Splinter haemorrhages, Osler's nodes, Janeway lesions and Roth spots: the peripheral stigmata of endocarditis

Introduction

Infective endocarditis is a serious endovascular infection, potentially affecting not only native heart valves, but also intravascularly implanted foreign materials such as valvular prostheses and pacemaker electrodes (Westphal et al, 2009). The worldwide incidence of infective endocarditis has been estimated to be 3–10 episodes per 100 000 patient-years (Tornos et al, 2011).

The disease was first described in the 16th century by Jean Francois Fernel, a French renaissance physician (Fye, 1997). For some 200 years following this, much of the pathophysiology of endocarditis was elucidated in sketches made after post-mortem examination. Signs and symptoms of endocarditis, including cardiac murmurs and fever, were only described in live patients in the early to mid-19th century. However, it was not until the late 19th century that a comprehensive amalgamation of information regarding the pathophysiology of endocarditis was made by various scholars (Millar and Moore, 2004). In 1885 Sir William Osler delivered, in his Gulstonian (now Gouldstonian) Lecture Series, a comprehensive account of the disease, highlighting the difficulties in diagnosis as being 'practically insurmountable'. After Osler's landmark reports, at a time where the fields of microbiology and imaging were immature, extra-cardiac physical findings became important clues to earlier diagnosis of the disease (Silverman and Upshaw, 2007).

Despite advances in diagnostic imaging and microbiology, diagnosis of infective endocarditis remains a clinical challenge. Today, diagnosis of infective endocarditis integrates an initial clinical suspicion with microbiological data and echocardiographic findings (Haldar and O'Gara, 2006). Although prized extra-cardiac clinical findings are rare, they still provide excellent clues to the diagnosis of infective endocarditis. This review outlines these peripheral stigmata of endocarditis (*Table 1*), and explores their historical descriptions.

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Splinter haemorrhages

Splinter haemorrhages are a recognized characteristic physical sign of endocarditis. In 1920, Sir Thomas Horder first described these lesions in relation to infective endocarditis. His account was of 'minute petechiae, in the form of a vivid linear splash of red, at the side of the bed of a fingernail' and he believed them to be a harbinger of more definite signs of endocarditis (Horder, 1909). In 1923, Blumer depicted them as 'curious sub-ungual linear haemorrhages (akin to a wood) splinter under the nail'. From this, the label 'splinter haemorrhages' was coined (Silverman and Upshaw, 2007).

The pathophysiology of these lesions has been a matter of conjecture. Horder (1909) assumed them to be a vascular phenomenon, either caused by increased capillary fragility or minute emboli. Although some studies (Platts and Greaves, 1958) have shown them to be more common in conditions in which micro-emboli are a feature, suggesting them to be embolic in nature, the fact that they may also be seen in healthy patients whose occupations expose the fingertips to frequent trauma is more suggestive of a haemorrhagic origin (Gross and Tall, 1963). It is unlikely that these lesions are petechial in origin, as initially proposed by Lewis (1942) and

Table 1. Peripheral signs of endocarditis

	Splinter haemorrhages	Osler's nodes	Janeway lesions	Roth spots
Macroscopic features	Multiple linear lesions, 1–3 mm in length, initially red then turn brown or black in a few days	Small, painful nodular lesions; pea-sized but can be up to 1.5 cm diameter; erythematous	Painless, macular lesions, few millimetres in diameter, erythematous	Pale-centred retinal haemorrhages
Microscopic features	Stain positive for altered blood; arise from capillaries in the dermal papillae of the nail	Endothelial inflammation, peri-vasculitis, thrombosis of superficial arterial lumina; few studies have revealed positive cultures	Dermal micro-abscesses; no evidence of vasculitis; studies have shown the lesions to be culture-positive	Fibrin and platelet aggregate in white centre
Significance	Non-specific	Prevalence 3–5% in cases of 'definite' infective endocarditis (low sensitivity)	Prevalence 5–11% in cases of 'definite' infective endocarditis (low sensitivity)	Non-specific sign
Commonest site	Long axis of the distal third of the nail, move distally as the nail grows	Pads of fingers and toes	Palmar surfaces of hands and feet	Retina
Pathophysiology	Vascular in origin: some studies suggest an embolic cause, others suggest a haemorrhagic origin	Sterile vasculitis, mainly seen in sub-acute endocarditis	Septic micro-embolization	Retinal capillary rupture and subsequent repair

White (1945), as in cases of splinter haemorrhages capillary fragility is not increased (Platts and Greaves, 1958).

Macroscopically, 'splinters' appear as multiple linear lesions, 1–3 mm in length, orientated to the long axis of the distal third of the nail (*Figure 1*). When first formed, they are red, then brown or black within a few days (Martin and Platts, 1959). They move distally with the growth of the nail, and can be scraped off from the underside of the nail. Studies have shown them to stain positive for altered blood (Platts and Greaves, 1958). Histological studies have shown splinter haemorrhages to arise from large, spirally wound capillaries lying in the dermal papillae deep to the hyponychium of the nail (Martin and Platts, 1959). Other systemic conditions associated with splinter haemorrhages include systemic lupus erythematosus, rheumatoid arthritis, antiphospholipid syndrome, peptic ulcer disease, malignancies, use of the oral contraceptive pill, pregnancy and psoriasis (Fawcett et al, 2004).

Osler's nodes

Osler's nodes are described as small, painful, nodular lesions usually found on the pads of the fingers and toes (Maestre et al, 2001) (*Figures 2* and *3*).

In 1909, Sir William Osler highlighted the occurrence of 'ephemeral spots of a painful nodular erythema' as being a very interesting feature of infective endocarditis. Quoting his colleague, Dr JA Mullen, Osler further described these lesions as being small swollen areas, red in colour with a white point in the centre, ranging from the size of a pea to 1.5 cm in diameter. 'They come out at intervals, and [sometimes] pass away in a few hours, but more commonly last for a day or longer. The [most common site] is near the tip of the finger.'

It was, however, F Parkes Weber in 1913 who assigned the name 'Osler's node' or 'Osler's sign' to these lesions, reiterating their great diagnostic importance and crediting Sir William Osler for recognizing their significance.

Osler's initial tenet was that these lesions were caused by a micro-embolic phenomenon. However, further histological studies went on to emphasize the absence of bacteria or emboli in these lesions. Instead, they reported findings of endothelial swelling and inflammation, peri-vasculitis, focal inflammatory destruction of the dermal glomus body and thrombosis of superficial arterial lumina (Maestre et al, 2001; Gunson and Oliver, 2007). From this, it was suggested that Osler's nodes were caused by an immunological cross-reaction to the offending infective agent in endocarditis. Only very few biopsies of Osler's nodes have revealed positive cultures for the pathogenic organism (Alpert et al, 1967). Despite considerable ongoing debate regarding their pathogenesis, the current opinion is that Osler's nodes are a form of sterile vasculitis, caused by the deposition of circulating immune complexes in small blood vessels, mainly seen in the sub-acute form of endocarditis (Silverman and Upshaw, 2007).

Figure 1. Splinter haemorrhages. Two parallel streaks in the distal third of the nail.

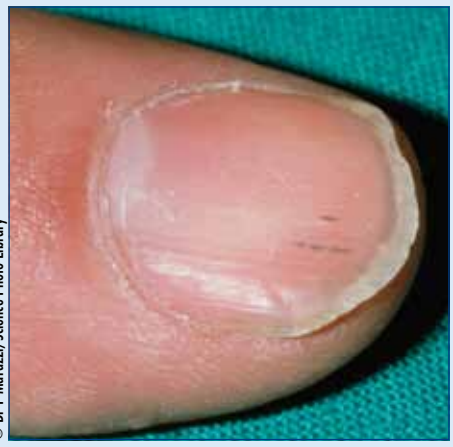
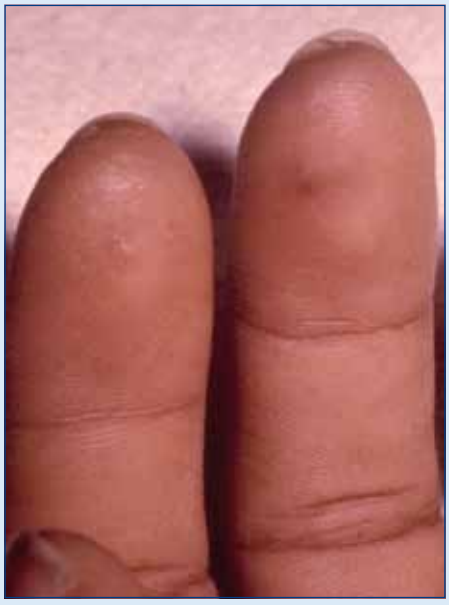


Figure 2. An Osler's node on the distal phalange of the finger.



Janeway lesions

Janeway lesions are painless, macular, haemorrhagic lesions that occur most commonly on the palmar surface of the hands and feet (Maestre et al, 2001) (*Figures 4–6*).

In 1899, Edward Janeway reported noticing small haemorrhages on the palms and soles of the hands and feet in patients with malignant (acute) endocarditis. He described these lesions as a way of distinguishing between acute endocarditis and other processes likely to be mistaken for it. In 1906, Emmanuel Libman, a pupil of Janeway, provided the name 'Janeway's

Figure 3. An Osler's node on the pad of the fourth toe.

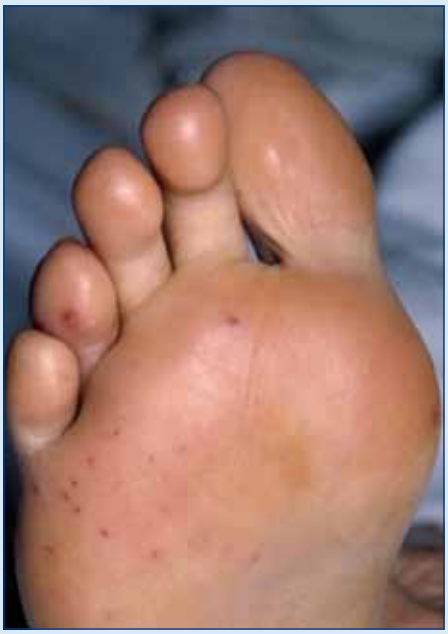
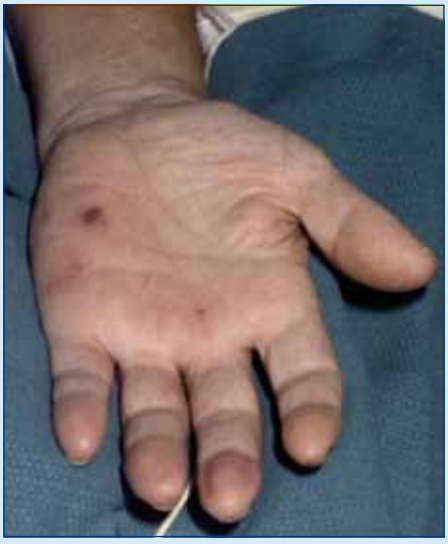


Figure 4. A Janeway lesion on the hypothenar eminence of the palm.



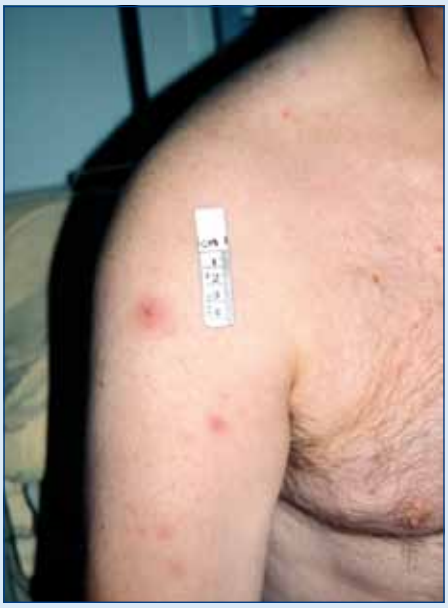


Figure 5. Janeway lesions on the shoulder of a patient with infective endocarditis.

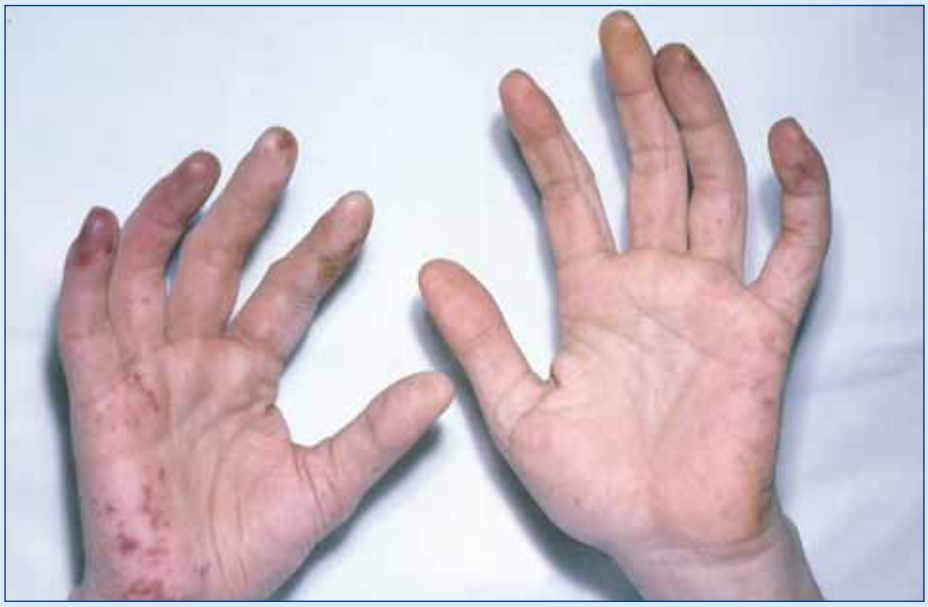


Figure 6. Janeway lesions on the hypothenar eminence of the palms in a patient with subacute bacterial endocarditis.

lesion' and remarked that these lesions were non-tender, in contrast to the exquisitely painful Osler's node. He highlighted them as being pathognomonic of endocarditis, later commenting that they were mainly seen in acute endocarditis (Libman, 1918, 1923).

Most histological studies of Janeway lesions have revealed dermal micro-abscesses, without evidence of vasculitis (Gunson and Oliver, 2007). Bacterial cultures are often positive, leading to the conclusion that these lesions are caused by septic micro-emboli (Farrior and Silverman, 1976; Kerr and Tan, 1979).

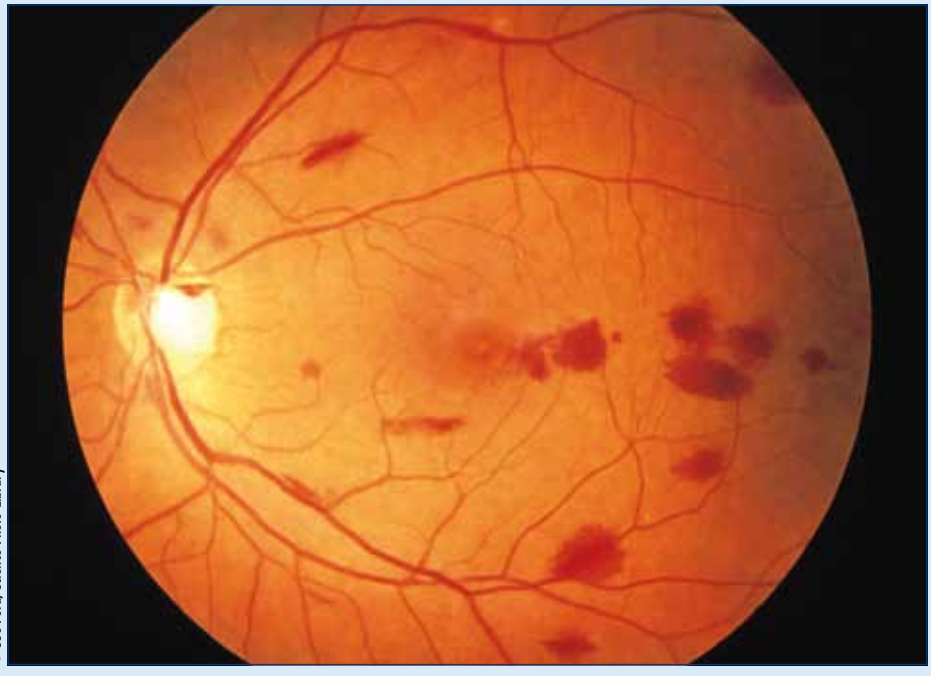
Roth spots

Roth spots are pale-centred retinal haemorrhages. Initially described in 1872 by Moritz Roth, a pathologist at the University of Basel, as 'round or flame shaped with a white spot in the centre', these white centres were thought to represent products of emboli from infective valve vegetations (Roth, 1872). Litten (1878) named these lesions 'Roth spots' and claimed that they occurred in 80% of patients with subacute bacterial endocarditis.

Roth spots have, however, been observed in a wide variety of other conditions such as leukaemia, anaemia, carbon monoxide poisoning, anoxia, pre-eclampsia, hypertensive retinopathy, neonatal birth trauma and intracranial haemorrhage from arteriovenous malformation, thereby making it inconceivable that the white centres of these lesions in all other cases represented infected emboli or a concentration of leukocytes (Ling and James, 1998) (*Figure 7*).

More recent investigators have given prominence to the presence of fibrin in the centre of these lesions and have concluded that the white centre of the Roth spot represents a fibrin thrombus at the site of a vessel rupture (Wong and Bodey, 1968; Duane et al, 1980). It has therefore been concluded that the white-centred haemorrhage thus results from the rupture of retinal capillaries and extrusion of blood, with subsequent platelet adhesion to damaged endothelium and the formation of a platelet–fibrin thrombus (Ling and James, 1998). Roth spots occur in a variety of seemingly diverse conditions, but the common predisposition to Roth spot formation appears to be retinal capillary rupture and the reparative process. They are therefore a non-specific sign in infective endocarditis.

Figure 7. Retina damage in leukaemia, showing Roth spots.



Discussion

Although rare peripheral manifestations of infective endocarditis still occur and may be invaluable clues to diagnosis, it must be remembered that their absence does not refute the diagnosis. Durack et al (1994), in their famous cohort that led to the formulation of the Duke criteria, reported the prevalence of Osler's nodes and Janeway lesions in definite cases of infective endocarditis to be 5% and 11% respectively. They excluded splinter haemorrhages from their proposed new diagnostic criteria for infective endocarditis, considering them to be 'non-specific'. They should be considered an important positive clinical sign, but have a poor correlation with disease activity and their presence must be weighed up appropriately within the clinical context.

Murdoch et al (2009), in their study of 2781 patients with definite endocarditis, found the prevalence of Osler's nodes and Janeway lesions to be 3% and 5% respectively. Although infective endocarditis is the most common condition associated with these lesions, it is important to note that these lesions are not pathognomonic for endocarditis. Osler's nodes have been reported as a result of bacteraemia without endocarditis and also distal to an infective intravascular graft. Rarely, systemic lupus erythematosus (without the presence of Libman–Sack's endocarditis) may cause Osler's nodes (Yee and McAllister, 1987). Other lesions mimicking Osler's nodes and Janeway lesions, which should be thought of in the differential diagnosis of these lesions, include cutaneous vasculitis, meningococcaemia, gonococcaemia, disseminated intravascular coagulation, thrombocytopenia, enterovirus infections and cholesterol emboli (Dalton and Robinson, 2001).

Conclusions

While these are considered 'classic' clinical signs of infective endocarditis, and their presence may be highly relevant, they are infrequently found, and their absence alone should never lead to the rejection of possible endocarditis from the differential diagnosis. BJHM

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Conflict of interest: none.

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KEY POINTS

- The peripheral stigmata of endocarditis have been recognized for many years, and Osler's nodes and Janeway lesions are among the diagnostic criteria for infective endocarditis.
- Splinter haemorrhages are found in the nail and may be either embolic or haemorrhagic in aetiology.
- Osler's nodes are painful nodular erythematous lesions on the pads of fingers and toes, thought to be vasculitic in nature.
- Janeway lesions are painless macular erythematous lesions found on the palmar surfaces of hands and feet, and are considered the result of septic embolization.
- Roth spots are pale-centred retinal haemorrhages that result from vessel rupture and repair.
- The absence of peripheral stigmata of endocarditis alone should not lead to the rejection of the diagnosis, as their presence is not sensitive for infective endocarditis.