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Review

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Review**Diagnosis and treatment of novel coronavirus pneumonia based on the theory of traditional Chinese medicine**

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ABSTRACT

Since the outbreak of novel coronavirus pneumonia (coronavirus disease 2019, COVID-19) in December 2019, it has rapidly spread to 187 countries, causing serious harm to the health of people and a huge social burden. However, currently, drugs specifically approved for clinical use are not available, except for vaccines against COVID-19 that are being evaluated. Traditional Chinese medicine (TCM) is capable of performing syndrome differentiation and treatment according to the clinical manifestations of patients, and has a better ability of epidemic prevention and control. The authors comprehensively analyzed the etiology and pathogenesis of COVID-19 based on the theory of TCM, and discussed its syndrome differentiation, treatment and prevention measures so as to provide strategies and reference for the prevention and treatment with TCM.

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1. Introduction

Since December 2019, the novel coronavirus pneumonia (coronavirus disease 2019, COVID-19) outbreak in Wuhan, Hubei Province, China has rapidly spread across the world and has now infected a total of 348678 people in 187 countries (March 21, 2020) [1]. China has listed COVID-19 as a class B infectious disease and has undertaken preventive and control measures according to class A infectious diseases [2]. With the spread of the epidemic, presently, patients infected with the novel coronavirus, as well as those with asymptomatic infection, are the main sources of infection; thus, COVID-19 is an infectious disease with a medium to slightly high contagious capacity [3]. The incubation period of the disease is generally 7 days, and the longest is 14 days; however, some cases have reported an incubation period of 24 days as well [4]. Common clinical manifestations include fever, dry cough and fatigue. Computerized tomography of the chest can show multiple ground glass shadows of the pulmonary lobes, indicative of conditions such as respiratory distress syndrome, shock and sepsis, which can even lead to death [5]. Thus far, although China has announced six trials and strategies for the diagnosis and treatment of the disease, the focus remains mainly on symptomatic treatment, new drugs specifically approved for the infection are not available. Clinical trials for new drugs such as remdesivir and coolidge are underway; however, the clinical promotion and short-term use of these drugs is unlikely. Therefore, given the particularities of this disease, it is of critical clinical value to formulate a set of treatment plans using integrated traditional Chinese medicine (TCM) and Western medicine, based on the concept of prevention and treatment. To utilize the advantages of integrated traditional Chinese and Western medicine in the prevention and treatment of COVID-19, this paper discussed the

etiology and pathogenesis of COVID-19 from the viewpoint of integrated TCM and Western medicine, the treatment measures for different susceptible groups, and the effect along with matters needing attention, so as to provide a reference for the prevention and treatment of COVID-19.

2. Etiology

Coronavirus is a type of a ribonucleic acid virus with an envelope structure, characterized by rod-like protuberances on the surface and can infect multiple host species, causing a variety of diseases [6]. The COVID-19 pathogen is a novel coronavirus (2019-nCoV), which can infect humans and is significantly clustered with the bat-like severe acute respiratory syndrome coronavirus (SARS-CoV) sequence isolated in 2015, with a nucleotide similarity of 88%. Based on these results, it can be concluded that 2019-nCoV is similar to SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) [7]. It is a zoonotic pathogen that can cause severe respiratory diseases in humans and can be transmitted from person to person [8]. Therefore, the International Committee on Taxonomy of Viruses announced that the official classification of the novel coronavirus is SARS-CoV-2.

There is no virus theory in TCM, and according to the clinical characteristics of COVID-19, the disease belongs to the category of “plague” [9]. As the *General Treatise on the Etiology and Symptomology* says [10], “if a person feels grumpy and gets sick, he will be easily infected by evil Qi, which may even exterminate the family, and extend to outsiders.” The common symptoms in the early stage of COVID-19 in mildly infected patients include fever, fatigue and dry cough, which could be easily confused with other common exogenous diseases. However, according to Wu You-ke’s *The Treatise on Epidemic Febrile Diseases* [11], which mentions “the febrile disease is non-wind, non-cold, non-heat and non-damp; it is a different feeling between heaven and earth,” the cause of this disease is very clear, differing from the other six exotic evils, and presenting characteristics of a strong and contagious epidemic virus.

Wuhan, the center of the outbreak pathogen, is located in the east of Jiangnan Plain of China. The vertical and horizontal water areas of the city’s rivers account for one-fourth of the total city area, demonstrating the natural environmental basis of

“damp evil” [12]. At the initial stage of this epidemic, most patients presented symptoms of fever; however, there were also patients with no fever or low fever, and some patients presented gastrointestinal symptoms, such as indigestion and loose stool, as well as chest tightness and fatigue, coinciding with the characteristics of “damp evil” in TCM. Hence, this disease is an epidemic, with the primary nature of “damp” and “toxic,” and thus can be termed “damp toxin disease.” Furthermore, in 2019, Wuhan experienced a warm winter climate, with incoming heat instead of cold. From the perspective of TCM, this kind of climate change is prone to generate damp-heat in the human body, which persists and is difficult to eliminate from Sanjiao (one of the six fu-organs in TCM theory). Some patients have a recurrent fever, bitter mouth, insomnia, upset, chest tightness and shortness of breath, fatigue, yellow or greasy tongue coating, and slippery pulse, which are manifestations of the evil underlying Shaoyang meridian according to the six-meridian syndrome differentiation theory [13]. Notably, the most severe cases developed dyspnea one week later, which even progressed to acute respiratory distress syndrome, septic shock, intractable metabolic acidosis, and coagulation dysfunction, leading to death [14]. According to TCM, the toxins from these patients not only hurt the Qi but also injure the nutrient blood and result in blood stasis; the pericardium transmission channel is also reversed, resulting in mental changes. Dampness stagnates for a prolonged period and turns into heat; heat toxin accumulates for a long time, resulting in stasis; stasis and heat combine mutually and then generate syncope, which consumes Qi and Yin and leads to a deficiency. According to the principle of “three factors and measures,” there exist various etiological characteristics in different regions, as well as climatic factors. Fan et al. [15] observed and analyzed the TCM pathological characteristics of “dryness” in Hunan cases, and concluded that dryness and dampness are mainly due to “child disease to mother” in the course of the disease. In the theory of TCM, dryness evil can easily injure the lung. Lung and spleen belong to “gold” and “soil” in the five-element theory of TCM. Dryness turns into dampness. Dampness easily traps spleen. Wet soil is the mother of dryness “gold.” Furthermore, excessive lung dryness injures the spleen “soil”; hence, both lung dryness and spleen dampness are significant. In contrast, Yu et al. [16] summed up the data and concluded that the diseases in Guangdong Province and Gansu Province were caused by warm-heat toxin or epidemic toxin, which was closely related to their regional environment. Guangdong

Province is hot and humid all year round, and the epidemic Qi can easily mix with evils of damp and heat to attack the lung; however, the overall 2019 winter temperature in Gansu Province was higher than that experienced in previous years. Additionally, Gansu is located in the northwest region of China, which is mostly dry and warm, and susceptible to the evil of dryness that can cause lung disease. TCM runs through the whole idea of disease differentiation all the time, and the unified relationship between man and nature has been called “correspondence between man and nature” in ancient books, which presents considerable advantage in the treatment of COVID-19 in different populations and regions.

3. Pathogenesis

Compared with other diseases, the evil Qi of the “damp toxin epidemic” is relatively fixed, and hence, the etiology and pathogenesis are relatively fixed, with obvious stages of disease progression in clinical settings. Understanding the consistency of the stages also allows for clinical diagnosis and evidence-based treatment. After careful assessment of the four pieces of diagnostic evidence available regarding the confirmed cases, it was observed that this epidemic is mainly caused by a dampness pathogen, with the disease location of mainly Sangjiao, and the core pathogenesis is “dampness, heat, poison, blood stasis and deficiency,” which runs through the whole process of dampness and intoxication and closure of the lung. The *Treatise on Epidemic Febrile Diseases* [11] ascertains that typhoid fever does not infect people, but epidemic diseases can infect people. The evil of typhoid fever enters from the orifices, while the evil of epidemic disease enters only from the mouth and nose; it has been observed that during an epidemic, the evil comes from the mouth and nose, remains in the membrane, and unconsciously lurks in the human body [17].

COVID-19 is located in the lung, where evil Qi first invades the body from the mouth and nose, repressing the lung Qi. In turn, the lung fails to disperse and descend, with symptoms of dry cough. The “damp evil” is heavy and viscous, blocking the Qi mechanism and causing chest tightness, body heat, and muscle soreness. “Damp evil” traps the spleen, easily injuring Yang Qi. The spleen dominates and transports water and food through the body. When the Qi fails to rise, the spleen cannot be nourished, and symptoms begin to appear, including fatigue, gastric congestion and loose stool.

The spleen and stomach act as the exterior and interior of each other; hence, the spleen's dysfunction affects the stomach's absorption. The dampness accompanying the epidemic toxin into heat is manifested as high fever, occasional yellow phlegm, obvious asthma due to the dampness toxin, and sticky stool due to the stagnation of dampness. Wang Qingren stated in *Correcting Mistakes in Medicine* that "the plague toxin burns its blood inside, and if the blood is burned and refined, the blood will coagulate [18]." During this period, the heat toxin burns the body fluid, and dampness suppresses the Qi mechanism, resulting in the stasis of blood, manifested in the form of increased dyspnea and additional mental problems occurring during the reverse transmission of the pericardium. In the later stage, the body is damaged by fluid consumption, and is deficient in both Qi and Yin. During this period of treatment, attention should be paid to whether there is any residual evil in the body.

Given the differences in etiology and pathogenesis attributed to climatic factors in different regions, Fan et al. [19] observed and stated that owing to climatic factors, dryness has been present in the lung for a prolonged period. On encountering the epidemic toxin, dampness and cold will collide with each other, and obstruct the lung and chest, injuring vital Qi, leading to the stagnation of the Qi mechanism and abnormal rise and fall of evil Qi, finally leading to a deficiency of vital energy. Although there exist differing opinions, combined with the clinical manifestations of the published and confirmed cases, the main etiology and pathogenesis can be attributed to "dampness, heat, toxin, blood stasis and deficiency." Furthermore, the pathogenesis may differ among individuals. In the case of adults without underlying diseases, because of being in the prime of life, the presence of vital Qi, as well as the balance and coordination of movement and transformation of Qi, blood, Yin and Yang, is sufficient to resist external evil, demonstrating no susceptibility or mild susceptibility, with a short disease course and a good prognosis. In children, for the viscera are not well developed, presenting delicate viscera, unfilled shape and Qi, and immature Yin and Yang, they fall sick easily and quickly [20]. However, in the overall growing phase, they are made up of "pure Yang", are robust, and will recover easily. Patients with underlying diseases, such as diabetes, hypertension, heart disease, chronic tracheitis, tumors, or other diseases, usually suffer from a deficiency of vital Qi; if they experience the external evil, the disease is often characterized by severe illness, rapid progression, and rapid transmission, resulting in critical illness and even

death. Pregnant women have a special physiological state, with a relative deficiency of Yin-blood and relative hyperactivity of Yang Qi. The growth of the fetus blocks the rise and fall mechanism of the Qi in pregnant women, which may lead to poor operation of Qi and blood. Therefore, the elderly, the infirm, children and pregnant women require close monitoring.

4. Treatment

Currently, there are no drugs specifically approved for COVID-19. In the treatment plan announced by the National Health Commission of the People's Republic of China [21], Western medicine offers mainly symptomatic treatment support, including early oxygen therapy and the use of corticosteroids. The treatment plan comprises antiviral therapies, including interferon- α , lopinavir, ritonavir and ribavirin; however, the curative effect remains unsatisfactory.

Referring to the experience of TCM in the treatment of patients with SARS in 2003, Chinese medicine is now fully involved in the treatment of COVID-19 patients [21–39], utilizing the advantages of TCM syndrome differentiation and treatment, improving the cure rate, and reducing mortality (Table 1).

Table 1. Specific measures of syndrome differentiation and treatment by disease stages.

Stage	Symptoms and signs	Therapeutic principle	Prescription	Reference
Initial stage	Fever is the main symptom of the disease, with most hiding fever not accompanied by a cold. Other symptoms include sleepiness and discomfort, dry cough and less phlegm, thirst without the desire to drink, chest tightness and palpitation, occasional muscle aches, nasal congestion and runny nose, and loose stools. No sweat, no sthenic heat or irritable heat sensation, and no sore throat. The tongue is dark red, or its edge is red, the moss is thin and white, and the pulse has no fixed point.	Eliminating the filth with aromatics, promoting Qi mechanism, separating and dissipating damp-heat, removing blood stasis, and freeing the network vessels.	Modified Huopu Xialing Decoction and Sanren Decoction	[13,19,39]
Progressive stage	The main characteristics of the progressive stage include high fever, asthma and shortness of breath, difficulty in movement, aggravation of fatigue and tiredness, aggravation of cough, persistent dry cough or less phlegm, white or yellow, sticky cough, thirst without the desire to drink, cyanosis of lips and nails, or with delirium, increased palpitation, dizziness, indigestion, abdominal distention, loose stools or constipation, difficult urination, dark red tongue, greasy fur, and smooth pulse.	Eliminating dampness and dispersing the lung with aromatics, clearing Ying heat, cooling blood, and detoxifying.	Lei's aromatic turbid-resolving method and Jiedu Huoxue Decoction combined with Shengjiang Powder	[29,31–33,35,39]
Extreme stage	In the advanced stage, without proper treatment, the disease is further aggravated, with high fever, dyspnea, cyanosis of lips, dark complexion, extreme fatigue, restlessness, syncope, hot hands and feet or cold hands and feet, oliguria, dark red tongue, turbid or yellow greasy fur, and rapid and thinning pulse. It should be noted that some patients during this period may have a moderate or low fever or even no obvious fever.	Dispersing Qi of the lung, healing the body's essence Qi and blood, detoxifying, and rescuing the inverse.	Shenfu Sini Decoction, Angong Niu Huang Pill, Zhibao Dan, Zixue Dan, and Suhe Xiang Pill	[22–25,28,39]
Recovery stage	The recovery period is mainly characterized by high fever that has subsided, mental improvement, low fever, fatigue, poor appetite, sticky stool, and other symptoms. Computed tomography shows absorption or fibrosis. The disease pathogenesis demonstrates that the damp toxin is eliminated, but the residual evil is still present, with deficient lung and spleen Qi.	Clearing the residual evil, promoting lung circulation, activating spleen and strengthening healthy Qi.	Modified Xue's Wuye Lugen Decoction	[14,16,20,21]

4.1. Treatment of patients with the disease

Currently, according to published data, COVID-19 clinically manifests as different stages of disease progression. TCM treatment requires syndrome differentiation and treatment based on the stages, which are defined as initial stage (mild), progressive stage (severe), extreme stage (extremely severe) and recovery stage (convalescent stage). The medicines' sources, medicines' names in Latin and English are presented in Table 2.

Table 2. List of medicine's sources, and Chinese, Latin and English names.

Chinese name (pin yin)	Medicine source	Latin name	English name (common name)
Anxixiang	<i>Styrax tonkinensis</i> (Pierre) Craib ex Hart.	Benzoinum	Benzoin
Baishao	<i>Paeonia lactiflora</i> Pall.	Paeoniae Radix Alba	White peony root
Baizhu	<i>Atractylodes macrocephala</i> Koidz	Atractylodis Macrocephalae Rhizoma	Bighead atractylodes rhizome
Banxia	<i>Pinellia ternata</i> (Thunb.) Breit	Pinelliae Rhizoma	Pinellia ternata
Bibo	<i>Piperi longum</i> L.	Piperis Longi Fructus	Long pepper
Bohe	<i>Mentha haplocalyx</i> Briq.	Menthae Haplocalycis Herba	Wild mint herb
Cangzhu	<i>Atractylodes lancea</i> (Thunb.) DC.	Atractylodis Rhizoma	Rhizoma atractylodis
Chaihu	<i>Bupleurum Chinese</i> DC.	Bupleuri Radix	Chinese thorowax root
Chantui	<i>Cryptotympana pustulata</i> Fabriciu	Cicadae Periostracum	Cicada slough
Chenpi	<i>Citrus reticulata</i> Blanco	Citri Reticulatae Pericarpium	Tangerine peel
Chenxiang	<i>Aquilaria sinensis</i> (Lour.) Gilg.	Aquilariae Lignum Resinatum	Rosewood heart wood
Chishao	<i>Paeonia lactiflora</i> Pall.	Paeoniae Radix Rubra	Red peony root
Dafupi	<i>Areru catechu</i> L.	Arecae Pericarpium	Shell of areca nut
Dahuang	<i>Rheum palmatum</i> L.	Rhei Radix Et Rhizoma	Rhubarb root and rhizome
Daimao	<i>Eretmochelys imbricata</i>	Hawkbill Turtle	Hawkbill turtle
Danggui	<i>Angelica sinensis</i> (Oliv.) Diels	Angelicae Sinensis Radix	Chinese angelica
Danshen	<i>Salviae miltiorrhiza</i> Bge.	Salviae Miltiorrhizae Radix Et Rhizoma	Red sage root
Danzhuye	<i>Lophatherum gracile</i> Brongn.	Lophatheri Herba	Lophatherum gracile
Dazao	<i>Ziziphus jujuba</i> Mill.	Jujubae Fructus	Chinese date
Dingxiang	<i>Ewgewia caryophyllata</i> Thunb.	Caryophylli Flos	Clove
Doukou	<i>Amomum kravanh</i> Pierre ex Gagnep.	Amomi Fructus Rotundus	Round cardamom
Dongguazi	<i>Benincasa hispida</i> (Thunb.) Cogn.	Wax Gourd Seed	Seed of Chinese waxgourd
Fangfeng	<i>Saposhnikovia divaricate</i> (Turcz.) Schischk.	Saposhnikoviae Radix	Saposhnikovia divaricata
Fuling	<i>Poria cocos</i> (Schw.) Wolf	Poria	Poria mushroom filament
Fuzi	<i>Aconitum carmichaelii</i> Debx.	Aconiti Lateralis Radix Praeparaia	Monkshood
Gancao	<i>Glycyrrhiza uralensis</i> Fisch.	Glycyrrhizae Radix Et Rhizoma	Liquorice root
Ganjiang	<i>Zingiber officinale</i> Rose.	Zingiberis Rhizoma	Dried ginger
Gegen	<i>Pueraria lobata</i> (Willd.) Ohwi	Puerariae Lobatae Radix	Lobed kudzu vine root
Guanghuoxiang	<i>Pogostemon cablin</i> (Blanco.) Benth	Pogostemonis Herba	Cablin potchouli herb
Guizhi	<i>Cinnamomum cassia</i> Presl.	Pinnamomi Ramulus	Cassia twig
Hanshuishi	Limestone and marble	Calcite	Gypsum rubrum
Heye	<i>Nelumbo nucifera</i> Gaertn.	Nelumbinis Folium	Lotus leaf
Hezi	<i>Terminalia chebula</i> Retz.	Chebulae Fructus	Medicine terminalia
Honghua	<i>Carthamus tinctorius</i> L.	Carthami Flos	Safflower carthamus
Houpo	<i>Magnolia officinalis</i> Rehd. et Wils.	Magnoliae Officinalis Cortex	Bark of magnolia
Hupo	Fossil resin	Succinic	Amber
Huanglian	<i>Coptis chinensis</i> Franch.	Coptidis Rhizoma	Chinese goldthread

Huangqi	<i>Astragalus membranaceus</i> (Fisch.) Bge. var. <i>mongholicus</i> (Bge.) Hsiao	Astragali Radix	Milkvetch root
Huashi	Magnesian minerals	Talcum	Talc
Jiangcan	<i>Bombyx mori</i> Linnaeus.	Bombyx Batryticatus	Stiff silkworm
Jianghuang	<i>Curcuma Longa</i> L.	Curcumae Longae Rhizoma	Turmeric
Jinbo	Natural gold	Aurum	Gold foil
Jinyinhua	<i>Lonicera japonica</i> Thunb.	Lonicerae Japonicae Flos	Wild honeysuckle flower
Lianqiao	<i>Glechoma longitruha</i> (Nakai) Kupr.	Forsythiae Fructus	Weeping forsythia
Lingyangjiao	<i>Saiga tatarica</i> Linnaeu	Saigae Tataricae Cornu	Antelope horn
Longnao	<i>Cinnamomum camphora</i> (L.) Presl	Borneolum	Synthetic borneol
Lugen	<i>Phragmites communis</i> Trin.	Phragmitis Rhizoma	Reed root
Mangxiao	Glauber's salt of family sulfates	Natrii Sulfas	Mirabilite
Maidong	<i>Ophiopogon japonicus</i> (L.f) Ker-Gawl.	Ophiopogonis Radix	Dwarf lilyturf tuber
Mudanpi	<i>Paeonia suffruticosa</i> Andr.	Moutan Cortex	Tree peony bark
Muxiang	<i>Aucklandia lappa</i> Decne.	Aucklandiae Radix	Aucklandia lappa
Niuhuang	<i>Bos taurus domesticus</i> Gmelin	Calculus Bovis	Bezoar
Peilan	<i>Eupatorium fortunei</i> Turcz.	Eupatorii Herba	Eupatorium fortunei
Pipaye	<i>Eriobotrya japonica</i> (Thunb.) Lindl.	Eriobotryae Folium	Loquat leaf
Renshen	<i>Panax ginseng</i> C. A. Mey.	Ginseng Radix Et Rhizoma	Ginseng
Ruxiang	<i>Boswellia carterii</i> Birdw	Olibanum	Frankincense
Sangbaipi	<i>Morus alba</i> L.	Mori Cortex	White mulberry root-bark
Sangye	<i>Morus alba</i> L.	Mori Folium	Mulberry leaf
Sharen	<i>Amomum villosum</i> Lour.	Amomi Fructus	Villous amomum fruit
Shengdihuang	<i>Rehmannia glutinosa</i> Libosch.	Rehmanniae Radix	Rehmannia glutinosa
Shengjiang	<i>Zingiber officinale</i> Rosc.	Zingiber Rhizoma Recens	Ginger
Shengma	<i>Cimicifuga heracleifolia</i> Kom.	Cimicifugae Rhizoma	Large trifolious bugbane rhizome
Shexiang	<i>Moschus berezovskii</i> Flerov	Moschus	Forest musk abelmosk
Shigao	<i>Gypsum</i>	Gypsum Fibrosum	Gypsum
Shuiniujiao	<i>Bubalus bubalis</i> Linnaeu	Bubali Cornu	Buffalo horn
Suhexiang	<i>Liquidambar orientalis</i> Mill	Styrax	Storax
Tanxiang	<i>Santalum album</i> L.	Santali Albi Lignum	Sandalwood
Taoren	<i>Prunus persica</i> (L.) Barsch	Semen Persicae	Peach seed
Tongcao	<i>Tetrapanax papyrifer</i> (Hook.) K. Koch	Tetrapanacis Medulla	Rice paper plant pith
Wuweizi	<i>Acanthopanax gracilistylus</i> W. W. Smith	Schisandrae Chinensis Fructus	Chinese magnolcavine fruit
Xiangfu	<i>Cyperus rotundus</i> L.	Cyperis Rhizoma	Nutgrass galingale rhizome
Xiaoshi	Minerals in aragonite group and calcite group	Nitrum	Niter
Xingren	<i>Prunus armeniaca</i> L. var. <i>ansu</i> Maxim.	Armeniaca Semen Amarum.	Bitter apricot seed
Xionghuang	Arsenic sulfide mineral	Realgar	Red orpiment
Xuanshen	<i>Scrophularia ningpoensis</i> Hemsl.	Scrophulariae Radix	Figwort root
Yiyiren	<i>Coix lacryma-jobi</i> L. var. <i>mayuen</i> (Roman.) Stapf	Coicis Semen	Semen coicis
Yinbo	Native silver	Argentum	Silver foil
Yujin	<i>Curcuma wenyujin</i> Y. H. Chen et C. Ling	Curcumae Radix	Aromatic turmeric root tuber
Zexie	<i>Alisma orientale</i> (Sam.) Juzep.	Alismatis Rhizoma	Rhizoma alismatis
Zhenzhu	<i>Pteria martensii</i> (Dunker)	Margarita	Pearl
Zhiqiao	<i>Citrus aurantium</i> L.	Aurantii Fructus	Immature trifoliate orange fruit
Zhizi	<i>Gardenia jasminoides</i> Ellis	Gardeniae Fructus	Common gardenia fruit
Zhusha	<i>Cinnabaris</i>	Cinnabaris	Cinnabar

4.1.1. Initial stage

The damp toxin in the Shangjiao membrane should be treated for “damp-heat

clearance to cure the lung,” including separating and dissipating the damp-heat, paying critical attention to the smooth release of lung Qi. Furthermore, it is crucial to closely monitor the potential of the toxin to enter the blood in order to resolve the dampness, eliminate the filth, promote the Qi mechanism, resolve blood stasis, and relieve the blood vessel networks, thereby following the principles of the Huopu Xialing Decoction and Sanren Decoction [14]. The combination prescription includes Guanghuoxiang, Peilan, Banxia and Doukou for aromatizing, drying and regulating Qi; Xingren for promoting lung Qi; Fuling, Zexie, Huashi, Tongcao, Danzhuye and Yiyiren for relieving and removing dampness or allowing the removal of dampness; and Mudanpi and Chishao for resolving blood stasis. The combination of these herbs can smoothen the Sanjiao Qi mechanism, dissipate and dissolve the dampness, resolve blood stasis, and dredge collaterals.

4.1.2. Progressive stage

Toxins causing dampness can increase the heat in the body; this dampness and heat can lead to infection of the lung and negatively affect the functioning of the lung. Hence, the treatment methods include elimination of dampness, transportation of aromatics to the lung, removal of Ying heat and subsequent cooling of the blood, and detoxification. This treatment strategy utilizes Lei’s aromatic turbid-resolving method and the Jiedu Huoxue Decoction combined with Shengjiang Powder [29], in which Guanghuoxiang, Peilan and Banxia are fragrant and are used for removing dampness and invigorating the stomach and spleen; Chenpi is used for promoting Qi circulation; Dafupi and Houpo are combined to promote circulation and remove dampness; and Heye can reduce the heat produced in the body and turbidity in the lung. In the Jiedu Huoxue Decoction, Chaihu can dredge the liver and the Qi; Taoren and Honghua can improve blood flow and resolve blood stasis; Chishao, Shengdihuang and Danggui can reduce the heat in the body, thereby cooling the blood and improving its nutrient composition; Lianqiao and Gegen can reduce the heat in the body and enable body detoxification; Gancao can replenish the Qi to stimulate the spleen and be combined with other Chinese medicines, including Jiangcan and Chantui of Shengjiang Powder, to reduce the gas produced and dampness in the body, reduce the heat in the body, and detoxify; Jianghuang can disperse Qi and reduce blood stasis; and Dahuang can reduce heat by causing it to descend. These drugs are used in a combination to improve their effectiveness.

4.1.3. Extreme stage

During the progressive stage, if the disease is not properly treated, the heat and dampness cause the lung to close, with the possibility of internal closure and external prolapse appearing. It is necessary to discuss treatment from the point of Qi and Yin, and treatment should be based on dispersing the Qi of the lung and fixing the body's essence Qi, improving blood flow, enabling detoxification, and rescuing the inverse. Based on these principles, the Shenfu Sini Decoction and three treasures (Angong Niu Huang Pill, Zhibao Dan, and Zixue Dan) or the Suhe Xiang Pill can be utilized [22]. In the Shenfu Sini Decoction, Fuzi warms and strengthens the kidney Yang; Gancao is beneficial to the Qi; Ganjiang can warm the spleen and stomach to dispel cold, and help Yang to dredge the blood vessels; Suhexiang can promote Qi, remove phlegm, and open the orifices to awaken the mind; and Longnao can also awaken the mind. Anxixiang is capable of circulating the Qi and blood and removing the filth; Xiangfu is used to soothe the liver, regulate Qi, and relieve depression; Muxiang soothes Sanjiao; Tanxiang relieves Qi stagnancy in the stomach; Chenxiang can warm the middle energizer and descend Qi, and warm the kidney to control Qi; Ruxiang can improve blood circulation; Dingxiang and Bibo can warm the spleen and stomach, promoting Qi and reducing cold symptoms; Baizhu invigorates the spleen and transports dampness, and it can be used together with various aromatic herbs to remove dampness and turbidity of Sanjiao; Hezi is used to relieve pain, with its astringency preventing all kinds of heat from consuming Qi; Zhusha can enhance heart detoxification and calm the mind; and Shuiniujiao can purge fire and remove toxins. Lastly, Angong Niu Huang Pill or Zixue Dan can be utilized when the heat is removed, and the Suhe Xiang Pill when Yin is closed.

4.1.4. Convalescent stage

This period is dominated by asthenia, with many changes necessitating individual syndrome differentiation and treatment. Some studies have emphasized that Xue's Wuye Lugen Decoction can be used as reference to clear the residual evil and promote lung circulation, activate the spleen, and strengthen healthy Qi [14]. The five leaves in the formula float and bring the evil to the surface. Among them, Huoxiang leaf, Bohe, fresh lotus leaf and Peilan leaf are all fragrant and good at invigorating the spleen. Lugen and Dongguazi can be used for infiltration. The formula is light and nimble and can be used for dispersing, purging, and infiltration.

Additionally, it is necessary to pay attention to the following points. (1) Focus on removing dampness. The process of dampness removal is considered during diagnosis and treatment of the disease. Although the epidemic toxin is mainly characterized by toxic heat, dampness and turbidity, it is difficult to separate the heat and dampness characteristics from the initial stages of the infection to the end. It is also difficult to only get rid of heat without removal of dampness as well. Dampness is Yin evil, and it is unsuitable to use cold and cool drugs during the early stage; warm and tonic herbs in the later stage should also be used cautiously. Furthermore, it is permissible to use a combination of drugs to resolve dampness, dry dampness, and drain dampness during different stages. (2) Promoting blood circulation and resolving blood stasis. The patients should be treated with drugs for promoting blood circulation and resolving blood stasis immediately after the appearance of lung shadow. During COVID-19, the patients present high fever, sputum mixed with blood, dark purple-colored tongue, and consolidation or ground glass shadows in early lung images. Pathological reports indicated diffuse alveolar damage, hyperemia, hemorrhage, edema, and pulmonary interstitial inflammation, which are all manifestations of blood stasis. Therefore, during the different stages of treatment, it is necessary to combine products promoting blood circulation and eliminating blood stasis, dredging blood vessels, removing blood stasis, reducing alveolar damage, preventing pulmonary interstitial fibrosis, and reducing sequelae, which is conducive to the comprehensive rehabilitation of patients. Additionally, there are no specific Chinese medicine prescriptions for the elderly, pregnant women, children, and patients with underlying diseases. Hence, it is essential to study the signs and symptoms of COVID-19 cases to provide effective treatment.

4.2. Prevention of disease

TCM focuses on the idea of “prevention of disease,” advocating prevention before the disease occurs and prevention of change after disease. Therefore, those who have a history of exposure or have been in close contact with epidemic areas should be prioritized with the treatment principles, including stabilizing Qi and strengthening the exterior, removing heat, and detoxifying the body according to the composition of the prescription and climatic factors in different regions, to practice prevention before disease occurrence. In the cases of patients with chronic illness or those susceptible to infection, emphasis should be given to strengthening the vital energy, improving

immunity, and using Yupingfeng Powder to invigorate Qi and solidify the exterior [26]. Individuals with underlying diseases can be treated regionally according to their diseases. According to TCM, after conception, the whole body's Yin-blood is gathered in Chong Meridian, Ren Meridian, and the uterus, placing the pregnant women in a special physiological state of a relative deficiency of Yin-blood and relative hyperactivity of Yang Qi. The growing fetus will block the rise and fall of Qi and blood, resulting in poor operation of Qi and blood. "It should be cool before pregnancy and warm after birth" is the general principle of regulation and stabilization in TCM before and after pregnancy. This can be adjusted and treated in advance to prevent the occurrence of disease, and the method of nourishing Yin and clearing heat, regulating the Qi mechanism, and calming the fetus is adopted. Young children are not full of Qi; their Yin and Yang are immature, and their viscera are delicate, especially, the lung, spleen and kidney [26]. Hence, it is recommended to protect the Qi of the spleen and stomach in advance to nourish other organs, strengthen their physique, and resist the evil of epidemic disease, utilizing Sijunzi Decoction or Yupingfeng Powder to invigorate the Qi for consolidating superficies [26]. According to TCM, different people have different physical characteristics, and hence, different treatment principles and medication plans should be generated based on their physical characteristics (Table 3). Based on the existing treatment schemes, the prescription composition and dosage recommended for prevention and treatment of COVID-19 during different stages are introduced in Table 4.

Table 3. Specific prevention measures for different groups of people.

Crowd type	Features	Therapeutic principle	Prescription
Contacts	Close contacts or healthy people returning from the epidemic area	Invigorate Qi for consolidating the exterior of the body, remove heat, and detoxify.	Yupingfeng Powder
Children	Under 14 years of age	Invigorate Qi for consolidating superficials, and remove heat and detoxify.	Yupingfeng Powder or Sijunzi Decoction
People with underlying diseases	High blood sugar	Remove heat and promote fluid retention in the body, and enrich Yin and consolidate superficials.	Yupingfeng Powder
	High blood pressure	Remove heat and nourish Yin, and calm the liver and consolidate superficials.	Yupingfeng Powder
	Coronary heart disease and cardiocerebrovascular diseases	Remove heat, detoxify blood, and promote blood circulation to alleviate blood stasis.	Shengmai Drink
Women during pregnancy	Pregnant women	Nourish Yin and remove heat, regulate Qi flow for soothing the fetus, and strengthen healthy Qi for consolidating superficials.	Yupingfeng Powder
Normal adults	Uninfected adults	Regulate Ying and Wei, invigorate Qi for consolidating superficials, invigorate Qi and nourish Yin, strengthen healthy Qi, remove heat and detoxify, and resolve dampness and exterior symptoms.	Guizhi Decoction, Yupingfeng Powder, Shenzhu Powder, or Huangqi Guizhi Wuwu Decoction

Table 4. Composition and dosage of the prescriptions.

Stage	Prescription	Composition
Prevention	Yupingfeng Powder	Fangfeng 30 g, Huangqi 60 g, Baizhu 60 g
	Sijunzi Decoction	Renshen 9 g, Baizhu 9 g, Fuling 9 g, Gancao 6 g
	Shengmai Drink	Renshen 9 g, Maidong 9 g, Wuweizi 6 g, Danshen 6 g
	Guizhi Decoction	Guizhi 9 g, Shengjiang 9 g, Dazao 9 g, honey-fried Gancao 6 g
	Shenzhu Powder	Cangzhu 1000 g, Chenpi 1000 g, Houpo 1000 g, honey-fried Gancao 360 g, Guanghuoxiang 250 g, Sharen 120 g
	Huangqi Guizhi Wuwu Decoction	Huangqi 15 g, Guizhi 12 g, Baishao 12 g, Shengjiang 25 g, Dazao 4 g
Initial stage	Huopu Xialing Decoction and Sanren Decoction	Guanghuoxiang 6 g, Peilan 6 g, Banxia 9 g, Doukou 6g, Xingren 9g, Fuling 9 g, Zexie 6 g, Huashi 18 g, Tongcao 6 g, Danzhuye 6 g, Yiyiren 12 g, Mudanpi 6 g, Chishao 6 g
Progressive stage	Lei's aromatic turbid-resolving method	Guanghuoxiang 3 g, Peilan 3 g, Chenpi 6 g, Banxia 6 g, Dafupi 3 g, Houpo 3 g, Heye 9 g
	Jiedu Huoxue Decoction combined with Shengjiang Powder	Lianqiao 6 g, Gegen 6 g, Chaihu 9g, Danggui 6g, Shengdihuang 15g, Chishao 9g, Taoren 24g, Honghua 15 g, Zhiqiao 3 g, Gancao 6 g, Jiangcan (wine fried) 6 g, Chantui 3 g, Jianghuang 9 g, Dahuang (raw) 12 g
Extreme stage	Shenfu Sini Decoction	Honey-fried Gancao 12 g, Fuzi 10 g, Ganjiang 6 g, Renshen 15 g
	Angong Niuhuang Pill	Niuhuang 30 g, Yujin 30 g, Shuiniujiao 30 g, Huangqi 30 g, Huanglian 30 g, Xionghuang 30 g, Zhizi 30 g, Zhusha 30 g, Longnao 7.5 g, Shexiang 7.5 g, Zhenzhu 15 g
	Zhibao Dan	Shuiniujiao 30 g, Daimao (raw scute) 30 g, Hupo 30 g, Zhusha 30 g, Xionghuang 30 g, Niuhuang 0.3 g, Longnao 0.3 g, Shexiang 0.3 g, Anxixiang 4.5 g, Jinbo 50 layers, Yinbo 50 layers
	Zixue Dan	Shigao 1500 g, Hanshuishi 1500 g, Huashi 1500g, Shuiniujiao 500 g, Lingyangjiao crumbs 500 g, Muxiang 500 g, Chenxiang 500 g, Xuanshen 500 g, Shengma 500 g, Gancao 240 g, Mangxiao 5000 g, Xiaoshi 930 g, Shexiang 38 g, Zhusha 90 g, Jinbo 3000 g, Dingxiang 30 g
	Suhe Xiang Pill	Suhexiang 60 g, Baizhu 60 g, Muxiang 60 g, Shuiniujiao 60 g, Xiangfu 60 g, Zhusha 60 g, Hezi 60 g, Tanxiang 60 g, Anxixiang 60 g, Chenxiang 60 g, Shexiang 60 g, Dingxiang 60 g, Bibo 60 g, Longnao 60 g, Ruxiang 60 g
Recovery stage	Xue's Wuye Lugen Decoction	Huoxiang leaf 6 g, Bohe leaf 1.8 g, fresh lotus leaf 3 g, Pipaye 15 g, Peilan leaf 4.5 g, Lugen 30 g, Dongguazi 15 g

4.3. Evaluation of the curative effect

According to the description of discharge criteria in the *Diagnosis and Treatment Protocol for COVID-19 (Trial Version 7)* [40], the evaluation of COVID-19 should be based on body temperature (more than 3 days after returning to normal), obvious improvement of respiratory symptoms, and pulmonary imaging (obvious alleviation of inflammation). If the above symptoms and signs are relieved and the respiratory pathogen nucleic acid test is negative for two consecutive times (the sampling interval is at least 24 hours), patient can be considered to be cured.

However, we believe that the quantification of lung imaging related to the above efficacy evaluation index is insufficient. Hence, we suggest that the lung imaging of patients with COVID-19 should be comprehensively evaluated, based on the definition of the lung segment and the density criteria of high, medium and low grades, to better evaluate the treatment efficacy.

5. Prospect

The use of TCM adopts the holistic concept, combined with symptoms, signs and other corresponding manifestations, to examine the syndromes and seek the causes, to support the selection of drugs based on syndrome differentiation. Syndrome differentiation and treatment, as one of the characteristics and advantages of TCM, is very important in diagnosis and treatment. For example, in the treatment of COVID-19, the syndrome types differ among individuals in different regions, under different climatic conditions, and for relatively different physiques. Syndrome differentiation should be clearly defined in combination with different factors and clinical syndrome characteristics. Prescriptions are mainly used to improve immunity, balance human Qi, blood, Yin and Yang, and recover organ function. According to the study of COVID-19 treatment herbs [41,42], Chinese herbal medicines with a higher probability to directly inhibit SARS-CoV-2 have been selected, including Lianqiao, Gancào, Sangbaipi, Jinyinhua, Sangye, Pipaye, and other herbs, commonly used to treat viral pneumonia. Drugs should be selected and utilized according to the corresponding syndrome types. Furthermore, with disease development, the drugs should be given the flexibility to deal with different syndrome types, and the whole process should be adjusted according to the principle of “three factors and measures,”

undertaking multi-target treatment. TCM also plays a leading role during the recovery period and post-discharge convalescence. Currently, although some patients present a negative nucleic acid test accompanied by alleviated pneumonia and recovered body temperature, they may still demonstrate symptoms, including fatigue, shortness of breath, loss of appetite, and anxiety. Some patients may present pulmonary fibrosis due to poor absorption of pulmonary inflammation, which may affect the quality of life; additionally, some patients may suffer adverse reactions during drug therapy. It is crucial to resolve such related issues when TCM is involved. However, we do not advocate taking medicine without incident, and the preventive prescription is only a corresponding choice for people with an imbalance of Qi, blood, and Yin and Yang. When selecting the prescription, attention should be paid to the syndrome and symptoms, especially in special groups, such as children, pregnant women, and the elderly. Moreover, any special physique should be closely monitored when using medicines, and the improper use of interventions is not recommended; the overuse of cold or hot drugs should be avoided. Current research on Qingfei Paidu Decoction, a combination of prescriptions from the *Treatise on Febrile and Miscellaneous Diseases* written by Zhang Zhongjing in the Han Dynasty, has made progress in the special project documented by the National Administration of Traditional Chinese Medicine of China on screening effective prescriptions for the prevention and treatment of the novel coronavirus pneumonia [43]. As of February 5, four pilot provinces have used the Qingfei Paidu Decoction to treat 214 confirmed cases, with a treatment course of 3 days, demonstrating a total efficacy rate exceeding 90%, among which over 60% of the patients showed significant improvement in symptoms and imaging manifestations, and 30% patients demonstrated stabilized symptoms without aggravation. Concurrently, Lianhua Qingwen Granule [44] is used in clinical treatment based on the principle of clearing away epidemic toxin, dispersing the lung, and expelling heat. Reportedly, it has been confirmed to significantly improve fever, cough, expectoration, and shortness of breath in confirmed cases of COVID-19. According to the feedback of clinical data, the efficacy of TCM in the clinical treatment of COVID-19 is great, and it still needs to be adjusted and improved with the clinical accumulation. In brief, the combination of Chinese and Western medicine can complement each other's advantages, which can improve the comprehension of the core of the disease, and cooperate actively and effectively in clinical settings to

enhance overall efficacy.

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Authors' contributions

WSX and LYB wrote the article; WY revised part of the article and made grammatical corrections; WXX provided research ideas; LJY reviewed the article and provided guidance; NM and SYJ collated the data.

Conflicts of interest

The authors declare that they have no conflict of interest.

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