‘Why do we itch and scratch?’

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Introduction:

Pruritus is to mean ‘an itching’. The response generated; *the* scratch equates to a physiological protective mechanism to protect the skin barrier from external harmful irritants in an acute setting. However, chronic itch, defined as a persistent pruritic urge lasting longer than six weeks is associated with significant negative impact on ones quality of life. No major classification of pruritus exists, except for broad classification into four major causes; dermatological, systemic, neuropathic and psychogenic. Whether the aetiology is dermatological or not, the act of itching can produce lichenification and excoriations of the skin which can predispose to an increased risk of infection.

Discussion:

Pruritus is a protective mechanism. This reflex is thought to be modulated neurologically from the level of the skin, with peripheral and/or central neurological signalling components. Therefore a complex pathway of mediators are involved.

Histamine, a known puritogen, was shown to be involved in transmitting the signal from the periphery to the spinothalamic tract. These primary afferent neurons synapse with cell bodies located in the dorsal root ganglia (DRG). Itch sensing neurons were believed to be a subpopulation of nociceptive neurons as proposed by the intensity-coding theory. The proposition of this theory was that low firing rates from specific nociceptive neurons generated the sensation of itch but once a higher firing frequency was attained the activity would be centrally interpreted as pain.

Cytokines have also been well established as signalling molecules of both the immune system and ‘*itch-transducers*’. Signalling between the primary epithelial cell; the keratinocyte, and the immune system via cytokines was shown to be the driver of the atopic dermatitis. This cytokine was denoted as Thymic Stromal Lymphopoietin (TSLP).

Afferent fibres express a host of channels and receptors in order to generate and appropriate response to stimuli. A study on mouse DRG demonstrated the expression of three G-protein coupled receptors (GPCR) as three separate classes of itch sensitive afferent neurons; 5-hydroxytryptamine, receptor 1F and Mrgpra3/d. However, only Mrgpra3 and Mrgprd were specific to itch sensitive neurons with minimal expression detected elsewhere. The idea of an itch specific pathway was coined.

However, different TRP channels were known to mediate either pain or itch, but as a class, they act as a functional molecular connection in mediating both pain and itch supporting an intensity-coding theory. It is now well established that many receptors are involved in the transmission of *itch signalling* to the level of DRG and spinal cord. However, it still is needed to be proven if these signals are relayed centrally.

Conclusion:

Pruritus is a primary symptom of many dermatological conditions with a significant effect on a patient's morbidity. The mechanism is thought to be neuroprotective but the pathways that are involved in its signalling are poorly understand, but ever so slowly being elicited. A peripheral and central signalling pathway is thought to exist after instigation of a signal at the level of the skin, with multiple signalling molecules and receptors involved. The new advances with JAK however, have postulated the existence of a core molecule as the ultimate signal through which multiple puritogenic signals may converge. JAK inhibition may be the key process involved in blockade of multiple puritogens signalling through a central mediator. Many chronic dermatological conditions have shown a beneficial response to the use of JAK inhibition to support this suggestion including alopecia universalis and vitiligo.