Case Report

Adrenal Fatigue Syndrome May be Due to Kidney Deficiency

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Abstract

According to Chinese medicine, chronic illness may cause a Kidney deficiency syndrome. In modern Chinese medical literature, Kidney deficiency syndromes have been associated with dysfunction of the neuroendocrine system, especially the hypothalamus-pituitary-adrenal axis.

This long-term case, which follows a menopausal patient with insomnia, appears to show a correlation between her Kidney deficiency diagnoses and adrenal fatigue. Free saliva cortisol tests of this patient at various intervals, when compared with her symptomatic presentation, indicate that the stressed stage and fatigued stage of adrenal fatigue syndrome may be related to Kidney *yin* deficiency and Kidney *yang* deficiency categories, respectively.

This case suggests that the free saliva cortisol test may possibly be useful as an objective biomarker indicating a likelihood of a Kidney deficiency syndrome diagnosis. To further study the correlation of adrenal fatigue syndrome and Kidney deficiency syndrome, and to assess clinical applications of the free saliva cortisol test in diagnosis of Kidney deficiency syndrome, larger clinical studies are warranted. Making connections between Chinese medicine syndromes and biomedical pathophysiology may facilitate the development of objective instruments to inform diagnosis, which may in turn improve clinical outcomes of traditional Chinese medicine.

Key Words: Chinese medicine syndrome, Kidney deficiency syndrome, pattern differentiation, *bian zheng*, adrenal fatigue syndrome, free salivary cortisol test, hypothalamus-pituitary-adrenal axis

Introduction

Chinese medicine syndrome diagnosis, also known as *bian zheng* or pattern differentiation, is an integral and essential part of traditional practice.[1] A Chinese medicine

syndrome is a characteristic profile, based on traditional theory, of all clinical manifestations that can be identified. Biomedical diagnosis is based on a pathophysiological state of disease.[1] Successful Chinese medicine treatment relies on correct pattern differentiation.[2,3] Recent advances in biomedical technologies make new biomedical interpretations of pattern diagnoses possible.[2-5] However, due to the philosophical nature of Chinese medicine theories, making definitive connections to biomedical pathophysiology remains challenging.

The efficacy of Chinese medicine therapies has been the subject of study for the past several decades. Adapting Chinese medicine therapies to fit within a well-designed clinical trial has been difficult, due in part to the subjective nature of Chinese medicine diagnosis—the consistency rate of Chinese medicine syndrome diagnosis can be as low as 30% among TCM practitioners.[6] Objectivity in the diagnostic process becomes urgent and necessary in Chinese medicine research.[7,8]

Kidney deficiency syndromes, including Kidney *yin*, Kidney *yang*, and Kidney *qi* deficiency, are among the most commonly observed patterns for chronic illnesses, such as autoimmune,[9] neurodegenerative,[10] female hormonal, metabolic, and cardiovascular diseases.[11] In one study, rheumatoid arthritis patients with Kidney deficiency syndromes were associated with a more severe autoimmune response and faster disease progression.[9]

Attempts have been made to correlate Kidney deficiency syndromes with biomedical markers, such as low cortisol,[12] low levels of reproductive hormones,[13] and low bone density.[14] Chinese kidney-tonic herbs such as *yin yang huo* (Epimedium)[15] and *gu sui bu* (Drynariae),[16] as well as classical formulas, such as *Zuo Gui Wan* (Restore the Left Kidney) and *You Gui Wan* (Restore the Right Kidney),[17] have also been studied regarding their effect on dysfunction of the hypothalamus-pituitary axis.

Various laboratory studies suggested that the dysfunction of the hypothalamus-pituitary-thyroid axis,[18] hypothalamus-pituitary-thymus axis,[17] and hypothalamus-pituitary-gonadal axis[19] are all associated with Kidney *yang* deficiency. Despite these findings, it remains unclear whether Kidney patterns truly reflect these biomedical pathological states.

Clinical study of identification of Kidney patterns has been limited to patient-reported outcomes and symptom analysis.[20] Symptoms of both Kidney *yin* and *yang* deficiencies may include joint weakness and pain, forgetfulness and dizzy spells, tinnitus, low libido and vaginal dryness, and increased nocturnal urination.[21] The symptoms specific to Kidney *yin* deficiency syndrome may include hot flashes, night sweats, feeling hot in palms and soles, thirst, dry eyes and skin, insomnia, and increased dreaming.

Those specific to Kidney *yang* deficiency syndrome are an overall feeling of cold, the feeling of cold in the lower back, frequent urination, increased urine volume, urinary incontinence and edema, and lethargy.[21] A questionnaire was developed to measure Kidney *yin* and *yang* deficiency clinically for middle-aged women with menopausal symptoms.[21] However, objective validation of the syndrome is still not available.

Adrenal Fatigue Syndrome

Adrenal fatigue syndrome (AFS) is a collection of signs and symptoms that results when the function of the hypothalamic-pituitary-adrenal axis (HPA) decreases below normal. It consists of many nonspecific but debilitating symptoms, such as fatigue that cannot be relieved by sleep, difficulty concentrating, insomnia, inability to lose weight, feeling anxious, allergies, or brain fog.[22]

There are two collective stress responding systems in the body—the autonomic nervous system (ANS) and the HPA axis. These two systems are mediated by largely overlapping circuits in the brain. The ANS provides the most immediate response to stressor exposure through

"When under chronic stress in the early stage of HPA dysfunction, known as the stressed stage, the adrenal glands increase cortisol output but are unable to keep up with the body's demand. Dysfunction of the HPA system causes disruption of the cortisol circadian rhythms, where cortisol production starts to rapidly decline during the day and increase at night. This results in clinical symptoms, such as insomnia, fatigue, and mood disorders."

its sympathetic and parasympathetic branches.[23] Activation of the HPA axis results in elevations in circulating epinephrine and cortisol. The hormonal mechanism of HPA induction is slower than the mechanisms that drive sympathetic activation, but it provides an amplified and prolonged systemic reaction.[23]

Cortisol is the primary hormone responsible for the stress response and maintaining homeostasis after exposure to stress.[24] The circadian rhythm of cortisol is regulated by the hypothalamus. Normal individuals have very low cortisol levels at midnight, which increase to a peak in the morning and then decline slowly throughout the day.[25] Cortisol influences a wide range of cognitive functions, including memory performance and executive function. The free salivary cortisol test (FSCT) is a common test of the cortisol circadian rhythm used to determine proper stages of AFS. The test has been studied extensively to assess HPA function for related diseases.[26, 27]

When under chronic stress in the early stage of HPA dysfunction, known as the stressed stage, the adrenal glands increase cortisol output but are unable to keep up with the body's demand. Dysfunction of the HPA system causes disruption of the cortisol circadian rhythms, where cortisol production starts to rapidly decline during the day and increase at night. This results in clinical symptoms, such as insomnia, fatigue, and mood disorders.[22, 28]

In the later stage of HPA dysfunction, called the fatigued stage, the adrenals are exhausted due to dramatic reduction of total cortisol output. The HPA system is unable to maintain homeostasis, and cortisol circadian rhythm shows reduction to a flat line. Symptoms may include fatigue that is not relieved by sleep, brain fog, lethargy, hypoglycemia, and the inability to maintain sleep at night.[22, 28] The HPA axis controls homeostasis of all hormones, and dysfunction affects multiple endocrine pathways, including thyroid metabolism.[31, 32] Pregnenolone metabolism is also affected, which influences the production of progesterone, aldosterone, estrogen, and testosterone.[32]

Case Description

Patient History

This patient, a married Caucasian housewife with two adult children, suffered from insomnia and fatigue for many years. She and her husband had a busy lifestyle and traveled abroad extensively. She was tested with FSCT at her first clinic visit. For the nine years following, she periodically took nutritional supplements for symptoms only, but she never completed any systematic treatment due to her busy schedule. At that point, she had a second FSCT test and received treatment for approximately a year before a third test was performed. Her symptoms, treatment protocols and FSCT results are presented here.

Test-1 Period

During her first test period, she was 44 years old; her main complaint was difficulty falling asleep. Once she fell asleep, she was able to sleep through the night, but she felt unrested in the morning. Overall, she had low energy during the day and experienced sugar cravings between 2 pm and 4 pm.

The patient also experienced perimenopausal symptoms. Although she still had a regular menstrual cycle, she started to show hot flashes, night sweats, dry skin, low libido, vaginal dryness, and irritability. She had an overall warm body and felt hot in her hands and feet. She also complained of food sensitivities and indigestion, including symptoms of bloating, gas, constipation, hives and skin rashes.

Her tongue was red with a dry thick white coating, and her pulse was deep and taut. According to Chinese medicine pattern differentiation, the patient's insomnia, fatigue, perimenopausal symptoms and red tongue indicated Kidney *yin* deficiency with Heat. Her digestive symptoms, skin breakout, and thick white tongue coating were clear signs of Spleen Dampness and Heat. Her emotions and irritability indicated Liver *qi* stagnation.

The first FSCT showed an increase in production of free salivary cortisol. The morning cortisol level was extremely high, followed by a gradual drop, with the lowest level around 4 pm, and with a slight increase at night. The overall cortisol production was much higher than normal range (Table 1a and Figure 1).

Figure 1. Salivary Cortisol Rhythm

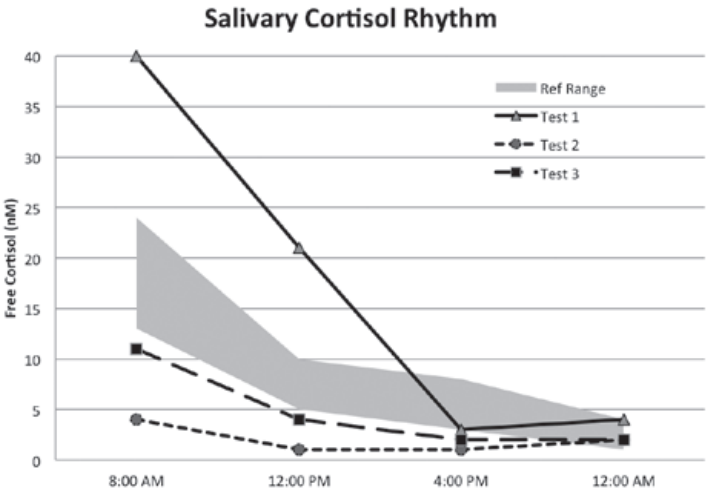

Table 1. Free Salivary Cortisol Test

A. Test 1

Time	Result (nM)	Description	Reference Values (nM)
08:00 AM	40	Elevated	13-23
12:00 Noon	21	Elevated	5-10
04:00 PM	3	Borderline	3-8
12:00 Midnight	4	Borderline	1-3
Total	68	Elevated	23-42

B. Test 2

Time	Result (nM)	Description	Reference Values (nM)
08:00 AM	4	Depressed	13-24
12:00 Noon	1	Depressed	5-10
04:00 PM	1	Depressed	3-8
12:00 Midnight	2	Normal	1-4
Total	8	Depressed	23-42

C. Test 3

Time	Result (nM)	Description	Reference Values (nM)
08:00 AM	11	Depressed	13-24
12:00 Noon	5	Borderline	5-10
04:00 PM	2	Depressed	3-8
12:00 Midnight	2	Normal	1-4
Total	20	Depressed	23-42

Patient information, AFS stages, and corresponding Chinese medicine diagnoses are summarized in Table 2.

Table 2. Summary of Patient Information with Corresponding CMSs and AFS Stages

	Test-1 Period	Test-2 Period	Test-3 Period
Patient Age	44	53	54
Free Cortisol Salivary Test	Elevated (Table 1a and Figure 1)	Depressed (Table 1b and Figure 1)	Depressed (Table 1c and Figure 1)
Other Tests	Not available	Elevated thyroid peroxidase antibodies with normal free T3/ T4 and TSH level	Not available
Tongue	Red with thick white coating	Purple and pale with white coating	Pale and light red color with white coating
Pulse	Deep and taut	Deep, thin and weak pulse	The same as Test-2 period
Main CMS or Patterns	Kidney *yin* deficiency with Heat Spleen Dampness and Heat Liver *qi* stagnation	Kidney *yin* and *yang* deficiency Spleen Dampness and Heat Heart *qi* and *yin* deficiency with Heat Disharmony of Heart and Kidney	The same as Test-2 period
HPA Stress Response	Resisted or maladapted	Exhausted	Exhausted
AFS Stages	Stressed stage	Fatigued stage	Fatigued stage

*AFS-adrenal fatigue syndrome; CMS-Chinese medicine syndrome; HPA-hypothalamus-pituitary-adrenal axis

Test-2 Period

The patient was 57 years old when the test-2 was performed. Her insomnia symptoms changed from difficulty falling asleep to difficulty staying asleep and waking up too early in the morning, with inability to fall back asleep. Her symptoms also included fatigue, lethargy, brain fog, poor memory, anxiety, frequent heart palpitations, cold hands and feet, cold body overall, and sweating and agitation, especially before meals. At night she would often wake up hungry, with heart palpitations and night sweats. Her allergy and sensitivities persisted.

Menstruation stopped four years prior to her second test. She continued to suffer from low libido and vaginal dryness and she occasionally felt warm at night. She craved salt and sugar and had frequent urination with clear urine and increased urine volume. Her blood work showed elevated thyroid peroxidase antibodies with normal free T3/T4 and TSH levels. Her tongue looked dark, pale, and purplish, with watery white coating. Her pulse was deep, thin, and weak.

Chinese medicine pattern differentiation of the patient at the time of the second test had shifted from Kidney *yin* deficiency to Kidney *yang* deficiency as evidenced by the presence of cold hands and feet, feeling of cold, and frequent clear urination. Meanwhile, she also showed symptoms of heart palpitation and anxiousness during the day as well as waking up at night with heart palpitation and difficulty in falling back asleep again. These are signs of Heart *qi* and *yin* deficiency with Heat and disharmony of Heart and Kidney, respectively.

The second FSCT showed a depressed production of cortisol level, with a cortisol rhythm as nearly a flat line. All four time points except the one at midnight were below normal range and overall cortisol production was much lower than normal range as well (Table 1b and Figure 1).

Treatment

The treatment principle for this patient was to tonify Kidney *yang* with Chinese herbs and to support adrenal function with nutritional supplementation. All Chinese herbal formulae were from the *Guang Ci Tang*, and nutritional supplements were from Apex Energetics, except for Probiotic Pearls (Enzymatic Therapy). She was prescribed *Shi Quan Da Bu Wan* (TotalTonic) for tonifying *qi*, blood, *yin* and *yang*, and *An Shen Bu Xin Wan* (SpiritCalm) for supporting Heart *yin* and clearing Heat. Both herbal formula were taken five pills twice a day. She was also prescribed nutritional supplement Adreno-Zyme one pill in the morning to support adrenal function and Glysen one pill at bedtime to stabilize blood glucose. The ingredients of the herbal formula are listed in Table 3.

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Table 3. Ingredients of Chinese Herbal Formula

Name	Ingredients
An Shen Bu Xin Wan (SpiritCalm)	Dan Shen (Radix Salviae Miltiorrhizae), Wu Wei Zi (Fructus Schisandrae Chinensis), Shi Chang Pu (Rhizoma Acori Tatarinowii), Zhen Zhu Mu (Concha Margaritifera Usta), Shou Wu Teng (Caulis Polygoni Multiflori), He Huan Pi (Cortex Albiziae), Tu Si Zi (Semen Cuscutae Chinensis), Mo Han Lian Herba Ecliptae Prostratae), Nu Zhen Zi (Fructus Ligustri Lucidi), and Sheng Di Huang (Radix Rehmanniae Glutinosae)
Shi Quan Da Bu Wan (TotalTonic)	Dang Shen (Radix Codonopsis Pilosulae), Bai Zhu (Rhizoma Atractylodis Macrocephalae), Fu Ling (Sclerotium Poriae Cocos), Gan Cao (Radix Glycyrrhizae Uralensis), Dang Gui (Radix Angelicae Sinensis), Bai Shao (Radix Paeoniae Lactiflorae), Chuan Xiong (Rhizoma Ligustici Chuanxiong), Shu Di Huang (Radx Rehmanniae Preparata), Huang Qi (Radix Astragali Membranacei), and Rou Gui (Cortex Cinnamomi Cassiae)
Gui Pi Wan (SpleenVive)	Dang Shen (Radix Codonopsis Pilosulae), Bai Zhu (Rhizoma Atractylodis Macrocephalae), Huang Qi (Radix Astragali Membranacei), Gan Cao (Radix Glycyrrhizae Uralensis, Fu Ling (Sclerotium Poriae Cocos), Yuan Zhi (Radix Polygalae Tenuifoliae), Suan Zao Ren (Semen Ziziphi Spinosae), Long Yan Rou (Arillus Euphoriae Longanae), Dang Gui (Radix Angelicae Sinensis), Tu Mu Xiang (Radix Inulae, Da Zao (Fructus Jujubae), and Sheng Jiang (Rhizoma Zingiberis Officinalis Recens)
Te Xiao Zao Ren An Mian Wan (Sleepeace)	Suan Zao Ren (Semen Ziziphi Spinasae), Yuan Zhi (Radix Polygalae Tenuifoliae), Shou Wu Teng (Caulis Polygoni Multiflori), Dan Shen (Radix Salviae Miltiorrhizae), Wu Wei Zi (Fructus Schisandrae Chinensis), Zhi Mu (Rhizoma Anemarrhenae Asphodeloidis), Bai Zi Ren (Semen Biotae Orientalis), Hu Po (Succinum), and Gou Teng (Ramulus Uncariae Cum Uncis)

Source: http://www.activeherbwholesale.com/GCT.html

The patient came back for re-evaluation once a month. Her symptoms, tongue, and pulse were checked. After two months of treatment, her Chinese herbal formula was changed from the earlier combination to *Gui Pi Wan* (SpleenVive) supporting Heart and Spleen *qi* and *Te Xiao Zan Ren An Mian Wan* (Sleepeace) tonifying Blood. The two herbal combinations were alternated every two months to prevent sensitivity reactions.

Her nutritional supplements were also changed from the earlier combination to Proglyco-SP and StressZyme to support adrenal function and reduce stress to improve sleep, respectively. The two nutritional supplements were also alternated every two months for the same purpose.

After six months of therapy, her fatigue, sleeping, and anxiety symptoms were improved, although her pulse and tongue did not show significant change. She then started receiving intestinal cleansing therapy using Myco-Zyme and liver support using Metacrine-DX periodically. Both supplements were taken one pill a day to address Spleen Dampness and Heat and Liver stagnation. Probiotic Pearls were also used to supply healthy bacteria in the gut. The three supplements were given in addition to the above treatment. The whole treatment lasted for about a year until a third FSCT was done.

Result and Test-3 Period

About one year after the above treatment started, the patient's overall condition showed improvement, with better sleep and more energy during the day. She reported that half the time she slept through the night and felt more rested in the morning. Her cold hands and feet were warmer, and she was no longer feeling cold all the time. Her sensitivity and digestive issues were also improved significantly. Her skin breakouts were minimal.

Her anxiety symptoms still showed fluctuation, depending on the stress level in her life. She still craved salt and sugar and had frequent urination with clear urine and increased urine volume. Her tongue looked pale with slight red color and thin white coating. Her pulse was still deep, thin and weak. Chinese medicine pattern differentiation of the patient at this period of time remained the same as that of the Test-2 period.

The third FSCT, taken one year after the patient had been treated, still showed a depressed production of cortisol level but did indicate an improved cortisol rhythm—higher in the morning and lower in the night. All four time points except the one at midnight were still below normal range, and overall cortisol production was still lower than normal level. However, the cortisol circadian curve improved from the second test (Table 1c and Figure 1). This test still showed a profile of adrenal fatigue but some improvement compared to the second one.

Discussion

During the Test-1 period, the patient was experiencing much stress in her life. The cortisol diurnal rhythm and higher-than-normal total cortisol production indicated a maladapted or stressed HPA response. The lower-than-normal cortisol level at 4 pm was consistent with her symptoms of fatigue and sugar craving around that period of time, and the increase in cortisol level at midnight was likely the reason for her insomnia symptoms such as difficulty to fall asleep. This was a typical case of AFS stressed stage. The above symptoms of AFS stressed stage shows consistency with the pattern differentiation of Kidney *yin* deficiency with Heat. Thus, it is likely that the AFS stressed stage and Kidney *yin* deficiency with Heat describes the same functional condition for this patient.

In addition to insomnia, the patient had clear signs of parasympathetic suppression, such as dry skin, dry mouth, indigestion, and constipation. Her sensitivity-related symptoms were likely related to neuroimmune dysfunction due to autonomic and HPA stresses. She also showed perimenopausal symptoms including hot flashes, night sweats, low libido and vaginal dryness, which are a result of female hormone imbalance possibly caused disruption of the HPA axis.

Test-2 showed that cortisol diurnal rhythm and total cortisol production changed from a stressed profile to an exhausted one. The flat-line cortisol rhythm indicated a depressed and fatigued HPA function after nine years of chronic stress. Her insomnia symptoms were consistent with the FSCT. Overall low cortisol production helped her to fall asleep, but the low cortisol level caused her difficulty in staying asleep.

At the time of the second test, she had persistent menopausal symptoms. However, her body temperature changed from extremely hot to cold hands and feet and a general feeling of cold. This suggests that her estrogen and progesterone continued to drop to a lower level, while her thyroid function may have been affected by long-term cortisol suppression. Other symptoms, such as fatigue, lethargy, and brain fog support the diagnosis of functional hypothyroidism, although her lab test showed normal T3 and T4 levels.

The symptoms of anxiousness and heart palpitation can be a result of neurotransmitter imbalance, including epinephrine and norepinephrine. Meanwhile, hypoglycemia, often seen in AFS fatigue stage, may be a trigger for heart palpitation, sugar craving, and anxiousness. Aldosterone is a mineralocorticoid that is crucial for sodium conservation in the kidney, salivary glands, sweat glands, and colon.[29] Hypoaldosteronism due to adrenal insufficiency in AFS fatigue stage may result in loss of sodium and water, frequent urination, increased urine volume, dehydration, and salt craving.

The above symptoms of AFS fatigued stage, such as cold hands and feet and feeling of cold as well as frequent clear urination, are consistent with a pattern of Kidney *yang* deficiency. This suggests that AFS fatigued stage may describe a functional status similar to a Kidney *yang* deficiency pattern.

In the Test-3 period, the patient's symptoms and FSCT showed improvement. The sign of Kidney *yang* deficiency—cold hands and feet, and feeling of cold—was improved. Her tongue color changed from dark and purplish to pale with slight red color. The results showed clearly that the patient improved from both HPA function and Chinese medicine perspectives.

It is noteworthy that with long-term stress, HPA stressed response occurs prior to a fatigued response, as Kidney *yin* deficiency generally does precede the Kidney yang deficiency pattern.[30, 31] This case report suggests that cortisol as an objective biomarker may be helpful in informing the diagnosis of Kidney deficiency syndromes as well as improving consistency in Chinese medicine research. Further studies verifying a correlation of FSCT values with AFS are recommended, and if successful, other diseases with KDS patterns may be studied for a similar correlation.

Conclusion

This single case study suggests a notable relationship between cortisol levels as determined by FSCT testing and Chinese medicine Kidney deficiency syndromes. It appears that the AFS stressed stage and fatigued stage may be associated with Kidney *yin* and Kidney *yang* deficiency patterns, respectively. The study also suggests that in addition to traditional diagnostic method, FSCT may provide an objective biomarker for Chinese medicine clinicians and researchers to diagnose Kidney deficiency syndromes and improve clinical outcomes. To further assess the clinical applications of FSCT in Kidney deficiency syndrome diagnosis and treatment assessment, additional clinical studies are warranted.

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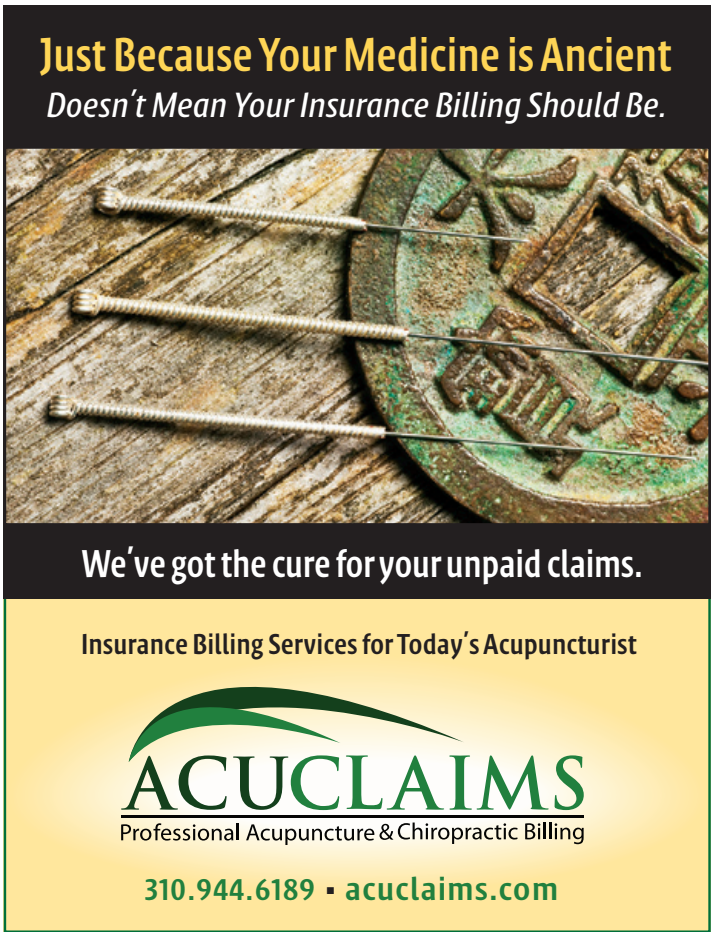

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