

# Traditional Chinese Medicine and Human Immunodeficiency Virus-Associated Neuropathy

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## Abstract

Peripheral neuropathy is one of the most common neurological complications of human immunodeficiency virus (HIV) infection and continues to impact people living with HIV/AIDS. The pain associated with peripheral neuropathy can be severe and debilitating. Most pharmacological agents are inadequate in symptom management and are accompanied by adverse side-effects. Acupuncture and moxibustion offer treatment approaches that can reduce HIV symptoms and/or the side-effects of anti-retroviral therapy and improve patients' quality of life.

## Introduction

Peripheral neuropathy is one of the most common neurological complications experienced by patients with HIV.<sup>1</sup> Despite advances in highly active anti-retroviral therapy (HAART), which have reduced morbidity and mortality, patients still often develop complications of the peripheral or central nervous system.<sup>2,3</sup> While the incidence and prevalence rates of neurological complications of the central nervous system such as HIV dementia<sup>3</sup> have declined, distal sensory peripheral neuropathy (DSP) continues to be a common complication occurring in approximately one-third of HIV patients.<sup>4,5,6</sup> Pre-HAART studies showed that the risk and severity of DSP was associated with advanced immuno-suppression and increased plasma viral load.<sup>7</sup> Post-HAART, with improvements in immune function and viral suppression, DSP persists with concomitant risk factors including advanced age, co-morbidities such as diabetes, nutritional deficiencies, mitochondrial polymorphisms and anti-retroviral medications.<sup>3</sup> DSP presents with aching or burning pain (dysaesthesia), and/or numbness or pins and needles (paraesthesia) in the distal extremities, usually symmetrical and predominantly in the toes and soles of the feet.<sup>8</sup> Reduced functional capacity has also been reported, including decreased or absent ankle reflexes, impaired pain and temperature perception, elevated vibratory threshold and occasional intrinsic muscle weakness.<sup>7,9</sup>

The pathophysiology of HIV neuropathy is not completely understood. DSP is characterised by degeneration of axonal sensory fibres and loss of both large and small myelinated and unmyelinated nerves, with inflammation mediated by macrophage infiltration and activation.<sup>2</sup> DSP may be due to HIV itself, medication, advanced immuno-suppression or

nutritional deficiency.<sup>10</sup> Direct infection of the nervous system appears to be an unlikely cause.<sup>11</sup> A possible mechanism may be binding of the viral envelope protein gp120 to chemokine receptors, leading to axonal injury.<sup>12</sup> Immunological dysfunction may promote macrophage infiltration and the resulting local release of pro-inflammatory neurotoxic cytokines.<sup>13</sup> Anti-retroviral agents used in the primary treatment of HIV, such as the nucleoside reverse transcriptase inhibitors (NRTI) and particularly the dideoxynucleoside analogues, which include didanosine (ddI), zalcitabine (ddC) and stavudine (d4t), exhibit recognised dose-dependent peripheral nerve neurotoxicity.<sup>14</sup> Though the use of these 'd-drugs' has declined, protease inhibitor (PI) therapies may be associated with DSP.<sup>15,16</sup> The drug-induced neuropathies may be mediated by disruption of DNA synthesis causing interference with mitochondrial function.<sup>17</sup> Clinically, it is often difficult to differentiate between drug-related neuropathy and that caused by HIV infection alone.<sup>13</sup>

If left untreated, many patients experience gait difficulties, and contact with everyday stimuli such as socks, shoes and bedsheets can cause extreme discomfort. The debilitating pain, difficulty walking, inability to exercise, emotional stress and resulting sleep disturbance can all significantly impact quality of life. Current treatment approaches for HIV-associated DSP aim primarily at symptomatic management of pain with non-steroidal anti-inflammatory drugs (NSAIDs), tricyclic anti-depressants, opioids and anti-convulsants. However, available treatment options are insufficient and often accompanied by side-effects such as sedation, dizziness and peripheral oedema.<sup>18</sup> Topical analgesics such as a high-concentration capsaicin<sup>19</sup> patch may reduce pain but lidocaine has demonstrated limited efficacy.<sup>20</sup>

Non-pharmacological interventions such as

acupuncture and moxibustion can serve as valuable and effective approaches to managing DSP and improving quality of life. Studies have demonstrated acupuncture to be effective in the treatment of neuropathic pain.<sup>21,22</sup> To date, there have been four published studies examining acupuncture for peripheral neuropathy in patients with HIV/AIDS.<sup>23,24,25,26</sup> Three of these showed improvement in pain and functional status, although the sample sizes were small and all studies lacked a control group. In the larger randomised placebo-controlled trial, controversy over acupuncture point selection<sup>27</sup> and modifications with the randomisation scheme yielded inconsistent results.<sup>28</sup> No studies were conducted using acupuncture in conjunction with moxibustion. Traditionally, acupuncture has been used together with moxibustion, although few clinical studies have demonstrated the effectiveness of moxibustion except in cases of breech presentation,<sup>29</sup> menopausal hot flashes<sup>30</sup> and Crohn's disease.<sup>31</sup>

### Traditional Chinese medicine and peripheral neuropathy

The foundation of Chinese medicine is a philosophy of correspondences based on the concepts of yin and yang and the five phases. Interplay of the natural phenomenon of duality with the fundamental qi in all aspects of the body preserves a state of balance. Disease is viewed as a disharmony of the body and treatment is directed towards harmonising the whole body system.<sup>32</sup> The diagnostic system of traditional Chinese medicine relies on identifying patterns based on signs and symptoms presented by the patient. Once patterns are determined, the main principle of treatment discerns between the ben (root) and the biao (branch). Often a practitioner will treat the outward manifestation (biao) and the root simultaneously, providing symptomatic relief while addressing the underlying pattern.<sup>33</sup>

In Chinese medicine, pain is due to imbalance within the body, which may lead to reduced flow of qi and blood through the channels and organs. As the flow of qi is affected, stagnation, obstruction or dampness may occur in the channels. The pathogenesis of DSP is primarily associated with deficiency of both yin and yang aspects of the Spleen, Liver and Kidney. As the deficiency progresses, stagnation may occur and heat or cold signs may predominate.

In Chinese medicine, organs are defined primarily by their function rather than their physical structure, as in Western medicine.<sup>34</sup> The Kidney produces the Sea of Marrow, which encompasses the brain, spinal cord and bone marrow. The central nervous system or brain is filled by the yuan qi (prenatal energy) of Kidney jing (essence). This essence is essential to the

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development and maintenance of the nervous system. As HIV infection progresses, viral heat moves into the interior and depletion of Kidney yin and jing occurs. The Kidney function of building the Sea of Marrow, which provides the myelin for the nervous system,<sup>35</sup> thus deteriorates. Changes in pain perception and temperature sensation may result as nerve conduction is impaired.

### The Kidney

Kidney yin is the foundation of the jin ye (body fluids), which moisten and nourish the organs, tissues and muscles. Jin are the thin, clear watery fluids found in tears, sweat and saliva, which moisten the skin and are controlled by the Lung. The ye are the thicker, more viscous fluids found in synovial and joint cavities and marrow, which nourish the inner organs and brain. They are controlled by the Spleen and Kidney and facilitate the movement of bones and joints. Without the proper lubrication and moistening provided by Kidney yin, heat or burning sensations along with numbness may occur in the extremities and thus impair movement.

As yin deficiency increases, its paired yang aspect also becomes weak. Kidney yang deficiency affects the circulation of qi and blood, causing pain and coldness in the extremities, possibly leading to ice-cold limbs. All organs rely on the yang energy provided by the Kidney's Mingmen (Gate of Life) for proper functioning. The Stomach needs it to receive and ripen the food before sending it to the Spleen. The Spleen needs the heat to convert and transport the food essence. If the fire of the Gate of Life is deficient, the Spleen and Stomach cannot transform nutrients, leading to dampness and resulting in heaviness and/or numbness in the limbs.

### The Stomach and Spleen

In the early stages of HIV infection, patients often present with symptoms of fatigue, diarrhoea, loss of appetite and inability to gain weight, possibly due to pathogens from the illness, but also as a result of the side-effects of medication. During the symptomatic phase of HIV infection, anti-retroviral agents and medications used to treat opportunistic infections damage the Spleen and Stomach, affecting the production of blood and qi, as well as depleting the Kidney and Liver. As the functions of the Stomach and Spleen are weakened, fluid retention occurs and leads to dampness. Dampness is heavy and cloying and

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obstructs the circulation of qi and blood.<sup>36</sup> This dampness may accumulate in the channels causing numbness, aching and decreased sensitivity of the extremities.

### **The Liver**

During activity, the Liver blood is responsible for circulating through the ligaments, tendons, muscles and peripheral nerves. Its paired organ, the Gallbladder, ensures the proper supply of qi to the sinews for agility and movement.<sup>33</sup> At rest, blood flows back to the Liver. If the Liver function is compromised, blood stagnation occurs, resulting in stiffness, throbbing or pins and needles in the limbs. If dysfunction leads to vacuity of Liver blood, then cold sensations or tingling in the extremities may manifest<sup>37</sup> and any deficit in Liver blood supply to the peripheral nerves makes them more sensitive and irritable.<sup>38</sup> The Liver and Kidney share the same source of yin. If the Kidney yin is lacking, then Liver yin may also be deficient and result in burning sensations in the limbs. As the disease progresses and Liver yin deteriorates, Liver yang may begin to rise or internal wind may develop, causing spasms, paralysis or difficulty in moving. Liver yang rising, often characterised as an excess condition, can arise from severe yin deficiency resulting in the separation of Liver yin and yang.<sup>38</sup>

### **Case study one**

A 45-year-old male diagnosed with HIV since 1995 presented with severe chronic bilateral numbness and pins and needles in his lower legs and burning pain in his feet and toes. The patient was referred by his primary care physician. His neuropathy symptoms began in 1999 and he was started on gabapentin with little resulting relief. His primary TCM diagnosis was Liver wind/blood deficiency with underlying Liver and Kidney yin deficiency. The patient's HIV RNA level was 150 copies/mL and his CD4+ cell count was 250 cells/ $\mu$ L while on ritonavir (PI), tenofovir (NRTI) and emtricitabine (NRTI). Using a scale of severity from zero (=no discomfort) to six (=very severe discomfort), his symptoms of pain, pins and needles and numbness were self-rated as very severe (six).

The patient had an absence of sensation to pin prick, light touch and temperature in both feet and legs. Pressure sensation using monofilament testing was absent bilaterally, as were his Achilles reflexes. His tongue was pale with a red tip, deviated, and had a peeled coat. His pulse was 84 beats per minute and had a forceful, wiry quality.

Treatment used the following acupuncture points: Quchi L.I.-11, Xuehai SP-10, Yanglingquan GB-34, Zusanli ST-36, Sanyinjiao SP-6 and Taixi KID-3. Needles were inserted to a depth that elicited deqi sensation and retained for 20 minutes using a reinforcing technique. Then the patient lay prone and Ququan LIV-8 and Xuanzhong GB-39 were needled and retained for 20 minutes. Simultaneously, indirect pole moxibustion was applied for two minutes to each of the following points using a clockwise circular motion: Geshu BL-17, Ganshu BL-18, Pishu BL-20 and Yongquan KID-1.

The treatment focused on the multiple underlying deficiencies of the Kidney and Spleen by tonifying the blood (Zusanli ST-36, Sanyinjiao SP-6, Ququan LIV-8) and strengthening marrow and Kidney yin and yang (Xuanzhong GB-39, Taixi KID-3), while moving blood and qi (Xuehai SP-10, Yanglingquan GB-34) and clearing heat (Quchi L.I.-11). Indirect pole moxibustion was applied to blood-related points (Geshu BL-17, Ganshu BL-18, Pishu BL-20) to further nourish blood and yin.

After 12 sessions (twice a week for six weeks), the patient experienced improved sensation, which was now normal in response to pinprick, temperature and light touch in both legs and feet. Pressure sensation had also improved and was present bilaterally. The patient reported his pain score to be mitigated and his overall symptom severity was reported as minor (one on the severity scale) in a follow-up session one month later.

### **Case study two**

A 50-year-old female diagnosed with HIV since 2004 presented with pins and needles in her lower extremities in June 2007. She reported that walking up stairs was very difficult and painful. Her primary TCM diagnosis was Spleen and Kidney qi deficiency with dampness and underlying Liver and Kidney yin deficiency. Her HIV RNA level was <50 copies/mL and her CD4+ cell count was 450 cells/ $\mu$ L while on ritonavir (PI), tenofovir (NRTI) and emtricitabine (NRTI). At baseline she rated her symptoms of pins and needles as very severe (six on the severity scale). She had an absence of sensation to pin prick, light touch and temperature in both feet and legs. Plantar reflexes and pressure sensation were absent bilaterally. Her tongue was pink and wide, with a thin, white coat. Her pulse was 77 beats per minute and had a thin, slippery quality. Given the similar underlying diagnosis of Liver and Kidney yin deficiency as the case study above, the treatment principles focused on the root and utilised the same acupuncture points and moxibustion to nourish her blood and yin. After 12 sessions (twice a week for 6 weeks) of treatment, she reported that her pain had moderately improved (three on the severity scale) and she had intact thermal, light touch and pin prick sensation, which was sustained at follow up eight weeks later.

Pattern	Signs/Symptoms	Tongue and Pulse
Liver yin deficiency	Burning sensation in limbs, blurred vision, dry eyes, dizziness, tinnitus, thirst, dry throat, headache, night sweats, insomnia, irritability, anxiety.	Red, no coat. Thready, wiry, rapid.
Liver blood deficiency	Cold extremities, tingling and occasional twitching, numbness, weakness of limbs, blurred/poor vision, floaters, dry eyes, tinnitus, dizziness, irritability, insomnia with excessive dreaming, pale complexion, pale lips and nail beds.	Pale, no coat. Thready.
Liver qi stagnation	Intermittent cold and numb extremities, distending pain in ribs, chest tightness, sighing, depression, irritability.	Dusky, thin white coat. Wiry.
Kidney qi deficiency	Cold limbs, numbness, urinary incontinence or frequency, vaginal discharge, back pain, poor libido, impotence, shortness of breath, shallow breathing, soft voice, sweating, tinnitus, dizziness, poor appetite, general weakness, pallor.	Pale, swollen, teethmarks, thin white coat. Deep, thready.
Kidney yin deficiency	Burning sensation in limbs with numbness, dry mouth and throat, thirst, malar flush, night sweats, afternoon fever, dry stools, darkish scanty urine.	Red with little or no coat. Thready, rapid.
Kidney yang deficiency	Ice-cold limbs with numbness, cold feeling, copious urination, nocturia, early morning diarrhoea, weak aching knees.	Swollen, wet. Slow.
Spleen qi deficiency with dampness	Feeling of heaviness of the limbs, swelling of the legs, numbness, anorexia, distention after eating, acid reflux, nausea, vomiting, loose stools, sallow complexion, fatigue, heaviness, shortness of breath.	Pale, flabby, toothmarks, white or greasy, thick coat. Weak or deep and slippery.
Spleen yang deficiency	Cold limbs, heavy, numbness, epigastric pain with cold sensation, watery stools with undigested food, chilled feeling.	Pale, puffy, thin white coat. Deep, weak.
Qi and blood stasis	Numbness/tingling of limbs, discomfort/stiffness and throbbing pain, burning, fatigue, depression, menstrual irregularities, PMS, headaches, facial flushing.	Dusky, dry. Thin, choppy.
Qi and blood deficiency	Numbness, tingling of limbs, fatigue, heaviness, spontaneous sweating, shortness of breath, pallor, dizziness, chilliness, sensory impairment.	Pale, toothmarks, no coat. Deep, weak, thready.

## Discussion

The development and predominance of neuropathic symptoms varies for each HIV patient. The above cases illustrate that despite the differing presentation of pain symptoms, both patients shared an underlying root of severe blood and yin deficiency. Clinically, cases are often complicated with multiple roots and manifestations, leaving the practitioner with the challenge of choosing what to treat first. With a chronic illness like HIV, where multiple deficiencies at various organ levels coincide, the manifestations may emerge, blend, overlap and recede. By focusing treatment on the root imbalances and nourishing blood and yin, particularly with the use of indirect pole moxibustion on blood-related points, both patients were able to experience significant relief.

## Conclusion

As people with HIV are living longer, HIV has transformed into a chronic and manageable disease. However, patients still experience additional

complications and side-effects of longterm medication use. TCM can provide beneficial and effective non-pharmacological approaches to reduce HIV symptoms and/or HAART side-effects and to improve quality of life. Other studies conducted with acupuncture have shown its effectiveness in reducing diarrhoea<sup>39</sup> and improving quality of life in patients with HIV/AIDS.<sup>40</sup>

Acupuncture and moxibustion have traditionally been combined as one therapy. The paucity of studies in the English language literature on the combined usage of acupuncture and moxibustion demonstrate the need for further research. As acupuncture research evolves, the need arises for further discussion on how to maintain the integrity of the therapy, while applying the high methodological standards of biomedical research. Ultimately, the integration of Western and Chinese medicine expands patients' choice to include treatments that are effective and low-cost, have few adverse side-effects, and which can significantly improve their overall quality of life. ■

**Table 1:**  
**Traditional Chinese medicine patterns of distal sensory peripheral neuropathy.**

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