BMJ Best Practice

Buerger's disease

The right clinical information, right where it's needed

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Summary

- A non-atherosclerotic vasculitis resulting in segmental occlusions of small and medium-sized arteries.
- Highest incidence is in young men of southeast Mediterranean origin and of Middle and Far Eastern origin who smoke.
- Presents as an acutely ischaemic limb, more commonly affecting the lower limb. Claudication is rarely described.
- Laboratory investigations exclude other vascular disease. Appropriate imaging shows medium and small vessel occlusion. Histological analysis of arterial specimens shows preservation of the internal elastic lamina.
- Best outcomes are associated with smoking cessation.
- Life expectancy is not altered.

BASICS

Definition

A non-atherosclerotic vasculitis resulting in segmental occlusions of small and medium-sized arteries, commonly affecting the lower limbs of young men who smoke. A hypercellular thrombus fills the lumen. Patients usually present with rest pain or tissue loss, and rarely present with claudication. Also known as thromboangiitis obliterans.

Epidemiology

Most commonly seen in young men (i.e., 20-40 years of age) of southeast Mediterranean origin and of Middle and Far Eastern origin.[1] It has a higher incidence in the Jewish population. A decrease in the prevalence rate of diagnosis of Buerger's disease was observed in the US between 1947 and 1986 (104 per 100,000 cases in 1947 to 13 per 100,000 cases in 1986).[2] The decline in morbidity may be associated with better health education, improved awareness of disease aetiology, improved imaging modalities, and effectiveness of antibiotics. Although Buerger's disease is more commonly seen in men, its incidence in women between 1970 and 1987 was reported to be as high as 23% in North America.[3] Increased female incidence may be associated with an increase in female smoking habit.[4] The prevalence of Buerger's disease is 0.5% to 5.6% in Western European countries, 45% to 63% in India, and 16% to 66% in Asia and the Far East.[5]

Aetiology

Buerger's disease was initially described by Leo Buerger in 1908 as "a strange endarteritis and endophlebitis with gangrene of the feet";[6] its exact aetiology remains unknown. It is likely to be related to tobacco constituents with a genetic predisposition, associated with immunological, endothelial, and coagulation responses. An increased risk of Buerger's disease has been seen in Bangladeshi patients who smoke >20 'bidis' a day (a home-made cigarette consisting of low-quality tobacco and smoked without filters).[7] Cannabis arteritis closely resembles Buerger's disease and has been reported in people who smoke cannabis.[8]

An infectious agent has been suggested as the cause of Buerger's disease, although no pathogen has been identified. One early study reported that 75% of people with Buerger’s disease had periodontal infections,[9] and an association with periodontal bacteria, in particular *Porphyromonas gingivalis* , has been made.[10] [11] It is postulated that a platelet thrombus containing oral bacteria does not adhere to the vessel wall and lodges distally as an embolus.

A genetic predisposition has been suggested due to the higher incidence of Buerger's disease in Ashkenazi than in non-Ashkenazi Jews in Israel.[12] The gene myeloid differentiation primary-response protein 88 (MyD88) has been identified as potentially offering resistance to Buerger's disease in Japanese people.[13]

The multi-factorial aetiology of Buerger's disease involves interactions between hereditary susceptibility, tobacco exposure, and immune and coagulable responses.

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Pathophysiology

Buerger's disease is a vasculitis affecting crural and brachial arteries. Advanced disease may include subclavian and axillary artery involvement. It has been known to affect cerebral, coronary, renal, gonadal, and mesenteric vessels to a much lesser degree.

In the acute pathological phase, active inflammation of all 3 vessel layers is seen. In the chronic pathological phase, the thrombus is organised with revascularisation of the medial and adventitial layers. A hypercellular thrombus rich in lymphocytes, fibroblasts, and giant cells fills the vessel lumen. The internal elastic lamina remains intact, with no vessel wall necrosis, calcification, or atheromatous plaques. Upon limb or digit amputation of chronically diseased tissue, the lumen is often found to be narrowed or occluded with fibrous thickening of the tunica intima. The vasculitis may be triggered by a hypersensitivity to tobacco constituents. Impaired endothelium-dependent vasodilation has been identified in patients with thromboangiitis obliterans, which may encourage thrombus formation.[14]

A cell-mediated immune response to artery collagen components has been suggested. The histocompatibility leukocyte antigen (HLA)-DRA was more frequently found and HLA-DRW6 less frequently found in patients with Buerger's disease compared with smokers without Buerger's disease and non-smokers.[15]

Plasma levels of kallikreins and kininase II (components of the kinin system of blood proteins) are higher in patients with Buerger's disease who are active smokers compared with non-Buerger's disease patients, whether or not they smoke. These protein levels were significantly greater in patients with Buerger's disease who were active smokers than in those who were ex-smokers. This may indicate that vasodilatation occurs in response to the vascular changes taking place, supporting a theory of immune complex deposition due to nicotine stimulation.[16]

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Primary prevention

The disease is rarely seen in people who do not smoke.

Secondary prevention

Patients should be advised to avoid restarting their smoking habit.

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Case history

Case history #1

A 36-year-old male smoker presents with a painful forefoot, which is worse at night, with no history of claudication. Examination confirms a sinus heart rhythm with a cold, pulseless foot with ulceration at the distal phalanges. Femoral and popliteal pulses are present, but foot pulses are absent.

Case history #2

A 35-year-old female smoker with a history of Raynaud's phenomenon presents with a cold, painful fingertip with ulceration. Examination reveals absent brachial, ulnar, and radial pulses.

Step-by-step diagnostic approach

It is important to first exclude other vascular diseases, such as atherosclerosis, emboli, and autoimmune diseases, before diagnosing Buerger's disease. Diagnosis is often made after the exclusion of other vascular diseases.

History

A current smoking history is almost always present. The absence of diabetes mellitus, hypertension, and hypercholesterolaemia and the presence of venous thrombophlebitis is a common feature of the history.

The lower limb is often painful and can be eased by hanging the leg over the edge of the bed at night. This suggests ischaemia and is not specific for Buerger's disease. Claudication of the arch of the foot may be described. A history of recurrent superficial thrombophlebitis of either the arms or the legs may be given.

A Japanese survey reported the following symptom frequency in patients with Buerger's disease:[22]

- Paraesthesia/cold sensation/cyanosis (37%)
- Plantar claudication (15%)
- Sural claudication (16%)
- Rest pain (10%)
- Ulceration/gangrene (19%).

The same study identified involvement of the ulnar artery (12%), anterior tibial artery (41%), and posterior tibial artery (40%) in patients with Buerger's disease.[22]

A history of recurrent episodes of large joint arthritis before their arterial occlusion presentation may be given by 12.5% of patients.[23] Single-joint inflammation is most often described affecting the wrists and knees, lasting up to 2 weeks. The diagnosis of Buerger's disease is often not made until 10 years after the joint symptoms.

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Physical examination

Critical ischaemia is defined as gangrene or rest pain lasting >2 weeks and requiring regular opioid analgesia. Its definition may also include ankle pressure <50 mmHg. People with non-critical ischaemia present with either claudication or new onset of rest pain.

An acutely ischaemic limb is a common presentation. The limb is cold with absent infrapopliteal pulses or absent brachial and distal forearm pulses. A sinus heart rhythm is detected. Gangrene or ulceration of the distal phalanges may be noted.
[Fig-1]

Upper limb involvement is clinically evident in 50% of patients.

The Allen test may detect Buerger's disease in 63% of patients.[3] The Allen test is performed by occluding both radial and ulnar arteries and observing whether the patient's hand becomes ischaemic. The pressure on the radial and ulnar arteries is then released 1 artery at a time. The release of each artery should reperfuse the hand individually. A negative Allen test reveals no ulnar or radial artery occlusion. An abnormal test in a young patient is highly suggestive of Buerger's disease. A positive test in a patient with lower limb disease may indicate the presence of upper limb disease.

Superficial thrombophlebitis is present in 40% to 60% of patients.[24] [25]

Laboratory investigations

Investigations should be aimed at ruling out other causes of vascular disease. Blood glucose should be normal, and Buerger's disease can be excluded in patients with diabetes. Biochemical evidence of renal failure (elevated urea and creatinine) may suggest the presence of an autoimmune disease. ESR, CRP, anti-nuclear antibody, rheumatoid factor, anti-neutrophilic cytoplasmic antibody (ANCA), and complement measurements should all be normal. Anti-cardiolipin antibodies may be elevated and are associated with periodontal destruction.[20] Anti-centromere antibodies should be normal to excludecalcinosis, Raynaud's phenomenon, oesophageal dysmotility, sclerodactyly, and telangiectasia (CREST) syndrome. Topoisomerase I antibodies (Scl-70) should be normal to exclude scleroderma. FBC may indicate evidence of infection or myeloproliferative disease. Coagulation studies should be normal to exclude a hypercoagulable state. Thrombophilia screen should exclude protein C, protein S, and anti-thrombin III deficiencies.

Arterial Doppler

An arterial Doppler confirms the absence of infrapopliteal, brachial, or distal pulses.

Radiological imaging

Arterial duplex, CT angiography, magnetic resonance angiography, and digital subtraction angiography are all useful radiological imaging techniques that show medium and small vessel occlusion, often with 'corkscrew'-shaped collateral vessels (Martorell's sign) seen. Digital subtraction angiography, CT angiography, and magnetic resonance angiography identify diseased vessels. Arterial duplex identifies non-atherosclerotic occluded vessels. Digital subtraction angiography also demonstrates normal non-atherosclerotic proximal arteries and shows occluded distal small and medium-sized vessels. The choice of imaging technique depends on what services are available at each hospital. Arterial duplex is simple, quick, and cheap, whereas magnetic resonance angiography is expensive, takes longer, and often has a waiting list. CT angiography and magnetic resonance angiography may be better for distal vessel disease.

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An echocardiogram should be completed to rule out a cardiac source of distal embolism.

Tissue biopsy

Arterial biopsy may aid diagnosis but should be avoided in ischaemic tissue. In the acute phase, active inflammation of all 3 vessel layers is seen. In the chronic phase, the thrombus is organised with revascularisation of the medial and adventitial layers. The elastic lamina is preserved.

Risk factors

Strong

smoking

- An association with tobacco smoking has suggested a possible hypersensitivity to tobacco constituents. Less than 5% of Buerger's disease patients are non-smokers. Smoking cessation reduces amputation risk.[3] A return to smoking following cessation may lead to a flare-up of the disease. Risk of Buerger's disease is thought to be increased by 'bidi' (a home-made cigarette consisting of low-quality tobacco and smoked without filters) smoking, which is possibly related to cannabis arteritis associated with cannabis consumption.[7] [8]
- Smoking only 1 or 2 cigarettes a day, using smokeless tobacco (chewing tobacco), or using nicotine replacement therapy may all keep the disease active.[17] [18]

age <40 years

- Buerger's disease is most common in those <40 years of age, although the incidence in older patients is increasing.

region of origin: southeast Mediterranean, Middle East, and Far East

- Buerger's disease is most commonly seen in people of southeast Mediterranean origin and of Middle and Far Eastern origin.[1] It is becoming less common in Western countries.

male sex

- For years it was thought to be a disease of men, but the incidence is rising in women, with the proportion of female patients varying from 11% to 23%.[3] [2]

periodontal infection

- There is a prevalence of anti-cardiolipin antibodies in patients with Buerger's disease with high levels associated with increased morbidity.[19] Anti-cardiolipin antibodies have an association with periodontal infection.[20]

Weak

human leukocyte antigen (HLA) haplotypes

- In areas of India and Japan where Buerger's disease has a high prevalence, an association with HLA-DRB1*1501 has been identified.[21] However, no HLA haplotype has been associated with Buerger's disease in North America.

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History & examination factors

Key diagnostic factors

presence of risk factors (common)

- Key risk factors include age <40 years, male sex, and history of smoking.

Other diagnostic factors

paraesthesias/cold sensation/cyanosis in limb or finger (common)

- Paraesthesias/cold sensation/cyanosis occur in approximately 37% of patients.[22]

ulceration/gangrene (common)

- Ulceration or gangrene on the distal phalanges may be noted. [Fig-1]
- Occurs in approximately 19% of patients.[22]

claudication (common)

- Plantar claudication occurs in approximately 15% of patients, and sural claudication occurs in approximately 16% of patients.[22]
- Claudication of the arch of the foot may be described by the patient.

rest pain (common)

- Occurs in approximately 10% of patients.[22]
- The lower limb is often painful and can be eased by hanging the leg over the edge of the bed at night. This suggests ischaemia and is not specific for Buerger's disease.

superficial thrombophlebitis (common)

- A history of recurrent superficial thrombophlebitis of either the arms or legs may be given.

cold limb or finger (common)

- A cold ischaemic limb or finger is present in acute ischaemia. [Fig-2]

pale limb or finger (common)

- A pale ischaemic limb or finger is present in acute ischaemia.

absence of distal pulses (common)

- Popliteal pulses are present, but foot pulses are absent.
- In the forearm, brachial and distal forearm pulses may be absent.

positive Allen test (common)

- Allen test may detect Buerger's disease in 63% of patients.[3] Performed by occluding both radial and ulnar arteries and observing whether the patient's hand becomes ischaemic. The pressure on the radial and ulnar arteries is then released 1 artery at a time. The release of each artery should reperfuse the hand individually. A negative Allen test reveals no ulnar or radial artery occlusion.

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- An abnormal test in a young patient is highly suggestive of Buerger's disease, although may be negative in 25% of patients; a positive test in a patient with lower limb disease may indicate the presence of upper limb disease.

joint arthritis (uncommon)

- 12.5% of patients may give a history of recurrent episodes of large joint arthritis before their arterial occlusion presentation.[23]

duration of joint symptoms up to 2 weeks (uncommon)

- Single-joint inflammation, most often described affecting the wrists and knees, lasting up to 2 weeks. The diagnosis of Buerger's disease is often not made until 10 years after the joint symptoms.

Diagnostic tests

1st test to order

Test	Result
blood glucose • Buerger's disease can be excluded in patients with diabetes.	**normal**
urea • Biochemical evidence of renal failure may suggest the presence of an autoimmune disease.	**normal**
serum creatinine • Biochemical evidence of renal failure may suggest the presence of an autoimmune disease.	**normal**
FBC with differential • Excludes a myeloproliferative disease. WBC count may be elevated if infection present.	**normal**
coagulation screen • Excludes a hypercoagulable state.	**normal**
thrombophilia screen • Excludes protein C, protein S, and anti-thrombin III deficiencies.	**normal**
CRP • May be elevated if wet gangrene present.	**normal**
ESR • May be elevated if wet gangrene present.	**normal**
arterial Doppler • An arterial Doppler confirms absence of arterial flow.	**confirms the absence of infrapopliteal, brachial, or distal pulses**

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Other tests to consider

Test	Result
anti-nuclear antibody	**normal**
rheumatoid factor	**normal**
anti-neutrophilic cytoplasmic antibody (ANCA)	**normal**
complement levels	**normal**
anti-centromere antibody • To exclude calcinosis, Raynaud's phenomenon, oesophageal dysmotility, sclerodactyly, and telangiectasia (CREST) syndrome.	**normal**
topoisomerase I antibodies (Scl-70) • To exclude scleroderma.	**normal**
echocardiogram • An echocardiogram looks for evidence of an embolic source. It is used to exclude embolic causes and is normal in Buerger's disease.	**normal**
arterial duplex • 'Corkscrew' collaterals are dilated vasa vasorum of the occluded main artery.	**identifies non-atherosclerotic occluded vessels; shows medium and small vessel occlusion, often with 'corkscrew'-shaped collateral vessels (Martorell's sign)**
digital subtraction angiography • Demonstrates normal non-atherosclerotic proximal arteries and shows occluded distal small and medium-sized vessels. • 'Corkscrew' collaterals are dilated vasa vasorum of the occluded main artery. • Arterial lesions are usually confined to the popliteal, crural, and below-knee vessels in the lower limb, and the forearm vessels in the upper limb.	**identifies diseased vessels; classical tortuous 'corkscrew'-shaped collaterals (Martorell's sign) connect unaffected segments of distal vessels**
anti-cardiolipin antibodies • Associated with periodontal infections and destruction seen in Buerger's disease.[20]	**elevated**

Emerging tests

Test	Result
CT angiography • 'Corkscrew' collaterals are dilated vasa vasorum of the occluded main artery. • Arterial lesions are usually confined to the popliteal, crural, and below-knee vessels in the lower limb, and the forearm vessels in the upper limb.	**identifies diseased vessels; shows medium and small vessel occlusion, often with 'corkscrew'-shaped collateral vessels (Martorell's sign)**

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Test	Result
magnetic resonance angiography • 'Corkscrew' collaterals are dilated vasa vasorum of the occluded main artery. • Arterial lesions are usually confined to the popliteal, crural, and below-knee vessels in the lower limb, and the forearm vessels in the upper limb.	**identifies diseased vessels; shows medium and small vessel occlusion, often with 'corkscrew'-shaped collateral vessels (Martorell's sign)**
tissue biopsy • Tissue biopsy shows evidence pathognomonic of Buerger's disease.	**highly cellular arterial thrombus; non-disrupted internal elastic lamina; evidence of segmental lesions of collateral vessels**
genetic testing • Myeloid differentiation primary-response protein 88 (MyD88) is a gene for which identification may suggest resistance to Buerger's disease, especially in Japanese people.[13]	**positive or negative for MyD88 gene resistance polymorphism**

Differential diagnosis

Condition	Differentiating signs / symptoms	Differentiating tests
Embolic disease	• Often affects only 1 limb but can affect more. Recent chest pain suggesting a myocardial infarction.	• In embolic disease, an echocardiogram may show a valve lesion or thrombus; ECG and troponin may show evidence of myocardial ischaemia. • Echocardiogram, ECG, and troponin blood tests show no dysrhythmia and no evidence of recent myocardial infarction in Buerger's disease. • Duplex imaging may reveal the embolised thrombus.
Hypercoagulable state	• Multiple limbs affected. Known history or family history of thrombophilia disease.	• Coagulation profile: PT, PTT, and INR may be elevated. • Thrombophilia screen: may be positive for protein C, protein S, or anti-thrombin III deficiencies.
Raynaud's phenomenon (RP)	• Painful extremities associated with cold weather exposure and a lack of skin loss. • Onset of symptoms with limb immersion in cold water.	• ANA, FBC, ESR, metabolic panel, and urinalysis may be normal in primary RP and abnormal in secondary RP.

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Condition	Differentiating signs / symptoms	Differentiating tests
Atherosclerosis	• Claudication history. Absent femoral pulses. • Associated with hypercholesterolaemia, hypertension, and diabetes.	• Atherosclerotic plaques seen on radiological imaging of arteries.
Rheumatoid vasculitis	• Usually known long-standing rheumatoid arthritis. • Active symmetric arthritis lasting >6 weeks, most commonly affecting the metacarpophalangeal (MCP), proximal interphalangeal (PIP), and metatarsalphalangeal (MTP) joints. • Skin rash is the most common vasculitic manifestation.	• Rheumatoid factor positive in up to 70% of cases. • Anti-cyclic citrullinated peptide (anti-CCP) positive in 70-80% of cases. • Joint x-rays reveal erosions.
Systemic lupus erythematosus	• Patients may have skin manifestations including malar, photosensitive, or discoid skin rash, mouth or nose ulcers, or diffuse patchy alopecia. • Other features include constitutional symptoms (e.g., fever, fatigue, weight loss), lymphadenopathy, musculoskeletal symptoms, Raynaud's phenomenon, and symptoms of CNS, gastrointestinal cardiopulmonary, or haematological involvement.	• Anti-nuclear antibodies, dsDNA, and Smith antigen are positive.
Wegener's granulomatosis	• Classic triad consists of upper and lower respiratory tract involvement and pauci-immune glomerulonephritis, producing renal symptoms. Involvement of cutaneous, ocular, musculoskeletal, and peripheral nervous system tissue is also common. • Constitutional symptoms include fatigue, malaise, fever, night sweats, anorexia, and weight loss.	• Positive cANCA (cytoplasmic pattern on immunofluorescence testing) combined with positive proteinase 3 antibody testing by enzyme immunoassay (EIA). • Positive pANCA (perinuclear pattern on immunofluorescence testing) combined with positive myeloperoxidase antibody testing by EIA.

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Condition	Differentiating signs / symptoms	Differentiating tests
CREST syndrome	• Acronym for calcinosis, Raynaud's phenomenon, oesophageal dysmotility, sclerodactyly, and telangiectasia. • Disease typically limited to distal upper and lower extremities; may involve face and neck. • Oesophageal dysmotility produces dysphagia and GERD. Sclerodactyly produces bright shiny skin of hands and feet. • Other features include dilated nailbed capillaries, symmetrical swelling of the fingers with reduced range of motion, contractures affecting joints in the hand, claw hand deformities, digital ulcers, and carpal tunnel syndrome.	• Anti-centromere antibody may be positive and is strongly suggestive of the disease. • Serum anti-nuclear antibody may be positive but is not specific. • Serum extractable nuclear antigens may be positive. • FBC with peripheral fragmentation of red blood cells is associated with systemic disease. • Serum creatinine elevated in presence of renal crisis.

Diagnostic criteria

Shinoya clinical criteria of diagnosis[26]

All 5 criteria must be met:

- Smoking history
- Onset before the age of 50 years
- Infrapopliteal arterial occlusive lesions
- Upper limb involvement of phlebitis migrans (also known as thrombophlebitis migrans)
- Absence of atherosclerotic risk factors aside from smoking.

These criteria were described in 2006 to make the diagnosis of Buerger's disease.[26] However, patients >50 years of age have been given the diagnosis. Probable Buerger's disease is considered when all but the fourth criterion are met.

Point scoring system of diagnosis[27]

Positive points:

- Age at onset: less than 30 years (+2) / 30-40 years (+1)
- Foot intermittent claudication: present (+2) / by history (+1)
- Upper extremity: symptomatic (+) / asymptomatic (+1)
- Migrating superficial vein thrombosis: present (+2) / by history only (+1)
- Raynaud colour changes: present (+2) / by history only (+1)

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- Angiography; Biopsy: if typical, both (+2) / either (+1)

Negative points:

- Age at onset: 45-50 years (-1) / >50 years (-2)
- Sex, smoking: female (-1) / non-smoker (-2)
- Location: single limb (-1) / no lower extremity involved (-2)
- Absent pulses: brachial (-1) / femoral (-2)
- Arteriosclerosis, diabetes mellitus, hypertension, hypercholesterolaemia: discovered after diagnosis 5.1-10 years (-1) / 2.1-5 years (-2)

Total of points defines the probability of the diagnosis:

- 0-1 points: Diagnosis excluded
- 2-3 points: Suspected, low probability
- 4-5 points: Probable, medium probability
- ≥6 points: Definite, high probability

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Step-by-step treatment approach

Patients often present with critical ischaemia and need admission to hospital at the time of diagnosis. Critical ischaemia is defined as gangrene or rest pain lasting >2 weeks and requiring regular opioid analgesia. Its definition may also include ankle pressure <50 mmHg. Patients with non-critical ischaemia present with either claudication or new onset of rest pain.

Initial admission to the hospital involves confirming diagnosis, excluding differential diagnosis, and arterial imaging. Vasoactive dilation is done during initial admission to hospital, along with debridement of any gangrenous tissue. Further treatments are given depending on severity of ischaemia and degree of pain.

Smoking cessation

Smoking cessation reduces the incidence of amputation.[3] It improves patency and limb salvage rates in those who do undergo surgical revascularisation.[28] [29]
[Fig-2]

[Fig-3]

[Fig-4]

Smoking increases flare-ups and reduces ulcer healing. A return to smoking following cessation may lead to a flare-up of the disease. Risk of Buerger's disease is thought to be increased by 'bidi' (a home-made cigarette consisting of low-quality tobacco and smoked without filters) smoking, which is possibly related to cannabis arteritis associated with cannabis use.[7] [8]

Smoking only 1 or 2 cigarettes a day, using smokeless tobacco (chewing tobacco), or using nicotine replacement therapy may all keep the disease active.[17] [18]

Additional therapies

Several additional therapies have shown some benefit, but the definitive treatment for Buerger's disease is smoking cessation.

Vasoactive drugs

- Nifedipine, a calcium-channel blocker, may cause peripheral vasodilation and improve distal blood flow.[3] It has been shown to be of benefit in patients with lower limb trophic changes and symptoms, and is often given in combination with other therapies such as cessation of smoking, antibiotics, and iloprost.[30] [31]
- Pentoxifylline and cilostazol have had good effects, although there are few supportive data. They are not routinely used. Pentoxifylline has been shown to improve pain and healing in ischaemic ulcers.[32] Treatment with pentoxifylline can be tried after other medical therapies have failed. Cilostazol could be tried in conjunction with or following failure of other medical therapies (e.g., nifedipine).[33] It is contra-indicated in the following: patients with unstable angina, recent myocardial infarction, or coronary intervention (within 6 months); patients receiving 2 or more other antiplatelet agents or anticoagulants; and patients with history of severe tachyarrhythmia.
- Iloprost is a prostacyclin glandin analogue that may be given intravenously. It has been shown to be beneficial in relieving rest pain and in healing 62% of ulcers within 4 weeks following a 24-day course.[34] [35] The effects of intravenous prostacyclin analogue iloprost, intravenous prostacyclin

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analogue clinprost, and intravenous prostaglandin analogue alprostadil have been compared and showed no significant difference between them, suggesting they are all beneficial at healing ulcers and resolving rest pain at 28 days. However, the quality of evidence in these studies was low to very low.[36] Iloprost, when given orally, shows little significant benefit in regards to ulcer healing, pain, and amputation rates.[37]

Antibiotics

- The choice of antibiotics depends on local hospital policies. Antibiotics are indicated only in the presence of infection or wet gangrene. Aerobic and anaerobic cover is needed. Amoxicillin/clavulanate may be adequate, or a penicillin plus metronidazole, or ciprofloxacin (if *Pseudomonas* is present), or a third-generation cephalosporin plus metronidazole. If admission to hospital is recommended (when patients present with critical ischaemia), the antibiotics can be given intravenously.

Analgesia

- Ischaemic pain may require opioid analgesia. Tramadol can be used to treat ischaemic pain. Alternatively, immediate-release oral morphine can be used in severe cases and substituted with modified-release morphine when pain is controlled. Severe pain requiring analgesia often requires admission to hospital so that disease can be controlled or the extent of disease can be assessed.
- Non-steroidal anti-inflammatory drugs (NSAIDs) can be used to treat superficial venous thrombophlebitis. Admission to hospital is not a requirement for giving NSAIDs but may occur if several medical options are being tried while observing disease severity.
- Spinal cord stimulation may also be beneficial. It has been shown to benefit patients with lower limb symptoms ranging from claudication and pain to ulceration and trophic changes. It is often used after medical therapy has failed. Spinal cord stimulation is performed by an implantable stimulator.[38] [39] [40]

Intravenous guanethidine

- Guanethidine reduces catecholamine release by acting on the Na+-ATPase-dependent pump. Reduction of rest pain and ulceration healing have been reported with guanethidine injections into the affected limb, sometimes with the additional use of a Bier block (intravenous regional sympathetic blockade).[41] [42] Injections can be easily repeated if beneficial effects are seen. Data on its effectiveness are limited.

Sympathectomy

- This can be chemical or surgical, lumbar, or thoracopic. Both positive and negative results have been reported with lumbar sympathectomy.[43] [35] Sympathectomy may be sufficient to enable necrotic lesions to heal.[44] It is thought to reduce pain by reducing peripheral resistance and promoting collateral development.[45] Thoracopic sympathectomy can be used for upper limb symptoms, and lumbar sympathectomy for lower limb symptoms. Due to the invasiveness of the procedure, sympathectomy is often a treatment tried when medical therapy has failed and there is no revascularisation option. It is often used in the more severe cases where there is tissue loss. However, its use has been reported in patients presenting with claudication.[46]

Intra-arterial thrombolysis

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- Revascularisation of crural vessels has been reported using intra-arterial thrombolysis, although it is not a commonly performed treatment modality in Buerger's disease.

Surgical revascularisation

- Due to the lack of patent distal vessels, bypass is often not an option. Angiography may reveal potential distal anastomotic sites, allowing bypass to help ulcer healing. However, primary graft patency rates are 41% at 1 year, 32% at 5 years, and 30% at 10 years; secondary patency rates are 54% at 1 year, 47% at 5 years, and 39% at 20 years.[29]
- Surgical revascularisation is indicated mainly in patients with critical ischaemia. Patients with non-critical ischaemia are only indicated for surgical revascularisation if there is severe claudication and a good vessel to anastomose on to distally.

Intramuscular bone marrow cell administration

- Improved ankle-brachial index, transcutaneous oxygen concentration, rest pain, pain-free walking distance, ulcer healing, and limb salvage have been reported with stem cell therapy.[47] However, no large-scale, multi-centre, placebo-controlled trials have been conducted to confirm its efficacy or safety.

Treatment details overview

Consult your local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing. (see Disclaimer)

Acute (summary)

Patient group	Tx line	Treatment
critical ischaemia	**1st**	**hospital admission + immediate smoking cessation**
	plus	**vasoactive medication**
	adjunct	**surgical debridement**
	adjunct	**intravenous antibiotic therapy**
	adjunct	**analgesia**
	adjunct	**spinal cord stimulation**
	adjunct	**intravenous guanethidine**
	adjunct	**surgical revascularisation**

Ongoing (summary)

Patient group	Tx line	Treatment
non-critical ischaemia	**1st**	**urgent smoking cessation**

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Ongoing		(summary)
	adjunct	vasoactive medication
	adjunct	oral antibiotic therapy
	adjunct	analgesia
	adjunct	spinal cord stimulation
	adjunct	sympathectomy

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Treatment options

Acute

Patient group	Tx line	Treatment
critical ischaemia	**1st**	**hospital admission + immediate smoking cessation**
		» Patients often present with critical ischaemia and need admission to hospital at the time of diagnosis. Critical ischaemia is defined as gangrene or rest pain lasting >2 weeks and requiring regular opioid analgesia. Its definition may also include ankle pressure of <50 mmHg. Initial admission to hospital involves confirming diagnosis, excluding differential diagnosis, and arterial imaging.
		» Smoking cessation reduces the incidence of amputation.[3] From a group of 43 patients who stopped smoking, 94% avoided an amputation.[48] It improves patency and limb salvage rates in those who do undergo surgical revascularisation.[28] [29] Patients who continue to smoke have a 19% major amputation rate;[29] this is thought to be 2.73 times greater than for people who have ceased smoking.[49] Smoking increases flare-ups and reduces ulcer healing. A return to smoking following cessation may lead to a flare-up of the disease. Smoking only 1 or 2 cigarettes a day, using smokeless tobacco (chewing tobacco), or using nicotine replacement therapy may all keep the disease active.[17] [18]
	plus	**vasoactive medication**
		» Vasoactive dilation (e.g., with nifedipine) is done during initial admission to hospital, along with debridement of any gangrenous tissue. Further treatments are given depending on severity of ischaemia and degree of pain. Pentoxifylline and cilostazol have had good effects, although there are few supportive data. They are not routinely used. Pentoxifylline has been shown to improve pain and healing in ischaemic ulcers.[32] Treatment with pentoxifylline can be tried after other medical therapies have failed. Cilostazol could be tried in conjunction with or following failure of other medical therapies (e.g., nifedipine).[33] It is contra-indicated in the following: patients with unstable angina, recent myocardial infarction, or coronary intervention (within 6 months); patients receiving 2 or more other antiplatelet agents

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Acute

Patient group	Tx line	Treatment
		or anticoagulants; and patients with history of severe tachyarrhythmia. » Intravenous iloprost may improve ulcer healing rates, but is not available in many countries. **Primary options** » nifedipine: 5 mg orally (immediate-release) three times daily initially, increase according to response, maximum 120 mg/day; 30 mg orally (extended-release) once daily initially, increase according to response, maximum 90 mg/day **OR** **Secondary options** » pentoxifylline: consult specialist for guidance on dose **OR** **Secondary options** » cilostazol: consult specialist for guidance on dose
	adjunct	**surgical debridement** » Initial admission to hospital involves confirming diagnosis, excluding differential diagnosis, and arterial imaging. Vaso-active dilation is done during initial admission to hospital, along with debridement of any gangrenous tissue. Further treatments are given depending on severity of ischaemia and degree of pain.
	adjunct	**intravenous antibiotic therapy** » Antibiotics are indicated only in the presence of infection or wet gangrene. Aerobic and anaerobic cover is needed. » Regimens include a penicillin plus metronidazole, or ciprofloxacin (if *Pseudomonas* is present), or a third-generation cephalosporin plus metronidazole. However, local protocols should be followed. **Primary options** » metronidazole: 500 mg intravenously every 6-8 hours **-and-** » benzylpenicillin sodium aqueous: 900 mg intravenously every 6 hours

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Acute

Patient group	Tx line	Treatment
		OR **Primary options** » ciprofloxacin: 400 mg intravenously every 12 hours **OR** **Primary options** » cefuroxime sodium: 750 mg intravenously every 8 hours **-and-** » metronidazole: 500 mg intravenously every 6-8 hours
	adjunct	**analgesia** » Tramadol may be sufficient to relieve ischaemic pain. Alternatively, morphine can be used in severe cases. Severe pain often requires admission to hospital so that disease can be controlled or the extent of disease can be assessed. » Non-steroidal anti-inflammatory drugs (NSAIDs) can be used to treat superficial venous thrombophlebitis. Admission to hospital is not a requirement for giving NSAIDs but may occur if several medical options are being tried while observing disease severity. **Primary options** » tramadol: 50-100 mg orally every 4-6 hours when required, maximum 400 mg/day **OR** **Primary options** » morphine sulfate: 10 mg orally (immediate-release) every 3-4 hours when required, may switch to modified-release formulation when pain controlled; 2.5 to 5 mg intravenously every 3-4 hours when required **OR** **Secondary options** » ibuprofen: 300-400 mg orally every 6-8 hours when required, maximum 2400 mg/day **OR** **Secondary options**

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Acute

Patient group	Tx line	Treatment
		» diclofenac sodium: 50 mg orally (immediate-release) two or three times daily
	adjunct	**spinal cord stimulation**
		» Spinal cord stimulation may be beneficial in alleviating ischaemic pain. It is performed by an implantable stimulator.[38] [39] [40]
	adjunct	**intravenous guanethidine**
		» Guanethidine reduces catecholamine release by acting on the Na+-ATPase-dependent pump. Reduction of rest pain and ulceration healing have been reported with guanethidine injections into the affected limb, sometimes with the additional use of a Bier block (intravenous regional sympathetic blockade).[41] [42] Injections can be easily repeated if beneficial effects are seen.
		» Data on the effectiveness of guanethidine are limited, and it is not available in many countries.
	adjunct	**surgical revascularisation**
		» Due to the lack of patent distal vessels, bypass is often not an option. Angiography may reveal potential distal anastomotic sites, allowing bypass to help ulcer healing. However, primary graft patency rates are 41% at 1 year, 32% at 5 years, and 30% at 10 years; secondary patency rates are 54% at 1 year, 47% at 5 years, and 39% at 10 years.[29]
		» Surgical revascularisation is indicated mainly in patients with critical ischaemia. Patients with non-critical ischaemia are indicated for surgical revascularisation only if there is severe claudication and a good vessel to anastomose on to distally.

Ongoing

Patient group	Tx line	Treatment
non-critical ischaemia	**1st**	**urgent smoking cessation**
		» Patients with non-critical ischaemia present with either claudication or new onset of rest pain.
		» Smoking cessation reduces the incidence of amputation.[3] From a group of 43 patients

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Ongoing

Patient group	Tx line	Treatment
		who stopped smoking, 94% avoided an amputation.[48] It improves patency and limb salvage rates in those who do undergo surgical revascularisation.[28] [29]
		» Patients who continue to smoke have a 19% major amputation rate;[29] this is thought to be 2.73 times greater than for people who have ceased smoking.[49]
		» Smoking increases flare-ups and reduces ulcer healing. A return to smoking following cessation may lead to a flare-up of the disease.
		» Smoking only 1 or 2 cigarettes a day, using smokeless tobacco (chewing tobacco), or using nicotine replacement therapy may all keep the disease active.[17] [18]
	adjunct	**vasoactive medication**
		» Nifedipine, a calcium-channel blocker, may cause peripheral vasodilation and improve distal blood flow.[3]
		» It has been shown to be of benefit in patients with lower limb trophic changes and symptoms, and is often given in combination with other therapies, such as cessation of smoking, antibiotics, and iloprost.[30] [31]
		» Pentoxifylline and cilostazol are vaso-active drugs that have had good effects, although there are few supportive data. They are not routinely used. Pentoxifylline has been shown to improve pain and healing in ischaemic ulcers.[32] Treatment with pentoxifylline can be tried after other medical therapies have failed. Cilostazol could be tried in conjunction with or following failure of other medical therapies (e.g., nifedipine).[33] It is contraindicated in the following: patients with unstable angina, recent myocardial infarction, or coronary intervention (within 6 months); patients receiving 2 or more other antiplatelet agents or anticoagulants; and patients with history of severe tachyarrhythmia.
		» Intravenous iloprost may improve ulcer healing rates, but is not available in many countries.
		Primary options
		» nifedipine: 5 mg orally (immediate-release) three times daily initially, increase according to response, maximum 120 mg/day; 30 mg orally (extended-release) once daily initially,

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Ongoing

Patient group	Tx line	Treatment
		increase according to response, maximum 90 mg/day **OR** **Secondary options** » pentoxifylline: consult specialist for guidance on dose **OR** **Secondary options** » cilostazol: consult specialist for guidance on dose
	adjunct	**oral antibiotic therapy** » Antibiotics are indicated only in the presence of infection or wet gangrene. Aerobic and anaerobic cover is needed. » Amoxicillin/clavulanate may be adequate, or a penicillin plus metronidazole, or ciprofloxacin (if *Pseudomonas* is present), or a third-generation cephalosporin plus metronidazole. However, local protocols should be followed. **Primary options** » metronidazole: 500 mg orally three times daily **-and-** » phenoxymethylpenicillin potassium: 500 mg orally four times a day **OR** **Primary options** » amoxicillin/clavulanate: 500 mg orally three times daily Dose refers to amoxicillin component. **OR** **Primary options** » ciprofloxacin: 500 mg orally twice daily **OR** **Primary options** » cefuroxime axetil: 250-500 mg orally twice daily **-and-**

TREATMENT

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Ongoing

Patient group	Tx line	Treatment
		» metronidazole: 500 mg orally three times daily
	adjunct	**analgesia**
		» Ischaemic pain may require opioid analgesia. Tramadol may be sufficient to relieve ischaemic pain. Alternatively, immediate-release oral morphine can be used in severe cases and substituted for modified-release morphine when pain is controlled.
		» Non-steroidal anti-inflammatory drugs (NSAIDs) can be used to treat superficial venous thrombophlebitis.
		Primary options
		» tramadol: 50-100 mg orally every 4-6 hours when required, maximum 400 mg/day
		OR
		Primary options
		» morphine sulfate: 10 mg orally (immediate-release) every 3-4 hours when required, may switch to modified-release formulation when pain controlled
		OR
		Secondary options
		» ibuprofen: 300-400 mg orally every 6-8 hours when required, maximum 2400 mg/day
		OR
		Secondary options
		» diclofenac sodium: 50 mg orally (immediate-release) two or three times daily
	adjunct	**spinal cord stimulation**
		» Spinal cord stimulation may be beneficial in alleviating ischaemic pain. It has been shown to be of benefit in patients with lower limb symptoms ranging from claudication and pain to ulceration and trophic changes. Often used after medical therapy has failed. Spinal cord stimulation is performed by an implantable stimulator.[38] [39] [40]
	adjunct	**sympathectomy**
		» Sympathectomy can be chemical or surgical, lumbar, or thorascopic. Both positive and

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Ongoing

Patient group	Tx line	Treatment
		negative results have been reported with lumbar sympathectomy.[43] [35] » Sympathectomy may be sufficient to enable necrotic lesions to heal.[44] It is thought to reduce pain by reducing peripheral resistance and promoting collateral development.[45] » Thorascopic sympathectomy can be used for upper limb symptoms, and lumbar sympathectomy for lower limb symptoms. Due to the invasiveness of the procedure, sympathectomy is often a treatment tried when medical therapy has failed and there is no revascularisation option. Often used in the more severe cases where there is tissue loss. However, its use has been reported in patients presenting with claudication.[46]

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Emerging

Free and pedicled omental flaps

Thought to improve claudication, reduce rest pain, and promote ulcer healing.[50]

Gene transfer

Intramuscular injections of vascular endothelial growth factor have had some encouraging preliminary results at improving collateral vessel formation.[51]

Autologous bone marrow cell transplantation

Implantation of autologous bone marrow cells by multiple injections into the gastrocnemius muscle may increase collateral vessel formation. Improved ankle-brachial index, transcutaneous oxygen concentration, rest pain, pain-free walking distance, ulcer healing, and limb salvage has been reported.[52] [47] Autologous bone marrow mononuclear cell (BM-MNC) implantation has been shown to reduce amputation rates in those unsuitable for angioplasty or surgical revascularisation. In a non-randomised trial, patients with Buerger's disease who had rest pain and non-healing ulcers had a 4-year amputation-free rate of 95% with BM-MNC (n=26) compared with 6% in those who did not receive BM-MNC (n=16).[53]

Bosentan

This endothelin receptor antagonist has been reported to improve digital necrosis in 2 patients.[54]

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FOLLOW UP

Recommendations

Monitoring

Acutely ischaemic limbs are managed during admission to hospital. Dry gangrenous limbs should be reviewed monthly to monitor for evidence of infection. Interval follow-up is rarely needed, because the patient will present acutely when ulcers or gangrene recur.

Patient instructions

To reduce recurrent disease, patients should be advised to stop smoking.

Complications

Complications	Timeframe	Likelihood
atherosclerosis	**long term**	**low**
Symptomatic Buerger's disease for >8 years has been associated with premature atherosclerosis.[58]		
gangrene	**variable**	**high**
Patients often present with an acutely ischaemic leg, where gangrene develops over the next few days following admission to hospital as the tissue demarcates. Often a gangrenous toe is present.		
amputation secondary to continued smoking	**variable**	**high**
Patients who continue to smoke have a 19% major amputation rate;[29] this is thought to be 2.73 times greater than for people who have ceased smoking.[49] Smoking increases flare-ups and reduces ulcer healing. A return to smoking following cessation may lead to a flare-up of the disease. Smoking only 1 or 2 cigarettes a day, using smokeless tobacco (chewing tobacco), or using nicotine replacement therapy may all keep the disease active.[17] [18]		

Prognosis

Buerger's disease often involves repeated acute episodes of ischaemia over several years. The disease intensifies at 30 to 40 years of age and then regresses. It is rarely present in patients >60 years of age.[55]

Smoking cessation

Patients who continue to smoke have a 19% major amputation rate;[29] this is thought to be 2.73 times greater than for people who have ceased smoking.[49] Smoking increases flare-ups and reduces ulcer healing. A return to smoking following cessation may lead to a flare-up of the disease. Smoking only 1 or 2 cigarettes a day, using smokeless tobacco (chewing tobacco), or using nicotine replacement therapy may all keep the disease active.[17] [18] Smoking is best stopped through smoking cessation classes, although varenicline has been shown to be beneficial. Varenicline is a selective nicotinic receptor partial agonist that is used as an aid for smoking cessation.

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Amputations

Within 5 years of diagnosis, 25% of patients will have undergone an amputation. This may rise to 38% by 10 years.[56] Repeated amputations are often needed and are an indication of the disease severity. [Fig-5]

Life expectancy

Life expectancy is not altered in patients with Buerger's disease: 90% to 95% survive for 10 years;[57] [1] 85% survive for 25 years.[29] This is probably because Buerger's disease is not associated with cardiovascular risk factors, aside from smoking.

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Key articles

- Mills JL, Porter JM. Buerger's disease (thromboangiitis obliterans). Ann Vasc Surg. 1991;5:570-572. Abstract
- Lie JT. The rise and fall and resurgence of thromboangiitis obliterans (Buerger's disease). Acta Pathol Jpn. 1989;39:153-158. Abstract
- Olin JW, Young JR, Graor RA, et al. The changing clinical spectrum of thromboangiitis obliterans (Buerger's disease). Circulation. 1990;82(5 suppl)IV3-IV8. Abstract
- Buerger L. Thrombo-angiitis obliterans: a study of the vascular lesions leading to presenile spontaneous gangrene. Am J Med Sci. 1908;136:567-580.
- Shionoya S. Pathology. In: Shionoya S, ed. Buerger's disease. Nagoya: University of Nagoya Press; 1990:57-79.
- Papa MZ, Rabi I, Adar R. A point scoring system for the clinical diagnosis of Buerger's disease. Eur J Vasc Endovasc Surg. 1996;11:335-339. Abstract
- Ohta T, Ishioashi H, Hosaka M, et al. Clinical and social consequences of Buerger disease. J Vasc Surg. 2004;39:176-180. Abstract
- Cacione DG, Macedo CR, Baptista-Silva JC. Pharmacological treatment for Buerger's disease. Cochrane Database Syst Rev. 2016;(3):CD011033. Abstract

References

1. Mills JL, Porter JM. Buerger's disease (thromboangiitis obliterans). Ann Vasc Surg. 1991;5:570-572. Abstract
2. Lie JT. The rise and fall and resurgence of thromboangiitis obliterans (Buerger's disease). Acta Pathol Jpn. 1989;39:153-158. Abstract
3. Olin JW, Young JR, Graor RA, et al. The changing clinical spectrum of thromboangiitis obliterans (Buerger's disease). Circulation. 1990;82(5 suppl)IV3-IV8. Abstract
4. Yorukoglu Y, Ilgit E, Zengin M, et al. Thromboangiitis obliterans (Buerger's disease) in women (a reevaluation). Angiology. 1993;44:527-532. Abstract
5. Arkkila PET. Thromboangiitis obliterans (Buerger's disease) Orphanet J Rare Dis. 2006; 1: 14. Full text
6. Buerger L. Thrombo-angiitis obliterans: a study of the vascular lesions leading to presenile spontaneous gangrene. Am J Med Sci. 1908;136:567-580.

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REFERENCES

7. Rahman M, Chowdhury AS, Fukui T, et al. Association of thromboangiitis obliterans with cigarette and bidi smoking in Bangladesh: a case-control study. Int J Epidemiol. 2000:29:266-270. Full text Abstract

8. Disdier P, Granel B, Serratrice J, et al. Cannabis arteritis revisited - ten new case reports. Angiology. 2001;52:1-5. Abstract

9. Allen EV, Brown GE. Thrombo-angiitis obliterans: a clinical study of 200 cases: I. etiology, pathology, symptoms, diagnosis. Ann Intern Med. 1928;1:535-549.

10. Iwai T, Inoue Y, Umeda M, et al. Oral bacteria in the occluded arteries of patients with Buerger disease. J Vasc Surg. 2005;42:107-115. Abstract

11. Iwai T. Periodontal bacteremia and various vascular diseases. J Periodontal Res. 2009;44:689-694. Abstract

12. Kjeldsen K, Mozes M. Buerger's disease in Israel. Investigations on carboxyhemoglobin and serum cholesterol levels after smoking. Acta Chir Scand. 1969;135:495-498. Abstract

13. Chen Z, Nakajima T, Inoue Y, et al. A single nucleotide polymorphism in the 3'-untranslated region of MyD88 gene is associated with Buerger disease but not with Takayasu arteritis in Japanese. J Hum Genet. 2011;56:545-547. Abstract

14. Makita S, Nakamura M, Murakami H, et al. Impaired endothelium-dependent vasorelaxation in peripheral vasculature of patients with thromboangiitis obliterans (Buerger's disease). Circulation. 1996;94(9 suppl):II211-II215. Abstract

15. Papa M, Bass A, Adar R, et al. Autoimmune mechanisms in thromboangiitis obliterans (Buerger's disease): the role of tobacco antigen and the major histocompatibility complex. Surgery. 1992;111:527-531. Abstract

16. Dellalibera-Joviliano R, Joviliano EE, Evora PR. Determination of kininogens levels and kallikrein/kininase II activities in patients with thromboangiitis obliterans. Scand J Immunol. 2010;72:128-133. Abstract

17. Lie JT. Thromboangiitis obliterans (Buerger's disease) and smokeless tobacco. Arthritis Rheum. 1988;31:812-813. Abstract

18. Joyce JW. Buerger's disease (thromboangiitis obliterans). Rheum Dis Clin North Am. 1990;16:463-470. Abstract

19. Maslowski L, McBane R, Alexewicz P, Wysokinski WE. Antiphospholipid antibodies in thromboangiitis obliterans. Vasc Med. 2002;7:259-264. Abstract

20. Chen YW, Nagasawa T, Wara-Aswapati N, et al. Association between periodontitis and anti-cardiolipin antibodies in Buerger disease. J Clin Periodontol. 2009;36:830-835. Abstract

21. Chen Z, Takahashi M, Naruse T, et al. Synergistic contribution of CD14 and HLA loci in the susceptibility to Buerger disease. Hum Genet. 2007;122:367-372. Abstract

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22. Sasaki S, Sakuma M, Kunihara T, et al. Distribution of arterial involvement in thromboangiitis obliterans (Buerger's disease): results of a study conducted by the Intractable Vasculitis Syndromes Research Group in Japan. Surg Today. 2000;30:600-605. Abstract

23. Puechal X, Fiessinger JN, Kahan A, et al. Rheumatic manifestations in patients with thromboangiitis obliterans (Buerger's disease). J Rheumatol. 1999;26:1764-1768. Abstract

24. Juergens JL. Thromboangiitis obliterans (Buerger's disease, TAO). In: Juergens JL, Spittel JA, Fairbairn JF, eds. Peripheral vascular disease. Philadelphia, PA: WB Saunders; 1980:469-491.

25. Hill GL. A rational basis for management of patients with Buerger syndrome. Br J Surg. 1974;61:476-481. Abstract

26. Shionoya S. Pathology. In: Shionoya S, ed. Buerger's disease. Nagoya: University of Nagoya Press; 1990:57-79.

27. Papa MZ, Rabi I, Adar R. A point scoring system for the clinical diagnosis of Buerger's disease. Eur J Vasc Endovasc Surg. 1996;11:335-339. Abstract

28. Sasajima T, Kubo Y, Inaba M, et al. Role of infrainguinal bypass in Buerger's disease: an eighteen-year experience. Eur J Vasc Endovasc Surg. 1997;13:186-192. Abstract

29. Ohta T, Ishioashi H, Hosaka M, et al. Clinical and social consequences of Buerger disease. J Vasc Surg. 2004;39:176-180. Abstract

30. O'Dell JR, Linder J, Markin RS, et al. Thromboangiitis obliterans (Buerger's disease) and smokeless tobacco. Arthritis Rheum. 1987;30:1054-1056. Abstract

31. Palomo Arellano A, Gomez Tello V, Parilla Herranz P, et al. Buerger's disease starting in the upper extremity: a favorable response to nifedipine treatment combined with stopping tobacco use. An Med Interna. 1990;7:307-308. Abstract

32. Agarwal P, Agrawal PK, Sharma D, et al. Intravenous infusion for the treatment of diabetic and ischaemic non-healing pedal ulcers. J Eur Acad Dermatol Venereol. 2005;19:158-162. Abstract

33. Ohashi S, Iwatani M, Hyakuna Y, et al. Thermographic evaluation of the hemodynamic effect of the antithrombotic drug cilostazol in peripheral arterial occlusion. Arzneimittelforschung. 1985;35:1203-1208. Abstract

34. Fiessinger JN, Schafer M. Trial of iloprost versus aspirin treatment for critical limb ischaemia of thromboangiitis obliterans. The TAO study. Lancet. 1990;335:555-557. Abstract

35. Bozkurt AK, Koksal C, Demirbas MY, et al. A randomized trial of intravenous iloprost (a stable prostacyclin analogue) versus lumbar sympathectomy in the management of Buerger's disease. Int Angiol. 2006;25:162-168. Abstract

36. Cacione DG, Macedo CR, Baptista-Silva JC. Pharmacological treatment for Buerger's disease. Cochrane Database Syst Rev. 2016;(3):CD011033. Abstract

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REFERENCES

37. The European TAO Study Group. Oral iloprost in the treatment of thromboangiitis obliterans (Buerger's disease): a double-blind, randomised, placebo-controlled trial. Eur J Vasc Endovasc Surg. 1998;15:300-307. Full text Abstract

38. Donas KP, Schulte S, Ktenidis K, et al. The role of epidural spinal cord stimulation in the treatment of Buerger's disease. J Vasc Surg. 2005;41:830-836. Abstract

39. Manfredini R, Boari B, Gallerani M, et al. Thromboangiitis obliterans (Buerger disease) in a female mild smoker treated with spinal cord stimulation. Am J Med Sci. 2004;327:365-368. Abstract

40. Broseta J, Barbera J, de Vera JA, et al. Spinal cord stimulation in peripheral arterial disease: a cooperative study. J Neurosurg. 1986;64:71-80. Abstract

41. Stümpflen A, Ahmadi A, Attender M, et al. Effects of transvenous regional guanethidine block in the treatment of critical finger ischemia. Angiology. 2000;51:115-122. Abstract

42. Paraskevas KI, Trigka AA, Samara M. Successful intravenous regional sympathetic blockade (Bier's Block) with guanethidine and lidocaine in a patient with advanced Buerger's Disease (thromboangiitis obliterans) - a case report. Angiology. 2005;56:493-496. Abstract

43. Chander J, Singh L, Lal P, et al. Retroperitoneoscopic lumbar sympathectomy for Buerger's disease: a novel technique. JSLS. 2004;8:291-296. Abstract

44. Lau H, Cheng SW. Buerger's disease in Hong Kong: a review of 89 cases. Aust NZ J Surg. 1997;67:264-269. Abstract

45. Kothari R, Sharma D, Thakur DS, et al. Thoracoscopic dorsal sympathectomy for upper limb Buerger's disease. JSLS. 2014;18:273-276. Full text Abstract

46. Segers B, Himpens J, Barroy JP. Retroperitoneal laparoscopic bilateral lumbar sympathectomy. Acta Chir Belg. 2007;107:341-342. Abstract

47. Fadini GP, Agostini C, Avogaro A. Autologous stem cell therapy for peripheral arterial disease: meta-analysis and systematic review of the literature. Atherosclerosis. 2010;209:10-17. Abstract

48. Olin JW. Thromboangiitis obliterans (Buerger's disease). N Engl J Med. 2000;343:864-869. Abstract

49. Sasaki S, Sakuma M, Yasuda K. Current status of thromboangiitis obliterans (Buerger's disease) in Japan. Int J Cardiol. 2000;75(suppl 1):S175-S181. Abstract

50. Talwar S, Jain S, Porwal R, et al. Free versus pedicled omental grafts for limb salvage in Buerger's disease. Aust NZ J Surg. 1998;68:38-40. Abstract

51. Isner JM, Baumgartner I, Rauh G, et al. Treatment of thromboangiitis obliterans (Buerger's disease) by intramuscular gene transfer of vascular endothelial growth factor: preliminary clinical results. J Vasc Surg. 1998;28:964-973. Abstract

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52. Tateishi-Yuyama E, Matsubara H, Murohara T, et al. Therapeutic angiogenesis for patients with limb ischaemia by autologous transplantation of bone-marrow cells: a pilot study and a randomized controlled trial. Lancet. 2002;360:427-435. Abstract

53. Idei N, Soga J, Hata T, et al. Autologous bone-marrow mononuclear cell implantation reduces long-term major amputation risk in patients with critical limb ischemia: a comparison of atherosclerotic peripheral arterial disease and Buerger disease. Circ Cardiovasc Interv. 2011;4:15-25. Full text Abstract

54. Todoli Parra JA, Hernández MM, Arrébola López MA. Efficacy of bosentan in digital ischemic ulcers. Ann Vasc Surg. 2010;24:690.e1-e4. Abstract

55. Szuba A, Cooke JP. Thromboangiitis obliterans: an update on Buerger's disease. West J Med. 1998;168:255-260. Full text Abstract

56. Cooper LT, Tse TS, Mikhail MA, et al. Long-term survival and amputation risk in thromboangiitis obliterans (Buerger's disease). J Am Coll Cardiol. 2004;44:2410-2411. Abstract

57. Ates A, Yekeler I, Ceviz M, et al. One of the most frequent vascular diseases in northeastern of Turkey: thromboangiitis obliterans or Buerger's disease (experience with 344 cases). Int J Cardiol. 2006;111:147-153. Abstract

58. Szuba A, Wysokinski W, Czarnacki M, et al. Coexistence of Buerger's disease with atherosclerosis obliterans. In: 9th International symposium on atherosclerosis. 1991; abstract 178.

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Images

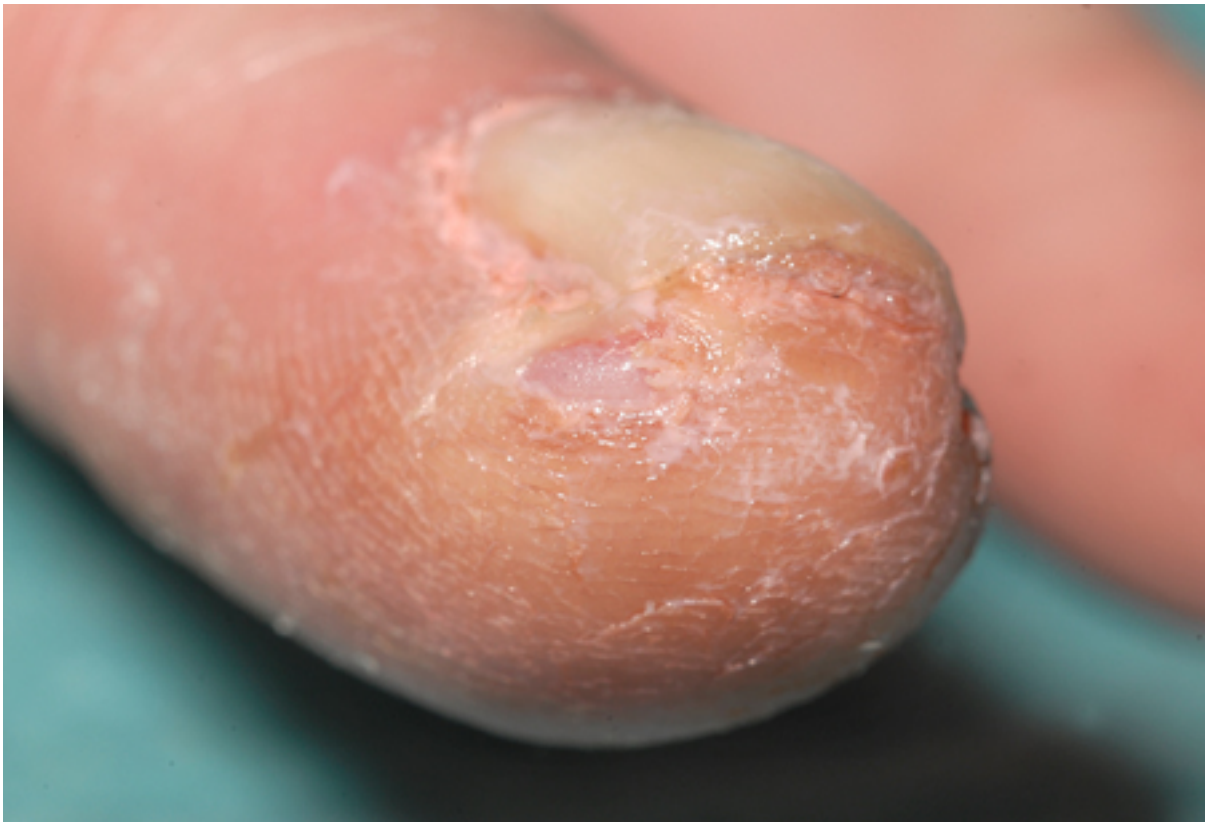

Figure 1: Fingertip ulceration in a woman who smokes

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Figure 2: A cold, ischaemic middle finger in a woman who smokes

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Figure 3: Subsequent middle finger amputation in a woman who continued to smoke

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Figure 4: Subsequent index finger amputation in a woman who continued to smoke

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Figure 5: Multiple amputations

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