CHAPTER 1

Introduction

Thermoregulation is an important mechanism for human homeostasis and a complex interaction among the central nervous system, the cardiovascular systems and the skin to maintain a core body temperature of 37°C. The hypothalamus receives information about body core and shell temperatures from peripheral skin receptors and the circulating blood. The information is used for regulating the body's core temperature through negative feedback to the thermostat in the brain [Binkley et al., 2002]. Moreover, the hypothalamus plays a central role in autonomic thermoregulation. Especially, the preoptic area in the hypothalamus is thought to be the most important region [Nagashima, 2006]. The hypothalamus has a neural structure with the highest level of heat-sensitive neurons and one-third as cold-sensitive neurons in preoptic and anterior nuclei of the hypothalamus [Cooper, 2002]. These thermo-sensitive neurons effectively monitor the temperature of blood flowing to brain and can thus detect changes in core temperature [Boulant, 2000]. The critical threshold temperature at the hypothalamus above or below which processes are initiated to increase heat production or heat loss is about 37°C [Wendt et al., 2007]. Thermoregulation is a balance between heat production and heat loss mechanisms that occurs to maintain a constant body temperature. Moreover, thermal factors such as core and skin temperatures are the primary feedback signals for sweat rate and skin blood flow, and these responses are represented as a function of internal or mean body temperatures [Kondo et al., 2009].

Heat dissipation is vital for mammalian survival during exercise and heat stress. The body can dissipate heat by convection (by warming of air or water around the body),

conduction (by contacting with solid objects such as the floor), radiation and evaporation of sweat. Important mechanisms for heat loss include sweat production which promotes heat loss from skin and radiation which transport heat from body core and muscle to skin via skin blood flow. In humans, an important heat dissipation mechanism occurs through evaporation of sweat secreted from eccrine sweat glands. Evaporation of sweat is an important heat loss process to control internal body temperature in a hot environment, in which ambient temperature is higher than skin temperature. The thermoregulatory sweating is affected by many internal factors including gender, physical fitness, menstrual cycle and circadian rhythm as well as external factors like air humidity [Shibasaki et al., 1997a].

Cutaneous vasodilation and sweating are the two main heat loss responses to internal and external heat stress in humans. Thermoregulatory sweating serves as a system for temperature reduction under heat stress conditions. During heat stress, both sweating and vasodilation systems are essential for thermal regulation. If this function cannot match the thermoregulatory requirement, excessive heat strain on the body may cause heat-related illnesses including skin eruptions, heat fatigue, heat cramps, heat syncope, heat exhaustion and heat stroke. Most heat-related illnesses (except for skin eruptions and heat cramps) are in essence consequences of varying severity of failure in the thermoregulatory system. Moreover, this failure of thermoregulatory system can lead to heat stroke and death [Wilke et al., 2007].

Sweating, an important heat-loss mechanism, is produced in response to body overheat. Its evaporation transfers heat from skin surface to the environment. Eccrine sweat glands produce sweat by plasma ultra filtration. The gland consists of two portions: a coiled secretory portion in dermis and a straight duct through the epidermis including a pore opening on skin surface. Secretory cells of a sweat gland produce isotonic secretion in the proximal part of the gland. Cells in distal part of the gland subsequently reabsorb electrolytes. Evaporation of 1 mL of sweat from the skin surface removes about 560 calories of heat from the body [Hoath and Maibach, 2003].

As a primary gland responsible for thermoregulatory sweating in humans [Shibasaki et al., 2006], eccrine sweat gland begins to develop from the sweat gland germ in fetus on palms and soles at 4th month, on axillae at early 5th month, and on the rest of skin surface at late 5th month. The total number of eccrine sweat glands found over almost the entire skin surface is about 2–5 million glands [Freinkel and Woodley, 2001].

Evidence from animal studies found that efferent signals from the preoptic hypothalamus travel via the tegmentum of the pons and the medullary raphe regions to the intermediolateral cell column of the spinal cord. In the spinal cord, axons emerge from the ventral horn, pass through the white ramus communicans, and then form synapse in the sympathetic ganglia. Postganglionic non-myelinated C fibers pass through the gray ramus communicans, combined with peripheral nerves and travel to sweat glands [Low, 2004].

Post ganglionic sympathetic fibers innervating eccrine sweat glands uses acetylcholine as a transmitter [Wilke et al., 2007]. Acetylcholine activates sweat gland by two different mechanisms: direct stimulation of muscarinic M3 receptor on the sweat gland (DIR) and indirect stimulation through local axon reflex (AXR) via nicotinic receptors on the axon terminal. Stimulation of nicotinic receptors produces retrograde impulses travelling to distant axon branches causing eventual stimulation of adjacent sweat glands. The muscarinic DIR response is of short latency and long duration while the nicotinic AXR response is of longer latency but shorter duration [Vilches and Navarro, 2000].

Binding of acetylcholine to muscarinic receptors on the sweat gland raises intracellular calcium concentration resulting in an increased permeability of potassium and chloride channels. Changes in permeability cause isotonic precursor fluid to be released from the secretory cells. As the precursor fluid passes along the duct towards skin surface, sodium and chloride are reabsorbed causing the precursor fluid to become hypotonic [Burns et al., 2010].

Increases in sweating can occur from the combination of increasing density of activated sweat glands and increasing the sweat output amount of sweat output per gland [Shibasaki et al., 2006]. Inefficient thermoregulation and circulation may lead to hyperthermia during exercise in hot weather resulting in heat illness. Heat illnesses, including heat syncope, heat exhaustion, heat cramps and heat stroke, occur as a result of hypotension caused by cutaneous vasodilation and the pooling of blood, dehydration due to excessive sweating, imbalance of sodium ions loss, and extreme hyperthermia leading to thermoregulatory failure [Koppe et al., 2004]. Previous studies reported that children and the elderly were generally more susceptible to hyperthermia and heat illness than young adults as confirmed by the report that half of heat-related deaths in Japan occurred in children and elderly [Inoue et al., 2002].