THE SWEAT GLAND, HOW DOES IT WORK, AND WHAT FACTORS AFFECT SWEAT RATE AND COMPOSITION?

Introduction

Humans are second only to camels in their ability to remain moderately active during the day, in the hottest regions of the world, due largely to their capacity to sweat. In humans, the eccrine sweat gland is probably the most active exocrine gland in terms of fluid and electrolyte secretion.

Humans have one of the most efficient evaporative cooling systems, which is evidenced by the efficiency of the thermoregulatory system, for three reasons: 1) the thermal sweat is produced by eccrine sweat glands, 2) there are two to three million eccrine sweat glands which are distributed over the skin surface, and their secretions cover the whole body, and, 3) the relative lack of body hair. These factors allow maximal sweat evaporation and, therefore, heat loss. Due to the importance of sweating for evaporative heat loss, however, the major limiting factor for the human animal in maintaining thermal homeostasis is the availability of sufficient water intake to compensate for sweat fluid losses.

Types of Exocrine Sweat Glands

There are three types of sweat gland in the human: the eccrine, apocrine and apoeccrine, but it is the eccrine sweat glands that are involved in thermoregulation. The eccrine glands secrete a hypotonic solution to plasma, with variable obligatory amounts of electrolytes, mainly sodium, chloride and potassium together with other compounds in very small amounts, namely: lactate, urea, ammonia, proteins and peptides. Apocrine and apoeccrine glands, in contrast, generally produce secretions which are richer in fats, proteins and salts, and which evaporate at a slower rate than eccrine secretions, and thus reduce the rate of heat loss. In humans, apocrine glands are mainly restricted to the face and hands, but are also located with apoeccrine glands in the mammary, axillary, anal and genital areas, whereas eccrine glands are distributed widely over the body surface.

Structure of the Eccrine Sweat Gland

The eccrine sweat gland consists of a simple tubular epithelium, and is comprised of the reabsorptive sweat duct (RSD) and the secretory coil. The coiled portion of the gland consists of the secretory coil and the proximal portion of the RSD, which are located in the dermis of the skin. The RSD of the sweat gland consists of the proximal coiled segment, a distal straight segment that traverses the dermis, and the intraepidermal sweat duct unit which opens directly onto the skin surface.

Secretory Coil

The secretory coil is comprised of three types of cells: dark, clear (secretory) and myoepithelial cells. The clear cell of the secretory coil is characterised by the presence of basal membrane infoldings (the reported site of Na - K ATPase), membrane villi, intercellular canaliculi which open into the lumen, and abundant mitochondria located near the basolateral membrane (BLM), which indicates that the clear cell is involved in the active secretion of electrolytes and water. The clear cell also reportedly has receptor sites for cholinergic and adrenergic neurotransmitters.

The myoepithelial cells are located near the BLM of the secretory coil, and are filled with dense myofilaments, which contract in response to cholinergic, but not adrenergic, stimulation. The function of the myoepithelial cells is believed to be structural in providing mechanical support for the secretory coil wall against the increase in luminal hydrostatic pressure during sweating, rather than the pumping out of preformed sweat. The dark cells are located near the lumen of the secretory coil, but their function is as yet unknown.

Reabsorptive Sweat Duct

The RSD is composed of two layers of cells - the basal ductal (peripheral) cells and the luminal cells. The basal ductal cells are rich in mitochondria, and the entire circumference of the cell membrane shows evidence of Na^+-K^+ATPase activity, suggesting that the entire cell membrane is involved in sodium pumping for ductal sodium reabsorption. In addition, it appears that the basal ductal cells also have receptor sites for sympathetic nervous system neurotransmitters. In contrast, the luminal cells of the duct have fewer mitochondria and only a small number of Na^+-K^+ATPase pumps, but a dense layer of tonofilaments near the luminal membrane,

which appear to function to provide structural resilience to the tubular lumen. In addition, the luminal cells contain channels for both sodium and chloride, and appear to act as the absorptive surface for passive diffusion of sodium, for ultimate active reabsorption by the basal ductal cells.

Sympathetic Nervous System Control of Sweating

Sweat gland activation occurs as a result of the discharge of cholinergic fibres, whose activity is controlled by the thermoregulatory centre located in the hypothalamus. Efferent nerves, originating from the sweat centre, presumably in the preoptic region of the hypothalamus, descend through the ipsilateral brain stem and medulla, and synapse in the intermediolateral cell columns of the spinal cord. The myelinated axons arising from the intermediolateral horn of the spinal cord (preganglionic fibres), pass out in the anterior roots to reach (through white rami communicantes) and synapse with postganglionic fibres, in the sympathetic chain ganglia. These sympathetic post ganglionic fibres are the nerves which innervate the sweat glands and consist of unmyelinated C class fibres, and which terminate, with other peripheral nerves, surrounding the sweat glands. Efferent nervous innervation to all sweat glands of the body leaves the spinal column at the thoracic and lumbar regions of T1 - L2. The term 'sudomotor' pertains to the efferent nerves that control the activity of the eccrine sweat glands.

In contrast to ordinary sympathetic innervation, acetylcholine is the principle neurotransmitter of the sudomotor system, although it also has an adrenergic component. Sweat cells exhibit cholinergic and alpha and beta adrenergic receptors on the BLM. Vasoactive intestinal peptide (VIP), atrial natriuretic peptide, ATP, and other substances, have also been located in the periglandular nerves of the sweat gland. However, the role and function of most of these peptides and neurotransmitters on sweat gland function is not fully understood.

Substances Used To Determine Sweat Gland Function *In Vitro*

Cultured sweat gland cells retain the ability to respond to a variety of secretagogues by receptor mediated processes, including the adrenergic agonists isoproterenol (ISO), prostaglandin E_2, phenylephrine, and the cholinergic agonists methacholine (MCh) and pilocarpine. Cultured human sweat cells also respond to acetylcholine and adrenaline.

In vitro, the addition of ISO to cultured sweat cells results in sweat secretion, reportedly via the beta adrenergic receptor. Phenylephrine, an alpha adrenergic agonist also results in sweat secretion, but significantly less than beta adrenergic sweat stimulation by ISO. Sweat secretion induced by the beta adrenergic agonist ISO, may be due in large part to accumulated cAMP because this substance collects in the sweat gland during stimulation with ISO, but not with acetylcholine. External calcium is not required for the ISO induced cAMP response. Furthermore, sweat secretion can be induced by theophylline which enhances cAMP. It is believed that a minimum level of intracellular calcium may be required for beta adrenergic sweating.

Acetylcholine and adrenaline stimulate sweat secretion in isolated human sweat glands, but adrenaline appears to activate calcium influx without mobilising intracellular calcium, in contrast to acetylcholine. Adrenaline reportedly acts via alpha adrenergic receptors.

Formation of Primary Sweat

The secretory portion of the eccrine sweat gland secretes isotonic fluid into the lumen. The primary fluid is rendered hypotonic during its passage to the skin surface by reabsorption of sodium chloride in excess of water, a process performed by the epithelial cells lining the duct.

The series of events leading to the secretion of an isotonic fluid into the sweat duct are as follows: acetylcholine is released from periglandular cholinergic nerve endings in response to nerve impulses from the CNS, and binds to cholinergic receptors located in the BLM of the clear cell of the secretory coil. Activation of cholinergic receptors results in the mobilisation of intracellular calcium, and influx of extracellular calcium into the clear cells' cytoplasm, which results in the commencement of sweat secretion.

Sweat secretion is sustained by acetylcholine in two phases: a transient extracellular calcium independent stage, and a sustained extracellular calcium dependent stage. The transient component is attributed to the release of calcium from bound intracellular stores, and therefore acetylcholine can increase intracellular calcium in the absence of extracellular calcium, but only for a short period. The sustained phase, however, appears to result from calcium influx, and occurs only in the presence of extracellular calcium.

Calcium Mobilisation Mediators

Calcium ions are ubiquitous regulators of many cellular processes, and eukaryotic cells have evolved a complex system of channels, pumps and exchangers, and transmembrane molecules, which maintain intracellular calcium concentrations at very low levels 10-100nM. This allows for rapid metabolic responses to calcium fluxes. Inositol polyphosphates (IPP's) are important mediators of intracellular calcium mobilisation and calcium influx, and are rapidly generated following cholinergic stimulation.

The signal transduction pathway for calcium's rapid agonist responses in many tissues involves the activation of the enzyme phospholipase C, which acts on the substrate phosphatidylinositol 4,5 biphosphate, and which results in the formation of inositol 1,4,5 triphosphate (IP_3) and diacylglycerol. The second messenger of this reaction - IP_3, generated at the cell membrane, causes the rapid release of calcium from intracellular stores by activating specific receptors and directly opening calcium channels, on the membranes of these stores in specific organelles, such as the endoplasmic reticulum.

Cytoplasmic calcium is significantly reduced when extracellular calcium is removed, and thus the formation of IP_3 may be of limited importance in the sustained elevation of cytoplasmic calcium during sweat gland stimulation. However, it has been speculated that IPP's could also mediate calcium entry from the ECF, and not just from intracellular stores. It has recently been reported that depletion of internal stores of calcium triggers a capacitative influx of extracellular calcium across the plasma membrane. Because internal calcium stores are finite, prolonged bouts of signalling depend on the influx of external calcium through store operated channels (SOC's) in the

plasma membrane. The influx of calcium can be recorded as SOC in the plasma membrane, or as a current known as the calcium release activated current (I_{crac}) An as yet unanswered question in cell signalling is how SOC and I_{crac} sense and respond to intracellular calcium store depletion. It is postulated that IP_3 receptors in intracellular stores are coupled to SOC and I_{crac} by a tight functional interaction with Htrp3 protein channels.

Effect of Increased Intracellular Calcium on Sweat Secretion

The increased cytoplasmic calcium, due to the transient and sustained acetylcholine phases through the activation of IPP's, stimulates chloride channels in the apical (luminal) membrane, and potassium channels in the BLM of the secretory clear cell, resulting in the efflux of both ions. The rise in cytoplasmic calcium is reportedly the key factor in the activation of the potassium channels, although not fully elucidated it may shift the voltage threshold for potassium channel opening. It has recently been reported that calcium activated potassium channels, which are gated by intracellular calcium, result in the coupling of intracellular calcium levels and membrane potential. Chloride enters the secretory cell via either a Na- 2Cl -K or Na - Cl cotransport system, and leaves the cells by diffusion into the lumen of the sweat duct.

The cholinergic stimulation of eccrine sweat secretory cells, and the associated rise in intracellular calcium concentration, is also associated with an influx into the cells of sodium, along with the efflux of potassium and chloride. Mch induces potassium and chloride efflux through their respective channels, activated in a calcium dependent fashion, and a sodium influx which can increase threefold the intracellular sodium concentration. During steady state Mch stimulation, the potassium concentration of clear cells reportedly decreases by approximately 45%, whereas sodium concentration increases in such a way as to maintain the constancy of the sum of sodium and potassium concentrations. In the secretory cells, blockade of the BLM potassium conductance inhibits sweat secretion, and a fall in cytoplasmic potassium accompanies secretion, showing the importance of potassium efflux in sweat secretion.

The movement of chloride across the apical membrane depolarises the apical membrane and generates a negative luminal potential. This negative lumen charge then attracts sodium into the lumen across the intercellular junction (ie., paracellular pathway), and therefore, osmotically water, for the formation of sweat, which is reportedly isotonic to plasma.

Other Biochemical Requirements for Sweat Secretion

The acetylcholine responses could not be obtained for either the transient or sustained phase in a bicarbonate free medium, and the human sweat gland in vitro appears to have a strict requirement for bicarbonate. Potassium efflux is drastically reduced in the absence of bicarbonate. Removal of extracellular bicarbonate influences intracellular pH, and reduces cytoplasmic hydrogen ion buffering capacity which may affect sweat gland secretion. In addition, secretagogues which mobilise calcium are known to effect cytoplasmic pH by stimulating proton extrusion via Na - H counter-transport. It is possible that in the human sweat gland, the cytoplasmic calcium store is pH sensitive and becomes depleted during periods of acidosis, thereby inhibiting secretagogue-evoked calcium mobilisation.

In addition, the transient phase of acetylcholine stimulation was abolished when external sodium was replaced with a similar compound, suggesting that the mobilisation of cytoplasmic calcium is dependent, in some way, on external sodium. In contrast, the sustained phase of the response was not affected by the removal of external sodium, suggesting that calcium influx does not occur via a sodium dependent system.

Sodium Chloride Reabsorptive Process

Although the biochemical reactions which result in primary sweat formation are essentially the same as those for sodium reabsorption in the sweat duct, ie. an intracellular rise in calcium concentrations following acetylcholine stimulation, there is differing selective permeability for certain ions in the ductal cells, as sodium is actively transported back into the blood.

The RSD is a unique tissue compared with many sodium chloride absorbing epithelia, in that it has low cell membrane electrical potential (BLM potential is approximately -7.0mV, and the apical membrane -19.0mV), and an extremely high transepithelial chloride conductance. The sodium absorbing tissue has a poor BLM potassium permselectivity, a relatively large BLM chloride conductance, and the transepithelial potential in vivo human sweat ducts is measured as -40Mv (lumen negative), that is due to sodium reabsorption. Other authors have recorded the transepithelial potential as -30mV at the opening of the duct.

The capacity of in vivo human sweat ducts to absorb sodium was estimated at 400pmmol/mm.min, which corresponds to 20nmol/cm.second, assuming a diameter of 10um for the duct lumen. The cholinergic agonist, Mch, stimulates sodium transport in cultured epithelia, and with a few minute delay, evokes oscillations in the transepithelial potential difference and short circuit current (>5um concentrations).

Sodium transport, in cultured sweat gland epithelia, is thought to result from an increase in intracellular calcium, which in turn activates calcium-sensitive potassium channels in the BLM, as with sweat formation. As a result of activation of these potassium channels in the BLM, the apical membrane hyperpolarizes, thereby increasing the electrochemical gradient for sodium entry. The results of studies indicate that Na^+-K^+ATPase pump activity in the BLM of the basal ductal cells is mainly responsible for the high intracellular potassium activity (above equilibrium) evidenced in the RSD cells. However, the role of other transport carriers such as Na - 2Cl - K or K - Cl cotransporters, which in turn depend on the Na - K pump activity, to maintain the higher potassium activity, is also possible. The apical membrane of the reabsorptive sweat duct does not seem to possess a potassium conductance. The intracellular potassium activity may also be modulated by the sodium transport status in the apical membrane.

As aforementioned, the apical membrane of the reabsorptive sweat duct does not seem to possess a potassium conductance. Regarding the serosal membrane, the potassium conductance of differentiated cells is localised in this membrane, but under selective conditions. The basal ductal cells show high activity of Na^+-K^+ATPase, with potassium conductance on the BLM, but not on the luminal membrane, and amiloride sensitive sodium channels on the luminal membrane. The duct is highly permeable to chloride,

and it appears that sodium enters passively from the lumen through amiloride sensitive channels, and is pumped out through the BLM in exchange for potassium. At the new steady state, the large influx of sodium across the apical membrane is equal to the flux of sodium carried by the pump in the BLM. Amiloride, or specific antagonists (atropine after carbachol, mepyramine after histamine), prevent sodium entry into the sweat gland epithelial cells. Exposure to mucosal amiloride, or sodium free solution, caused the cells to hyperpolarise, the fractional resistance of the apical membrane to increase, and the short circuit current to decrease to zero, i.e., sodium transport has ceased.

Evidence for Calcium Oscillations in RSD Cells

Cytosolic calcium oscillations are a nearly universal mode of signalling in excitable and non excitable cells. Although calcium is known to mediate a diverse array of cell functions, it is not known whether oscillations contribute to the efficiency or specificity of signalling or are merely a consequence of the feedback control of intracellular calcium.

Calcium signals can either activate highly localized cellular processes in the immediate vicinity of the channels, or by recruiting channels throughout the cell, can activate processes at a 'global' level. In many cells, IP3 is a global signalling molecule that liberates calcium throughout the cytoplasm. For sites of elementary calcium release to produce global responses, the individual channels must communicate with each other to set up calcium waves. If cells are connected, such intracellular waves can spread into neighbouring cells and become intercellular waves to coordinate cellular responses within a tissue.

It is believed that the increase in intracellular calcium is the primary event for sodium reabsorption, and with many cells behaving in synchrony. The spread of intracellular calcium waves is dependent on the presence of gap junctions, and although the presence of gap junctions in ductal cells has not been reported, electrophysiological studies indicate that the basal ductal cells are electrically coupled. In contrast, other studies unequivocally state that cultured sweat glands have prominent gap junctions, and are electrically coupled. The luminal and basal ductal cells appear to behave like a syncytium, presumably through intercellular communication, i.e. gap junctions. It is also reported that gap junctions are calcium controlled.

Sweat stimulation also reportedly results in oscillatory changes in membrane potential, and which is believed to be due to the potassium activated channels which appear synchronous in their opening and closing following cholinergic stimulation. It is postulated that the oscillations in cytoplasmic calcium are responsible for the cyclic changes in potassium channel activity. However, it is not understood how this specialized coupling between cytoplasmic calcium and potassium channels is achieved, but preliminary data indicate an absolute segregation of coupling between channels, and illustrates the functional importance of submembrane calcium microdomains.

Transient increases, or oscillatory behaviour, in intracellular calcium levels may be important to protect cells from injury which would occur upon prolonged elevation of intracellular calcium. The best way to achieve this, however, is if cells behave asynchronously so that intracellular calcium can be dissipated through gap junctions to quiescent cells. In sweat glands, however, whose function is to reabsorb salts from

small luminal volumes, asynchronous behaviour would mean that cells downstream would perform the absorptive task from an already depleted fluid. Synchronous behaviour results in intermittent waves of absorption, followed by periods of rest during which the luminal fluid is renewed, as appropriate flow rates are needed to ensure maximal efficiency. However, data shows that in the monkey palm sweat gland, the proximal duct contains approximately 10 times higher Na^+-K^+ATPase activity than the distal segments, indicating possibly greater sodium reabsorption in this area. (This is contradicted by other authors who suggest that the RSD acts in syncytium, i.e. constant reabsorption throughout duct, otherwise cells upstream would have a depleted fluid)

Recent results have shown that calcium oscillations increase both the efficacy and information content of calcium signals that lead to gene expression and cell differentiation. IP_3 releases calcium from intracellular stores and triggers complex waves and oscillations in the levels of cytosolic free calcium. The physiological functions of oscillations in cytosolic free calcium levels and the existence of IP_3 oscillations remain controversial. It is reported that IP_3 pulses mimic the natural cycle of calcium release from internal stores. Oscillations in IP_3 levels may be due to the fact that cells may only be able to generate a limited total amount of IP_3, because it's biosynthesis uses many ATP molecules and depletes stores of the scarce lipid, phosphatidylinositol 4,5 biphosphate. Repetitive pulses are more effective than a continuous supply of the same total amount of IP_3 for producing large and reliable calcium spikes, which in turn results in optimal signalling.

Three isoforms of the IP_3 receptor have been identified - I, II and III. Although the isoform of the receptor within the eccrine sweat gland has not been identified, the presence of calcium oscillations may be determined by elucidating the isoform. The Type III IP_3 receptor is restricted to the trigger zone from which calcium waves originate, and has distinctive IP_3 binding properties. Activation of type III isoform, in cells that express only this isoform, results in a single transient, but global, increase in intracellular calcium concentration. The bell shaped calcium dependence curve of type I IP_3 receptor indicates that it is ideal for supporting calcium oscillations, as it provides amplification of the initial IP_3 signal, and negative feedback inhibition of further IP_3 stimulated calcium release. The feedback inhibition is important because it provides autoregulation, and is essential for calcium oscillations and for the propagation of regenerative intracellular calcium waves. The properties of type III IP_3 are better suited to signal initiation as calcium dependent inhibition is lacking in this isoform, i.e., there is positive feedback as calcium is released. As far as cell function is concerned, oscillations proved to be more efficient than stable increases in calcium - but only when the average concentration of cytosolic calcium remains below ~300nM. In addition, the oscillations appear to be generated at the cell surface, without any involvement of intracellular receptors.

Factors Effecting Sweat Gland Function

As aforementioned, the preoptic/anterior region of the hypothalamus has an essential role in the control of thermoregulation. However, sweating does not commence until a specific temperature setpoint, T_S, has been exceeded, at which point there is a linear increase in sweat rate with T_{cor}. For a given person, sweat rate is dependent on environmental conditions (T_a, dew point temperature, radiant load and air velocity),

clothing (insulation and moisture permeability), degree of acclimatisation and physical activity level.

The rate of local sweat output can be mathematically represented as the sum of afferent inputs from internal and mean skin temperatures, and modified by local T_{sk}. In addition, it has been suggested that sweat output is also influenced by non thermal factors, such as changes in blood osmotic pressure.

Effect of Cardiovascular and Thermoregulatory Systems

Isotonic hypovolemia reportedly reduces the sensitivity of the sweating response and increases the T_{cor} threshold for sweating and cutaneous vasodilatation. This indicates that blood volume may also have an effect on sweat gland function, however this is also inconclusive. The effect of skin blood flow on sweat rate is also inconclusive, but some authors report that a decrease in skin blood flow is associated with reduction in sweating rates. The altered function of sweat glands, occasionally reported in the literature, during hypovolemia has been attributed to the lack of oxygen for sweat gland function.

Recent studies have indicated that the T_S or core temperature threshold for sweating can be changed by altering the homeostasis of the body. The infusion of a hypertonic sodium chloride solution reportedly results in an increase in T_{cor} of 1°C, which alters the threshold for sweating in defence of T_{cor}. In addition, it has been reported that during exercise, the increase in plasma sodium concentration, results in a slowing of the onset of sweating, and also raises the plateau for steady state T_{cor}. The effect of plasma osmolality, however, on sweat gland function is inconclusive.

Effect of Local Skin Temperature (T_{sk})

Local T_{sk} also reportedly modifies the effect of T_{cor} on sweating rate in a cumulative fashion. An increase in local T_{sk} is associated with a decrease in the T_{cor} threshold for sweating. However, this response is not universal, and there is a wide variability in responses between individuals. For some individuals, an increase in local T_{sk} results in increased sensitivity of the sweat gland to periglandular neurotransmitters. It has been observed, however, that an increase in T_{cor} is nine times more efficient in stimulating the sweat centre, and therefore sweat rate, than an increase in mean T_{sk}. The mechanism(s) for the effects of local T_{sk} on sweat gland function is unknown, but the periglandular temperature on glandular metabolism, neurotransmitter release and metabolism, membrane transport and/or receptor affinity has been postulated.

Effect of Sweat Gland Morphology

The quantity of sweat secreted from glands depends on the size, sensitivity and overall activity of the glands. The maximum sweat rate per gland is directly proportional to the sensitivity of the gland, and linearly related to the size of the gland. The size of the sweat gland varies almost fivefold between individuals, and this largely correlates with the individual (and perhaps regional) differences in sweat rates. As the size of the sweat gland increases, there is: 1) a higher sweat rate per gland, 2) a higher sweat rate per unit tubular length of the secretory coil, 3) a higher sweat rate per unit volume of

the secretory coil, and 4) an increase in cholinergic sensitivity of the sweat gland. Maximal sweat rate per gland ranges between 2-20nL/min.

There is reportedly no difference in the ability of males and females to sweat as the total number of sweat glands is fixed and does not change throughout life, in both sexes. There is, however, a significant regional difference in gland number, with the highest number on the palms and soles, followed by the forehead, forearms and the back. It has been reported that sweat glands use glucose as their primary energy source, but they also may utilise mannose, lactate and pyruvate. The total sweating rate does not seem to differ as a function of adiposity, and this seems to be true in both men and women.

Effect of Training and Acclimatisation

As sweat rate and blood volume are strongly correlated with VO_2max and degree of acclimatisation, physical training and acclimatisation results in improvement in glandular function. It has been reported that the enhancement of sweating can occur with physical training and heat acclimatisation. Acclimatisation is usually associated with an increased sweat rate by an increased sweating response to a given increase in T_{cor}. However, it is not clear whether the improved ability to sweat after acclimatisation is achieved at the central level, at the peripheral level (i.e., the level of the sweat gland and the periglandular nerves and vascularity), or both levels. Although the mechanisms for improved glandular function during acclimatisation remains unresolved, the maximal sweat rate increases after a number of days with heat exposure, and the rate of sweating is inversely proportional to the degree of acclimatisation. After approximately five days of initial heat exposure, however, there is no further increase in sweat rate.

The higher sweat rates observed in trained subjects is reportedly to be largely due to an increased sensitivity to the central sweating drive, at the peripheral level. Consequently, a relatively unfit person requires a higher central thermoregulatory drive to dissipate a given thermal load than a fitter person. It is speculated that this increased sweat gland response is mediated by 1) increased periglandular concentrations of acetylcholine, 2) increased cholinergic sensitivity of the sweat gland, 3) glandular hypertrophy, and 4) a combination of these factors. As the sweat rates increase with training and acclimatisation, the sweat electrolyte concentration decreases.

Effect of Maturation

Maximum sweat rate is not affected until at least the '60's, but gland function does decline during the 70's and 80's. This may be attributed, in part, to skin changes associated with many years in the sun, as the density of glands is unchanged throughout life. Maximal sweat rate per gland, which is an indicator of the functional capacity of the sweat gland, does not appreciably decrease until age 70.

Subjects of varying ages, from prepubescent (9 years), pubescent (12 years) and adult (21 years), males and females cycled at 50% VO_2max in 42°C; 18% RH for 40 minutes. Sweat was collected from a plastic bag attached to the back. Sweat sodium and chloride losses tended to increase with maturation (children ~40mmol/L and adults ~60mmol/L), while sweat potassium was lower in adults compared to the

prepubescents. Children have a lower sweating rate than adults, even when corrected for BSA, and per active gland. As a result, the amount of sodium chloride lost in the sweat of children is lower than that of adults, in absolute and per kg of body weight, with no maturational difference found in potassium loss. Within the same maturational group, there were no gender differences in sweat electrolyte loss or sweat rate when matched for aerobic power.

Local sweat rate is a product of sweat rate per gland and the number of activated sweat glands. Sweat rate per gland correlates with BSA. Both BSA and sweat gland size increase with age and these changes may contribute to the increased sweat rate per gland as a person matures. Data suggest that in children there is a lower population density of sweat glands in those with a higher surface area for older than for younger children. The changes in sweat rate and sweat gland population density with physical maturation may be attributed to geometric changes i.e., increase in body size and SA. However, the differences in sweat electrolyte composition between children and adults suggest that there are qualitative differences occurring in the sweat response during puberty.

The maturational differences in sweat sodium loss may be related to differences in sensitivity of the duct cells to plasma aldosterone levels, or that sodium loss in the sweat is a function of sweat rate, and occurs in the reabsorptive duct rather than in the acinus of the gland. However, there are reportedly no significant differences in plasma aldosterone levels between young and adult individuals, suggesting that difference in sweat sodium is probably not related to aldosterone, unless the sensitivity of the receptor to aldosterone is altered by maturation. It has been reported, however, that hormones do not affect the eccrine sweat cells in many of the ways that they affect the kidney.

Measurement of Sweat Electrolyte Composition

The sweat, which is secreted onto the skin, contains a wide variety of organic and inorganic solutes, with variable quantities of electrolytes. The amount of electrolytes lost depends on a number of factors, including the concentration of individual electrolytes, as well as the total sweat volume. The sweat composition undoubtedly varies between individuals, but may also vary within the same individual depending on the rate of secretion, the state of acclimatisation and the degree of physical fitness i.e. state of training. Well trained people, and those who are heat acclimatised, have attained the ability to minimise the excretion of electrolytes by the sweat glands, and have generally lower sweat electrolyte concentrations than unacclimatised and less fit individuals. The quantity of electrolytes excreted from different regions of the body is not uniform, and there are also differences in sweat electrolyte concentrations with maturation, with prepubescent individuals having lower sweat sodium concentrations. Apocrine apoeccrine sweat also differs in composition to eccrine sweat. For these reasons, it seems impossible to determine the one and only electrolyte composition of human sweat.

The knowledge of sweat electrolyte composition has been derived from a variety of studies, and there is wide variability in the results. There are a number of factors responsible for the variability in the composition of sweat: a large biological variability, variable electrolyte losses from different body sites, and methodological problems in the collection procedure including evaporative loss, incomplete collection and

contamination with sloughed skin cells. Some studies use a washdown technique for the collection of sweat, others use bags or capsules for sweat collection.

In order to determine the accuracy and reproducibility of different sweat collection procedures, collections of sweat were made in six subjects, utilising a total body washdown technique, and collections from one arm in an occlusive arm bag. Arm occlusive bags gave higher readings of sweat electrolyte losses than other measures, possibly due to the change in local T_{sk} and humidity at the sweat collection site. However, given that there are regional variations in sweat sodium loss, and that whole body sweat collection includes eccrine, apoeccrine and apocrine secretions, whereas arm sweat consists only of eccrine sweat, differences in results between the methods are to be expected. Pore occlusion, by sweat collection methods, influences excretion rate and the electrolyte concentrations in sweat.

Influence of Sweat Rate on Sweat Electrolyte Composition

Some authors report that sweat sodium concentrations are influenced by the flow rate of sweat, whereas other authors have found that sweat sodium concentrations are not related to the sweat flow rate. It has been suggested that sodium loss in the sweat increases with increasing sweat rates, with the explanation that a high sweat rate decreases the time available for sodium reabsorption in the duct of the sweat gland. However, the correlation between sweat sodium loss and sweat rate is low. In addition, within the same individual, there are also significant regional differences in sweat rate and sweat composition, which makes the relationship between sweat rates and sweat electrolyte composition difficult to quantify.

Source of Potassium in Sweat

The potassium concentration in human sweat is much higher than in blood. Results indicate that there is no potassium conductance or potassium - dependent carrier system to account for any potassium secretion across the apical membrane of the RSD. In addition, there are tight junctions between the cells of the RSD so it is unlikely that potassium could leak into the lumen as a consequence of luminal negativity. Since potassium concentration in the sweat reportedly increases with decreasing sweat rates, water reabsorption across the potassium impermeable luminal membrane may result, to some extent in an increase in luminal potassium concentration, but it is not the sole cause of potassium accumulation in the lumen of the RSD. However, it is more likely that primary sweat from the secretory coil is the source of the higher potassium concentration in human sweat. Although the concentration of potassium in the sweat is high compared to the plasma values of potassium, the plasma content represents only a fraction of the whole body stores.

Values for Sweat Electrolytes

Mean sweat sodium concentration has been reported as 33mmol/L with a range of 20-80mmol/L. However, other authors report the upper limit for sodium in the sweat as 60mmol/L with a range of 10-50mmol/L. The sweat from these studies was obtained using a whole body washdown technique or arm occlusive bags, and it is unclear in some studies as to the training or acclimatisation status of the subjects and the

environmental conditions. Sweat sodium losses for 233 children, aged from 1-15 years of age, have been reported as 5-46mmol/L.

Sweat potassium losses range between 4-8 mmol/L. The mean value of potassium in the RSD was measured at 4.1mmol/L. In contrast, it is also reported that mean potassium loss in the sweat varies between 8-10mmol/L (range 2.5-21.0mmol/L).

Sweat Rates

Depending on the exercise intensity, level of training and state of heat acclimatisation, sweat rates have been reported to rise as high as 2-3L/hr. For athletes, the highest sweat rates occur during prolonged, high intensity activity in the heat.

Sweat rates of 1L/hr are very common
In a study the average sweat loss of marathon runners 1.325L/hr.

Hidromeiosis

Hidromeiosis is the decline in sweat rate during repeated or prolonged sweating. The reason for hidromeiosis has yet to be ascertained but it may represent a decrease in the sweat rate due to poral occlusion or sweat gland fatigue. However, there is evidence that hidromeiosis is not associated with a decrease in sweat gland density or poral occlusion, and appears only to occur in acclimatised individuals. The sweat gland fatigue hypothesis has also been disputed. If an individual is put in a heat chamber, the hidromeiotic phenomenon can be observed as the sweating rate decreases over time. However, if the subject is removed and the skin dried, the sweat rate begins to increase again which indicates that the hidromeiotic phenomenon has little to do with sweat gland fatigue. In addition, in those subjects that exhibit a reduction in sweating over time, after prolonged heat exposure, there is no increase in T_{cor}. Consequently, hidromeiosis is believed to represent a physiological adaptation to acclimatisation that is apparently designed to minimise the loss of sweat water from the skin by dripping, without resulting in a rise in T_{cor}.

Other Mineral Losses in Sweat

It has been reported that copper lost in the sweat can vary from negligible to 4.9mg/L, and therefore, the nutritional significance of this loss is questionable, although there is some evidence that indicates copper excretion may take place in the sweat, as well as in the bile. There is also extremely variable sweat losses reported for zinc, from negligible to substantial. Some authors suggest that there are excessive losses of iron in sweat, with one author suggesting a loss of 2.5mg of iron per litre of sweat during a marathon race. However, this has not been supported by other authors, and results also range from negligible to substantial. Iron excretion in the sweat, from the whole body washdown technique (filtered for cellular material), is significantly lower than that reported from other methods where the sweat may be contaminated with sloughed cells. However it is generally agreed that there is not a significant amount of minerals lost in sweat and there is no need for rehydration drinks to add these minerals. This is especially so when maximal absorption is required, as any additional molecules will alter the tonicity of the drink and slow down absorption.