found to enhance mitochondrial respiration, as indicated by a significant increase in ATP-GC and mitochondrial state 3 respiration in H9c2 cells and in isolated rat heart mitochondria [37]. Cistanches Herba was also shown to induce mitochondrial uncoupling in both cell and animal models. The induction of mitochondrial uncoupling constitutes a substrate cycle involving the mitochondrial electron transport chain, which results in an increase in responsiveness of mitochondria to cellular energy demand [38]. The induction of mitochondrial uncoupling can in turn activate mitochondrial electron transport, which is associated with increased mitochondrial ROS production [37]. The sustained low level of mitochondrial ROS production triggers a series of cellular responses, including mitochondrial biogenesis, via the activation of AMP-activated protein kinase (AMPK) pathway [39,40]. Taken together, the Cistanches Herba-induced increase in mitochondrial number, together with the augmented mitochondrial responsiveness to energy demand, allow sufficient energy generation to maintain physical and mental activities and thereby produce beneficial effect in CFS patients with Yang deficiency (Fig.3).

Schisandrae Fructus (namely Wu-Wei-Zi in Chinese), the fruit of Schisandra chinensis, is a Qi-invigorating herb. Schisandrae Fructus possesses five tastes, namely sweet, sour, bitter, astringent and salty, which, according to "Five-Element Theory", correspond to five visceral organs (spleen, liver, heart, lung and kidney, respectively) in TCM [41]. According to TCM, Schisandrae Fructus can invigorate the Qi of these five visceral organs [41]. Over the past few decades, extensive research has focused on investigating the pharmacological activities of Schisandrae Fructus, particularly those of its polysaccharide and lignan components. Polysaccharides isolated from Fructus Schisandrae (namely SCP-IIa and SCPP11) were found to produce an immunomodulatory effect on peritoneal macrophages and lymphocytes in mice [42,43]. Among the lignans, schisandrin B (Sch B), the most abundant dibenzocyclooctadiene lignan in Schisandrae Fructus, was shown to possess antioxidant and anti-inflammatory activities [44]. A huge body of experimental evidence has shown that Sch B can enhance mitochondrial glutathione antioxidant status and thus protect against oxidant-induced injury under both in vitro [45] and in vivo [46] experimental conditions. Mechanistic studies have demonstrated that Sch B is metabolized by cytochrome P-450, with a concomitant production of a low level of ROS [47]. Conceivably, these "signaling ROS" then stimulate a redox-sensitive ERK (extracellular signal-regulated kinases) / Nrf2 (nuclear factor erythroid-2 related factor 2)/ EpRE (electrophile responsive element) signaling pathway, with a resultant expression of antioxidant proteins [47]. As proposed by the "Mitochondrial Theory of Aging", mitochondrial dysfunction is mainly caused by cumulative oxidative damage [48]. The Sch B-elicited glutathione antioxidant response can preserve the structural integrity of mitochondria in the face of oxidative challenge, which in turn can indirectly improve the functional capacity of mitochondria, as evidenced by an elevation of ATP-GC in Sch B-treated mice [49]. These findings therefore suggest that the Qi-invigorating action of Sch B may also be beneficial

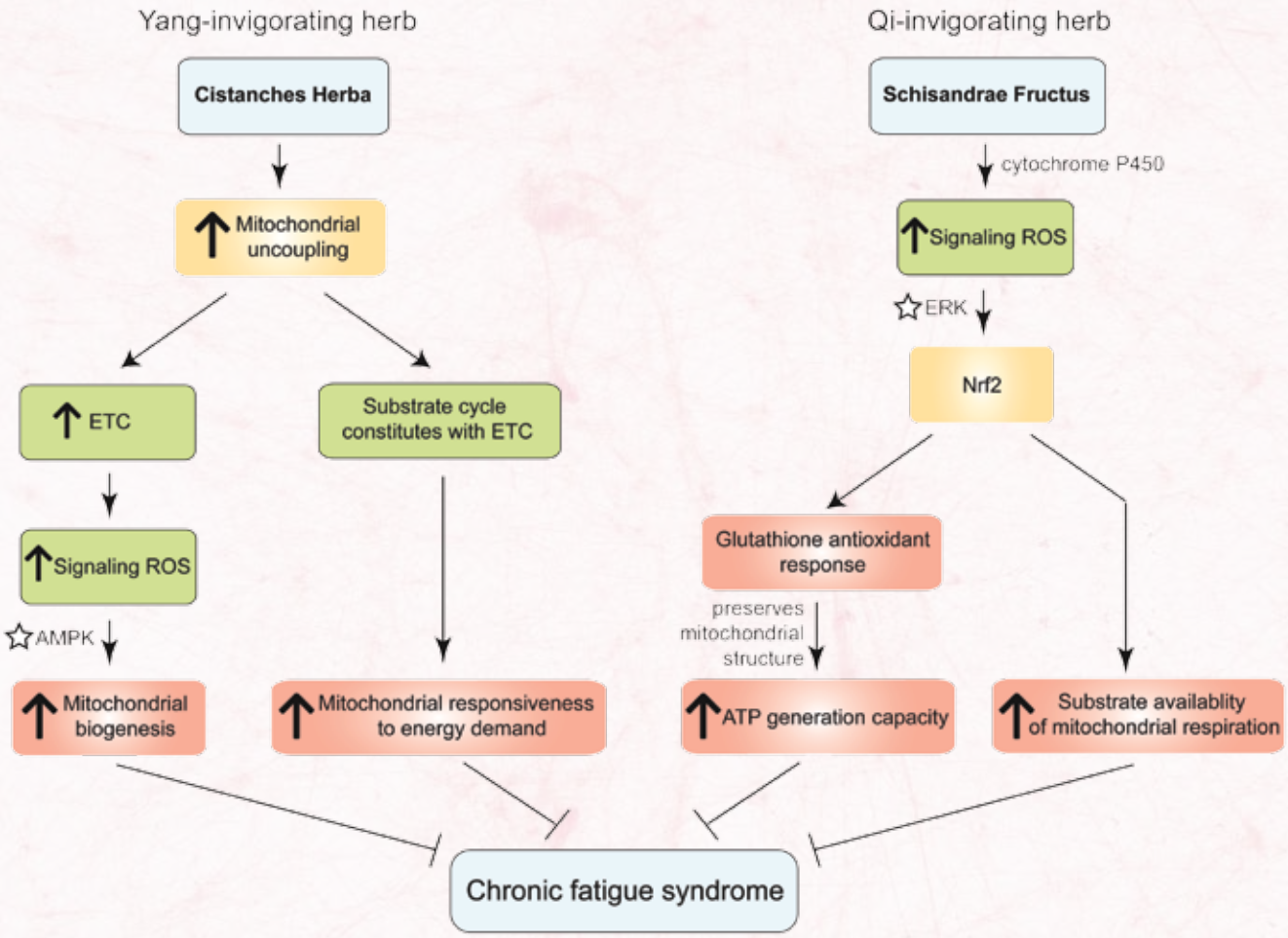

Fig.3. A potential treatment for chronic fatigue syndrome using Yang/Qi-invigorating herbs
ERK, extracellular signal-regulated kinases; ETC, electron transport chain; Nrf2, nuclear factor erythroid 2-related factor 2; ROS, reactive oxygen species; ☆, activation

in patients suffering from CFS with Yang-deficiency (Fig.3). In addition, the activation of Nrf2 by Sch B can not only enhance antioxidant defense components and reduce the extent of inflammation [44,45], but it can also produce a positive impact on cellular bioenergetics by controlling substrate availability for mitochondrial respiration [50].

Conclusion

Based on the crucial role of mitochondria in energy metabolism, we propose an extended view of Yang and Qi in the context of mitochondrion-driven cellular and body function. Yang and Qi likely connote mitochondrion-driven biological processes in the human body. The manifestation of Yang/Qi deficiencies in TCM is in common with CFS of Yang deficient type, for which a huge body of clinical evidence has accumulated linking mitochondrial dysfunction to CFS. By virtue of their ability to enhance mitochondrial function and its regulation, Yang- and/or Qi-invigorating herbs, such as Cistanches Herba and Schisandrae Fructus, respectively, may prove useful for the treatment of CFS with Yang deficiency. Moreover, the astringent and immunomodulatory actions of Fructus Schisandrae may also be beneficial to CFS patients with Yin deficient symptoms such as increased sweating, dry mouth and immune dysfunction. Future clinical studies on Cistanches Herba and Schisandrae Fructus or their combination in CFS patients, particularly those with Yang deficiency are therefore warranted. ■

References

1. Zhen, Z. (1995) Advanced textbook on traditional Chinese medicine and pharmacology Vol. 1. Beijing: New World Press.

2. Yin, H. and Shuai, X. (1992) Fundamentals of traditional Chinese medicine, Beijing: Foreign Languages Press.

3. O'Brien, K.A. and Xue, C.C. (2003) "The theoretical framework of Chinese medicine," in A comprehensive guide to Chinese medicine, Leung, P.C., Xue, C.C. and Chen, Y.C. Eds., Singapore: World scientific publishing Co. Pte. Ltd.

4. Liu, Z. and Liu, L. (2009) Essentials of Chinese medicine, London: Springer.

5. Zhang, D. and Wu, X. (1991) "Chapter 5 Qi, Blood, Body fluid, Essence of life and spirit," in The basic knowledge of traditional Chinese medicine, Liu, Y. Eds. Hong Kong: Hai Feng Publishing Co.

6. Gustafsson, A.B. and Gottlieb, R.A. (2008) "Heart mitochondria: gates of life and death," Cardiovascular Research, vol. 77, pp. 334-343.

7. Hand, S.C. and Menze, M.A. (2008) "Mitochondria in energy-limited states: mechanisms that blunt the signaling of cell death," The Journal of Experimental Biology , vol. 211, pp. 1829-1840.

8. Wang, Y.Y., Chang, S.L., Wu, Y.E., Hsu, T.L., and Wang, W.K., (1991) "Resonance. The missing phenomenon in hemodynamics," Circulation Research, vol. 69, pp. 246-249.

9. Wang, Y.Y.L., Hsu, T.L., Jan, M.Y., and Wang, W.K., (2010) "Theory and

Applications of the Harmonic Analysis of Arterial Pressure Pulse Waves," Journal of Medical and Biological Engineering, vol. 30, pp. 125-131.

10. Cannizzo, E.S., Clement, C.C., Sahu, R., Follo, C., and Santambrogio, L., (2011) "Oxidative stress, inflamm-aging and immunosenescence," Journal of Proteomics, vol. 74, pp. 2313-2323.

11. de la Fuente, M., Hernanz, A., and Vallejo, M.C. (2005) "The immune system in the oxidative stress conditions of aging and hypertension: favorable effects of antioxidants and physical exercise," Antioxidants & Redox Signaling, vol. 7, pp. 1356-1366.

12. Yu, Y.M., and Qiu, M.Y., (2005) "A preliminary epidemiological study and discussion on traditional Chinese medicine pathogenesis of chronic fatigue syndrome in Hong Kong," Journal of Chinese Integrative Medicine, vol. 3, pp. 359-362.

13. Wu, L., and Yan, C. (2004) "[Functions of visceral organs in energy metabolism and body temperature regulation in tradition Chinese medicine] [Article in Chinese]," Journal of Gansu College TCM, vol. 21, pp. 12-13.

14. Zhao, L., Wu, H., Qiu, M. et al. (2013) "Metabolic Signatures of Kidney Yang Deficiency Syndrome and Protective Effects of Two Herbal Extracts in Rats Using GC/TOF MS," Evidence-Based Complementary & Alternative Medicine, vol. 2013, article id 540957.

15. Lu, X., Ziong, Z., Li, J., Zheng, S., Huo, T., and Li, F., (2011) "Metabonomic study on 'Kidney-Yang Deficiency syndrome' and intervention effects of Rhizoma Drynariae extracts in rats using ultra performance liquid chromatography coupled with mass spectrometry" Talanta ,vol. 83, pp. 700-708.

16. Huang, X., Chen, Q., Yang, G., et al. (2012) "Metabolic profiling study of Yang deficiency syndrome in hepatocellular carcinoma by 1H NMR and pattern recognition," Evidence-Based Complementary and Alternative Medicine, vol. 2012, article id 843048.

17. Chen, R., Moriy, J., Yamakawa, J., Takahashi, T., and Kanda, T., (2010) "Traditional Chinese medicine for chronic fatigue syndrome," Evidence-Based Complementary and Alternative Medicine, vol. 7, pp. 3-10.

18. Afari, N., and Buchwald, D., (2003) "Chronic fatigue syndrome: a review," The American Journal of Psychiatry, vol. 160, pp. 221-234.

19. Brenu, E.W., Ashton, K.J., Atkinson, G.M., Staines, D.R., and Marshall-Gradisnik, S. (2012) "Gene expression in chronic fatigue syndrome," in An International Perspective on the Future of Research in Chronic Fatigue Syndrome, C.R. Snell, Eds., InTech, Croatia.

20. Plioplys, A.V., and Plioplys, S., "Electron-microscopic investigation of muscle mitochondria in chronic fatigue syndrome," Neuropsychobiology, vol. 32, pp. 175-181.

21. Myhill, S., Booth, N.E., and McLaren-Howard, J., (2009) "Chronic fatigue syndrome and mitochondrial dysfunction," International journal of clinical and experimental medicineis, vol. 2, pp. 1-6.

22. Jones, D.E., Hollingsworth, K.G., Taylor, R., Blamire A.M., and Newton, J.L. (2010) "Abnormalities in pH handling by peripheral muscle and potential regulation by the automatic nervous system in chronic fatigue syndrome," Journal of Internal Medicine, vol. 26, pp. 394-401.

23. Jones, D.E., Hollingsworth, K.G., Jakovljevic, D.G., et al. (2011) "Newton. Loss of capacity to recover from acidosis on repeat exercise in chronic fatigue syndrome: a case-control study," European Journal of Clinical Investigation, vol. 42, pp. 186-194.

24. Wyller, V.B., Godang, K., Mørkrid, L., Saul, J.P., Thaulow, E., and Walløe, L. (2007) "Abnormal Thermoregulatory Responses in Adolescents With Chronic Fatigue Syndrome: Relation to Clinical Symptoms," Pediatrics, vol. 120, pp. e129-e137.

25. Hamilos, D.L., Nutter, D., Gershtenson, J., et al. (1998) "Core body temperature is normal in chronic fatigue syndrome," Biological Psychiatry, vol. 43, pp. 293-302.

26. Priceand, E.J., and Venables, P.J. (2002) "Dry eyes and mouth syndrome--a subgroup of patients presenting with sicca symptoms," Rheumatology (Oxford), vol. 41, pp. 416-422.

27. Morris, G., Berk, M., Galecki, P., and Maes, M. (2014) "The Emerging Role of Autoimmunity in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/cfs)," Molecular Neurobiology, vol. 49, pp. 741-756.

28. VanElzakker, M.B., (2013) "Chronic fatigue syndrome from vagus nerve infection: a psychoneuroimmunological hypothesis," Medical Hypotheses, vol. 81, pp. 414-423.

29. Jeppesen, T.D., Schwartz, M., Olsen, D.B., et al. (2006) "Aerobic training is safe and improves exercise capacity in patients with mitochondrial myopathy," Brain, vol.129, pp. 3402-3412.

30. Van Cauwenbergh, D., De Kooning, Me., Ickmans, K., and Nijs, J. (2012) "How to exercise people with chronic fatigue syndrome: evidence-based practice guidelines," European Journal of Clinical Investigation, vol. 42, pp. 1136-1144.

31. Chambers, D., Bagnall, A.M., Hempel, S., and Forbes, C., (2006) "Interventions for the treatment, management and rehabilitation of patients with chronic fatigue syndrome/myalgic encephalomyelitis: an updated systematic review," Journal of the Royal Society of Medicine, vol. 99, pp. 506-520.

32. Whiting, P., Bagnall, A.M., Sowden, A.J., Cornell, J.E., Mulrow, C.D., and Ramírez, G. (2001) "Interventions for the treatment and management of chronic fatigue syndrome: a systematic review," JAMA, vol. 286, pp. 1360-1368.

33. Kindlon, T., (2011) "Reporting of harms associated with graded exercise therapy and cognitive behavioural therapy in myalgic encephalomyelitis/chronic fatigue syndrome," Bulletin of the IACFS/ME, vol. 19, pp. 59–111.

34. Ko, K.M., Leon, T.Y., Mak, D.H., Chiu, P.Y., Du Y., and Poon, M.K. (2006) "A characteristic pharmacological action of 'Yang-invigorating' Chinese tonifying herbs: enhancement of myocardial ATP-generation capacity," Phytomedicine, vol. 13, pp. 636-642.

35. Ko, K.M., and Leung, H.Y., (2007) "Enhancement of ATP generation capacity, antioxidant activity and immunomodulatory activities by Chinese Yang and Yin tonifying herbs," Chinese Medicine, vol. 2, pp. 3.

36. Leong, P.K., Chen, N., and Ko, K.M. (2012) "Mitochondrial decay in ageing: 'Qi-invigorating' schisandrin B as a hormetic agent for mitigating age-related diseases," Clinical and Experimental Pharmacology and Physiology, vol. 39, pp. 256-264.

37. Wong, H.S., and Ko, K.M. (2013) "Herba Cistanches stimulates cellular glutathione redox cycling by reactive oxygen species generated from mitochondrial respiration in H9c2 cardiomyocytes," Pharmaceutical Biology, vol. 51, pp. 64-73.

38. Bains, W., (2008) "Treating chronic fatigue states as a disease of the regulation of energy metabolism," Medical Hypotheses, vol. 71, pp. 481-488.

39. Zong, H., Ren, J.M., Young, L.H., et al. (2001) "AMP kinase is required for mitochondrial biogenesis in skeletal muscle in response to chronic energy deprivation," Proceedings of the National Academy of Sciences, vol. 99, pp. 15983-15987.

40. Kukidome, D., Nishikawa, T., Sonoda, K., et al. (2006) "Matsumura and E. Araki. Activation of AMP-activated protein kinase reduces hyperglycemia-induced mitochondrial reactive oxygen species production and promotes mitochondrial biogenesis in human umbilical vein endothelial cells," Diabetes, vol. 55, pp. 120-127.

41. Ko, K.M., and Chiu, P.Y., (2006) "Biochemical basis of the "Qi-invigorating" action of Schisandra berry (wu-wei-zi) in Chinese medicine," The American Journal of Chinese Medicine, vol. 34, pp, 171-176.

42. Chen, Y., Tang, J., Wang, X., Sun, F., and Liang, S. (2012) "An immunostimulatory polysaccharide (SCP-IIa) from the fruit of Schisandra chinensis (Turcz.) Baill," International Journal of Biological Macromolecules,

vol. 50, pp. 844-848.

43. Zhao, T., Mao, G., Mao, R., et al. (2013) "Antitumor and immunomodulatory activity of a water-soluble low molecular weight polysaccharide from Schisandra chinensis (Turcz.) Baill," Food and Chemical Toxicology, vol. 55, pp. 609-616.

44. Checker, R., Patwardhan, R.S., Sharma, D., et al. (2012) "Schisandrin B exhibits anti-inflammatory activity through modulation of the redox-sensitive transcription factors Nrf2 and NF-κB," Free Radical Biology and Medicine, vol. 53, pp. 1421-1430.

45. Lam, P.Y., Leong, P.K., Chen, N., and Ko, K.M. (2011) "Schisandrin B enhances the glutathione redox cycling and protects against oxidant injury in different types of cultured cells," Biofactors, vol. 37, pp. 439-446.

46. Chiu, P.Y., Leung, H.Y., Poon, M.K., and Ko, K.M., (2006) "Chronic schisandrin B treatment improves mitochondrial antioxidant status and tissue heat shock protein production in various tissues of young adult and middle-aged rats," Biogerontology, vol. 7, pp. 199-210.

47. Leong, P.K., Chiu, P.Y., Chen, N., Leung H.Y., and Ko, K.M. (2011) "Schisandrin B elicits a glutathione antioxidant response and protects against apoptosis via the redox-sensitive ERK/Nrf2 pathway in AML12 hepatocytes," Free Radical Research, vol. 45, pp. 483-495.

48. Wang, C.H., Wu, S.B., Wu, Y.T., and Wei, Y.H. (2013) "Oxidative stress response elicited by mitochondrial dysfunction: Implication in the pathophysiology of aging," Experimental biology and medicine (Maywood), vol. 238, pp. 450-460.

49. Ko, K.M., Chen, N., Leung, H.Y., et al. (2008) "Long-term schisandrin B treatment mitigates age-related impairments in mitochondrial antioxidant status and functional ability in various tissues, and improves the survival of aging C57BL/6J mice," Biofactors, vol. 34, pp. 331-342.

50. Holmström, K.M., Baird, L., Zhang, Y., et al. (2013) "Nrf2 impacts cellular bioenergetics by controlling substrate availability for mitochondrial respiration," Biology Open, vol. 2, pp. 761-770.

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探討社區長者跌倒效能與運動的關係

【摘要】

目的

探討社區長者跌倒效能與運動模式的關係及其影響因素。

方法

在中文版國際跌倒效能量表基礎上增加一般狀況及運動模式調查形成調查問卷，於澳門14間長者日間活動中心以便利抽樣方式對481名社區長者進行問卷調查。

結果

481名社區長者跌倒效能總平均分為43.58±12.542，當中67.2%的長者有規律運動的習慣；人口學特徵方面，女性、低教育程度、獨居、飲酒、服藥、使用輔具、有跌倒史、罹患慢性疾病、白內障、青光眼、腦血管疾病及感知害怕跌倒等組別跌倒效能得分較高，有顯著性差異；運動方面，做保健操長者跌倒效能得分顯著較高，相反跳舞長者跌倒效能得分顯著較低；而多因素分析顯示感知害怕跌倒、年齡、跌倒史、罹患慢性疾病、患有骨質疏鬆及腦血管疾病是跌倒效能最具影響力的因素。

結論

社區長者害怕跌倒是普遍又嚴重的長者健康問題，研究進一步確認社區長者害怕跌倒的影響因素，同時發現進行高運動量運動如跳舞組別的長者跌倒效能得分較低；因此，針對長者進行跌倒影響因素的篩查及跌倒效能的評估，結合適當的運動鍛鍊計劃，除有助提升長者生理功能外，並能改善長者害怕跌倒的心理。

背景

跌倒是普遍又嚴重的長者健康問題[1]，可導致長者身體機能衰退和死亡[2]；據國外統計，約有28%至35%的65歲以上長者在一年內曾發生跌倒；跌倒除可導致身體損傷外，還可引發害怕跌倒的心理表現[3]；而害怕跌倒是指身體和健康功能上缺乏獨立及失去信心的表現，除與生理及心理功能相關外，也受個人因素影響[1]，可透過跌倒效能測量工具來評估害怕跌倒的程度[4]；有研究指出長者不論有否跌倒經歷，普遍存在害怕跌倒的心理，導致長者避免活動、限制社交參與、身體功能衰退，惡性循環下將增加再跌倒的風

險，以致生活品質降低[5]；在國外害怕跌倒的盛行率為21%至85%[6]，反映害怕跌倒是比跌倒更常見、更嚴重的健康問題[7]，同時亦是一個值得關注的公共衛生問題[8]。然而，通過規律身體活動能促進力量、協調及平衡力，有助預防跌倒[9]；增加活動量亦有助長者提高執行日常生活自理的信心[10]，從而減少害怕跌倒心理。

近年澳門人口老化日趨嚴重，2013年長者人口比率達至8%[11]；為了提升長者運動水平，澳門特區政府過去投放了大量資源推廣大眾體育鍛鍊並聯同民間社團開辦不同類型的運動班，於2010年進行全澳市民監測報告中指出，長者進行體育鍛鍊比例高達84.8%[12]；因此，本研究旨在探討澳門社區長者跌倒效能與運動模式的關係，除了有助制訂害怕跌倒的干預策略外，亦可為日後澳門特區政府運動推廣提供重要依據。

對象與方法

調查對象

2014年6月至8月以便利抽樣方式對澳門14間受澳門社工局津助的長者日間活動中心的社區長者進行問卷調查。納入標準：年齡在65歲以上；具有一定的溝通及理解能力；能夠獨立行走（包括使用輔助工具）；知情同意。

研究工具

①一般狀況調查表：包括長者的性別、年齡、教育程度、居住狀況、飲酒習慣、服用藥物及精神科藥物、跌倒史、跌倒後有否出現損傷、罹患慢性疾病、使用輔助工具及感知害怕跌倒：長者口頭表述是否害怕跌倒及程度等。②運動模式：參考世界衛生組織對有關運動量的綜合量度方法，包括：運動鍛鍊情況、參與運動種類、頻率、強度及每週累計時間等項目，並運用代謝當量（Metabolic Equivalent-METs）[13]作客觀計算，劃分標準：每週累計<600 METs為低運動量組、600-1500 METs為中運動量組、1501-2400METs為重運動量組、>2400 METs為高運動量組[14]。③中文版國際跌倒效能量表〔Falls Efficacy Scale- International（ch）, FES-I（ch）〕：於2012年被Kwan, Tsang, Close, & Lord[15]等人翻譯國際版跌倒效能量表（Falls Efficacy Scale- International, FES-I）而成，能測量長者進行活動時擔憂自己會因此跌倒的程度，由16條條目組成，每條條目為1分（不關注）至4分（極度關注），總分最低16分、最高64分，跌倒效能總分越高，反映對跌倒關注越高，害怕跌倒的程度也越高[15，16，22]；劃分標準：16 - 19分為低關注組、20 - 27分為中關注組、28 - 64分為高關注組[16]；量表選擇了跨文化條目，曾應用於多個國家的社區長者，均有良好的結構效度，對害怕跌倒程度較低的測量敏感性較高，適合作為社區長者害怕跌倒的評估工具[4]；中文版經翻譯後進行測試，得出內部一致性信度Cronbach's Alpha為0.94，重測信度為0.89，評分者間信度為0.95[15]，信度良好。是次問卷經三位專家學者檢核及修正，總量表內容效度為0.85，各條目為0.75 - 1.00；並對30位社區長者進行了預測試，重測信度為0.90。

資料收集方法

由5位研究員進行培訓後，統一標準指導語，使用統一問卷，採用現場面對面訪談方式，由研究員詢問及準確填寫，問卷需時約15至20分鐘。問卷採用不記名方式，回收後以編號取代，再經編碼及計算代謝當量，資料經3位研究員輸入後再由另外2位研究員共同核實及查對，以確保準確性。

倫理考量

本研究經由香港理工大學人類實驗對象操守小組委員會（HSESC）審核通過，於進行問卷調查前向14間老人活動中心申請研究協議；問卷調查前向所有長者講解及簽署同意書，確保研究屬自願參與原則；完成後問卷會被保密並妥善上鎖保存，並於研究結束後銷毀。

統計學方法

數據收集後進行內容審查、覆核及進行邏輯性除錯，應用SPSS 20.0軟件進行數據分析，以次數分佈、百分比、均數、標準差對資料數據進行描述，樣本以Kolmogorov-Smiruov方法檢定是否呈正態分佈後，應用卡方檢定、t檢定、相關、迴歸分析等方法對人口學、運動等資料與跌倒效能的關係進行分析，應用t檢定比較參與不同運動項目下跌倒效能的差異；利用多元線性逐步回歸（Multiple regression analysis-Stepwise）進行分析，以確定影響跌倒效能的因素。

研究結果

基本情況

研究共訪問499名長者，其中18名因不諳廣東話、中途退出等原因未能成功訪問，最後共收取481份有效問卷，問卷有效率96.4%。當中男性121人（25.2%），女性360人（74.8%）；年齡最小值65歲，最大值99歲，平均年齡為76.55±7.422歲；長者的性別與教育程度（χ 2=50.121，P<0.01）、居住狀況（χ 2=5.849，P<0.05）及飲酒習慣（χ 2=59.186，P<0.01）具統計學的差異（見表一）。疾病方面，罹患一種或以上慢性病共455人（94.6%）；以罹患高血壓的比例最高，佔65.7%，其餘依次為骨質疏鬆（41.2%）、白內障（40.5%）、腰痛（36.8%）、糖尿病（25.8%）、心血管疾病（24.3%）、下肢關節炎（23.7%）、腦血管疾病（13.3%）、失禁（4.4%）、惡性腫瘤（3.7%）。

跌倒效能情況

481名長者在表示感知害怕跌倒的程度上，表示從不害怕有27人（5.6%）、一點害怕有80人（16.6%）、頗害怕有148人（30.8%）、十分害怕226人（47%）。從表二可見長者的FES-I總分及各條目得分情況、均數及標準差。結果顯示，長者的FES-I總分為43.58±12.542，各條目平均得分最大值為3.36、最小值為2.21。此外，女性的FES-I總平均分較男性高（t=-3.241，P<0.01）；在16條條目得分中，女性在家居清潔、煮飯、洗澡淋浴、上/落樓梯、在家附近行走、拿高過頭頂/撿地上的東西、趕接電話、走在濕滑的地面上、拜訪親友、在人很擠的地方走、走在崎嶇不平的路上、上/落斜坡等共12條條目的平均得分顯著較男性為高（P<0.05）；而性別在穿脫衣服、買東西購物、從椅子上站起來/坐下、出去參加活動等4條條目平均得分無顯著差異。

運動情況

67.2%的長者經常進行規律運動，64.9%的長者每週運動時間為120分鐘或以上，從表三可見男女長者的平均運動次數、時間及代謝當量並無顯著差異，但女性長者平均自覺運動強度較男性為高（t=-2.294，P<0.05）。從表四可見長者的每週運動頻率平均為4.62±2.770次，每次平均運動時間為39.57±29.559分鐘，運動時自覺強度平均為2.64±1.644分，持續運動時間平均為80.03±87.168月，每週代謝當量（METs）平均為868.76±805.471 METs/wk。長者較常參與的運動項目依次為：保健操（32.2%）、步行（26.0%）、公園健身器械（25.6%）、太極或八段錦（19.8%）、跑步（4.0%）、游泳（2.7%）、踏單車（1.7%）、跳舞（4.4%）。此外，34.7%的長者在過去一年曾參加由政府體育發展局主辦的運動班，當中最多長者參與為老年健身操班，佔20.8%；長者表示最喜愛的運動班為健身操（20.0%），其次為太極或八段錦（12.9%）、其他如扇舞等（8.5%）。

運動與跌倒效能的關係

長者的FES-I得分並不會因一年內運動習慣的不同而存在顯著差異；同時FES-I得分與每星期運動次數、每次運動時間、運動強度及代謝當量等無顯著相關，但研究結果揭示長者的FES-I得分與持續運動時間存在正向弱相關（P<0.01）；至於運動項目方面，參與保健操的FES-I平均分較沒有參與的為高（t=-3.029，P<0.05），而參與跳舞的FES-I平均分較沒有參與的為低（t=2.094，P <0.05）（見表四）。

跌倒效能的影響因素

從表四及表五中找出各變項中不同組別其FES-I存在差異的變項為性別、年齡、教育程度、居住狀況、飲酒習慣、服用藥物、跌倒史、跌倒次數、罹患慢性疾病、骨質疏鬆、白內障/青光眼、腦血管疾病、其他疾病、輔具使用、保健操、跳舞、感知害怕跌倒等共17項，連同6項運動變項包括一年內運動習慣、每星期運動次數、每次運動時間、持續運動時間、自覺運動強度、代謝當量等共23項作為自變量，FES-I作為依變量，進行多元線性逐步回歸，得出影響因素為感知害怕跌倒、年齡、跌倒史、其他疾病、骨質疏鬆、腦血管疾病（見表六）；從表七中可見模式6的複相關係數R=0.801，決定係數R2=0.642，達到統計學意義，反映這六個變項是跌倒效能最具影響力

的因素。

討論

長者跌倒與害怕跌倒現狀及分析

本研究顯示澳門社區長者一年內跌倒發生率為21.8%，與近年鄰近地區包括中國（12.5%）、南韓（13.0%）、香港（20.8%）及日本（26.0%）的跌倒發生率[14，15，17，18]相比，澳門跌倒發生率與香港相若但僅低於日本；當中105名發生跌倒的長者中，一年內重覆跌倒有34名，再次跌倒發生率為32.4%，運用卡方檢定發現獨居、患有慢性疾病、服藥及使用輔具的老年人跌倒比例較高（P<0.05），數字反映澳門長者跌倒情況不容忽視且需要針對跌倒高危人群作重點篩查及干預。感知害怕跌倒方面，77.8%的長者表示為頗害怕或十分害怕跌倒；而長者的FES-I總平均分為43.58分，屬高關注組別[16]，運用均數檢定方法發現女性、低教育程度、獨居、飲酒、服藥、使用輔具、有跌倒史、罹患疾病等組別的平均FES-I得分較高（P<0.05），反映FES-I得分偏高並受多種因素影響尤其受個人因素影響，結果與國外多份研究相似，符合年長者、女性及有跌倒史有較多害怕跌倒[1，6，19]、教育程度較高者害怕跌倒的程度較低[19 - 21]的結論，同時亦可能與女性佔74.8%、從未受教育者佔32.2%、長期服用藥物及患有慢性病者分別佔90.9%及94.6%等因素佔整體有較高的比例有關；在FES-I量表的16條條目得分中，女性在室內的家務工作、室外的社區活動及較易發生跌倒的環境等共有12條條目的平均得分顯著較男性為高，高分條目的分佈與Yardley等人於2005年的研究結果一致[19]。此外，除個人因素外，研究顯示跌倒史是FES-I的影響因素，一年內有跌倒史的FES-I平均分較無跌倒史為高（P<0.01），但兩者分數均達偏高程度，符合Cumming[5]等人2000年提出的不論有否跌倒史，長者害怕跌倒心理普遍存在的結論。研究結果揭示澳門社區長者FES-I得分高且普遍，是一種不良的心理反應，且進一步確認澳門社區長者害怕跌倒的相關因素、以及影響長者出現較害怕心理的日常活動條目。

長者運動現況及分析

有67.2%的澳門社區長者進行規律運動，64.9%長者每周運動時數累加達至120分鐘或以上，更有4成長者每天皆進行運動；只有19.1%長者從不或甚少進行運動，與台灣的41.0%[23]相比，比例較低。這可能與澳門特區政府大力推動運動政策有關，因此長者的運動次數和頻率均達到世界衛生組織針對65歲以上組別的建議[24]；然而，長者在自覺運動強度方面稍微偏低，未能達到世界衛生組織的建議，可能與大部份長者進行的運動為保健操（1.5 - 3.5METs）[25]、散步或公園器械等屬低強度的運動有關。在進行運動與跌倒效能的雙變量分析中，顯示長者的FES-I得分隨持續運動時間越長而越高，即越害怕跌倒，結果可能與長者持續運動時間越長、年齡越高身體功能越趨下降而出現更害怕跌倒的原因所引致；此外，結果同時顯示做保健操的長者比不做者FES-I得分較高，這可能與做保健操的多屬活動中心內較不活躍、體弱及對跌倒較為關注的長者有關，因此中心安排這些長者進行運動量較低的保健操，部份長者更坐在椅子上進行，因而造成運動強度參差、做保健操的FES-I得分反而較高；另外，跳舞的長者比不跳舞者FES-I得分較低，主要因跳舞需要較佳的平衡力及體能，代謝當量（5.0 - 7.8METs）[25]也較高，符合提出高運動量的組別有較佳的平衡力及較少害怕跌倒的結論[26]，也可能與參加跳舞的長者較不擔心跌倒，因此選擇與保健操性質大大不同的運動有關；由於跳舞能改善下肢肌肉耐受力、強度、靈活度、平衡、敏捷及步態，並能增加骨質及肌力，可減少跌倒的發生[27]，亦有研究指出太極能改善身體的柔韌性及平衡度[28]，長期練習更可增加姿勢的穩定性，導致跌倒風險降低[29]，加上有研究指出最有效的防跌運動是合併的、混合性的運動[30]；因此，從預防長者跌倒的層面上，澳門特區政府需持續推行大眾體育的方針，但應改變推行的策略，建議提供有目的性的、混合性的運動，循序漸進引導長者參與合適的運動鍛鍊計劃，逐漸提高運動強度，並在適當時機提供支持以強化持續運動的信心，以降低長者害怕跌倒的心理表現並能提升生理功能從而預防跌倒。

長者害怕跌倒影響因素的分析

多因素分析結果顯示，感知害怕跌倒、年齡、跌倒史、患有慢性疾病、骨質疏鬆及腦血管疾病等是跌倒效能最具影響力的因素；提示長者愈感知害怕跌倒、年齡愈高、有跌倒經歷、罹有多種慢性疾病，以及患骨質疏鬆症、腦血管疾病的長者，平均FES-I得分較高，有較高程度的害怕心理。結果雖然未顯示規律運動與FES-I得分有關，與Lim[14]等人於2011年研究結果相似，但本研究顯示跌倒與FES-I有顯著性關係，同時顯示規律運動與跌倒有顯著性關係，其中跳舞長者的平均FES-I比不跳舞的有顯著性差異，說明在跌倒、運動及FES-I之間，存在著相互影響的間接關係。因此，對社區長者進行跌倒影響因素的篩查及FES-I的評估，可有助預測其發生跌倒的風險[5]，更有助識別跌倒高危人群，作出重點干預措施；此外，研究發現高運動量的運動如跳舞有助減少長者發生跌倒的風險及降低害怕跌倒的心理，建議政府提供運動鍛鍊協助長者建立自信心，將有助提高長者的心理質素。

研究限制

本研究的運動類別較多，以致個別運動類別的樣本量不足，建議日後可以阻力運動或帶氧運動方式進行分類，以獲取較多的樣本量；此外，問卷屬自我報告形式，屬主觀性，運動時間由長者口述，結果可能被高估；而本研究未能以隨機抽樣方式進行，樣本可能屬社區較活躍的長者而出現樣本性別差異偏大的現象；最後，由於是橫斷面描述性研究，只能探討運動模式及個人因素與跌倒效能的關係，建議日後應進行縱貫性研究，並可探討更多變項間的變化及因果關係。

結論

澳門社區長者跌倒效能分數偏高，感知害怕跌倒、年齡、跌倒史、患有慢性疾病、骨質疏鬆及腦血管疾病是跌倒效能的影響因素。研究結果顯示跳舞組別的長者跌倒效能得分較低，害怕跌倒的程度較低。由於影響因素屬多因素性，建議實施多面性策略作為預防措施，同時針對長者進行跌倒影響因素的篩查及跌倒效能的評估，加強跌倒衛生教育及防跌意識，並建議在社區推廣有策略性、合適的運動鍛鍊計劃，除提高長者對運動的關注外，同時能提升長者日常生活自理能力，將有助改善長者害怕跌倒的心理。■

表一：研究對象的一般狀況及跌倒狀況

因素	男性n=121	女性n=360	N=481	χ2值	P值
	人數(%)	人數(%)	總數(%)		
年齡				4.449	0.108
65-74歲	52(43.0)	147(40.8)	199(41.4)		
75-84歲	56(46.3)	145(40.3)	201(41.8)		
≧85歲	13(10.7)	68(18.9)	81(16.8)		
教育程度				50.121	0.000*
從未受教育	16(13.2)	139(38.6)	55(32.2)		
小學	61(50.4)	176(48.9)	237(49.3)		
中學	38(31.4)	32 (8.9)	70(14.5)		
大專或以上	6 (5.0)	13 (3.6)	19 (4.0)		
居住情況				5.849	0.016*
獨居	32(26.4)	139(38.6)	171(35.6)		
與家人同住	89(73.6)	221(61.4)	310(64.4)		
飲酒習慣	59.186	0.000*			
從未飲酒	87(71.9)	346(96.1)	433(90.0)		
已戒酒	21(17.4)	8 (2.2)	29 (6.0)		
目前仍飲酒	13(10.7)	6 (1.7)	19 (4.0)		
服用藥物				1.142	0.285
否	14(11.6)	30 (8.3)	44 (9.1)		
是	107(88.4)	330(91.7)	437(90.9)		
使用精神科藥物				0.019	0.891
否	117(96.7)	349(96.9)	466(96.9)		
是	4 (3.3)	11 (3.1)	15 (3.1)		
輔具使用				0.521	0.470
否	95(78.5)	271(75.3)	366(76.1)		
有	26(21.5)	89(24.7)	115(23.9)		
一年內跌倒史				1.897	0.168
沒有	100(82.6)	276(76.7)	376(78.2)		
有	21(17.4)	84(23.3)	105(21.8)		
跌倒後損傷狀況				2.175	0.337
非跌倒者	100(82.6)	276(76.7)	376(78.2)		
無損傷	4 (3.3)	21 (5.8)	25 (5.2)		
出現損傷	17(14.1)	63(17.5)	80(16.6)		
罹患疾病				0.063	0.802
否	6 (5.0)	20 (5.6)	26 (5.4)		
是	115(95.0)	340(94.4)	455(94.6)		

卡方檢定(Chi-Square test)，*P<0.05表示有顯著差異

表二：研究對象跌倒效能量表各條目得分情況及與性別的分析

因素	男性n=121		女性n=360		N=481		t值	P值
	均數	標準差	均數	標準差	均數	標準差		
家居清潔	2.28	1.134	2.74	1.033	2.62	1.077	-3.926	0.000**
穿脫衣服	2.21	1.127	2.36	1.019	2.32	1.048	-1.216	0.225
煮飯	2.01	1.029	2.29	1.041	2.22	1.044	-2.624	0.009**
洗澡、淋浴	2.53	1.133	2.86	1.093	2.77	1.111	-2.818	0.005**
買東西、購物	2.31	1.111	2.53	.987	2.48	1.023	-1.937	0.055
從椅子上站起來／坐下	2.36	1.111	2.47	1.017	2.44	1.042	-0.967	0.334
上／落樓梯	2.71	1.129	3.08	.966	2.98	1.020	-3.180	0.002**
在家附近行走	2.19	1.051	2.41	.955	2.36	0.983	-2.147	0.032*
拿高過頭頂/撿地上東西	2.90	1.121	3.23	.935	3.15	0.994	-2.913	0.004**
趕接電話	2.15	1.062	2.38	.997	2.32	1.017	-2.151	0.032*
走在濕滑的地面上	3.08	.936	3.45	.730	3.36	0.802	-3.933	0.000**
拜訪親友	2.37	1.081	2.60	1.013	2.54	1.034	-2.106	0.036*
在人很擠的地方行走	2.82	1.041	3.33	.872	3.20	0.942	-4.818	0.000**
走在崎嶇不平的路上	3.08	1.021	3.44	.798	3.35	0.873	-3.522	0.001**
上／落斜坡	2.98	1.107	3.36	.820	3.27	0.915	-3.550	0.001**
出去參加活動	2.12	1.045	2.24	.987	2.21	1.002	-1.092	0.275
跌倒效能總分	40.12	14.184	44.75	11.733	43.58	12.542	-3.241	0.001**

獨立樣本T檢定(Independent t-test)，*P<0.05、**P<0.01表示有顯著差異

每條目最低1分、最高4分）

表三：研究對象性別與運動情況的分析

因素	男性n=121		女性n=360		t值	P值
	均數	標準差	均數	標準差		
每星期運動 (次)	4.81	2.853	4.56	2.743	0.864	0.388
每次運動時間 (分鐘)	39.69	31.186	39.53	29.036	0.054	0.957
持續運動時間 (月)	75.29	97.626	81.62	83.446	-0.691	0.490
自覺運動強度 (0-10分)	2.36	1.461	2.73	1.693	-2.294	0.023*
每週代謝當量 (METs/wk)	822.27	676.393	884.38	844.721	-0.818	0.414

獨立樣本T檢定(Independent t-test)，*P<0.05表示有顯著差異

表四：研究對象運動情況與跌倒效能的分析

變量	人數	均數	標準差	*t*值	*r*值	P值
保健操				-3.029		0.003*
否	326	42.46	12.975			
是	155	45.95	11.254			
步行				-1.794		0.073
否	356	42.98	12.663			
是	125	45.31	12.075			
跑步				1.122		0.262
否	462	43.71	12.407			
是	19	40.42	15.529			
太極或八段錦				1.267		0.207
否	386	43.91	12.901			
是	95	42.26	10.925			
游泳				0.529		0.597
否	468	43.63	12.479			
是	13	41.77	15.117			
踏單車				1.071		0.285
否	473	43.66	12.500			
是	8	38.88	14.980			
跳舞				2.094		0.037*
否	460	43.84	12.619			
是	21	38.00	9.295			
其他運動				0.824		0.411
否	358	43.86	12.668			
是	123	42.78	2.181			
一年內運動習慣				0.613		0.540
無規律運動	158	43.08	13.348			
規律運動	323	43.83	12.142			
每星期運動（次）	481	4.62	2.770		0.049	0.279
每次運動時間（分鐘）	481	39.57	29.559		0.005	0.906
持續運動時間（月）	481	80.03	87.168		0.177	0.000**
自覺運動強度（0-10分）	481	2.64	1.644		0.023	0.621
每週代謝當量（METs/wk）	481	868.76	805.471		0.038	0.403

獨立樣本T檢定(Independent t-test)，*P<0.05表示有顯著差異

皮爾森相關(Pearson's correlation)，**P<0.01表示有顯著差異

表五：跌倒效能的影響因素

變量	人數	均數	標準差	*t*值	*r*值	F值	P值
性別				-3.559			0.000**
男	121	40.12	14.184				
女	360	44.74	11.733				
教育程度				3.587			0.000**
從未受教育	155	46.52	12.299				
小學或以上	326	42.19	12.433				
居住狀況				2.987			0.003**
獨居	171	45.87	12.218				
非獨居	310	42.33	12.560				
飲酒習慣				2.841			0.005**
沒有	462	43.91	12.423				
有	19	35.63	13.145				
服用藥物				-2.881			0.004**
否	44	38.43	14.287				
是	437	44.10	12.251				
輔具使用				-5.068			0.000**
否	366	42.00	12.580				
有	115	48.63	11.042				
一年內跌倒史				-3.853			0.000**
沒有	376	42.52	12.736				
有	105	47.39	11.063				
罹患疾病				-3.052			0.002**
否	26	36.35	12.840				
是	455	44.00	12.412				
骨質疏鬆				-4.178			0.000**
否	283	41.66	12.898				
是	198	46.34	11.497				
白內障／青光眼				-2.578			0.010*
否	286	42.37	12.869				
是	195	45.36	11.857				
腦血管疾病				-2.112			0.035*
否	417	43.11	12.424				
是	64	46.66	12.968				
其他疾病				-2.267			0.024*
否	389	42.96	12.502				
是	92	46.24	12.430				
年齡	481	76.55	7.422		0.217		0.000**
跌倒次數	481	0.41	1.309		0.146		0.001**
感知害怕跌倒					238.825	0.000**	
從不害怕	27	20.89	4.126				
一點害怕	80	30.78	8.876				
頗害怕	148	41.22	8.211				
極度害怕	226	52.38	7.775				

獨立樣本T檢定(Independent t-test)，*P<0.05、**P<0.01表示有顯著差異

皮爾森相關(Pearson’s correlation)，**P<0.01表示有顯著差異

單因子變異數分析(ANOVA)，**P<0.01表示有顯著差異

表六：FES-I影響因素的多因素分析

影響因素	未標準化係數		標準化係數		
	B	Std.Error	Beta	*t*值	P值
常數	-6.964	3.706		-1.879	0.61
感知害怕跌倒	10.175	0.387	0.737	26.310	0.000**
年齡	0.206	0.047	0.122	4.352	0.000**
跌倒史	2.728	0.843	0.090	3.238	0.001*
其他疾病	2.768	0.886	0.087	3.124	0.002*
骨質疏鬆	2.111	0.708	0.083	2.982	0.003*
腦血管疾病	2.104	1.021	0.057	2.060	0.040*

多元線性逐步迴歸(Mutiple regression analyses-Stepwise)，依變量為FES-I；

*P<0.05, **P<0.01

表七：逐步回歸方程的決定係數

模式	複相關係數R	決定係數R2
1	.775[a]	.600
2	.784[b]	.614
3	.791[c]	.625
4	.795[d]	.632
5	.799[e]	.638
6	.801[f]	.642

a. 預測變數：感知害怕跌倒

b. 預測變數：感知害怕跌倒、年齡

c. 預測變數：感知害怕跌倒、年齡、跌倒史

d. 預測變數：感知害怕跌倒年齡、跌倒史、其他疾病

e. 預測變數：感知害怕跌倒、年齡、跌倒史、其他疾病、骨質疏鬆

f. 預測變數：感知害怕跌倒、年齡、跌倒史、其他疾病、骨質疏鬆、輔具使用、腦血管疾病

吳壽婷博士與碩士學生們合照
從左至右： 唐沛然、李春霞、吳壽婷博士、鄺凱青、曾紅燕、楊秀娟

參考文獻

1. Scheffer A.C., Schuurmans M.J., van Dijk, N., van der Hooft, T., de Rooij, S.E. (2008) Fear of falling: Measurement strategy, prevalence, risk factors and consequences among older persons. Age Ageing. 37(1):19.

2. Fox, P.J., Vazquez, L., Tonner, C., Stevens, J.A., Fineman, N., Ross, L.K. (2010) A randomized trial of a multifaceted intervention to reduce falls among community- dwelling adults. Health Education & Behavior. 37(6):831-48.

3. Landers, M.R., Durand, C., Powell, D.S., Dibble, L.E., Young, D.L. (2011) Development of a scale to assess avoidance behavior due to a fear of falling: The fear of falling avoidance behavior questionnaire. Phys Ther. 91(8):1253.

4. 李鶯，程雲孫，王麗娟. 害怕跌倒測評工具的研究進展. 護理學雜誌，28(15), 89-91.

5. Cumming, R.G., Salkeld, G., Thomas, M., Szonyi, G. (2000) Prospective study of the impact of fear of falling on activities of daily living, SF-36 scores, and nursing home admission. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. May 01;55(5):M299-305.

6. Hellström, K., Vahlberg, B., Urell, C., Emtner, M. (2009) Fear of falling, fall-related self-efficacy, anxiety and depression in individuals with chronic obstructive pulmonary disease. Clin Rehabil. 12;23(12):1136-44.

7. 包月. (2009) 老年公寓老年人害怕跌倒心理及影響因素的研究[D]. 中國醫科大學.

8. Li, F., Fisher, K.J., Harmer, P., McAuley, E. (2005) Falls self-efficacy as a mediator of fear of falling in an exercise intervention for older adults. The Journals of Gerontology Series B: Psychological Sciences and Social Sciences. January 01;60(1):P34-40.

9. Ullmann, G. (2008) The efficacy of feldenkrais in improving balance, mobility and health related factors in an older adult population [dissertation]. University of South Carolina.

10. Bishop, M.D., Patterson, T.S., Romero, S., Light, K.E. (2010) Improved fall- related efficacy in older adults related to changes in dynamic gait ability. Phys Ther. 90(11):1598.

11. 澳門統計暨普查局. (2014) 澳門人口統計，2014. 於2014年1月15日搜索自http://www.dsec.gov.mo/Statistic.aspx?NodeGuid=7bb8808e-8fd3-4d6b-904a-34fe4b302883

12. 澳門體育發展局. (2014) 澳門大眾體育，2014. 於2014年1月15日搜索自http://www.sport.gov.mo/zh/

13. Ainsworth, B.E., Haskell, W.L., Hermann, S.D., Meckes, N., Bassett, J.R.D.R., Tudor-locke, C., et al. (2011) 2011 compendium of physical activities: A second update of codes and MET values. Medicine & Science in Sports & Exercise. 08;43(8):1575-81.

14. Lim, J., Jang, S., Park, W., Oh, M.K., Kang, E.K., Paik, N. (2011) Association between exercise and fear of falling in community-dwelling elderly koreans: Results of a cross-sectional public opinion survey. Arch Phys Med Rehabil. 6;92(6):954-9.

15. Kwan, M.M.S., Tsang, W.W.N., Close, J.C.T., Lord, S.R. (2013) Development and validation of a chinese version of the falls efficacy scale international. Arch Gerontol Geriatr. 0;56(1):169-74.

16. Delbaere, K., Close, J.C., Mikolaizak, A.S., Sachdev, P.S., Brodaty, H., Lord, S.R. (2010) The falls efficacy scale international (FES- I): A comprehensive longitudinal validation study. Age Ageing.

17. 王慧. (2011) 社區老年人害怕跌倒心理與ADL能力及抑郁相關性的研究[D]. 河北醫科大學.

18. Yamada, M., Arai, H., Uemura, K., Mori, S., Nagai, K., Tanaka, B., et al. (2011) Effect of resistance training on physical performance and fear of falling in elderly with different levels of physical well- being. Age Ageing. 40(5):637-41.

19. Yardley, L., Beyer, N., Hauer, K. (2005) Development and initial validation of the falls efficacy scale-international (FES-I). Age Ageing. November 2005;34(6):614-9.

20. Curcio, C., Gomez, F., Reyes-Ortiz, C. (2009) Activity restriction related to fear of falling among older people in the colombian andes mountains. J Aging Health. 21(3):460-79.

21. Shin, K.R., Kang, Y., Kim, M.Y., Jung, D., Kim, J.S., Hong, C.M., et al. (2010) Impact of depression and activities of daily living on the fear of falling in korean community- dwelling elderly. Nurs Health Sci. 12(4):493-8.

22. Tinetti, M.E., Richman, D., Powell, L. (1990) Falls efficacy as a measure of fear of falling. Journal of Gerontology. November 01;45(6):P239-43.

23. 鄧瑞儀、林信宏. (2011) 如何運用轉型領導策略改善老人規律運動行為. 中華體育季刊. 25(2):283-9.

24. 世界衛生組織. (2014) 關於身體活動有益健康的全球建議，2010. 於2014年1月15日搜索自http://www.who.int/dietphysicalactivity/factsheet_recommendations/zh.

25. The Compendium of Physical Activities (2011) The compendium of physical activities: Tracking Guide. 2011. 於2014年4月15日搜索自https://sites.google.com/site/compendiumofphysicalactivities/tracking-guide.

26. McAuley, E., Mihalko, S.L., Rosengren, K. (1997) Self-efficacy and balance correlates of fear of falling in the elderly. J Aging Phys Act. 10;5(4):329-40.

27. Keogh, J.W.L., Kilding, A., Pidgeon, P., Ashley, L., Gillis, D. (2009) Physical benefits of dancing for healthy older adults: A review. J Aging Phys Act. 17(4):479.

28. Yu, D., Yang, H. (2012) The effect of tai chi intervention on balance in older males. Journal of Sport and Health Science. 5;1(1):57-60.

29. Chen, K., Chen, W., Huang, M. (2006) Development of the simplified tai chi exercise program (STEP) for frail older adults. Complement Ther Med. 14(3):200-6.

30. Shubert, T.E. (2011) Evidence-based exercise prescription for balance and falls prevention: A current review of the literature. Journal of Geriatric Physical Therapy. 34(3):100-8.

The Provisional Hong Kong Academy of Nursing Annual Fellowship Conferment cum Nursing Symposium

Date : 9th May 2015 (Saturday)

Time : 2:00pm to 6:00pm

Venue : Auditorium 3/F, Kowloon Bay International Trade and Exhibition Centre

Program Rundown:

1:30pm Reception and Video Show

2:00pm Conferment Ceremony officiated by Secretary for Food and Health
Conferment of Honorary Fellows

Nursing Symposium

Keynote Speakers:
Prof. LEONG Chi Yan John, Chairman of Hospital Authority, Hong Kong
Dr. LI Xiuhua, President of Chinese Nurse Association, Beijing

Paper Presentation by:
Ms. FAN Yuying, Head Nurse of Sun Yat-Sen University Cancer Center, Guangdong
Ms. VONG Kit Mei, Chief Nurse of Centro Hospitalar Conde de São Januário, Macau
Ms. SHUM Ngan Fun, Advanced Practice Nurse of Queen Mary Hospital, Hong Kong
Ms. WANG Li, Head Nurse of Peking University Shenzhen Hospital, Guangdong
Ms. CHAN Weng Sai, Chief Nurse of Macau Health Bureau, Macau
Mr. TO Hoi Chu, Nurse Consultant of Queen Elizabeth Hospital, Hong Kong

Q & A

6:00pm End of Event

A Force for Change : Care Effective Cost Effective

Symposium Co-organizers

1988 Guangdong Nursing Education Center 广东省护理教育中心

衛生局 Serviços de Saúde

Tehyen Chu
Tehyen earned her Ph.D. in Biochemistry from Stony Brook University and conducted postdoctoral research at Harvard University. She was a 2009 FDA Commissioner's Fellow and works in the medical device industry subsequently. She is now working at an industry incubation center to help foster more medical devices onto the global market.

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My Experience as an FDA Commissioner's Fellow

In the United States, it is said that for every one dollar spent, 25 cents to 33 cents are spent on FDA regulated products. This statement illustrates the size of the healthcare product market and the importance of FDA regulation in this industry. In addition to the importance of such regulations, initiatives to encourage the release of more novel products into the market, and to translate the advancements in science into relevant products, has driven the US FDA to set up several programs aimed at developing regulatory science and establishing regulations that are based on science and risk. One of the programs that was established is the FDA Commissioner's Fellowship.

The FDA Commissioner's Fellowship was established in 2008. The goal of this two-year program is to provide healthcare professionals, scientists and engineers a formal opportunity to learn, understand and contribute to FDA's mission and policy. This goal is achieved by gathering early career healthcare professionals, scientists and engineers at FDA to receive regulatory science training while conducting research related to scientific, policy, or regulatory issues with mentors at the agency. I was very fortunate to be part of the second class (Oct. 2009-Oct. 2011) of this fellowship program, and gained experience that exceeded my expectations.

There are seven Centers at the FDA – Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), Center for Veterinary Medicine (CVM), Center for Food Safety and Applied Nutrition (CFSAN), Center for Tobacco Products (CTP) and National Center for Toxicological Research. Except for CTP, which was established after our class was selected in August of 2009, all six Centers plus the Office of Regulatory Affairs (ORA) participated in providing preceptors to mentor fellows. There were fifty fellows in my class. My classmates were composed mostly of biologists, chemists, epidemiologists, engineers, as well as physicians and veterinarians. Some of us were fresh out of school with newly minted degrees, while others had a few years of work or research experience under their belts.

The selection of fellows was largely based on whether their skills and expertise fit with the research projects that were proposed by the preceptors. My research experience and expertise in developmental genetics in a model system fit with the research proposal that my preceptor put forward, and this placed me in the Center of Biologics Evaluation and Research (CBER) at the Office of Cellular, Tissue and Gene Therapies (OCTGT). My research at FDA was focused on how extracellular matrix components affect powerful morphogens that are widely used in the manufacturing of cell therapy products for inducing differentiation. While my research was bioscience-oriented, some of the research projects of my peers were in epidemiology, informatics, risk analysis, or related to policy and best practice studies.

The fellowship was designed to have the fellows spend 50% of the time on their research projects and 50% of their time on training courses. For research, fellows were encouraged to attend related conferences and meetings outside of FDA to interact with experts in their specific fields as well as broaden their connections and knowledge. For training courses, the fellowship provides graduate-level coursework that all fellows were required to attend. In addition, the fellows were encouraged to attend training courses offered by each Center, which were catered specifically to the Center needs. The graduate-level coursework was quite rigorous and requires lots of discussion and team effort to accomplish. Below, I have listed both the fellowship curriculum and the CBER training courses that I attended.

Fellowship curriculum:

Winter 2009
Introduction to FDA Law and Regulation
(Food and Drug Law Institute)

Spring 2010
Fundamentals of Epidemiology
(John Hopkins University, School of Public Health, Graduate Course)
Introduction to Clinical Trials
(John Hopkins University, School of Public Health, Graduate Course)
European Union Food and Drug Regulatory Framework
(EU regulators)

Summer - Fall 2010
Biotechnology: Management of Drug Discovery
(Duke University, Fuqua School of Business)

Fall 2010 - Spring 2011
Center Specific Training
(lectures focus on explaining the functions of the different Centers and Offices at FDA)

CBER training courses:

GS Review Hands-On Training	Winter 2009
eCTD- ICH Electronic Common Technical Document:	Spring 2010
New Reviewer Training and Medical Device Reviewer Training	1/2010
Biologics Law	4/2010
Introduction to Biostatistics	9/2010
Aseptic Process Training	11/2010
Risk Communication for Biologics	3/2011
Risk Assessment and Risk Management	4/2011
Introduction to Cell Culture for Biologics Production:	7/2011
(Fermentation and Bioreactor Technology)	
Introduction to Downstream Processing for Biologics Production	9/2011

Most courses in the list were directly relevant to the understanding of tasks that took place at the FDA. However, "Biotechnology: Management of Drug Discovery" was different. This course was included in our curriculum to give the fellows, who were mostly science-majors and illiterate about business decisions, an opportunity to understand how the biotechnology industry makes investment decisions. The purpose was to equip the future FDA regulators among us with an understanding of the business pressures that exist for the industry. FDA does not factor business considerations into its deliberations or decisions. FDA's mission is to protect public health and only concerns itself with safety and effectiveness issues. However, as a regulator, it is helpful to understand the behavior and concerns of the industry

representatives sitting across the negotiation table if the regulator is aware of the pressures and considerations that exist for the industry.

In addition to the above activities, the fellowship also arranged for all fellows to attend the annual Food and Drug Law Institute (FDLI) conference. FDLI is a non-profit organization, whose mission is to provide a platform for discussing food and drug law issues through conferences, publications and member interaction, but does not engage in advocacy activities. This annual conference is a forum that brings professionals from industry, consulting organizations and academia to hear directly from and interact with FDA leadership, and to engage in discussions and debates on the latest regulatory developments. It was eye opening for me to experience this gathering of people with vastly different professional backgrounds. This is very different from the research conferences I used to attend, where the majority of the attendants have very similar backgrounds (mainly Ph.D.). At the annual FDLI conference, in addition to attorneys, medical professions, patient advocates and industry leaders, there were experts in risk management, medical ethics and economics and all of them engaged in discussions. The diverse expertise of the participants at this conference clearly illustrated the complexity of the issues at hand.

As part of my experience in the Office of Cellular, Tissue and Gene Therapies (OCTGT) at CBER, I participated in weekly reviewer meetings and monthly office meetings to discuss the regulatory submissions that came before OCTGT. The novel and experimental nature of the products that OCTGT regulates resulted in most applications being INDs and some device submissions. The majority of reviewers in this group are Ph.D. level scientists and MDs. Some of the reviewers are Principal Investigators (PI) who run their own labs and conduct research in the related fields. These researchers help the office stay current on the latest advances in related therapeutic products and identify potential regulatory issues that may emerge as the science advances.

Under the supervision of experienced reviewers, I conducted a few reviews on 510(k) submissions and IND/IDEs. Through this invaluable experience, I gained first hand knowledge on what is considered crucial in determining "Substantial Equivalence" in a 510(k) application. I also understood that most reviews are team efforts with medical, pharm/tox and CMC reviewers. I saw that OCTGT took the review of all submissions seriously and decisions were never made lightly.

While at OCTGT, I had the opportunity to see how an FDA office tackles regulatory issues. Working committees may be formed to focus on the issue. A lot of the effort went into understanding the nuance of the issue at hand. Experts were invited to office meetings and gave staff an overview and analysis of the issues. The discussion at the end of the presentation between the guest speaker and the staff was often very informative and interesting. The spectrum of the regulatory issues can span from ethical discussions regarding pediatric clinical trials for biologic products to qualification concerns of companion diagnostic kits. For example, to understand the current thinking in assessing the need for pediatric clinical trials, an FDA medical ethicist was invited to give OCTGT a comprehensive and systematic over-

view of the ethical framework and principles applicable to pediatric clinical trials. The speaker pointed out why informed consent is a corner stone in participating in clinical trials. In a population who cannot give such informed consent, he described how people have sometimes followed different processes to try to obtain "consent". He further pointed out why some of these attempts are flawed and what ethical principals one should consider for such populations in conducting risk and benefit analyses. The speaker provided a moral structure to think through this difficult topic. It was thought provoking to see that such ethical rigor was applied when assessing the necessity of a pediatric trial. In addition to the office seminar, OCTGT also hosted a public workshop to have a wider discussion with practitioners and ethicists in the field. There was a continuous effort from FDA to have all the stakeholders in this issue to familiarize and further their understanding of risk-benefit analyses for pediatric clinical trials.

In addition to regulatory issues, knowledge of potential new therapeutic products was of considerable interest to the office. For example, stem cell research advances were closely followed. Staff members were encouraged to attend conferences on stem cell research. Academic researchers were invited for seminars. A Principal Investigator (PI) search for hiring stem cell experts was conducted while I was there. Having a PI would allow OCTGT to have an in-house expert on stem cell research. I was very impressed by such enthusiasm and the efforts made in acquiring scientific knowledge and expertise on stem cells and other potential therapies. Only by having a full understanding of the science behind the potential therapeutic products can the agency make a regulatory decision that is scientifically based and keep up with advancements in the applications of such products.

During my fellowship, I also took an interest in the mission of the International Office at FDA. As globalization of the manufacturing chain becomes more and more prevalent, FDA also has to come up with more effective regulatory policy to face such a reality in order to protect public health. One approach was to work with the regulatory counterparts in other countries to leverage resources and knowledge. The International Office at FDA is the primary contact window to communicate with counterparts in other countries. They also oversee the various overseas FDA offices. The first FDA overseas office was established in 2008 in China. One of the significant events that took place prior to setting up of the first overseas office was the Melamine tainted pet food scandal in 2007 [1]. (Commissioner's Fellows had the privilege to meet the FDA scientist who identified Melamine as the culprit in the pet food that made the animals sick[2]. During the outbreak of the contamination, she spent weeks locked up in her lab looking through pathological tissue slides of the sick animals and compared it to literature reports.) Another event was the contaminated Heparin incident in 2008[3]. These incidents clearly illustrated that country boundaries are no longer effective barriers to prevent the entry of ineffective or adulterated products. It requires a control of material at the origin of the manufacturing chain. In order to achieve this, it is paramount for countries to work together. The establishment of overseas offices is one step towards better communication with other regulatory authorities and foreign manufacturers who import regulated products into the US.

One special process that all FDA employees, including Commissioner's Fellows, have to go through is financial disclosure. No FDA employees, their spouses and children are allowed to have financial interests or holdings in the industry that FDA regulates. FDA officials with greater authorities have their personal finances scrutinized even further. In fact, during the second year of my fellowship, an FDA employee was prosecuted for illegally trading on company stocks based on product approval information before it went public [4]. The prosecutor built a tight case, which linked the timing of stock purchasing right after internal decisions on approval of the product were made. Through this legal case, I saw how much the US federal government values FDA's neutrality in the lucrative business that it regulates. Such neutrality is essential and lends credibility to the decisions that FDA makes.

My two-year fellowship built a solid understanding in my mind of the FDA and the regulation it promulgates. This enhanced my determination to develop my regulatory career. Through the training at FDA, I see this profession as a worthwhile occupation. The regulatory profession is not only about making sure a specific product meets the regulatory requirements; it is also about supporting the industry to make quality products. I see the regulation as a means to ensure the safety and effectiveness of medical products. This is not to say that there exist no unreasonable regulations in the books. When such issues are identified, FDA does work with the industry and relevant stakeholders to address the problems. In addition, FDA does have the goal of making its decision scientifically based and risk based. I certainly witnessed this on-going effort while at FDA and I believe the industry and other regulatory authorities will do well by adopting the same principals.

After FDA, I have spent over two years working as a regulatory affairs professional in the medical device industry, gaining experience on how industry complies with FDA regulations. Looking forward, with my current position at a medical device incubation center, I plan to apply my training to help medical device start-ups build a healthy respect for producing quality products that the FDA regulation is trying to ensure. ■

References:

1. The Associated Press. (2007). 104 Deaths Reported in Pet Food Recall. The New York Times.

2. Reimschuessel, R. (2008). CVM Researcher Renate Reimschuessel Nominated for Service to America Medal. FDA Veterinarian Newsletter March / April Volume XXIII, No II.

3. Harris, G. (2008). U.S. Identifies Tainted Heparin in 11 Countries. The New York Times.

4. Hilzenrath, D. S. (2011). FDA Chemist Charged with Insider Trading. The Washington Post.

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國際技術移轉項目管理：醫療器械

簡介

醫療器械的技術轉移包括：甲乙方之間的技術買賣、中試端到商業生產端的技術轉移和放大、內部製造外包給予合同製造商所牽涉的技術移轉、本身技術由甲地遷移到乙地、或是由甲地複製到乙地等。

“國際”技術轉移單純者包括將工藝、設備、檔等從甲地（或甲方）遷（或複製）到乙地（或乙方），複雜者——尤以如醫療器械類的高度管制產品——可牽涉到第三、第四地的上市法規、進而牽涉到生產工廠的全盤法規與技術規劃、關鍵物料及最終產品的運輸規劃、工藝流程同步抑或不同步的策略規劃、跨國知識財產權的保護策略等。

轉移的考慮可能來自於降低製造成本、靠近關鍵原物料來源、靠近消費市場、風險分散、品牌定位、法規策略、抑或其他商業策略等。其中，“法規策略”在醫療器械產業佔了舉足輕重的特有地位。

商業契機及挑戰

對於會考慮國際技轉的公司，常見的商業動機包括：

1. 降低製造、運輸成本：將現有的勞工地區移轉到勞工成本低廉的地區，自動化部分移轉到工業技術更穩定的地區，體積較大或脆弱之部分移到更近的地方生產等
2. 靠近消費市場：除了更接近消費者，對於“高度管制市場（highly-regulated markets）”以至於“未管制市場（unregulated markets）”採取分開的供應策略以提高成本效益
3. 風險分散：將生產基地擴展到第二地點，降低人力、物料、政治、財務風險
4. 國際政策走向：例如世界衛生組織促進未開發國家的醫藥品近用權利等
5. 其他商業考慮：例如品牌形象考慮等

醫療器械技轉主要的挑戰包括：

1. 高度管制產品：除了上市前審查時間擺長、上市後變更困難，各國法規尚存在高度差異（儘管有諸多國際組織致力於法規協和工作多年）造成合規成本高昂
2. 高知識、多學科人力需要：僅就技術呈面，醫療器械的研發、製造、質管制等可牽涉到醫療、生物、化學、機電、統計、法規等專業人才
3. 知識財產權保護：除了產品本身設計的知識財產權，還有生產工藝的知識財產權，甚至於跨學科專業人力所累積的“實際能力（know-how）”等無形資產

總論，我們可將醫療器械的國際技轉過程分為五大項規劃（圖 一）：

圖 一　五大項規劃

1. 知識財產權（Intellectual Property）規劃
2. 法規策略（Regulatory Strategy）規劃
3. 人事（Personnel）規劃
4. 原物料、零件（Raw Material, Parts）規劃
5. 工廠、設備（Facility, Equipment）規劃

在考慮技術轉移專案前，專案目標必須要清楚。承上述商業動機考慮，所有管理團隊必須非常清楚這個移轉的目的是降低製造成本、靠近市場、風險分散、或是其他品牌或商業考慮。

知識財產權規劃

知識財產權包括產品本身的設計、生產的工藝、以及公司人員所累積的實際能力。專利註冊是法律上最基本的保障機制，但是多國的專利註冊昂貴、執行也昂貴。

生產工藝和人員實際能力方面的產權難免會隨著時間及人員流動而流失。“禁止競爭”條款實際上執行並不易。將設計、工藝等步驟拆開分散是一個常見的知識財產權策略。當然，拆開分散是會提高行政、運輸、囤貨等的成本，對中小規模的企業較吃力。

當產品在多國上市，除了銷售管道、經銷商的考慮之外，大部分開發中國家至於先進國家的醫療器械法規都會要求有當地法定人為該產品負責、持有該產品的資料、持有該產品的上市許可、並對該產品如果造成的不良事件或賠償負責。因此，在多國上市有幾個可能考慮：

1. 當地代理商：

a. 考慮產品的所有資料必須交給代理商，是否會有複製或抄襲的風險。

b. 有些國家允許一個品牌的一個產品只能有一個上市許可，是否會有上市許可遭代理商“綁架”的風險。

c. 如果發生不良事件及賠償事件，且不論代理商與母公司之間的合同關係，當代理商缺乏專業的能力去妥善的處理技術、法務的糾紛時，可能直接影響到母公司品牌的名譽。

2. 當地合資夥伴或當地自立公司：對知識財產權的保護最有效，不過如果產品在許多國家上市，雖然當地自立公司的成本效益可能大幅減低但組織管理會越趨複雜。以人事管理管理為例，有些國家要求母公司的董監事也要有工作或居留簽證。

3. 協力廠商持有上市許可：當考慮過自立公司的成本，以及為了避免代理商握持所有的產權，協力廠商持有是一種中間解決方案。因為代理商與協力廠商獨立，當任一方出現問題時，對業務及產權的影響都可以大幅減低。

法規策略規劃

法規策略主要會牽涉到上市前及上市後的法規。

當該產品同時已經在多國上市，技術轉移可能會牽涉到各國的原上市許可。輕則者可能牽涉到變更、重則者可能牽涉到重新申請。

上市後的法規主要牽涉到公司內部對不良事件及賠償的處理體系將如何修改，什麼情況會由那一個部門負責等。所謂不良事件的處理體系大多是公司內部的問題，有些國家會有額外的法規限制，例如一個最終產品只能有一個工廠負責等。

就國際技術移轉來說，常見的法規策略有：

1. 完全複寫原則：即工廠設計、設備、工藝、標準作業程式（SOP）、以至於組織架構百分百的複製。出發點是將技術移轉定義為生產地的變更（有別于將其定義為“新”的工廠），避免產品需要重新上市註冊。實際上，些微的差異無法避免。目前各國法規少有對國際技轉的規範，因此與主管機關保持緊密的溝通格外重要。
2. 市場分割策略：即甲廠與乙廠分別負責供應不同的市場。

圖二　一些主要法規的考量範例如

主要法規考慮	甲地（技術輸出方）	乙地（技術輸入方）	丙地（第三地）
良好製造規範（GMP）	技術輸出是否會牽涉到甲地GMP申報內容變更	大部分國家認可ISO13485標準，少數國家有自有GMP標準，少數國家、產品可能牽涉到醫療器械以外之製造規範	有些國家的上市許可必須明列所有生產工廠
	需要新的GMP稽核或只需要通報	需要新的GMP稽核	需要新的GMP稽核抑或只需要通報
上市許可	技術輸出是否會牽涉到工藝變更（包括甲乙地的變更）	技術輸出是否會牽涉到工藝變更（包括甲乙地的變更）	技術輸出是否會牽涉到工藝變更（包括甲乙地的變更）
	需要新的上市許可抑或需要既有許可進行變更	需要新的上市許可抑或需要既有許可進行變更	需要新的上市許可抑或需要既有許可進行變更；當今國際間醫療器械的上市法規仍有相當大的差異
進出口法規	物料、半製成品、產品、耗材、設備等是否能出口，是否有高敏感物料需要特殊運輸條件	物料、半製成品、產品、耗材、設備等是否能進口	

人才規劃

人才規劃首要必然是新廠工人的招聘及培訓計畫。但是，員工培訓可能跟法規策略密不可分。

如果法規策略採取的是完全複寫原則，則甲、乙廠必須要遵循百分百同樣的品質系統及SOP。SOP必須翻譯成甲、乙地的語言，甚至如果有其他國家的稽核，可能也要翻譯成丙地語言。雙語的SOP維持不易，因此，SOP本身也需要策略（例如：高階SOP單一採國際慣用的英語、低階SOP采當地語言等）。

SOP必須要保持同步，任一廠的任何變更都會直接影響另一個廠。有可能因乙地的特殊情況迫使甲地也必須跟隨更改。有可能甲地稽核的結果造成甲、乙地都必須一併進行更改。例如，當甲乙廠使用同一個原物料來源，但是因運輸距離與方式不同，可能會有不同的處理方法需要整合。

如果採取的是市場分割策略，以合規的角度，甲乙廠彼此不影響。管理者可能要考慮的是，隨著時間過去甲乙廠將會開始有差異，這些漸增的差異是否會造成母公司控管的困難。

原物料、零件規劃

原物料及零件的規劃包括進出口考慮、長距離運輸的考慮、採購地點的考慮、以及是否會影響產品上市登記等。物料種類可分成：

1. 與產品直接相關物料、零件：該產品上市許可的產品規格中所舉列的物料、零件。因為會直接牽涉到產品品質以及上市許可，所以來源不能輕易變更、運輸及存放條件也不能輕易變更。
2. 與產品間接相關物料、零件：一般包括製造過程中會使用的耗材，品質管制的設備，品質管制的耗材等。這類耗材往往用量小、使用頻密，有些有機會會有效期出現較短、來源少等。
3. 與產品不相關物料、零件：物料當地採購一定是成本控管最好的方式。但是，當法規因素不能輕易更改，公司必須考慮運輸會增加多少成本、有多少運輸的風險、特殊物料是否有進出口的限制、是否有運輸方法的限制（例如只能海運不能空運）、敏感物料是否會因跨氣候帶的運輸過程受到影響。如果有敏感物料可能受到運輸方法和氣候帶的影響，視上市國法規，可能要執行更多試驗來證明它的穩定性以及對產品的影響。

耗材等也有類似的考量。許多品質管制用的耗材（例如標準液）用量小、有效期短，長距離運輸不易、如特有耗材也有可能當地採購不易。此情況需要制定另外的對策，甚至可能需要自己建立調配方法。

工廠、設備規劃

工廠與設備的規劃必然需要專業的建築及工程團隊，並且持有當地合法的執照。

就國際轉移來說，如果採取的法規策略是完全複寫原則，工廠與設備的規劃有兩大考量：

1. 工廠設計完全複製是否可行：尤以如果甲乙兩地之建築和工程的技術、法規如果有一段距離（例如從工程法規較不完善的國家移到法規較完善的國家、從人口密度低的國家移到人口密度高的國家），或是從舊建築法規移到新建築法規。

   以西方國家較常見的“祖父條款（Grandfather Clause）”為例，許多產品與車間因為在早年設計並且已在市場上成熟而得以（在沒有變更的情況下）規避新的法規要求。但是，一旦需要新建工廠，影響的可能不單只是建築與工程，有可能連上市許可都會受到影響（例如潔淨室的環境、設施的規格、滅菌環境與設備的規格等）。
2. 設備轉移問題：尤其以特殊設備、客制設備、或是老舊設備。同建築法規一事，設備進出口、安裝、使用等也有各國的法規差異以及新舊法規之分。常見的有高度管制的設備包括壓力鍋爐設備、蒸餾設備、高壓電動設備、高排放設備、放射性設備、自動化設備等。如果甲地的設備不能拿到乙地的認證，嚴重可能牽涉到必須修改工藝甚至重新申請上市。

風險管理

上述的五大項規劃——知識產權規劃、法規策略規劃、人工規劃、原物料和零件規劃、工廠和設備規劃——各有風險。

一個技術轉移專案的風險管理需要將可預期的風險逐一舉列，並且依成本、時間等評估優先順序，然後寫出具體計畫。高風險的專案應伴隨對其他備份方案的評估。

結論

由於醫療器械屬於高度管制產品，需要高知識、跨學科的專業人才，為高知識財產權產品，並且目前國際上仍存在相關法規的高度差異，因此國際技術移轉成了一個挑戰，也成了一個契機。■

參考文獻

World Health Organization. (2012). Local Production and Technology Transfer to Increase Access to Medical Devices.

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5 Steps to a Successful Product Launch

Abstract

In today's dynamic world, large medical companies develop countless innovative products and devices every year. With a growing industry and greater competition, an increasing number of products fail to impact the market. Pushing out new products is a common problem that even the most prominent of companies are facing. A product launch is often considered one of the most critical steps in determining the success of a product. No matter how novel or innovative a product may be, no matter how much money may have been spent on it, all of that could go to waste with a poorly launched product. A lack of knowledge regarding a proper product launch is a key factor leading to failure. To address this problem, we would like to introduce a streamlined and simple process to launch a new product. Our process involves 5 stages, namely, Product Evaluation, Team Formation, Planning, Implementation and Launch, implemented by 3 teams. An effective process requires transparency and good collaboration, which we offer in the article below, through the use of simple organizational charts, informative diagrams. We collected input from many industry experts in order to envision a process that would suit a wide range of products. Upon pilot testing our process on a real product, we received highly positive feedback, with each department representative being pleased overall. We also received constructive criticism, which we strived to apply. Currently, this project is nearing completion, with supporting materials, ready for implementation in companies around the world.

Introduction

Why?

In today's dynamic, fast-paced world, large medical companies develop countless innovative products and devices every year. According to 2010 survey by McKinsey Global, sales of medical devices are growing by over 9% annually, signifying powerful growth in this industry. However with growth, it is also becoming increasingly difficult to enter this market, with stiff competition all around. The same survey shows that only 39% of 2240 executives feel confident in their company's ability to introduce new products. Pushing new products out onto the market is a common problem that even the most prominent of companies encounter.

Introducing the Product Launch, considered one of the most critical steps in determining the success of a product. A product launch involves

the stages from when the product is developed to when it is first released to the market. No matter how novel or innovative a product may be, no matter how much money may have been spent on it, all of that could go to waste with a poorly launched product. To put this another way - even an average

product could be successful with the right launch process.

Our Role

Upon beginning our internship at Terumo BCT, we were firstly assessed by our tutor regarding our strengths and skills that we possessed. Recognizing both of us as strong communicators with a creative mind-set, we were assigned to this project, to find a solution for a smooth product launch.

In order to address this problem and simplify a product launch, we set about to design a unique process to achieve this. We researched through several sources as well as conducting interviews with experienced professionals in the Medical industry, who were able to provide us with greater insight into the common problems faced in a product launch. Our task of rectifying these issues was not an easy one, involving collaborating with many people and collecting regular feedback on our developments. The Commercial department was especially busy, however, with some persuasion and effective time management, we were able to get the job done. We also received a valuable opportunity to conduct a pilot test and apply process on a real product and gained a hugely positive response. Through this article, we would like to share our experiences, and provide a simple but effective process for a product launch.

Flow Chart showing the 5 steps in a Product Launch

The Process

Our process involves 5 stages, namely, Product Evaluation, Team Formation, Planning, Implementation and Launch, implemented by 3 teams primarily.

Commercial

The Commercial team is arguably the most important part of the product launch. As product launch is a direct business activity, they play the most crucial role in the process. Furthermore, they also hold most of the decision making power, necessary for passing through gates, from one stage to the next.

*Note that in our project, we define the Commercial Team as a collaboration of sales, marketing and finance. Also note that the Country Manager may be considered part of the commercial team.

Regulatory Affairs

The Regulatory team is also one of the core teams involved, particularly in a medical devices product launch. They have one primary job - to ensure the product meets every possible legal standard required to sell in the respective countries.

Logistics

Last but not least, the Logistics team too is one of the key teams in a product launch. While the commercial and regulatory team make sure about the market prospects and legality, logistics must provide the smoothest flow of goods from the point of origin to the point of consumption.

Supporting Teams

This includes departments that can help with the launch process, for example Human Resources or IT.

1. Product Evaluation

The first step in any product launch is to actually understand the product itself; its purpose, its merits, its applications. A good understanding of the product is very necessary as only then can it be determined whether or not this project is worth undertaking. The key here is to identify a unique selling point with which to identify the product's advantages.

To begin, the three major teams, commercial, logistics and regulatory respectively, must work individually to determine the feasibility of the project, from various aspects. One such way to do this, would be to conduct a SWOT Analysis, by identifying the product's Strengths, Weaknesses, Opportunities and Threats.

The Commercial team must assess the product's value in the market and potential customer prospects, as well as competitor products and risks involved. Here, the input of Key Opinion Leaders may be useful.

The Regulatory team must first determine whether or not any regulatory procedures are required. If not, then the product is clear to go ahead. However, if specific approval is required, the team must quickly get to work, as often, it is the regulatory process that can take the longest.

Finally the Logistics team must ensure that there is enough manufacturing capacity and warehousing abilities, as well as the necessary distribution methods in order for the product to be successfully sold

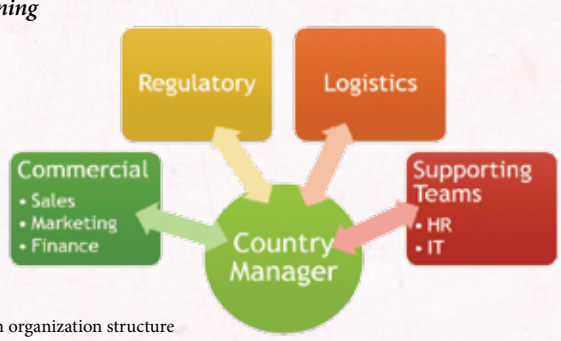
2. Team Formation

It is absolutely essential to have a well-functioning, collaborative team in order to achieve success. One cannot stress enough the importance of teamwork in a product launch. More than anything, a good team must have the motivation and drive to power the product.

Smaller teams are often more efficient, so it is recommended that you have no more than 4 or 5 people in the core team. For example, one member from each Commercial, Regulatory and Logistics as well as the Country Manager. Furthermore, HR and IT can play a supporting role.

Once the team has been formed, the next step is ensuring regular communication. In order to have effective communication, every team must have a leader. One suggestion is that the Country Manager be the leader, however this is not a must. The leader must be the crux of the team, responsible and accountable for the progress of the product launch.

3. Planning



Ideal team organization structure

Task	Country Manager	Commercial	Regulatory	Logistics	Human Resources	IT
Product Evaluation	A	R	R	R	I	I
Team Formation	R, A	C	C	C	S	I
Planning	A	R	S	S	C	C
Action & Monitoring	A	R	R	R	S	C
Launch	A	R	S	S	I	C

RASCI Chart for Responsibility Awareness

If you fail to plan, you plan to fail. A solid plan is the most vital aspect of a product launch. Without an effective plan, the product launch cannot move forward at all. Planning involves envisioning the desired outcome of the product launch, and charting a path towards success.

In this stage, first a foremost, the launch objectives of goals must be identified. These goals shouldn't be excessive or unachievable, rather, a simple but focused goal is much more beneficial. Every employee should be aware of this goal and share the same passion for success.

The next step involved responsibility awareness. Each team member should be fully aware of what their responsibilities are and what they are required to do. To help, it is recommended to use a RASCI chart, identifying

key personnel in each stage that is Responsible, Accountable, Supporting, Consulted, and Informed (as shown in the example).

Finally, it is necessary to timeline. This timeline should be shared each employee so as to ensure that that everyone is aware of what needs to be done at what time. The timeline should identify the task, expected date of completion and person responsible for it. One effective way to do this would be to use a Gantt chart, however any method can be suitable.

4. Implementation

Talk without action is meaningless; and the same goes for a product launch. Precise implementation of the timeline plan is crucial for success, with strict monitoring of progress as well as any unexpected circumstances if any.

Even though each person may be aware of their responsibility, they may tend to forget it. Enforcement of the RASCI can be particularly helpful here. An example of a project timeline is shown here, for easy monitoring.

The project timeline is designed to be simple on the top, to provide a quick overview of the situation, ideal for the country manager. The colour-coded dates give an idea of expected completion as well as whether or not the situation is on-track. Greater detail can be found below, with descriptions of tasks, completion dates and person responsible.

To avoid an ineffective process, or lapses in productivity, the country manager or leader must take control of the process. The leader must ensure that sufficient development is being made, and that everything is running smoothly. Another way to monitor this as well as improve communication would be to organize monthly meetings with the core team, where progress can be tracked and then the timeline updated accordingly.

	Regulatory			Logistics			Commercial		
G: On Time Y: Delay R: Urgent	Dec '14			Jan '15			March '15		
	Task	Date	Who	Task	Date	Who	Task	Date	Who
	Classify products	08/08	X	Manufacturing Capacity	05/08	X	Key selling points	08/08	X
	Authorized Representative	05/08	X	Raw Materials	15/09	X	Market Survey	01/09	X
	Begin Application	12/09	X	Distribution Line	15/10	X	Launch Country	15/09	X
	Clinical trials	28/10	X	Inventory	01/12	X	Marketing Strategy	15/02	X
	Secure license	15/11	X	Warehousing	20/12	x	Sales Training	24/02	X

Project timeline example for effient monitoring

5. Launch & Post Launch Review

The last step of the process is the probably the easiest step, the Launch itself. Given that the previous 4 steps have been followed well, the final launch should flow through successfully. Nevertheless, this step is still an important one, if the product is to make a solid impact on the market.

Each individual company will have their own marketing and launch strategies, and so we will not go into great detail. However a logical way would be to begin by preparing promotional materials and beginning a marketing campaign. Next, the product would be launched at a global stage, and the focus here would be educating potential customers on the key advantages. Finally, consumer feedback should be collected, providing a pathway for improvement on the next generation, and greater market expansion. At this point, the team can be terminated and the new product is now classified as a regular product (Cooper, 2008).

But most importantly, the post launch should be about celebrating the success of the product. This is one aspect that many companies forget about. A celebration can be the company's way to show its gratefulness and appreciation for its hardworking team and all its employees. Just a simple celebration can make every person involved feel truly rewarded, greatly enhancing their passion in future product launches.

Pilot Launch

Overview of Pilot

TRIMA Accel

After designing our product launch process, as detailed above, we decided to apply it to an actual product, in order to gain a better understanding of how our process would truly function. Therefore, a pilot launch was conducted on a real product called TRIMA, from Terumo BCT.

TRIMA is an existing medical device, performing automated blood collections. Currently, an update is being released, which includes new hardware and software products. Our role was to find a simplified solution to launch this product onto the market, in a quick, transparent and efficient manner.

Our Task

In order to set about our task, we began applying our process. As this was already an existing medical device, we were able to skip through some steps such as conducting a market survey. Nevertheless, keeping with the process, we first evaluated the product, assessing its commercial value as well as regulatory and logistics feasibility. Next, we made an outline for the team formation, and then designed a launch objective. We then used RASCI to assign responsibility and also created a project timeline (see examples above). Furthermore, we created a framework to ensure smooth implementation and launch, however these stages were more like guidelines, due to a lack of time.

After applying our process to this product launch for TRIMA, we presented our methods and results to senior members of Terumo BCT (Singapore), in order to judge how much of an impact our product could make, and to take a measure of our achievements.

Measurements of success

Once a product is launched, it is critical to evaluate it and consider areas for improvement. There are various criteria one can use to measure the success of a product launch.

First and foremost, if the launch objective are fulfilled, that is already one major step towards confirming a successful product launch. Also, during the process, the project should be tracked for punctuality and how closely it follows the timeline. This can be done again through monthly meetings. Another aspect to judge success by is through employee satisfaction. Whether or not the team enjoyed working with this process is a key indicator of its success, and so it highly recommended to conduct a review once the product launch is completed. Finally, other business aspects could be customer satisfaction due to the speed of the product getting onto the market, and also sales volume and profitability of the product itself.

Often, companies may find that this product launch isn't proceeding smoothly – and this may be due to a several reasons. Nevertheless, it is highly important to identify the key issue in the problem here, and then focus on how to rectify it. Some steps to take could be to perform an audit of the process, or maybe review why certain stages are proving ineffective as well as constantly listening to the feedback of team members.

Good Collaboration is the key to Success

Feedback

Collecting user feedback is an essential step in any process, and very necessary for continual improvement. After presenting our TRIMA pilot launch to experienced members of the industry, we received highly positive feedback on the process overall, as well as constructive criticism, which we strive to apply.

Feedback is necessary for improvement

When asked whether our process is simple and transparent, Umal Raskar (Country Manager of Terumo BCT Singapore) replied "The process is very systematic and helpful, especially for a country manager like me in order to understand who is responsible for what task, and also tracking the progress being made."

Caren Tan (HR Manager at Terumo BCT Singapore) stressed the importance of strong collaboration within the team, and was glad the process made note of this. "Having one project leader and regular monthly meetings ensures the effectiveness of the process. Also, RASCI helps keep track of accountability." Jack Wong (Regulatory Affairs at Terumo BCT) also echoed this. "The use of RASCI makes this process unique, with a clear representation of who does what".

When asked to rate the current product launch methods being used at Terumo BCT, Fredrick Dalborg (Vice President, Commercial Operations APAC) gave a rating of 4, saying they were limited to marketing, not accounting for logistics or distribution. He then gave our process a rating of 8, saying "Compared to the current product launch process, this process improves significantly on details, which ensures success."

For further improvements, we received suggestions to make a common template, which would enable the process to be easily and quickly implemented for any product. Furthermore, greater detail in the implementation stage would help to re-iterate individual tasks and responsibilities.

Nevertheless, we received extremely positive feedback overall, from each of the departments and the team as a whole too. The consensus was that the process was definitely worth implementing at Terumo BCT Singapore, and elsewhere around the world too. ■

References

1. Cooper, R. G. (2008). Perspective: The Stage-Gate Idea-to-Launch Process.

2. Fuhr, T., George, K., & Pai, J. (n.d.). The Business Case for Medical Device Quality. Retrieved from McKinsey & Company: http://www.mckinsey.com/~/media/McKinsey/dotcom/client_service/Public%20Sector/Regulatory%20excellence/The_business_case_for_medical_device_quality.ashx

3. Lavenda, D. (2013, January 24). 10 Steps for Successfully Launching a New Product or Service. Retrieved from FastCompany: http://www.fastcompany.com/3004920/10-steps-successfully-launching-new-product-or-service

4. Yu, J., & Kurwa, M. (2002). Ensuring a Successful New Product Launch.

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