Erythromelalgia is a rare clinical syndrome, originally described by Mitchell in 1878.

The term is a descriptive one, comprising *erythros* (red), *melos* (extremity) and *algos* (pain). This denotes the triad of redness, increased temperature and pain usually in the extremities.

Alternative terms include **erythermalgia** and **erythralgia**.

Usually the phenomenon causes bouts of painful redness affecting the lower extremities, commonly symmetrically; other body parts can also be affected.

These attacks can be relieved by immersion of the affected part in cool water.

Erythromelalgia can be primary (occurs on its own) or secondary, in conditions of various types including neurological, vascular and haematological.

Pathophysiology:

Charkoudian ([1]) suggests that, like Raynaud's, erythromelalgia may well "represent cutaneous microvascular disorder..." related to "disorders of local and/or reflex thermoregulatory control of the skin circulation."

Davis et al. ([2]) found that 86% of patients with erythromelalgia when screened for autonomic reflex, had abnormal results, with abnormal axon reflex test, adrenergic function and cardiovagal function. 94% had abnormal sweating (absent or severely reduced).

Electromyography and nerve conduction tests in these patients were often abnormal and vascular function studies showed an average increase in toe skin temperature of 7.8 degrees C during symptoms, with a 10- fold increase in blood flow.

The authors of the study concluded,

"most patients with erythromelalgia have small-fiber neuropathy."

Various other aspects of the arachnoiditis syndrome raise the suspicion that small fibre neuropathy is an element of the condition. Another possibility is decreased sympathetic vasoconstrictor response to certain stimuli.

Mork et al. ([3]) suggested that microvascular arteriovenous shunting was a possible mechanism.

This means that the very small blood vessels are not functioning normally.

Arteriolar fibrosis and occlusion with platelet thrombi may occur, but not in all cases.

Platelets have been demonstrated to have abnormal hyperaggregability and platelet kinetic studies show decreased platelet survival, predominantly due to increased consumption.

Prostaglandins and cyclooxygenase appear to play an important role.

Sandroni et al ([4]) found that during symptoms, an increase in blood flow and skin temperature is accompanied by a paradoxical decrease in oxygen supply to the affected area; they stated that a high proportion of patients have a distal small fibre neuropathy as well as large fibre neuropathy.

In Type 2 diabetes, the ability of skin blood vessels to dilate is impaired, and this may contribute to increased risk of heat illness in these patients when exposed to elevated ambient temperatures.

The same might be true for arachnoiditis patients and could thus account for heat intolerance. However, in many arachnoiditis patients, there is frequent fluctuation between feeling cold and feeling over-warm, despite no change in ambient temperature.

Indeed, many seem to have problems with Raynaud's and it now seems that some individuals have erythromelalgia in addition, so that they experience fluctuation between cold, white extremities and hot, red, swollen and painful extremities.

Berlin and Pehr ([5]) presented a case of co-existent erythromelalgia and Raynaud's phenomenon, so, whilst rare, this combination is recognised.

This may affect not only the feet (most commonly), causing burning sensation (which may, or may not, differ somewhat, qualitatively, from the nerve-related burning in areas of reduced sensation) but also the hands and even the face. Ramirez and Kirsner ([6]) recently described a refractory case involving the ears.

Orstavik et al. ([7]) suggest that the pain experienced in erythromelalgia has a neuropathic component and certainly arachnoiditis patients may find it hard to distinguish between nerve-related burning, dyaesthetic pain and the ?thermal' burning pain of erythromelalgia.

Indeed, it is feasible that an individual may experience both of these pains at different times and some may describe them as different pains.

Causes:

- Early onset erythromelalgia can be familial.
- Idiopathic erythromelalgia: in 60% of adult-onset erythromelalgia cases. Most early-onset

cases are idiopathic.

- Myeloproliferative disorders: mostly thrombotic in type e.g. polycythaemia, although prevalence of erythromelalgia in myeloproliferative disorders is uncertain. Erythromelalgia presents before diagnosis in 85% of cases.
- Medications that can cause erythromelalgia include: pergolide, bromocritpine, nifedipine, felodipine and nicardipine.
- Other disorders: include systemic lupus erythematosus (biopsya tends to show vasculitis), diabetes mellitus, venous insufficiency, astrocytoma, rheumatoid arthritis, and gout. It is not clear whether these conditions are coincidental.

Presentation:

- Attacks last minutes to days
- Triggers include exercise and increase in ambient temperature
- Attacks often begin with an itching sensation and progress to severe, burning pain that can prevent walking and may necessitate application of ice etc.
- Soles of the feet and toes are most commonly involved, usually bilaterally and may extend to the knees; hands, usually the palms, but may go as high as the elbow
- Exacerbating factors include warming the affected part or placing it in a dependent position (e.g. hanging leg down)
- Relieving factors include cooling and elevating the affected part. In myeloproliferative disorders*, dramatic relief from aspirin may occur.
- Differential diagnoses: menopausal hot flushes, cellulitis (infection), frostbite, vasculitis, neuropathic pain e.g. due to Complex Regional Pain Syndrome, peripheral neuropathy.
- Extremity becomes warm, tender, dusky in appearance, bright red and sometimes mottled. There may be oedema (swelling)
- Normal looking between attacks or possible blistering is constant or frequent flare-up; may alternate with Raynaud's.
- Pulses may be normal or bounding
- Ischaemic ulcers may occur
- Davis et al. ([8]) looked at presentation and outcome in 168 patients, of which 122 were female and 46 male. Another study of 60 patients found a male: female ratio of 3:2 in secondary erythromelalgia.

In Davis' study, average duration of symptoms ranged widely from 1 month to 26 years, with a mean of 48 months. 7 patients had experienced symptoms since childhood. 97% had intermittent symptoms, the other 3% were constant.

- 88% had involvement with the feet, 25% in the hands, 13% in the legs, and a few individuals with ears, neck or face.

- Patients described the affected part during the attack as ?hot' (48%), ?burning' (65.5%) and ?numb' by 3%.
- In 51%, symptoms were exacerbated by heat, and 29% made worse on exercise.
- In 67%, cooling the affected extremity with ice relieved the symptoms.
- Commonly patients employ a variety of strategies to avoid episodes (avoid exercise, sleeping without sheets and blankets, having a fan directed at the feet)
- Common behaviours adopted by patients to alleviate symptoms during an attack include: going barefoot, wearing open-topped footwear, avoiding socks; seeking cold surfaces to walk on, using a fan, immersing the part in cold or even iced water, sometimes for prolonged periods.
- Physical examination was abnormal in 66% of patients, of which signs included redness, acrocyanosis (a persistent blue or cyanotic discolouration of the fingers, which may worsen with exposure to cold and improve with rewarming, thought to be due to vasospasm in skin blood vessels), ischaemic ulcers (breakdown of skin due to inadequate circulation).
- 50% of the patients were smokers (note there is also a strong association between Raynaud's and smoking).
- 4 patients had diabetes
- various tests of autonomic and vascular function were abnormal as were nerve conduction and EMG in a significant number of patients.
- In terms of progression, after a mean follow-up of 8.7 years, 31% reported general worsening of the symptoms, 27% stayed the same and 31% said their symptoms were reduced; 11% reported complete resolution of the symptoms.
- Those who reported worsening noted an increase in frequency of attacks.
- In the 43% of the patients who reported an average annual rate of attacks, the average was 72 episodes a year, or 1.38 a week.
- 14% reported progression of symptoms from lower to upper and lower extremities, but those who presented only with upper extremity symptoms did not report progression down to the lower limbs.
- Local complications included: 22% skin damage due to ice/cold water, infections in 16%, ulcers (13%) and one case of gangrene. Soaking the affected part can lead to ?immersion foot' and irritant contact dermatitis. Allergic contact dermatitis in response to applied agents may also occur. Other vascular problems such as oedema, venous insufficiency and lymphoedema can be worsened by erythromelalgia.
- Functional impairment included inability to walk long distances, to stand for prolonged periods; 12.5% had to give up work, 12.5% stopped driving and 3% needed to use a wheelchair. 2 patients became bedbound.

Management:

Davis and Rooke ([9]) make the following suggestions:

"No treatment is consistently effective"

1. patient education about the condition and avoidance of precipitating factors
2. teach patients safe techniques to cool the affected parts
3. pain control using the same range of medication as for neuropathic pain; aspirin can have idiosyncratic effects, being highly effective in some patients but ineffective in others. Surveys suggest that most patients find it ineffective. Davis and Sandroni ([10]) reported benefit from topical lidocaine patch and Kuhnert et al. ([11]) found lidocaine intravenous infusion followed by oral mexiletine gave prolonged remission. Capsaicin was not found beneficial in Davis's study and less than half of those tried on beta-blockers experienced benefit. Cohen ([12]) found that Gabapentin reduced symptoms effectively. Antihistamines are not helpful in most patients. He more recently conducted a small study based on his own experiences with the condition, using high dose oral magnesium. ([13]) 8 out of 13 patients reported improvement, 4 had no response and one worsened. Note that Aldrete is currently investigating magnesium as a therapy for arachnoiditis.
4. Calcium antagonists such as diltiazem are strong vasodilators and do not seem beneficial in most patients and may indeed exacerbate the symptoms.
5. note that some of these treatment have also been reported to exacerbate the condition: e.g. sympathetic blocks, epidurals, sympathectomy, nitroprusside infusion and calcium antagonists.
6. control of secondary factors such as leg oedema etc.
7. correct underlying medical condition
8. direct patients to support groups such as: www.erythromelalgia.org (email erythro@ida.net)

* myeloproliferative disorders: e.g. chronic myeloid leukaemia, polycythaemia rubra vera; erythromelalgia may precede the diagnosis; this group of patients tend to respond dramatically to aspirin, which may help towards a diagnosis. ([14])

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