Why do we itch and scratch?

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Introduction

Itch is an increasingly common symptom presenting in both dermatology and primary care, which may significantly threaten physical and psychological wellbeing. Despite the prevalence of this sensation, underlying mechanisms of itch have been poorly characterised until recently. The development of reliable animal models has greatly improved our understanding of the molecular and neural pathways employed in itch signalling. On a cellular level it is important to appreciate the mechanisms involved in initiation of the itch signal. The underlying source of the pruritogenic stimulus must also be explored, as well as the functional purpose.

Causes of itch at a cellular level

On a molecular level, we itch because a variety of endogenous or exogenous stimuli activate specific receptors in the periphery. Neurotransmitters then facilitate propagation of itch signals to neurons in the dorsal horn, which subsequently undergo central modulation.

What stimulates release of pruritogens?

Pathological processes, which may be grouped according to their clinical time course, influence the concentrations of diverse pruriceptor agonists.

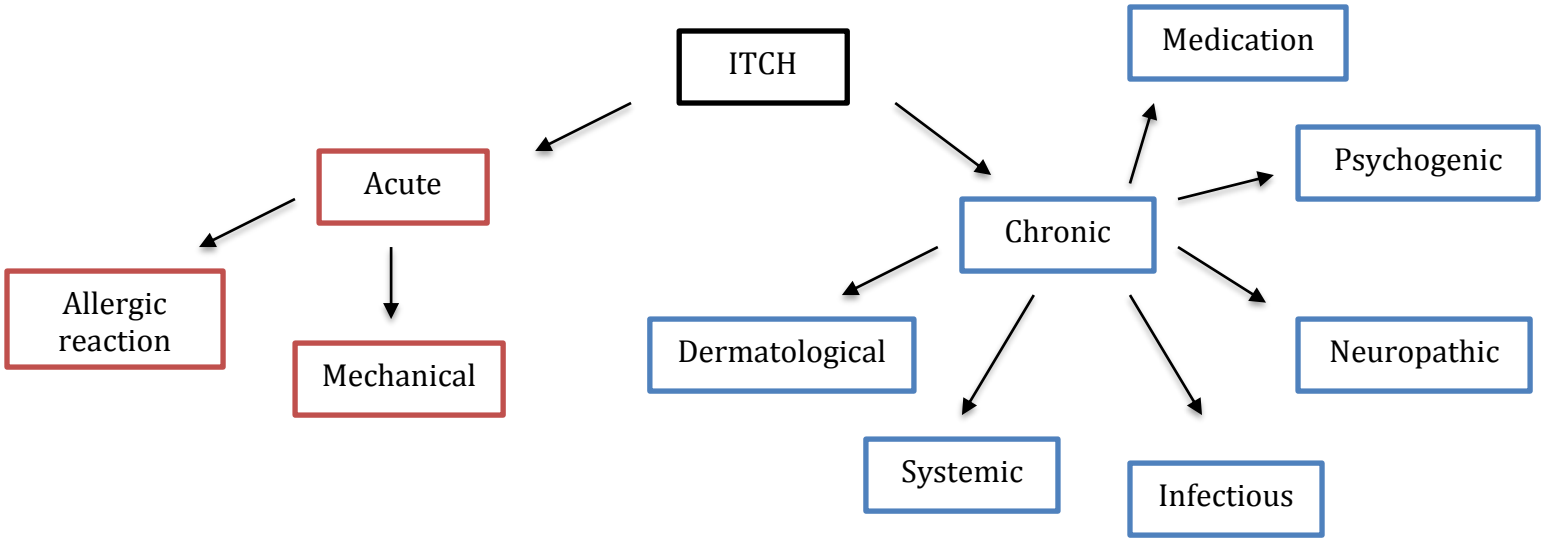

Figure.1: Causes of itch, grouped by clinical time-course.

Acute itch

Acute itch is perhaps best characterised by the allergic response. Stimulation of a type I hypersensitivity reaction evokes an IgE response with histamine-mediated release and downstream activation of TRPV1[1]. Mechanically induced itch may also be classified as acute, since removal of the stimulus terminates the itch sensation.

Chronic itch

In inflammatory dermatoses, itch is often associated with inflammation and dysfunction of the protective skin barrier. Itch may also be the primary manifestation of systemic disease, clearly appreciated in uraemic and cholestatic pruritus. Infectious diseases, most notably HIV and parasitoses, are also often burdened by chronic itch. The requirement for faithful communication of the itch stimulus, through complex neuronal circuitry, is emphasised by neuropathic itch. Damage to the signalling pathway can be appreciated in postherpetic itch and inflammatory transverse myelitis. Importantly, a rigid neuroanatomical pathway does not consider the role of behavioural or emotional contributions. Anxiety and depression share strong associations with pruritic skin disease[2,3], often with reciprocal causality. Pruritus can also be associated with psychotic disorders, including delusional parasitosis and impulse control disorders.

Why we scratch

Scratching is a conscious and voluntary response to itch, aiming to terminate the sensation. The mechanism employs the concept of surround inhibition. However, scratching does not always neatly terminate itching, as demonstrated by the perpetual itch-scratch cycle**.**

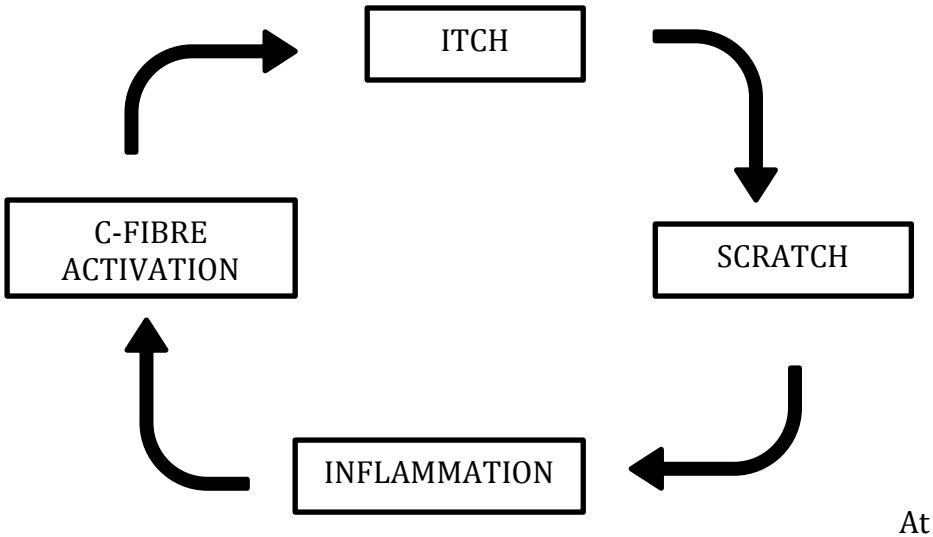

Figure.2: The itch-scratch cycle

At a molecular level, central serotonin signally has been implicated in potentiation of itch in mouse models[4]. Scratching also stimulates reward centres in the brain, detected by fMRI[5].

Does it serve any purpose?

The ability to sense itch may have previously offered a protective advantage in signalling the presence of parasites or toxic substances. In modern medicine, itch can provide useful clues to the astute clinician regarding diagnosis or progression of systemic conditions.

However, itch may also prove burdensome and harmful. Persistent scratching damages the protective barrier of the skin, risking secondary infection. Pruritus may also prove problematic when normal control mechanisms are deregulated, by means of peripheral and central sensitisation[6]. The psychological burden of living with a chronic itch condition is exemplified by studies reporting

impairment of sleep[7], appetite and concentration, as well as increased feelings of stigmatisation[8]. This suggests the need for liaison between dermatology and psychiatric services.

Conclusion

The skin is constantly bombarded by an array of stimuli, some of which activate pruriceptors and initiate itch signalling. Although the development of this sensation may have originally conferred some evolutionary advantage, overall the harms associated with chronic pruritus outweigh the protective benefits. The diversity of underlying causes evoking production of pruritogenic stimuli emphasises the fascinatingly broad differential diagnoses that the clinician may consider when faced with an itchy patient.

Word Count: 599

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