



Can Autoimmune Hepatitis Be Treated Without the Use of Corticosteroids and Immunosuppressive Drugs?

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Received: May 30, 2019; **Published:** June 27, 2019

Abstract

Introduction: Autoimmune Hepatitis (AIH) occurs when the Liver is attacked by immune cells that mistake it for foreign tissue or pathogen, causing inflammation [1]. The goal of the treatment is to slow or stop the immune system attack on the Liver [1,2]. Treatment with prednisone is generally used initially and a second medication, azathioprine may be recommended as well [2]. Prednisone, especially when taken in a long-term, can cause a wide range of serious side effects, including diabetes, thinning bones (osteoporosis), broken bones (osteonecrosis), high blood pressure, cataracts, glaucoma and weight gain [3]. Most people need to continue taking the prednisone for at least eighteen to twenty-four months, and many remain on it for life. Although the patient may experience remission a few years after starting treatment, the disease often returns if the drug is discontinued [1,2]. In Traditional Chinese Medicine (TCM), *Yin* deficiency plays a central role in autoimmune diseases [4].

Purpose: The purpose of this study is to demonstrate that autoimmune hepatitis can be treated without the use of corticosteroids or immunosuppressive drugs.

Methods: A case report of a female patient who had severe headache in the parietal region. "According to Traditional Chinese Medicine literature, this region corresponds to the Liver meridian. Auricular acupuncture with apex ear bloodletting sessions were started, as well as Chinese dietary counselling. Laboratory tests revealed low-prothrombin time and the presence of antinuclear antibody.

Results: After one month of treatment, the exams were repeated and the antinuclear antibody was negative.

Conclusion: The conclusion of this study is that Autoimmune Hepatitis can be treated without the use of corticosteroids and Immunosuppressive drugs according to the teachings of Traditional Chinese Medicine, reducing the side effects caused by these drugs.

Keywords: Autoimmune Disease; Corticosteroids; Immunosuppressive Drugs; Acupuncture; Traditional Chinese Medicine

Introduction

Autoimmune hepatitis (AIH) occurs when the liver is attacked by immune cells that mistake it for foreign tissue or pathogen, causing inflammation. Its alternative name is lupoid hepatitis [1].

Autoimmune hepatitis is classified as either type I or II, type I being the most common form. Type I commonly combines with other autoimmune disorders, such as type 1 diabetes, Proliferative Glomerulonephritis, Hashimoto's thyroiditis, Graves' disease,

Sjögren's syndrome, autoimmune anemia and ulcerative colitis. Type II of Autoimmune Hepatitis is less common, typically affecting girls aged 2 to 14, although adults can have it too [1].

The function of the immune system is to protect the body from viruses, bacteria and other living organisms. However, certain viral infections such as hepatitis B or toxins that change the antigenicity of the liver's cytomembrane may cause the immune system mistakenly to attack liver cells. In addition, a genetic factor may predispose some people to have AIH [5].

In the vast majority of patients, autoimmune hepatitis is marked by fluctuating levels of inflammation intensity, with relapses and remissions [5].

The diagnosis on Western medicine consists of laboratory blood tests, specific tests of liver enzymes, which may help to reveal a pattern typical of hepatitis. A liver biopsy may also generate a clear diagnosis [1-3].

Further tests for autoantibodies are needed to diagnose autoimmune hepatitis. In this disease, the immune system produces antinuclear antibodies, antibodies against smooth muscle cells or liver and kidney microsomes [4].

For more than three decades, corticosteroids, either alone or in combination with azathioprine, have been the mainstays of drug therapy for patients with autoimmune hepatitis.

Approximately 65% of patients respond to initial therapy and enter histological remission; however, 80% of these patients relapse after drug withdrawal [5]. According to Traditional Chinese Medicine (TCM), in the treatment of a disease, the therapeutic principles are based on the concept of holism. The concept of holism refers to unity and integration. Traditional Chinese Medicine, Hippocratic Medicine and other ancient traditions comprehend the human body as an organic unity in which the component parts are inseparable in structure. The body would be influenced by external environment and internal alterations (emotions and diet).

Different analysis in TCM literature demonstrated that the material structure of the Liver belongs to *Yin* and its function belongs to *Yang*. A subject can acquire *Yin* deficiency due to a genetic inheritance from their parents, an improper diet, after an illness treated by a medication that damaged Liver *Yin*, or even if the patient is in suffering from chronic emotional distress.

The concepts of *Yin* and *Yang* were previously exposed in previous articles of the author. Regarding the Liver meridian, an imbalance of the *Yin* and *Yang* energies leading to *Yin* deficiency can cause different Liver pathologies, including autoimmune hepatitis. The principle of treatment according to Traditional Chinese Medicine is to eliminate pathogenic Heat from the Blood, remove Blood stasis, and nourish Liver and Kidney *Yin* [6].

Purpose

The purpose of this study is to demonstrate that it is possible to treat Autoimmune Hepatitis without using corticosteroids or im-

munosuppressant's drugs. In addition, it is also a goal to present a deeper comprehension of how energy alterations may lead to varied pathologies.

Methods

The methods used consisted in a revision of literature regarding the treatment of autoimmune hepatitis both in Western and ancient medicines, as well as a report of a clinical case of a 58-year-old woman with a history of severe headaches, which did not improve with any type of medication.

Case Report 1:

The patient was a 58-year-old woman, with headaches in the parietal region for around 10 days. The pain was so intense that it would prevent her from leaving her bed in the morning. The patient sought an infectious disease specialist with background in ancient medical traditions.

The doctor required laboratory tests to investigate if there was an organic cause affecting the Liver meridian. According to Traditional Chinese Medicine, the area of the headache represented an imbalance of the energy meridian of the Liver.

In the same appointment, the patient began twice week's sessions of auricular acupuncture, associated with apex ear bloodletting. Chinese dietary therapy was also indicated, with the avoidance of dairy products, frying, eggs, chocolate, honey, coconut and alcohol, soda and mate tea.

The patient's laboratory tests revealed only 70% prothrombin time and serum glutamic-oxaloacetic and glutamic-pyruvic transaminases tests were normal. Serological markers for hepatitis B and C were negative. As the prothrombin time was below normal, other tests were ordered to investigate a possible autoimmune disease.

The exams revealed 1: 320 antinuclear antibody. Other antibodies, such as anti-smooth muscle and anti-microsomal antibodies were negative.

Results

After a month of treatment with auricular acupuncture, apex ear bloodletting and Chinese dietary therapy, new exams were required to evaluate the presence of these antibodies, and the result was negative.

Discussion

The immune system and autoimmune disease

In a healthy immune system, the body will attack foreign pathogens directly with white blood cells to remove them or create protein antibodies to neutralize or remove them from the body. This is done by a series of internal actions when injury or pathogens disrupt the normal flow of the body [2,5].

It is responsibility of a healthy immune system to create inflammation in order to heal a damaged tissue. Cortisol's function is to regulate the inflammation response by its anti-inflammatory abilities. It will be released constantly into the body, suppressing the inflammation in order to heal. When the immune system is repressed, the body is more susceptible to acquire diseases [2].

In the case of autoimmune disease, the body will create dysfunctional antibodies, called autoantibodies, which lose the ability to differentiate between foreign pathogens and healthy cells of the body; leading to a cascade of the body attacking its own healthy cells [2,5].

Autoimmune hepatitis in western medicine

The immune system usually protects the body from infection by identifying and destroying bacteria, viruses, and other potentially harmful foreign substances. Autoimmune hepatitis is a chronic disease in which the body's immune system attacks normal components or cells of the liver, causing inflammation and liver damage [2].

Autoimmune hepatitis affects the hepato-biliary system and is part of a broad clinical spectrum. It is important to have a clear diagnosis of autoimmune liver disease and to have interpreted the laboratory testing in order to identify the predominance of the active liver injury [5].

Autoimmune hepatitis is a serious condition that may worsen over time if not treated. A combination of autoimmunity, environmental triggers, and a genetic predisposition can lead to autoimmune hepatitis. The disease is more common in females and can occur at any age and affects all ethnic groups. Autoimmune hepatitis can lead to cirrhosis and liver failure. Cirrhosis occurs when scar tissue replaces healthy liver tissue and blocks the normal flow of blood through the liver. Liver failure occurs when the liver stops working properly [2].

The common symptoms of autoimmune hepatitis are fatigue, joint pain, nausea, loss of appetite, pain or discomfort on the liver, skin rashes, dark yellow urine, light-colored stools, jaundice, yellowing of the skin and eyes. Symptoms of autoimmune hepatitis range from mild to severe.

Some patients may feel as if they have a mild case of the flu. Others may have no symptoms when a health care provider diagnoses the disease; however, they can develop symptoms later [8].

Treatment for autoimmune hepatitis includes medication to suppress, or slow down the overactive immune system.

The primary goal of treatment is the complete resolution of symptoms and biochemistry, and the prevention of hepatocellular damage. Furthermore, as AIH is a chronic disorder, the secondary goal is preventing the progression of fibrosis leading to cirrhosis [3].

The standard treatment is done with corticosteroids and immunosuppressive drugs.

Corticosteroids

Corticosteroids are medications that decrease swelling and reduce the activity of the immune system. Health care providers treat both types of autoimmune hepatitis with a daily dose of a corticosteroid called prednisone [7]. When this treatment fails, other options may include a liver transplant [7].

However, the use of corticosteroids can have significant side effects, and alternative treatments are constantly sought for patients, particularly for long-term disease control [3].

International guidelines recommend a dose of prednisone of 1 mg/kg/day, up to a maximum of 60 mg/day, when used as the sole agent [10]. This dose is lowered to a maximum of 30 mg/day when used concurrently with azathioprine [3].

Immunosuppressive drugs

A research focusing on azathioprine demonstrated its use as an effective steroid sparing agent for maintenance of disease remission and it is the most widely used agent for this purpose today [3].

According to Cropley and Whiteman, prednisone should be used concurrently with azathioprine for induction of remission in AIH. Azathioprine is used at 1 mg/kg/day and is changed depending on disease response [3].

Which patients with autoimmune hepatitis require therapy?

Treatment for patients with autoimmune hepatitis is justified in all subjects with evidence of active disease, whether clinical, histological or serological, and especially in those with advanced liver disease [3].

The treatment should be offered for such patients because of the clear survival benefit and patient outcome with appropriate immunosuppressive therapy, with 10-year survival rates exceeding 80%. Patients with moderate-severe autoimmune hepatitis have 10-year survival rates exceeding 80%. Without the treatment these patients have a very poor prognosis, with a 5 year survival of 50% and 10-year survival of 10% [8].

According to Palack, one complication of autoimmune hepatitis is cirrhotic disease. Up to 30% of adults with autoimmune diseases may have cirrhotic disease at diagnosis. Cirrhosis develops in around 12% of these patients after 10 years despite immunosuppression, in 49% if there are persistent mild-moderate laboratory abnormalities and in 82% when bridging necrosis or multi-lobular necrosis are present [8].

In the same study, Palack exposes that according to Western medicine, for asymptomatic patients with autoimmune mild hepatitis, the treatment is not well established. This group have a 10-year survival rate, as high as 80%. Comparing them with the group of untreated patients with autoimmune mild hepatitis, the 10-year survival rate was significantly lower, when comparing with patients with severe disease that received treatment (67% versus 98%) [8].

Some patients with mild autoimmune hepatitis might do well without immunosuppression. Although the prognosis is not uniformly benign, spontaneous recovery may occur. It is also common for patients which are asymptomatic to become symptomatic. According to Palack, "between 26% and 70% of asymptomatic patients may develop symptoms during follow up" [8]. Treatment might not be indicated in patients with inactive cirrhosis, pre-existent comorbid conditions, or drug intolerances. On the other hand, patients with a histologic diagnosis of cirrhosis may respond well to therapy and should receive treatment in an attempt to slow the disease progression [2].

Treatment might also not be appropriate for patients with decompensated liver disease. Such individuals might be better served by a liver transplant [2].

For patients with autoimmune hepatitis the treatment must be individualized. This individualization is done based on common clinical questions, regarding the highness of the prednisone dose on the beginning of the therapy, the right timing for the addition of azathioprine, the right timing for a reduction in steroid dosing, the duration of the treatment beyond biochemical remission, and if a liver biopsy should be considered and performed in an attempt to withdrawal of immunosuppression and life-long low-dose maintenance therapy with azathioprine [2].

Autoimmune hepatitis affects the hepato-biliary system, and is part of a broad clinical spectrum with a variable and slow natural history. It is important to have a clear diagnosis of autoimmune liver disease and to have interpreted the laboratory testing in order to identify the predominance of the active liver injury [2-4,8].

A complete approach to the management of autoimmune liver diseases should also include adequate symptom control, early recognition of extra-hepatic manifestations and surveillance for complications.

Autoimmune hepatitis and ancient medical theories

Yin and Yang

In other articles of the author, the concepts of *Yin* and *Yang* were already broadly discussed [9-12]. Chinese medical treatment for autoimmune diseases is based on the theory of balancing the *Yin* and *Yang*.

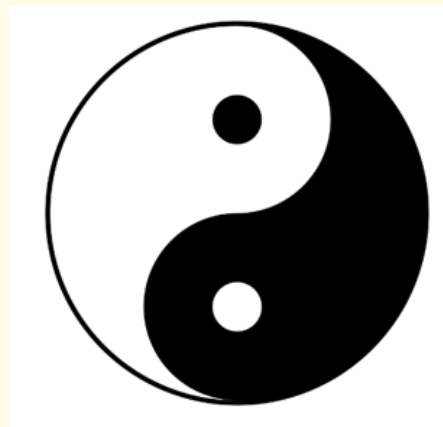


Figure 1: Yin-Yang.

The *Yin* and *Yang* theory is based on two basic components: *Yin* and *Yang* (Figure 4), which are neither materials nor energy [14,15]. They combine in a complementary manner and form a method for explaining relationships between objects. Gradually, this logic was developed into a system of thought that was applied to other areas. Traditional Chinese Medicine (TCM) is an example of one area where the *Yin-Yang* Theory is used to understand complicated relationships in the body [14,16].

The original concept of *Yin* and *Yang* came from the observation of nature and the environment. Later, this thinking was used in understanding other things, which occurred in pairs and had complementary and opposing characteristics in nature. Some examples include: sky and earth, day and night, water and fire, active and passive, male and female and so on. Working with these ideas, ancient people recognized nearly all things could have *Yin* and *Yang* properties [14,15].

Different researchers demonstrated the effectiveness of the use of *Yin* and *Yang* theories to develop diets based on Chinese Dietary concepts, as well as different treatments with Chinese herbs, systemic and auricular acupuncture [15,16].

Harmony is sought between *Yin* and *Yang* (Figure 4), and imbalances in these two energies are responsible for the formation of symptoms and diseases [9-12]. To maintain effective immunity, good health and normal physiological function, a person must have healthy reserves of *Yin*, which should be in harmony with *Yang*, as *Yin* and *Yang* are always in a state of dynamic flux [14,15].

Yin refers to formed substances, such as organs, tissues, cells and body fluids, which are visible and measurable things. *Yang* is the action potential, *Qi*, and heat in the body [14,15].

Yin and *Yang* in balance is a huge topic that involves all Chinese medical theory and treatment. *Yin* can be damaged by both excess and deficient Heat, as shown in figures 2 and 3.

The excess of *Yang* energy is linked to Heat in the energy meridians, which appears as symptoms such as irritability, thirst, dry throat, concentrated urine, constipation, red tongue with a yellow coat, and a full, rapid pulse.

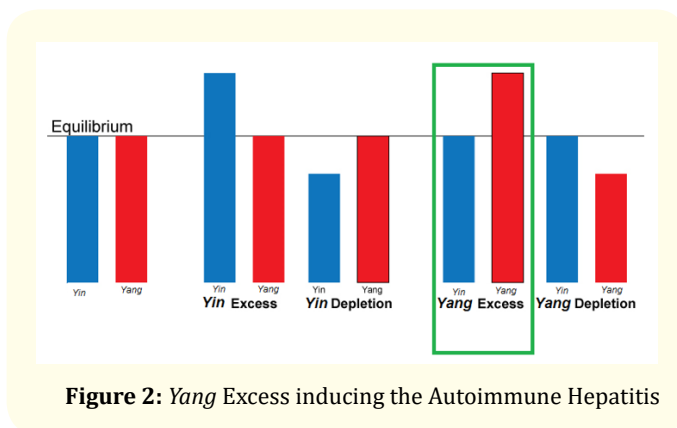


Figure 2: Yang Excess inducing the Autoimmune Hepatitis

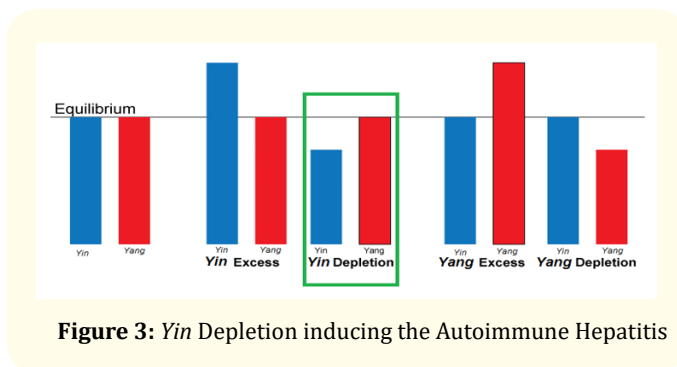


Figure 3: Yin Depletion inducing the Autoimmune Hepatitis

A deficiency in the *Yin* energy results on imbalance leading to excess of *Yang* energy. The general symptoms of *Yin* deficiency are red cheeks, night sweating, irritability, chronic inflammation, red tongue with no coat, and a thin, rapid pulse. *Yin* deficiency can also cause other physiological changes, leading to *Qi*, Blood and even *Yang* deficiency.

Figure 4 represents *Yin* Depletion. It may also be associated with age. A subject with *Yin* depletion will present symptoms as thinner skin and development of wrinkles, shorter stature, blurry vision, tinnitus and insomnia.

The Liver meridian and the Five Elements Theory

The Five Elements theory is another important cornerstone of Traditional Chinese Medicine, discussed and explored in other articles of the author. The theory proposes an interconnection between the energy meridians of the body, focused in five massive organs [17,18].

The Liver is one of these organs.

According to the theory, the Liver has as a hollow coupled organ, which is the gallbladder. The external sensory organ that it commands it is the eye and is responsible for the vision. It is very common for patients who have problems in the liver to have a headache in the parietal region (Figure 4). Other symptoms patients may experience bitter mouth, nausea and abdominal pain [17,18].

On the Figure 4, the headache is located at the top of the head, which corresponds to the imbalance of the Liver meridian [17,18].

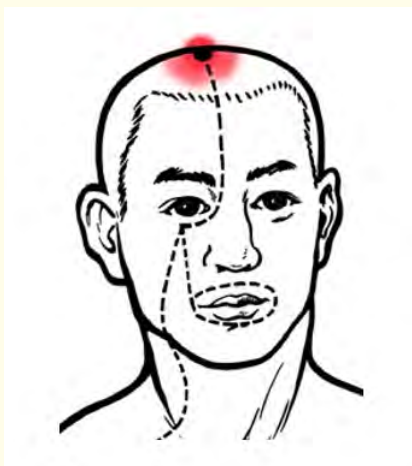


Figure 4: Headache location associated with Liver Meridian Disharmony.

When patients present headache due to energy imbalance of the Gallbladder meridian (Figure 5), the pain occurs on the temporal and supra-auricular region.



Figure 5: Headache location associated with the Gallbladder meridian.

The crucial point here is that the basic pathogenesis of many degenerative diseases is similar to the pathogenesis of autoimmune diseases. Therefore, it makes sense to apply theories related to the treatment of *Yin* deficiency for both autoimmune and degenerative diseases [17,18].

The general treatment principle in Traditional Chinese Medicine to treat autoimmune hepatitis is to eliminate pathogenic Heat from the Blood, remove Blood stasis, and nourish Liver and Kidney *Yin* [17-19].

One of the techniques used to remove the Heat from Blood is the use of apex ear bloodletting (Figure 6). Therapeutic bloodletting has been practiced at least 3000 years as one of the most frequent methods of treatment in general, whose value was not questioned until the 19th century, when it was gradually abandoned in Western medicine, while it is still practiced in Arabic and Traditional Chinese Medicine. It serves to remove excessive amount of blood as well as to remove toxic substances that accumulate in the human body [20].

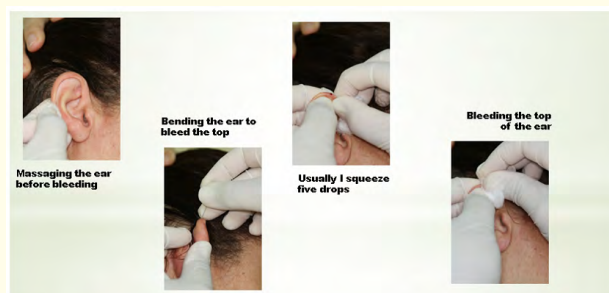


Figure 6: Apex Ear Bloodletting.

Liver *Yin* Deficiency

According to TCM, the patients with Liver *Yin* deficiency may present symptoms such as dry eyes, mouth and throat; Heat sensations in palms and soles; Dull intercostal pain; Nails are dry and without luster ; Impatience; Constipation with dry stools; Urine is dark and may be scanty; Low grade fever worse later in the day or evening; Restlessness; Insomnia (often after waking around 3am); Fatigue; Night sweats; Aversion to Heat; Shallow Breathing, dyspnea, sighing, taking deep breaths; Pain relieved by cool air or cool applications and pain also better for pressure or firm touch [17,18].

Febrile diseases may also lead to the impairment of Liver *Yin*. Sometimes, the Liver may not be moistened by Kidney water because of a deficiency of Kidney *Yin*. Deficiency of Liver *Yin* makes it impossible not only for the Liver to be nourished but also for *Yin*

to control *Yang*, so Fire flares up. At the same time, Fire can singe the Blood to cause Blood stasis, which blocks the Liver channel and prevent water flow and bile and blood transportation. The water, bile and blood exude from their regular pathways, causing edema, ascites, jaundice and bleeding [17,18].

It is important to emphasize that not all the patients with those symptoms have autoimmune hepatitis. The foods which can cause Fire in the Liver and Gallbladder, consequently causing Liver *Yin* deficiency are: fried foods, eggs, chocolate, honey, coconut, alcoholic beverages and dairy products as a whole, especially when the cheese is melted. The patient received indication to stop consuming these foods, as showed in the Case Report session [17,18].

Kidney *Yin* Deficiency

The signs and symptoms presented by the patient when he has Kidney *Yin* deficiency are afternoon or evening sweating; Dry mouth or throat; Thirst; Feeling of fever in afternoon or evening; Constant ringing in ears; Achy lower back and aching bones. When the doctor is aware of these symptoms, he can start to think about the possibility of autoimmune hepatitis as a diagnosis. However not all patients with these symptoms may have autoimmune hepa-

titis disease. Drinks that can cause Kidney *Yin* deficiency are: soda, coffee and mate tea [19].

Treatment of autoimmune hepatitis according to Traditional Chinese medicine

The studies in literature regarding Traditional Chinese Medicine demonstrated that autoimmune hepatitis is explained by *Yin* and *Yang* disturbances. Specifically, a deficiency of *Yin* affects cells negatively and may lead to tissue degeneration, apoptosis or programmed cell death [4].

On Traditional Chinese Medicine, all diseases treatments are based on the difference of pathogenesis of disease rather than the disease themselves. This is what is called treating the same syndrome with the same method and treating different syndromes with different methods [21].

Therefore, Traditional Chinese Medicine can treat different diseases and symptoms with similar prescriptions and methods. *Yin* deficiency is not unique to autoimmune diseases. Thus, the treatment of *Yin* deficiency should be the same regardless the disease [4].

	Liver <i>Yin</i> Deficiency	Extreme Heat Due To Liver and Kidney <i>Yin</i> Deficiency	<i>Yin</i> deficiency and Blood stasis
Treatment Principle	Nourish Liver <i>Yin</i> and regulate Blood flow.	Clear pathogenic Heat and remove Toxins, cool the Blood, and nourish Liver and Kidney <i>Yin</i> .	Nourish <i>Yin</i> , promote Blood circulation, remove Blood stasis and soften hepatosplenomegaly.
Herbal Treatment	YI GUAN JIAN	LONG DAN XIE GAN TANG	DA BU YIN WAN and HUA YU TANG
Acupuncture Points	BL-18 Ganshu, BL-17 Geshu, SP-6 Sanyinjiao, KI-3 Taixi and LIV-2 Xingjian.	BL-18 Ganshu, BL-19 Danshu, LI-11 Quchi, SP-10 Xuehai, LIV-2 Xingjian, KI-3 Taixi and SP-6 Sanyinjiao.	KI-3 Taixi, BL-23 Shenshu, BL-18 Ganshu, BL-17 Geshu, SP-10 Xuehai and KI-16 Huangshu

Table 1: Treatment of Autoimmune Hepatitis According to Traditional Chinese Medicine.

Western and Traditional Chinese Medicine Perspectives

The figure of the tree (Figure 7), places a good metaphor between the Western Medicine and the Traditional Chinese Medicine. This figure and this metaphor were previously exposed in other articles of the author. The use of a tree to create a metaphor for medicine use was also previously presented in books such as the I-Ching [9-12].

The part of the trunk, stem, and leaves are visible to the naked eye and represent the performance of Western Medicine currently, where each leaf of each stem represents each symptom of each specialty. The part of the tree that is below the earth, invisible to the naked eye, represents the root where in this drawing, represents the Five Elements Theory and *Yin* and *Yang* [9-12].

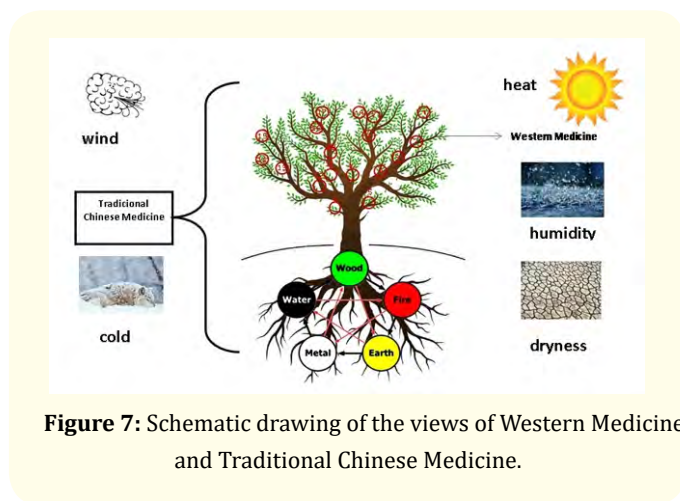


Figure 7: Schematic drawing of the views of Western Medicine and Traditional Chinese Medicine.

When treating autoimmune hepatitis with corticosteroids and other medications, the disease is comprehended in the leaf-level of the tree metaphor. When dealing with energy, the problem is being treated in the root-level, invisible to the naked eye [9-12].

In Traditional Chinese Medicine, diseases may be treated with the same method as a result of the occurrence of the same pathogenesis in their development.

The usual treatment of autoimmune hepatitis with the prescription of corticosteroids and azathioprine can lead to increased aggression toward the Liver energy, which can cause Liver Heat and decrease Liver *Yin* energy, thereby maintaining the energy imbalance that led to this autoimmune disease, according to Traditional Chinese Medicine [9-12].

Arndt Schultz’s law

According to the Arndt Schultz Law, substances vary in action depending on their concentration [13]. High concentrations kill; medium concentrations suppress or inhibit; and low, or minute concentrations stimulate [22,23].

Over a century ago Schultz’s experiments (1888) showed that many chemical agents had the effect of stimulating the growth and respiration of yeast. The phenomenon became known as the Arndt-Schultz Law and was widely referred to in the pharmacological literature for over 30 years and became one of the scientific principles [22,23].

According to Arndt-Schultz’s law, the use of medication in high concentrations decreases the vital energy and, in this way, causes

the formation of an Internal Heat, further unbalancing the energy condition that generated the pathology (Figure 8).

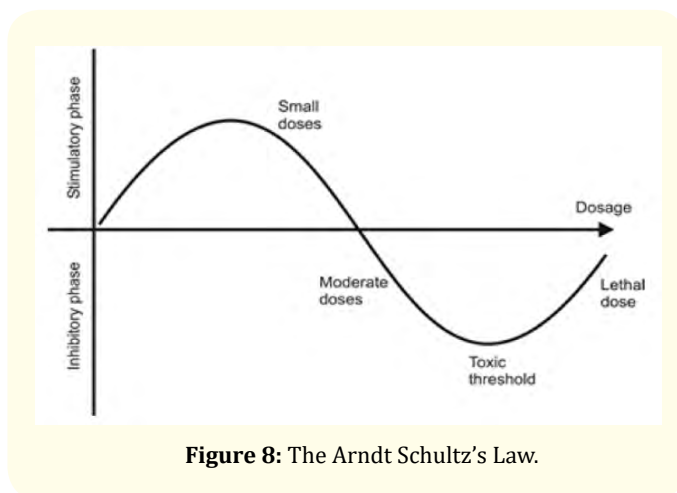


Figure 8: The Arndt-Schultz’s Law.

The Arndt-Schultz law was previously exposed in other articles of the author [9-12]. and in specific case of autoimmune hepatitis, the use of this theory can theorize a hypothesis of how the excessive use of corticosteroids and immunosuppressive drugs can influence the organism negatively.

Conclusion

The conclusion of this study is that there are other ways to treat autoimmune hepatitis, without using corticosteroids or immunosuppressive medications. Through the energy point of view of Traditional Chinese Medicine in which all autoimmune diseases are basically caused by *Yin* deficiency, all treatment is through dietary counselling, Chinese herbals, acupuncture sessions, all aiming to re-establish this basic imbalance, rebalancing *Yin* and *Yang* energy and consequently controlling autoimmune hepatitis.

The key for preventing and treating an autoimmune disease, in this case, autoimmune hepatitis, is keeping *Yin* and *Yang* balanced. Preventing invasion by the six external pathogens which are Wind, Cold, Heat, Dampness, Dryness and Fire, balancing *Yin* and *Yang*, vitalizing or removing Blood stasis, eliminating Phlegm and Dampness and clearing the Heat are the most important points of treatment, according to Traditional Chinese Medicine. More studies of this form of treatment should be realized in order to reaffirm the importance of the variety of treatments.

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Volume 3 Issue 7 July 2019

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