Scenario: Itch (widespread) - assessment

What should I ask and look for to determine if there is an underlying cause?

Ask the person about:

- o The characteristics of the itch:
- o Prickling itch of this nature can persist for hours after a hot shower or bath in people with polycythaemia vera.
- o Crawling a description of itch 'like insects crawling over the skin' may be psychogenic in origin and indicative of delusions of parasitosis.
- o Burning itch associated with burning may be a feature of dermatitis herpetiformis and some types of urticaria. Lymphoma can also present with burning itch. Stinging after contact with water is known as aquagenic pruritus and may be an isolated symptom, although it can be associated with myeloproliferative disorders such as polycythaemia vera.
- o Onset, timing, and duration of itch for example nocturnal itch can suggest scabies.
- o Location of itch consistently localized itch suggests a localized cause rather than systemic disease.
- o Relieving factors itch that is relieved with emollients or topical antipruritics is rarely associated with a serious cause.
- Associated symptoms (for example rash, fever, weight loss).
- o Drug history (to exclude medications that can cause itching, for example opioids).
- o Diet to identify features suggesting iron deficiency.
- o Itching in other people who have been contacts may indicate scabies.
- o Alcohol misuse may indicate liver disease.
- o Emotional stress and mental health history may indicate a psychogenic cause.
- Review all systems to identify symptoms associated with systemic disease. This may help focus the physical examination and laboratory tests.
- A full physical examination may be useful if there are no localizing clues from the history. Always examine:

- o The skin, for:
- o Lesions, rash, signs of infestation, or excoriation.
- o Dermographism (skin becomes raised and red when firmly stroked with a blunt object) indicative of a type of urticaria.
- o Colour may give clues about jaundice, renal failure, or anaemia.
- o Lymph nodes.
- o Liver and spleen, for enlargement.

The recommendation on what questions to ask and what examinations to perform is based on expert opinion in review papers [Krajnik and Zylicz, 2001; Moses, 2003; Greaves, 2004; Greaves, 2005; Roebuck, 2006; Davies, 2007].

What tests should I do?

- Request the following tests if there is no sign of active skin disease and an underlying cause is not obvious:
- Full blood count and blood film.
- Liver function tests.
- Renal function tests.
- o Serum iron and ferritin levels.
- o Thyroid function tests.
- o Fasting blood glucose.
- o ESR (erythrocyte sedimentation rate), CRP (C-reactive protein), or plasma viscosity, depending on local arrangements.
- Other tests should be guided by history and examination findings (for example chest radiography, urinalysis, faecal occult bloods).

Basis for recommendation

The recommended tests have been adapted for primary care by CKS from expert opinion found in narrative reviews [Greaves, 2004; Roebuck, 2006; Davies, 2007].

How should I manage itch while awaiting investigations?

- While awaiting the results of investigations, offer <u>self-care advice</u>.
- If the person has dry skin, offer an emollient (if this has not already been tried).
- o Use an emollient that is acceptable to the person.
- o Ointments are better at relieving dry skin than creams or lotions, but take longer to be absorbed into the skin and may not be as well tolerated.
- o Ointments or creams can also be used as a soap substitute if needed.
- o Advise the person to apply the emollient liberally as often as it is needed, and to use around 500 grams in a week.
- Apply emollients immediately after a bath or shower to keep moisture in the skin.
- o For more information on the use of emollients, see the section on <u>Prescribing information</u> in the CKS topic on <u>Eczema atopic</u>.
- o If an emollient alone does not provide adequate relief, consider a trial of an emollient with an active ingredient (for example menthol 0.5% or 1% in aqueous cream) or topical crotamiton (Eurax[®]).
- Once the results of investigations are available, see <u>Scenario: Itch (widespread) management</u> for information on management.

Basis for recommendation

Emollients

- Emollients are recommended as the first-line treatment for itch on the basis of expert opinion [Yosipovitch and Hundley, 2004; Proksch, 2008].
- Experts state that emollients are particularly helpful for people with dry skin, which is often the cause of widespread itch [Moses, 2003; Yosipovitch and Hundley, 2004]. Expert opinion suggests that ointments may be more effective at treating dry skin, but they are less well tolerated than creams or lotions [Dermatology UK, 2007].

Experts advise that effective use of emollients can also help to reduce complications from scratching

[Davies, 2007].

Emollients with active ingredients

Preparations such as menthol in aqueous cream are recommended by some experts and work by

stimulating nerve fibres which transmit the cold sensation, therefore distracting from the itch sensation

[Yosipovitch and Hundley, 2004]. They are usually used at a low concentration (for example 0.5–1%)

[Davies, 2007].

Some emollients contain active antipruritics, such as lauromacrogols, which are reputed by experts

to reduce itch by virtue of their mild anaesthetic effect [Davies, 2007]. However, CKS identified no trials

of emollients with these ingredients.

Topical crotamiton

CKS found no evidence on the use of topical crotamiton for widespread itch, although it is licensed

for use in people with scabies and itchy skin conditions [ABPI Medicines Compendium, 2007b]. Most CKS

expert reviewers consider a trial of its use for one or two weeks to be reasonable for widespread itch if

other treatments have been unsatisfactory. However, given the lack of evidence and its increased cost

compared with emollients, it is recommended as a second-line treatment by CKS.

Itch - widespread - Management

Scenario: Itch - widespread

How should I manage itch if the cause is known?

If the underlying cause of itch is treatable, manage it in primary care, or refer the person to

secondary care if appropriate.

Offer self-care advice.

If the person has dry skin, offer an emollient (if this has not already been tried).

Use an emollient that is acceptable to the person. 0

Ointments are better at relieving dry skin than creams or lotions, but take longer to be absorbed into

the skin and may not be as well tolerated.

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- o Ointments or creams can also be used as a soap substitute if needed.
- o Advise the person to apply the emollient liberally as often as it is needed, and to use around 500 grams in a week.
- o Apply emollients immediately after a bath or shower to keep moisture in the skin.
- o For more information on the use of emollients, see the section on <u>Prescribing information</u> in the CKS topic on <u>Eczema atopic</u>.
- o If an emollient alone does not provide adequate relief, consider a trial of an emollient with an active ingredient (for example menthol 0.5% or 1% in aqueous cream) or topical crotamiton (Eurax[®]).
- If the underlying cause cannot be treated (for example, chronic renal disease) and symptoms are not relieved by treatment of dry skin with emollients and self care:
- o Consider using a sedating oral antihistamine at night, such as hydroxyzine (which is licensed for pruritus) or chlorphenamine (off-label indication), as short-term treatment. Use sedating antihistamines with caution in people with liver impairment.
- o If, after 2 weeks of treatment, there is no relief of itch, stop the antihistamine.
- o Antihistamines are more likely to exert their effect through sedation than their antipruritic properties (unless there is an underlying histamine-related cause).
- Seek specialist advice about prescribing drug treatment to manage itch in the longer term (for example selective serotonin reuptake inhibitors, gabapentin, mirtazapine, or tricyclic antidepressants).

Treating the underlying cause

• The recommendation to treat the underlying cause of itch is based on expert opinion. If itch has a systemic underlying cause (for example hyperthyroidism, iron deficiency anaemia, or Hodgkin's lymphoma) the itching usually improves as the primary condition resolves [Moses, 2003].

Referral

• CKS found no evidence or guidelines on when to refer people with widespread itch. CKS has therefore based these recommendations on what is generally considered to be good clinical practice.

Emollients

- Emollients are recommended as the first-line treatment for itch on the basis of expert opinion [Yosipovitch and Hundley, 2004; Proksch, 2008].
- Experts state that emollients are particularly helpful for people with dry skin, which is often the cause of widespread itch [Moses, 2003; Yosipovitch and Hundley, 2004].
- Expert opinion suggests that ointments may be more effective at treating dry skin, but they are less well tolerated than creams or lotions [Dermatology UK, 2007].
- Experts advise that effective use of emollients can also help to reduce complications from scratching
 [Davies, 2007].

Emollients with active ingredients

- Preparations such as menthol in aqueous cream are recommended by some experts and work by stimulating nerve fibres which transmit the cold sensation, therefore distracting from the itch sensation [Yosipovitch and Hundley, 2004]. They are usually used at a low concentration (for example 0.5–1%) [Davies, 2007].
- Some emollients contain active antipruritics, such as lauromacrogols, which are reputed by experts to reduce itch by virtue of their mild anaesthetic effect [Davies, 2007]. However, CKS identified no trials of emollients with these ingredients.

Topical crotamiton

• CKS found no evidence on the use of topical crotamiton for widespread itch, although it is licensed for use in people with scabies and itchy skin conditions [ABPI Medicines Compendium, 2007b]. Most CKS expert reviewers consider a trial of its use for one or two weeks to be reasonable for widespread itch if other treatments have been unsatisfactory. However, given the lack of evidence and its increased cost compared with emollients, it is recommended as a second-line treatment by CKS.

Antihistamines

• CKS identified no controlled trials that investigated the use of antihistamines for widespread itch caused by cholestasis, renal failure, or malignancy [Davis et al, 2003; Greaves, 2005; O'Donoghue and Tharp, 2005], or itch of unknown cause. Some experts suggest that unless the itch is caused by a histamine-induced process (for example mastocytosis), the efficacy of antihistamines is limited [Summey and Yosipovitch, 2005; Lynde et al, 2008]. However, CKS expert reviewers were of the opinion that a trial of treatment with a sedative antihistamine at night for 2 weeks may offer relief from symptoms; it should be discontinued after this time if there is no effect.

- If an antihistamine is considered appropriate, first-generation antihistamines (for example chlorphenamine and hydroxyzine) are more sedating than second-generation antihistamines and may therefore be useful for night time use [O'Donoghue and Tharp, 2005].
- Experts postulate that sedating oral antihistamines probably provide a reprieve from nocturnal scratching by inducing sedation, helping to break the itch-scratch cycle (as occurs for other itchy conditions such as pruritus vulvae) [Weichert, 2004]. Therefore, they may have a beneficial effect in people with itch of unknown cause.

Additional drug treatment

- Experts recommend additional drug treatment for widespread itch if there is a specific indication or other treatments (such as self care and emollients) have been used without success [Lynde et al, 2008]. However, because of the weak evidence on drugs such as selective serotonin reuptake inhibitors, gabapentin, pregabalin, mirtazapine, and tricyclic antidepressants, and the fact that none of them are licensed for the treatment of itch, CKS does not recommend their use except on specialist advice.
- o **Selective serotonin reuptake inhibitors** there is weak <u>evidence</u> from small trials with methodological flaws (115 participants in total) and case studies that paroxetine, fluvoxamine, fluoxetine, and sertraline may be effective for reducing itch of a variety of causes. Although the evidence is very limited, it is stronger for paroxetine.
- o **Gabapentin** there is weak <u>evidence</u> from a randomized controlled trial (25 people) to suggest that gabapentin may be effective for the treatment of itch caused by renal failure, and <u>evidence</u> from another randomized controlled trial (16 people) that there may be no difference in efficacy between gabapentin and placebo for the treatment of cholestatic itch. In addition, <u>case reports</u> suggest gabapentin is effective for treating itch of unknown cause, brachioradial pruritus, and itch caused by multiple sclerosis.
- o **Mirtazapine** mirtazapine is an antidepressant with H1-antihistamine properties. There is weak evidence from <u>case studies</u> that suggest it may be effective for itch caused by malignancy, renal failure, and cholestasis. However, it has not been studied in controlled trials [<u>Greaves, 2005</u>]. Mirtazapine also has an anxiolytic effect, and can cause somnolence effects which may be beneficial for some people [<u>Summey and Yosipovitch, 2005</u>].
- o **Tricyclic antidepressants** (including doxepin and trimeprazine) have been reported in a few case studies to successfully treat pruritus, although predominantly that associated with skin disease [Davies, 2007]. They have the potential to help with anxiety and depressive symptoms that may be

associated with itch, but their use is limited by their adverse effect profile (anticholinergic and sedative effects), particularly in older people [Greaves, 2005; Summey and Yosipovitch, 2005].

How should I manage itch if the cause is unknown?

- Attempt to identify the cause of the itch, if this has not already been done. See <u>Scenario: Itch</u>
 (widespread) assessment.
- Offer <u>self-care advice</u>.
- If the person has dry skin, offer an emollient (if this has not already been tried).
- o Use an emollient that is acceptable to the person.
- o Ointments are better at relieving dry skin than creams or lotions, but take longer to be absorbed into the skin and may not be as well tolerated.
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- o Apply emollients immediately after a bath or shower to keep moisture in the skin.
- o For more information on the use of emollients, see the prescribing information section in the CKS topic on Eczema atopic.
- o If an emollient alone does not provide adequate relief, consider a trial of an emollient with an active ingredient (for example menthol 0.5% or 1% in aqueous cream) or topical crotamiton (Eurax[®]).
- If an underlying cause is unlikely and symptoms are controlled with emollients or self-care strategies, advise the person to continue with this and to return if there are any changes in their symptoms.
- If there is doubt about whether there is an underlying cause for the itch, or symptoms are not controlled with emollients or self-care strategies, refer the person to a dermatologist.

 While awaiting specialist assessment consider:
- A sedating oral antihistamine at night, such as hydroxyzine (licensed for pruritus) or chlorphenamine (off-label indication), as short-term treatment. Use sedating antihistamines with caution in people with liver impairment.
- o If after 2 weeks of treatment there is no relief of itch, stop the antihistamine.

- o Antihistamines are more likely to exert their effect through sedation than their antipruritic properties (unless there is an underlying histamine-related cause).
- o Seeking immediate specialist advice by telephone regarding alternative drug treatment for itch (for example gabapentin or pregabalin) while the person is awaiting the specialist appointment.

Emollients

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- Experts postulate that sedating oral antihistamines probably provide a reprieve from nocturnal scratching by inducing sedation, helping to break the itch-scratch cycle (as occurs for other itchy conditions such as pruritus vulvae) [Weichert, 2004]. Therefore, they may have a beneficial effect in people with itch of unknown cause.

Additional drug treatment for widespread itch

- CKS identified only weak evidence on gabapentin and pregabalin for the treatment of widespread itch of uncertain or no underlying cause. Because of the low quality of this evidence and the fact that neither of these drugs are licensed for treatment of itch, CKS recommends they are not prescribed in primary care except on specialist advice.
- Two case reports of people with intractable itch of uncertain cause, in whom numerous treatments had been tried with no relief, found symptoms were controlled within a month of starting gabapentin, with minimal adverse effects [Yesudian and Wilson, 2005].
- o Pregabalin has been used to treat widespread, severe itch with no underlying cause in case studies of three people [Ehrchen and Stander, 2008]. However, it is not licensed for itch, and further post-marketing safety data are needed (black triangle) [BNF 58, 2009].

What self-care advice should I give for itch?

- When bathing:
- o Reduce the amount of time spent in the bath to less than 20 minutes.

- o Bathe less frequently, if possible. Wash the axillae, genital area, and under the breasts daily, but other skin areas can be washed 2–3 times weekly.
- Use cool or lukewarm water (hot water can be drying).
- o Avoid bubble baths, soaps, and perfumed products. Use mild, alcohol-free cleansers, or use an emollient as a soap substitute.
- o If bath oils are used, use a non-slip bath mat to avoid injury.
- o Avoid vigorously drying the skin. Pat it dry instead.
- A cool shower may offer immediate short-term relief from itch, but avoid excessive showering as this may dry the skin.
- Keep nails short to minimize skin damage. Try to rub rather than scratch skin if the urge to relieve the itch is unavoidable.
- Keep the indoor environment cool (particularly the bedroom) and consider humidifying the air, particularly during the cold winter months.
- Wear clothing that does not irritate the skin (for example cotton or silk). Avoid wool or synthetic fabrics.
- Avoid spicy foods, alcohol, and caffeine as they may cause vasodilation.

These recommendations on self-care advice are based on expert opinion from a number of narrative reviews [Moses, 2003; Greaves, 2004; Yosipovitch and Hundley, 2004; Roebuck, 2006; Davies, 2007; Misery et al, 2007].

What treatments are not recommended for itch?

- A number of products are available that have been used to treat itch, but are *not* recommended by CKS for widespread itch when there is no identifiable underlying skin condition:
- o Topical anaesthetic.
- o Topical antihistamine.
- o Topical capsaicin.
- o Topical corticosteroids.

- o Topical doxepin.
- o Opioid antagonists (naloxone or naltrexone).
- Thalidomide.
- o Tricyclic antidepressants.

Topical anaesthetic

Topical anaesthetic is not recommended because expert opinion recommends avoiding excessive application and using it for a maximum of 3 days (because of the risk of systemic absorption) [BNF 58, 2009]. This is not a practical option for people with widespread itch. Topical anaesthetics are also associated with an increased risk of allergic sensitization [Moses, 2003; Lynde et al, 2008].

Topical antihistamines

• Topical antihistamines are not effective for widespread itch and expert opinion suggests there may be adverse effects (including allergic sensitization) [Moses, 2003; Hercogova, 2005].

Topical capsaicin

• Topical capsaicin is not recommended by experts as it requires frequent application and may cause a burning sensation [ABPI Medicines Compendium, 2007a; Davies, 2007]. These factors reduce its value for use over a wide body surface area, as is required in widespread itch.

Topical corticosteroids

• Topical corticosteroids are not recommended by experts for widespread itch because of their potential adverse effects, including skin atrophy [Moses, 2003; Yosipovitch and Hundley, 2004].

Topical doxepin

Topical doxepin is used for itch associated with atopic dermatitis [Lynde et al, 2008]. However, experts state that coverage should be limited to less than 10% of the body surface area because of the risk of sedation from percutaneous absorption [Yosipovitch and Hundley, 2004; Davies, 2007; BNF 58, 2009]; therefore, it is not suitable for widespread itch.

Opioid antagonists

Use of oral naltrexone has been shown to be effective for itch caused by cholestasis and uraemia [Davis et al, 2003; Greaves, 2005; Lynde et al, 2008]. However, the manufacturer's information states that naltrexone should only be initiated in specialist clinics for its licensed indication (to prevent relapse in detoxified, formerly opioid-dependent people) [ABPI Medicines Compendium, 2009]. Therefore, CKS does not consider it appropriate for off-label use in primary care.

Oral corticosteroids

Oral corticosteroids are not recommended by CKS for the treatment of itch, unless there is an underlying condition for which they are indicated. There are a number of potentially serious adverse effects associated with systemic corticosteroids, including adrenal suppression, immunosuppression, mood and behaviour changes, and increased susceptibility to infections [ABPI Medicines Compendium, 2008].

Thalidomide

Thalidomide has anti-itch activity, but is not recommended by experts because of its potentially serious adverse effects (including teratogenicity and peripheral neuropathy) [Summey and Yosipovitch. 2005].

Prescriptions

For information on contraindications, cautions, drug interactions, and adverse effects, see the electronic Medicines Compendium (eMC) (http://emc.medicines.org.uk), or the British National Formulary (BNF) (www.bnf.org).

Emollients

Age from 12 years onwards

Emulsifying ointment

Emulsifying ointment

Apply to skin frequently and liberally, as often as required. Use as a soap substitute. Supply 500 grams.

Age: from 12 years onwards

NHS cost: £2.38 OTC cost: £4.30 Licensed use: yes

Patient information: Apply gently in direction of hair growth, and avoid vigorous rubbing of skin.

Epaderm® ointment

Epaderm emulsifying ointment

Apply to skin frequently and liberally, as often as required. Use as a soap substitute. Supply 500 grams.

Age: from 12 years onwards

NHS cost: £6.14 OTC cost: £10.00

Licensed use: yes

Patient information: Apply gently in direction of hair growth, and avoid vigorous rubbing of skin.

Hydromol® ointment

Hydromol ointment

Apply to skin frequently and liberally, as often as required. Use as a soap substitute. Supply 500 grams.

Age: from 12 years onwards

NHS cost: £4.74 **OTC cost**: £8.35 Licensed use: yes

Patient information: Apply gently in direction of hair growth, and avoid vigorous rubbing of skin.

E45® cream

F45 cream

Apply to skin frequently and liberally, as often as required. Use as a soap substitute. Supply 500 grams.

Age: from 12 years onwards

NHS cost: £6.20 **OTC cost**: £9.69 Licensed use: yes

Patient information: Apply gently in direction of hair growth, and avoid vigorous rubbing of skin.

Diprobase® cream

Diprobase cream

Apply to skin frequently and liberally, as often as required. Supply 500 grams.

Age: from 12 years onwards

NHS cost: £6.76 **OTC cost**: £11.91 Licensed use: yes

Patient information: Apply gently in direction of hair growth, and avoid vigorous rubbing of skin.

Menthol in aqueous cream

Age from 12 years onwards

Menthol 0.5% in aqueous cream: apply once or twice a day

Menthol 0.5% in Aqueous cream

Apply to the affected area(s) once or twice a day. Supply 500 grams.

Age: from 12 years onwards

NHS cost: £15.30 Licensed use: yes

Menthol 1% in aqueous cream: apply once or twice a day

Menthol 1% cream

Apply to the affected area(s) once or twice a day.

Supply 500 grams.

Age: from 12 years onwards

NHS cost: £15.30 Licensed use: yes

Age from 12 years onwards

Crotamiton 10% cream: apply 2-3 times a day when required

Crotamiton 10% cream

Crotamiton

Apply to the affected area 2 to 3 times a day when required for relief of itching. Supply 500 grams.

Age: from 12 years onwards

NHS cost: £19.75 OTC cost: £35.16 Licensed use: yes

Crotamiton 10% lotion: apply 2-3 times a day when required

Crotamiton 10% lotion

Apply to the affected area 2 to 3 times a day when required for relief of itching. Supply 500 ml.

Age: from 12 years onwards

NHS cost: £14.95 OTC cost: £26.35 Licensed use: yes

Sedating antihistamine

Age from 12 years onwards

Chlorphenamine tablets: 4 mg at night when required

Chlorphenamine 4mg tablets

Take one tablet at night when required for relief of itching. Supply 28 tablets.

Age: from 12 years onwards

NHS cost: £1.08 OTC cost: £3.15

Licensed use: no - off-label indication

Hydroxyzine tablets: 25mg at night when required

Hydroxyzine 25mg tablets

Take one tablet at night when required for relief of itching. Supply 28 tablets.

Age: from 12 years onwards

NHS cost: £1.17 Licensed use: yes