SWEAT ANALYSIS: A PAINLESS ALTERNATIVE TO REAL-TIME VITAL SIGNS ANALYSIS

PART 2: THE PHYSIOLOGY OF SWEAT

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Production of Sweat

Sweat glands are accessories of the epidermal region of the skin and are normally distributed throughout the entire body except the lips, external genitalia and nipples. Sweat glands function in the process of perspiration to help to eliminate waste products from excretory organs such as the kidneys. These glands are classified based on their physical structure and mode of secretion as eccrine and apocrine glands. The average human being has about 4 million sweat glands, of which 3 million are eccrine glands (Asahina, Poudel and Hirano, 2015). Therefore, sweat glands permit secretion of sweat through the cell membrane without pinching off the external cell parts. Postganglionic sympathetic fibres innervate the apocrine and eccrine glands (Hu *et al.*, 2018).

The production of sweat is associated with fluctuations in body temperature. The major neurotransmitter for eccrine glands is acetylcholine, while catecholamines serve as the key neurotransmitters for apocrine glands. An increase in body temperature causes the sympathetic nervous system to activate the eccrine sweat glands to release water to the outer surface of the skin (Cui and Schlessinger, 2015; Owen, 2016). The water then evaporates and cools the body. Therefore, eccrine sweat is central to adjusting body temperature. When temperatures are extremely high, humans are capable of excreting more than a litre of sweat in an hour (Amano *et al.*, 2015).

Following the formation of sweat, the dermal ducts in the sweat glands convey this substance to the surface of the skin. Throughout this process, analytes such as metabolites, ions, hormones, acids and low molecular weight peptides are apportioned into sweat. The predominant

ions in sweat are sodium and chloride, which are conveyed through active transport from the blood and the secretory coil. Consequently, osmotic pressure builds up and propels water into the sweat gland. Sodium and chloride ions are then reabsorbed via openings situated in the walls of the dermal duct walls. The rate of reabsorption is relatively constant, leading to a corresponding increase in the levels of sodium and chloride ions in secreted sweat as the sweat rate increases.

Understanding of the actual mechanism involved in the secretion of other sweat analytes is limited. However, it has been hypothesised that other analytes are partitioned into sweat via active or passive transport from the blood or interstitial fluid in neighbouring blood vessels. The ultimate concentration of the analytes in sweat is determined by the precise method of partitioning together with aspects such as molecular size, charge and sweat rate.

Eccrine sweat in humans is basically a watery solution of sodium chloride with minimal quantities of other electrolytes that are usually found in plasma. Eccrine sweat may also exhibit a reddish pigment. People who do not sweat heavily can lose large quantities of sodium chloride when exposed to elevated temperatures or intensive labour, potentially leading to sodium deficiency (Hurley and Johnson, 2015; Turner and Avolio, 2016). This deficiency may be linked with inefficiencies of the eccrine gland (Cheshire, 2016). However, the efficacy of the gland improves with continued use, minimising salt loss. The secretory region of the eccrine glands secretes an ultrafiltrate, which is processed by cells that cover the duct area. Reabsorption of electrolytes such as sodium occurs in this area, leading to the production of hypotonic sweat and preserving electrolytes as a result.

The apocrine sweat glands in humans are found in areas of the body with hair, for example, the armpits, scalp and genital region (Borowczyk-Michalowska *et al*., 2017). These glands constantly produce a concentrated fatty sweat into the tubes within the glands. Emotional

stress triggers contraction of the glands, causing the glands to eject their contents. Normal flora (bacteria) on the exterior of the skin then act on the fat in the sweat to produce unsaturated fatty acids that have a pungent smell (Jobling, 2015; Lübke and Pause, 2015). In nonhuman species, an additional function of apocrine sweat is to provide pheromone signalling, which influences social activities such as parenting and mating (Mutic *et al*., 2016). The role of apocrine sweat in humans is unknown but is thought to contribute to sexual attractiveness (Motofei and Rowland, 2016).

There exist mixed sweat glands that are referred to as apoeccrine glands, which are located in the perianal and axillary areas in humans. Apoeccrine glands mature during adolescence from the predecessors of eccrine glands. Several investigations using the hormones epinephrine and methacholine as sweat stimulants have shown that the apoeccrine glands generate sweat at a rate five times higher than that of the eccrine glands (Vary, 2016).

The thermoregulatory hub in the hypothalamus, which is sensitive to temperature changes, is responsible for the regulation of body temperature by controlling the levels of eccrine sweat and the flow of blood to the skin. The thermoregulatory centre is also sensitive to other factors such as physical exertion, hormones, emotions and endogenous pyrogens. The impact of emotions and physical activity on the thermoregulatory centre is achieved via the limbic system (Asahina, Poudel and Hirano, 2015; Mogenson, 2018).

Sweat glands found on the palms as well as those on the soles of the feet are triggered mainly by emotional stimuli (Hashmonai *et al*., 2017). In comparison, axillary sweating is prompted by thermoregulatory modifications in addition to emotional impetus. However, no significant differences are evident in the morphology, nervous organisation and neurotransmitter responses between the palmar and plantar glands and other sweat glands. Therefore, it is

hypothesised that a unique thermoregulatory centre is responsible for sweating in the palms, soles and axillae (Kauffman, 2018). This hub is different from the control centre that influences sweating in other parts of the body and is believed to be directed by input from the cortex only, making it impervious to temperature alterations. The lack of sweat triggered by emotion during sleep as well as under the influence of sedatives is an observation that backs this theory.

Emotional sweating is believed to be a primitive human function of use while hunting or on the battlefield. Low quantities of sweat on the palms and soles are helpful in enhancing friction by regulating the humidity of the stratum corneum. Consequently, the ability to grip is enhanced. Apart from cooling the body during physical activity and under elevated temperatures, other benefits of sweating prompted by heat include lowering blood sugar levels (Emaminejad *et al.*, 2017), reducing alkali stores (Reis, 2017), augmenting the number or erythrocytes (*Asoglu et al.*, 2016) and boosting the specific gravity of blood. Furthermore, during emotional sweating, natural smells from the apocrine glands become aerosols and liberate pheromone signals (Banner, Frumin and Shamay-Tsoory, 2018).

The Chemical Basis of Sweat

Sweat is a clear biological fluid that is slightly acidic at a pH of 6.3, which makes it more acidic than blood (Nyein *et al.*, 2016). Typical concentrations of ions such as potassium and calcium in sweat are usually in the millimolar range. Similarly, weak acids or alkalis – for example, ammonia – can reach the sweat glands via diffusion and form ions because of the elevated pH of sweat, which entraps the ions in the secretory coil and generates millimolar concentrations exceeding those in blood. Other moieties such as urea and lactate can move into sweat from blood or be produced all through the metabolic activities of the sweat glands at millimolar levels. Molecules with high molecular weight, for instance, glucose, are found in

sweat in the micromolar range, which is lower than that found in blood by orders of magnitudes. Conversely, proteins such as neuropeptides or hormones can be found in blood in the nanomolar or picomolar range (Bariya, Nyein and Javey, 2018). In addition to naturally produced analytes, sweat may contain such extraneous molecules as drugs, alcohols and heavy metals as the body tries to eliminate toxins (Bariya, Nyein and Javey, 2018).

Consequently, based on the pH partition theory, alkaline drugs are more likely to build up in sweat than in blood (Sonner *et al*., 2015). The conveyance of a water-insoluble drug in blood as well as in other types of biological fluids is influenced by the acidity or alkalinity of the liquid and the drug's pKa. These strictures can be substituted into the Henderson-Hasselbalch equation and used in the computation of the hypothetical concentration ratio of biofluid to plasma (Jadoon *et al*., 2015). Drug levels are usually higher in plasma than in sweat, creating a concentration gradient that ultimately prompts the diffusion of the unbound drug from the plasma to perspiration via the lipid bilayer of the membranes (Nakata *et al*., 2017). Water is the main constituent of sweat, comprising approximately 99%. Other constituents include nitrogenous substances including urea and amino acids, metal ions such as sodium and potassium, non-metals such as chloride ions (Dam, Zevenbergen and Van Schaijk, 2016), metabolites such as pyruvate and lactate as well as xenobiotics including drug molecules.

The components of sweat are influenced by the mechanisms of analyte partitioning and the method of sweat stimulation (Bariya, Nyein and Javey, 2018). In the normal physiological state, urine contains these substances in specific quantities. However, in pathological or disease states, the levels of these components change. Such changes can serve as indicators of various disorders for diagnosis or prognostic purposes. Alternative biofluids include saliva, blood and urine. However, other impurities found in these substances can complicate their use in clinical

studies. Sweat, on the other hand, contains negligible impurities, easing its preparation and thus making it an ideal biofluid for use as a biomarker. Additionally, sweat is less susceptible to contamination, which implies that it is possible to store this substance for protracted periods.

Another benefit of using sweat as a biofluid is the non-invasive sampling associated with its collection. Sweat analysis is thus deemed a rapid and easy procedure compared to methods involving other biofluids, particularly blood, whose sampling is an intrusive process that necessitates surgery. Consequently, patients requiring frequent analyses are predisposed to infections. Furthermore, blood samples need additional processing to eliminate plasma proteins before analysis in comparison to sweat samples. For a practical example, the rapid processing of sweat samples is valuable in doping regulation where test outcomes are needed urgently (Liu *et al*., 2015).

Despite these benefits, the regular use of sweat samples for clinical purposes has been constricted by prohibitive costs, painstaking sampling, the risk of infection and the requirement for volume normalisation (Heikenfeld, 2016). Moreover, evaluating the metabolic products contained in sweat is a rigorous endeavour. Other limitations of sweat as a biofluid encompass difficulties in generating sufficient sweat for test purposes, evaporation of samples, inadequate or inappropriate sampling gadgets and the need for highly trained workers. The presence of pilocarpine in sweat also introduces errors in measurements. The small quantities of sweat also pose problems in the normalisation of sampled volumes when handling quantitative measurements (Luque de Castro, 2016).

Reference List

Amano, T. *et al*. (2015) 'Modulation of muscle metaboreceptor activation upon sweating and cutaneous vascular responses to rising core temperature in humans', *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 308(12), pp. R990-R997.

Asahina, M., Poudel, A. and Hirano, S. (2015) 'Sweating on the palm and sole: physiological and clinical relevance', *Clinical Autonomic Research*, 25(3), pp. 153-159.

Asoglu, M. *et al.* (2016) 'Mean platelet volume and red cell distribution width levels in initial evaluation of panic disorder', *Neuropsychiatric Disease and Treatment*, 12, pp. 2435-2438.

Banner, A., Frumin, I. and Shamay-Tsoory, S. G. (2018) 'Androstadienone, a chemosignal found in human sweat, increases individualistic behavior and decreases cooperative responses in men', *Chemical Senses*, 43(3), pp. 189-196.

Bariya, M., Nyein, H. Y. Y. and Javey, A. (2018) 'Wearable sweat sensors', *Nature Electronics*, 1(3), pp. 160-171.

Borowczyk-Michalowska, J. *et al*. (2017) 'Stage-Specific Embryonic Antigen-4 (SSEA-4) as a distinguishing marker between eccrine and apocrine origin of ducts of sweat glands', *Journal of Investigative Dermatology*, 137(11), pp. 2437-2440.

Cheshire Jr, W. P. (2016) 'Thermoregulatory disorders and illness related to heat and cold stress', *Autonomic Neuroscience*, 196, pp. 91-104.

Cui, C. Y. and Schlessinger, D. (2015) 'Eccrine sweat gland development and sweat secretion', *Experimental Dermatology*, 24(9), pp. 644-650.

Dam, V. A. T., Zevenbergen, M. A. G. and Van Schaijk, R. (2016) 'Toward wearable patch for sweat analysis', *Sensors and Actuators B: Chemical*, 236, pp. 834-838.

Emaminejad, S. *et al.* (2017) 'Autonomous sweat extraction and analysis applied to cystic fibrosis and glucose monitoring using a fully integrated wearable platform', *Proceedings of the National Academy of Sciences*, 114(18), pp. 4625-4630.

Hashmonai, M. *et al.* (2017) 'The etiology of primary hyperhidrosis: a systematic review', *Clinical Autonomic Research*, 27(6), pp. 379-383.

Heikenfeld, J. (2016) 'Non-invasive analyte access and sensing through eccrine sweat: challenges and outlook circa 2016', *Electroanalysis*, 28(6), pp. 1242-1249.

Hu, Y. *et al.* (2018) 'Neural control of sweat secretion: a review', *British Journal of Dermatology*, 178(6), pp. 1246-1256.

Hurley, S. W. and Johnson, A. K. (2015) 'The biopsychology of salt hunger and sodium deficiency', *Pflügers Archiv-European Journal of Physiology*, 467(3), pp. 445-456.

Imani, S. *et al.* (2016) 'A wearable chemical–electrophysiological hybrid biosensing system for real-time health and fitness monitoring', *Nature Communications*, 7, pp. 1-7.

Jadoon, S. *et al.* (2015) 'Recent developments in sweat analysis and its applications, '*International Journal of Analytical Chemistry*, 2015(164974), pp. 1-7.

Jobling, M. A. (2015) 'On the nose: genetic and evolutionary aspects of smell', *Investigative Genetics*, 6.

Kauffman, P. (2018) 'Primary hyperhidrosis', in Loureiro, M. P. *et al.* (eds) *Hyperhidrosis: a complete guide to diagnosis and management.* Cham: Springer, pp. 27-32.

Liu, G. *et al.* (2015) 'Real-time sweat analysis via alternating current conductivity of artificial and human sweat', *Applied Physics Letters*, 106(13), pp. 1-6.

Lübke, K. T. and Pause, B. M. (2015) 'Always follow your nose: the functional significance of social chemosignals in human reproduction and survival', *Hormones and Behavior*, 68, pp. 134-144.

Luque de Castro, M. D. (2016) 'Sweat as a clinical sample: what is done and what should be done', *Bioanalysis*, 8(2), pp. 85-88.

Mogenson, G. J. (2018) *The neurobiology of behavior: an introduction*. Abingdon: Routledge.

Motofei, I. G. and Rowland, D. L. (2016) 'Structural dichotomy of the mind; the role of sexual neuromodulators', *Journal of Mind and Medical Sciences*, 3(2), pp. 131-140.

Mutic, S. *et al.* (2016) 'Chemosensory communication of gender information: masculinity bias in body odor perception and femininity bias introduced by chemosignals during social perception', *Frontiers in Psychology*, 6, pp. 1-11.

Nakata, S. *et al.* (2017) 'Wearable, flexible, and multifunctional healthcare device with an ISFET chemical sensor for simultaneous sweat pH and skin temperature monitoring', *ACS Sensors*, 2(3), pp. 443-448.

Nyein, H. Y. Y. *et al.* (2016) 'A wearable electrochemical platform for noninvasive simultaneous monitoring of Ca^{2+} and pH', *ACS Nano*, 10(7), pp. 7216-7224.

Oh, S. Y. *et al.* (2018) 'Skin-attachable, stretchable electrochemical sweat sensor for glucose and pH detection', *ACS Applied Materials & Interfaces*, 10(16), pp. 13729-13740.

Owen, K. (2016) 'Excessive sweating: are patients suffering unnecessarily?', *The Journal for Nurse Practitioners*, 12(1), pp. 35-40.

Reis, A. H. (2017) 'Acidemia and blood free fatty acids: analysis of cardiovascular risk factors in a new context', *Discovery Medicine*, 23(126), pp. 183-188.

Sonner, Z. *et al*. (2015) 'The microfluidics of the eccrine sweat gland, including biomarker partitioning, transport, and biosensing implications', *Biomicrofluidics*, 9(3), pp. 1-19.

Turner, M. J. and Avolio, A. P. (2016) 'Does replacing sodium excreted in sweat attenuate the health benefits of physical activity?', *International Journal of Sport Nutrition and Exercise Metabolism*, 26(4), pp. 377-389.

Vary Jr, J. C. (2016) 'Selected disorders of skin appendages-acne, alopecia, hyperhidrosis', *The Medical Clinics of North America*, 99(6), pp. 1195-1211.