Interpretation of the Traditional Chinese Medicine portion of the diagnosis and treatment protocol for coronavirus disease 2019 (Trial Version 7)

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Traditional Chinese Medicine, based on the experience of a panel of experts, supported by evidence from fever clinics and from the outcomes of emergency (EM) observation rooms and inpatients throughout China (especially in Wuhan, Hubei Province) in combination with the latest scientific research results and data. The present interpretation of the TCM protocol is based on an overall understanding of the revised content, and aims to guide and standardize its clinical application to provide a reference for clinicians.

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Keywords: Medicine, Chinese traditional; Coronavirus disease 2019; Protocol interpretation

INTRODUCTION

Traditional Chinese Medicine (TCM) has a long history in the treatment of acute infectious diseases. Since the Western Han Dynasty more than 2000 years ago, 321 large-scale epidemics have occurred in China. The use of TCM has effectively prevented and controlled the spread of these epidemics in limited areas and spaces. In 2003, the World Health Organization (WHO) reported that 11 patients with severe acute respiratory syndrome (SARS) were cured by pure Chinese herbal decoction therapy, with no sequelae such as osteonecrosis of the femoral head during follow-up. Studies have shown that TCM prevents and treats disease by regulating the whole body, strengthening immunity, killing pathogens, eliminating pathological products, and restoring metabolism balance.

To contain the current coronavirus disease 2019 (COVID-19)
VID-19) epidemic, the Chinese government and society have taken strong measures, including comprehensive use of TCM. A series of Diagnosis and Treatment Protocols for COVID-19 was released by the National Health Commission and National Administration of TCM. A TCM treatment protocol was initially recommended in the third version of the Diagnosis and Treatment Protocol for COVID-19, while the fourth and fifth versions included adjustments and supplementations regarding disease staging, prevention, dosages, and Chinese patent medicines. In the sixth version of the Diagnosis and Treatment Protocol for COVID-19, the TCM disease staging, symptom patterns, and medicine recommendations were systematically revised. The TCM protocol contained in the Diagnosis and Treatment Protocol for COVID-19 (Trial Version 7) has been updated from previous versions. Under the direct leadership of the National Administration of TCM, this seventh version is based on the experiences of a panel of experts and is supported by evidence from fever clinics, emergency observation room and inpatient outcomes throughout China, especially in Wuhan, Hubei province, in combination with the latest scientific research data. To guide and standardize the clinical application of the TCM protocol included in the seventh version of the Diagnosis and Treatment Protocol for COVID-19, the present study presents an overall description of the revised content and an interpretation for its use in clinical practice.

OVERALL ANALYSIS OF THE TCM PROTOCOL

The TCM classification of COVID-19 is consistent with conventional medicine

TCM treatment divides the disease into periods of medical observation and clinical treatment (confirmed cases). During clinical treatment, cases are classified in TCM as mild, moderate, severe, and critical, which is consistent with conventional medicine. In addition, TCM recovery treatment is added for patients who satisfy the discharge criteria but still require quarantine and health monitoring, and discharged patients who have ended their quarantine period but still have symptoms such as lung function injury, pulmonary fibrosis, and asthenia. The updated TCM protocol is now consistent with the classification of conventional medicine, with stronger practicability and operability, which is conducive to the integration of the diagnosis and treatment philosophies of TCM and modern medicine.

TCM symptom patterns and recommended medicines

Based on accumulated experience in epidemic prevention and treatment, the TCM diagnosis and treatment protocols of various provinces and cities throughout China were analyzed and the treatment experience and prescriptions of many national TCM masters and doctors, including Prof. Zhou Zhongying and Prof. Xiong Jibai, were used to systematically update the section on TCM symptom patterns and drug recommendations. Lung cleansing and detoxifying is the key general prescription recommendation in clinical treatment, in accordance with the “The Research on screening the effective prescription for COVID-19” program. The TCM protocol in the seventh version of the Diagnosis and Treatment Protocol for COVID-19 includes additional detailed treatment methods and drugs for severe and critical cases of COVID-19; for example, the seventh version includes the TCM solution for desynchronization between the ventilator and patient. To provide further guidance to TCM doctors, the seventh version of the protocol contains all recommended doses of TCM prescriptions, which enables the frontline doctors to fully use the TCM protocol, and enables the combination of TCM and conventional medicine.

TCM prevention protocol in the medical observation period

Quarantine and self-isolation are effective measures with which to contain the spread of the COVID-19 epidemic. During the medical observation period, suspected cases of COVID-19 and those in self-isolation must stay at home; most of these patients have fever but no obvious respiratory symptoms. Chinese patent medicines are recommended for these patients.

Chinese patent medicines for severe and critical cases of COVID-19

With the sharp increase in the number of new patients with COVID-19, the use of a single TCM prescription restricts the treatment options of TCM clinicians and limits the clinical choices of conventional medicine doctors. Therefore, the recommendations for Chinese patent medicines are diversified in accordance with the pathogeneses of patients in different stages of the disease. For example, oral Chinese patent medicines are recommended for patients in the medical observation period, while TCM injections are recommended for severe and critical cases.

TCM PROTOCOL INTERPRETATION

The TCM protocol in the seventh version of the Diagnosis and Treatment Protocol for COVID-19 establishes the medical observation period and the clinical treatment period, which respectively correspond to the treatment of suspected cases of COVID-19 and home-isolated patients, and the treatment of confirmed cases. The protocol recommends TCM prescriptions and Chinese patent medicines for different symptom patterns. The following is a detailed interpretation of the disease patterns and prescriptions based on the disease stage and type. The italicized text is the original text of the Diagnosis and Treatment Protocol for COVID-19.
ID-19 (Trial Version 7), underlined text is not from
the TCM protocol of the Diagnosis and Treatment Pro-
tocol for COVID-19, and the text in normal font is the
interpretation of the TCM protocol.
In TCM, COVID-19 is classified as a plague with an
etiology of epidemic factor exposure. Different regions
should refer to the following plans for symptom pattern
identification and treatment in accordance with the
disease stage, local climate characteristics, and pa-

tient constitution. Prescriptions that exceed the maxi-
umum dose according to pharmacopoeia should only be
used under the guidance of a physician.

Yi means plague in Chinese, and is a general term used
to describe severe infectious diseases in TCM. Data
shows that COVID-19 is oral and nasal afferent and
highly contagious. Therefore, it is classified as Yi from
the TCM perspective. After visiting fever clinics and ex-
amining emergency patients and inpatients in Wuhan,
Prof. Tong Xiaolin (an academic from the Chinese
Academy of Sciences and leader of the expert group)
and Prof. Xue Boshu (a National TCM Master) decid-
ed that COVID-19 should be named Yi of cold-damp-
ness from the TCM perspective. Cold-dampness is a
qualitative analysis of COVID-19 from the perspective
of TCM etiology based on the following evidence.

First, the clinical manifestations of patients with COV-
ID-19 often show the clinical characteristics of cold
and dampness. Second, Wuhan had a cold and humid
climate during the COVID-19 outbreak, with a report-
ed mean temperature of 5-11 °C and relative humidity
of 47%-79%. Various infected areas had a similar aver-
age temperature, humidity, and latitude. In addition,
the outbreak point occurred at the time of the lowest
annual temperature. Overall, this evidence suggests
that a cold and damp environment is an important
contributing factor to the COVID-19 outbreak. How-
ever, although the disease is developed by cold and
dampness, the course of the disease will change because
of the influence of different regional climates and pa-
tient physiques. The following protocol for the TCM
treatment based on symptom pattern identification
should be adopted in accordance with the actual clini-
cal situation.

**TCM prescriptions in the medical observation period**

This period is mainly aimed at the treatment of sus-
pected cases of COVID-19. The diagnostic criteria for
suspected cases are any of the following epidemiologi-
ical history factors plus any two clinical manifestations,
or all three clinical manifestations if there is no clear ep-

demiological history.

Epidemiological history: (a) history of travel to or resi-
dence in Wuhan and its surrounding areas, or in other
communities where cases have been reported, within
14 d prior to the onset of the disease. (b) Contact with patients
with positive RT-PCR test results for SARS coronavirus 2 (SARS-CoV-2) within 14 d prior to the
onset of the disease. (c) Contact with patients who
have fever or respiratory symptoms and are from Wu-
han and its surrounding areas, or from communities
where confirmed cases have been reported, within 14 d before the onset of the disease. (d) Clustered cases (two
or more patients with fever and/or respiratory symp-
toms within a small area/group such as families, offic-
es, or schools within 2 weeks).

Clinical manifestations: (a) fever and/or respiratory
symptoms; (b) imaging findings characteristics of CO-
VID-19 (thoracic imaging shows multiple small patchy
pulmonary shadows and interstitial changes in the ear-
y stage, especially in the extrapulmonary bands, which
devlops into multiple ground-glass opacities and infiltr-
ates bilaterally; severe cases may have pulmonary con-
solidation, but pleural effusion is rare). (c) Normal or
decreased WBC count and lymphocyte count.

Clinical manifestations: fatigue with gastrointestinal
discomfort.

Recommended Chinese patent medicine: Huoxiang
Zhengqi capsule (pill, liquid, or oral liquid).

Clinical manifestations: fatigue with fever.

Recommended Chinese patent medicines: Jinhua Qin-
ggan granule, Lianhua Qingwen capsule (granule),
Shufeng Jiedu capsule (granule).

Interpretation: Huoxiang Zhengqi capsule (pill, tinc-
ture, oral liquid) should be administered to suspected
cases and home-isolated patients with fatigue and gas-
trointestinal discomfort that have chest oppression, ab-
dominal distension, nausea, vomiting, diarrhea, and
other symptoms.

Huoxiang Zhengqi capsule (pill, tincture, oral liquid)
is derived from Huoxiang Zhengqi San. The original
formula comes from the clinical TCM book called
"Formulas from the Imperial Pharmacy" (Tai Ping Hui
Min He Ji Fu Fang). Modern pharmacological research
shows that the medicinal effect of Huoxiang Zhengqi
capsule is to regulate gastrointestinal function, and to
enhance immunity and anti-inflammatory effects. 8-12

For suspected cases and home-isolated patients with fati-
tigue and fever, the recommended TCM prescriptions
are Jinhua Qinggan granule, Lianhua Qingwen cap-
sule (granule), and Shufeng Jiedu capsule (granule).

Jinhua Qinggan granule was developed during the A/
H1N1 influenza outbreak. Pharmacological and clinical
studies have shown that Jinhua Qinggan granule has
antipyretic and antiviral effects, and is effective in
treating influenza characterized by wind-heat invading the
lung. 11-13 Jinhua Qinggan granule is recommended
for patients with COVID-19 with slight fever, mild or
no aversion to cold, a red and sore throat, nasal conges-
tion, rhinorrhea, thirst, and cough or cough with sput-
tum. The formula of Lianhua Qingwen capsule (granule) is
derived from Ma Xing Shi Gan decoction and Yin
Qiao San. Lianhua Qingwen capsule has a broad-spect-
rum antiviral, antipyretic, and anti-inflammatory ef-
fet, and is clinically used for a variety of viral influen-
zia and respiratory infections. 14-17 Clinical studies show
that combined application of Lianhua Qingwen capsule for the treatment of COVID-19 increased the effective rate of the main symptoms by 17.7% compared with the control group, and reduced the probability of exacerbation during treatment by 13.8%.13

Shufeng Jiedu capsule (granule) is derived from Qudu San, which helps clear heat, resolve toxins, sooth the liver, and resolve constraint. Pharmacological studies indicate that Shufeng Jiedu capsule has antiviral, anti-inflammatory, antipyretic, and immunoregulatory effects, and is clinically used for acute upper respiratory infection with fever, such as community-acquired pneumonia.19,22 Shufeng Jiedu capsule is recommended for patients with COVID-19 with fever, aversion to wind, sore throat, headache, nasal congestion, rhinorrhea with turbid fluid, and cough.

**TCM prescriptions in the clinical treatment period (confirmed cases)**

Confirmed cases include suspected cases of COVID-19 with one of the following etiological or serological factors: (a) fluorescent RT-PCR positive for new coronavirus nucleic acid; (b) viral gene sequence highly homologous to known new coronaviruses; (c) SARS-CoV-2-specific IgM and IgG detected in serum (SARS-CoV-2-specific IgG is detectable or reaches a titer increment of at least four-fold during convalescence compared with the acute phase). For these patients, the new guidelines recommended general therapy and classification therapy.

**Qingfei Paidu decoction**

Scope of application: in accordance with the clinical observations of doctors in various locations, Qingfei Paidu decoction is suitable for mild, moderate, and severe cases of COVID-19, and may be used to treat certain critically ill patients.

Basic formula: Mahuang (Herba Ephedrae Sinica) 9 g, Stir-frying with liquid adjuvant Gancao (Radix Glycyrrhizae) 6 g, Kuixingren (Semen Armeniacae Amurum) 9 g, Shigao (Gypsum Fibrosum) (decocted first) 15-30 g, Guizhi (Ramulus Cinnamomi) 9 g, Zexie (Rhizoma Alismatis) 9 g, Zhuling (Polyporus) 9 g, Baizhu (Rhizoma Atractylodis Macrophalae) 9 g, Fuling (Poria) 15 g, Chaihu (Radix Bupleuri Chinensis) 16 g, Huangqin (Radix Scutellariae Baicalensis) 6 g, Banxia (Rhizoma Pinelliae) 9 g, Shengjiang (Rhizoma Zingiberis Recens) 9 g, Ziwan (Radix Asteris Tatarici) 9 g, Kuandonghua (Floks Farfarae) 9 g, Shegan (Rhizoma Baelanacae) 9 g, Xixin (Herba Asari Mandshurica) 6 g, Shanyao (Rhizoma Dioscoreae Opposita) 12 g, Zhishi (Fructus Aurantii Immaturus) 6 g, Chenpi (Pericarpium Citri Reticulatae) 6 g, Huoxiang (Herba Agastachis Rugosa) 9 g.

Administration: one package of traditional Chinese herbal pieces in a decoction per day, warmed and divided into two portions administered daily (40 min after a meal in the morning and evening). Three packages comprise one course of treatment.

If possible, patients are advised to consume half a bowl of rice soup after taking the decoction; one bowl of rice soup is suggested for patients with a dry tongue due to fluid depletion. If there is no fever, the dosage of gypsum should be reduced. For patients with fever or high fever, the amount of gypsum can be increased. If the symptoms improve but not do not totally resolve, a second course of treatment is required. If the patient has a special condition or other underlying diseases, the formula can be modified in accordance with the actual situation during the second course. If the symptoms disappear, the drug should be discontinued.

References: the General Office of the National Health Commission of the People’s Republic of China, Office of the National Administration of TCM “Notice on Recommending the Use of Qingfei Paidu decoction in Pneumonia Treated with Integrated Chinese and Western Medicine for the COVID-19 Infection” (National Administration of TCM Office Medical Letter [2020] No. 22).

Interpretation: Qingfei Paidu decoction is a general prescription for COVID-19 that effectively relieves the main symptoms in mild, moderate, and severe cases. Qingfei Paidu decoction is a combination of Maxing Shigan decoction, Wuling Powder, Xiaochaihu decoction, Shegan Mahuang decoction, and Sini Powder, with some adjustments. Administration of Qingfei Paidu decoction to more than 1100 patients with confirmed COVID-19 in 10 provinces (excluding Hubei) was effective in more than 90% of cases, and more than 50% of the patients showed a response after the first administration.23 A clinical retrospective analysis of 98 cases showed that the administration of Qingfei Paidu decoction for 3 d resulted in a significant reduction in the percentage of lymphocytes, aspartate aminotransferase, alanine aminotransferase, and D-dimer levels to normal values ($P < 0.01$); each observed laboratory index returned to normal in over 70% of patients. After taking Qingfei Paidu decoction for 6 d, the C-reactive protein level and erythrocyte sedimentation rate returned to normal ($P < 0.01$), and each observed laboratory index returned to normal in over 80% of patients. After taking Qingfei Paidu decoction for 9 d, each observed laboratory index returned to normal in over 90% of patients. No drug-related adverse reactions were observed during the study. Furthermore, 79 patients showed improvements on computed tomography after 6 d of treatment with Qingfei Paidu decoction, giving an improvement rate of more than 80%. Preliminary findings suggest that Qingfei Paidu decoction may affect Toll-like receptors and T cell receptors.24 Additionally, some core compounds of Qingfei Paidu decoction have a certain degree of affinity for the main protease (3C-like protease) and angiotensin-converting enzyme 2 of SARS-CoV-2.25

**TCM prescriptions for mild cases of COVID-19**

Mild cases involve mild clinical symptoms and no man-
Pattern of cold-damp constraint in the lung
Clinical manifestations: fever, fatigue, generalized body aches, cough, expectoration, chest tightness and labored breathing, poor appetite, nausea, vomiting and sticky stools, pale enlarged tongue with tooth marks or a light red tongue with coating that is white, thick, curd-like, and greasy or white and greasy, and a soggy or slippery pulse.

Recommended formula: Mahuang (Herba Ephedrae Sinica) 6 g, Shigao (Gypsum Fibrosum) 15 g, Kuvingen (Semen Armeniacae Amarum) 9 g, Qianghuo (Rhizoma et Radix Notopterygii) 15 g, Tinglizi (Semen Lepidii Apetali) 15 g, Guanzhong (Rhizoma Dryopteridis Crassirhizomatis) 9 g, Dilong (Pheretima Aspergillum) 15 g, Xuchangjing (Radix seu Herba Cynanchi Paniculata) 15 g, Huoxiang (Herba Agastaches Rugosa) 15 g, Peilan (Herba Eupatoriis Fortunei) 9 g, Canghuo (Rhizoma Atractyloidis Lanceae) 15 g, Fuling (Porzia) 45 g, Baihu (Rhizoma Atractyloidis Macrocephalae) 30 g, Jiao San Xian [stir-frying to brown Shanzha (Fructus Crataegi), Shenqi (Massa Medicata Fermentata), and Maiya (Fructus Hordei Germinati) 9 g each, Houpu (Cortex Magnoliae Officinalis) 15 g, Jiao Bing Lang (Arecae Semen) 9 g, Caoguo (Fructus Tiako) 9 g, Shengjiang (Rhizoma Zingiberis Recens) 15 g). Administration: one package daily, decocted to create 600 mL that is divided into three equal portions, each of which is administered before a meal in the morning, afternoon, and evening.

Scope of application: this prescription is suitable for patients with mild clinical symptoms such as fever, fatigue, generalized body aches, cough, poor appetite, and sticky stools.

Interpretation: this prescription, also known as the Wuhan Anti-Epidemic Formula, was developed by Tong Xiaolin and has been administered to more than 50,000 patients, most of which comprised suspected cases and confirmed cases with mild symptoms. Preliminary results show that this prescription is effective in treating fever, cough, fatigue, and muscle aches.

The prescription is a combination of Maxing Shigan decoction, Tinglizi Dazao Xiefei decoction, Huopo Xialing decoction, Shenzhu powder, and Da Yuan decoction, and has the functions of dispersing cold and degumifying, ventilating the lung to regulate the surface, invigorating the spleen and replenishing Qi, eliminating pathogenic factors from Moyuan, dispelling filth with aroma, and activating blood to dredge the collaterals. Maxing Shigan decoction has anti-viral effects, inhibits airway inflammation, and reduces colonic mucosal inflammation. Huopo Xialing decoction regulates gastrointestinal function and improves gastric mucosal defense. In mice infected with influenza virus FM1, modified Shenzhu Powder downregulates the secretion of NLRP3 inflammatory corpuscles and its downstream factors IL-1β and IL-18, which probably have immune-protective effects. Dayuan decoction attenuates the expression of NF-κB in the bronchial mucosal epithelium and lung tissues of rats with acute lung injury, and alleviates pulmonary edema associated with lipopolysaccharide-induced acute lung injury.

Clinical manifestations of damp-heat accumulation in the lung
Clinical manifestations: low-grade or no fever, slight aversion to cold, fatigue, heavy sensation in the head and body, muscle soreness, dry cough with little sputum, sore throat, thirst without the desire to drink or with chest tightness and epigastric fullness, anhidrosis or disturbed hidrosis, vomiting with anorexia, loose or sticky stools. The tongue is light red, and the tongue coating is white, thick, and greasy or thin and yellow. The pulse is slippery and rapid or soggy.

Recommended formula: Binglang (Semen Arecae) 10 g, Caoguo (Fructus Tiako) 10 g, Houpu (Cortex Magnoliae Officinalis) 10 g, Zhimu (Rhizoma Anemarrhenae) 10 g, Huangqin (Radix Scutellariae Baicalensis) 10 g, Chaihu (Radix Bupleuri Chinensis) 10 g, Chishao (Radix Paeoniae Rubra) 10 g, Lianqiao (Fructus Forsythiae Suspensae) 15 g, Qinhuo (Herba Artemisiae Annuae) (added later) 10 g, Canghuo (Rhizoma Atractyloidis Lanceae) 10 g, Daqingye (Folium Isatidis) 10 g, Gancao (Radix Glycerrhizae) 5 g.

Administration: one package daily comprising 400 mL after decocting, divided into two equal portions, one of which is taken in the morning and one in the evening.

Scope of application: this prescription is suitable for patients with mild clinical symptoms such as low-grade or no fever, fatigue, heavy sensation in the head and body, dry cough with minimal sputum, sore throat, poor appetite, nausea, and sticky stools.

Interpretation: the prescription is a modified combination of Dayuan decoction, Xiaoaihu decoction, and Haoqin Qingdan decoction, which has the effects of clearing heat and dampness, reconciling Shaoyang, eliminating pathogenic factors from Moyuan, dispelling filth and resolving turbidity, cooling blood, and detoxifying. Xiaoaihu decoction protects the gastrointestinal mucosa, and a variety of its extracts have varying degrees of antibacterial properties. Haoqin Qingdan decoction inhibits influenza virus proliferation by downregulating the expression of influenza virus genes, reduces the immune damage caused by inflammatory factors, and protects the lung tissue; it also improves gastric mucosal inflammation and protects the gastric mucosa of mice infected with Helicobacter pylori by downregulating the expressions of nuclear factor kappa-B P65, cyclooxygenase-2, and tumor necrosis factor-α, and adjusting the imbalance of Th1/Th2.
spiratory problems, with imaging findings suggestive of pneumonia. The guidelines recommend two treatment regimens based on the symptom patterns.

**Pattern of dampness and stagnation in the lung**

Clinical manifestations: fever, cough with minimal sputum or yellow sputum, chest tightness and shortness of breath, abdominal distension, and constipation. The tongue body is dark-red, and the tongue shape is enlarged. The tongue coating is dark-red and greasy or yellow and dry. The pulse is slippery and rapid or wiry and slippery.

Recommended prescription: Mahuang (Herba Ephedrae Sinica) 6 g, Kuxingren (Semenum Armeniacae Amarum) 15 g, Shigao (Gypsum Fibrosum) 30 g, Yiyiren (Semenum Coicis) 30 g, Cangzhu (Rhizoma Atractylodis Lanceae) 10 g, Huoxiang (Herba Agastaches Rugosa) 15 g, Qingshao (Herba Artemisiae Annuae) 12 g, Huzhangren (Radix Periisii Cuspidati) 20 g, Majorcao (Majorca Euphorbiae) 6 g, Banxia (Rhizoma Pinelliae) 10 g, Suweishigan decoction, and Shenshu Powder, and has the functions of ventilating the lung, relieving and dispersing cold, dehumidifying and regulating the stomach, and detoxification. Pingwei Powder promotes repair of the intestinal mucosal barrier, and regulates the expression of aquaporin (such as AQP2 and AQP9) in the gastric mucosal layer to protect the gastric mucosal layer. The mechanism of this prescription might be related to the reduction of bronchial mucosal damage and the repair of intestinal mucosa.

**TCM prescriptions for severe cases of COVID-19**

Severe cases include adult patients meeting any of the following criteria. (a) Respiratory distress (≧ 30 breaths/min); (b) oxygen saturation < 93% at rest. 3) Arterial partial pressure of oxygen (PaO) / fraction of inspired oxygen (FiO) ≧ 300 mm Hg (1 mm Hg = 0.133 kPa). In high-altitude areas (more than 1000 meters above sea level), PaO/FiO; is corrected to PaO/FiO × [atmospheric pressure in mm Hg/760]. 4) Patients with chest imaging that shows lesion progression of > 50% within 24-48 h. Depending on the symptom patterns, the guidelines recommend two treatment regimens for common cases.

**Pattern of epidemic toxin blocking the lung**

Clinical manifestations: fever with a red face, cough with minimal amounts of yellow and sticky or blood-stained sputum, chest tightness and shortness of breath, lassitude, dryness, bitterness, and stickiness in the mouth, nausea and loss of appetite, difficult defecation, and scant dark urine. The tongue is red with a yellow greasy coating. The pulse is slippery and rapid.

**Recommended prescription: Huashi Baidu Formula**

Basic formula: Mahuang (Herba Ephedrae Sinica) 6 g, Kuxingren (Semenum Armeniacae Amarum) 9 g, Shigao (Gypsum Fibrosum) 15 g, Gancao (Radix Glycyrrhizae) 3 g, Huoxiang (Herba Agastaches Rugosa) (added later) 10 g, Houpu (Cortex Magnoliae Officinalis) 10 g, Cangzhu (Rhizoma Atractylodis Lanceae) 15 g, Caoguo (Fructus Tsakho) 10 g, Banxia (Herba Euphorbiae) 6 g, Mahuang (Herba Ephedrae Sinica) 6 g, Qianghuo (Rhizoma et Radix Notopterygi) 10 g, Shengjiang (Rhizoma Zingiberis Recens) 10 g, Binglang (Semenum Arecae) 10 g.

Administration: one to two packages daily as a decoction, 100-200 mL administered two to four times per day orally or via a nasal feeding tube.

Scope of application: Huashi Baidu formula is suitable for patients with fever, cough with minimal amounts of sticky yellow sputum or blood-stained sputum plus gasping, fatigue, respiratory distress, tachypnea, nausea, poor appetite, and constipation.
with similar effects can be selected in accordance with injection, Xuebijing injection, Reduning injection, and Xingnaojing injection) or administering a TCM injection in combination with a TCM decoction to treat the disease, slow the disease progression, and prevent complications.

The main component of Xiyangping injection is the water-soluble andrographisulfonate, which eliminates heat and detoxifies, relieving cough and diarrhea. Pharmacological studies indicate that Xiyangping injection has certain antiviral, immune-boosting, anti-inflammatory, and antibacterial effects, and is suitable for the treatment of acute respiratory infection and other diseases. Xuebijing injection is derived from Xuefu Zhu Yu decoction, which includes Danshen (Radix Salviae Miltiorrhizae), Chuanxiong (Rhizoma Chuanxiong), and Danshen (Radix Salviae Miltiorrhizae), and has the functions of promoting blood circulation and removing blood stasis, eliminating heat, and detoxification. Xuebijing injection is often used as an adjuvant therapy in the treatment of severe pneumonia. Reduning injection is made of Qinghao (Herba Artemisiae Annuae), Jinyinhua (Florulae Forsythiae Suspensae), and Zhizi (Fructus Gardeniae), and has the functions of eliminating heat, detoxifying, cooling blood, and dispelling wind. Pharmacological studies indicate that Xuebijing injection has antivirus and anti-inflammatory effects, and is effective in treating severe cases of acute upper respiratory infection and viral pneumonia. Tanreqing injection is composed of Huangqin (Radix Scutellariae), Bear Gall powder, Cornu Oryzae, Jinyinhua (Florulae Forsythiae Suspensae), and Zhizi (Fructus Gardeniae), and has the functions of eliminating heat, resolving phlegm, and detoxifying. Tanreqing injection has a definite effect on patients with severe acute viral pneumonia and those with COPD associated with respiratory failure. The combination of Qingwen Baidu decoction and Tanreqing injection significantly reduces the inflammatory response of patients with A/H1N1 viral pneumonia and alleviates their symptoms, which may be related to the prevention and treatment of the cytokine inflammatory storm. Xingnaojing injection is composed of Shexiang (Moschus), Yujin (Radix Curcumae Wenyujin), Zhizi (Fructus Gardeniae), and Bingpian (Bormoeolum Syntheticaum), and has the functions of eliminating heat, detoxifying, cooling and activating blood, and refreshing the mind; it is used to treat the continuous high fever and multiple organ functional failure caused by sepsis.

**Pattern of Qi and Yin consumed by blazing heat**

Clinical manifestations: high fever with polydipsia, tachypnea and shortness of breath, delirium and unconsciousness, and blurred vision, possibly accompanied by macules and papules, hematemesis, epistaxis, or convulsion of the four limbs. The tongue is crimson with little or no coating. The pulse is deep, thready, and rapid, or floating, large, and rapid.

Recommended prescription: [Shigao (Gypsum Fibrosum) decocted first] 30-60 g, Zhumu (Rhizoma Anemarrhenae) 30 g, Dihuang (Radix Rehmanniae) 30-60 g, Shuniniujiao (Cornu Bubali) (decocted first) 30 g, Chishao (Radix Paeoniae Rubra) 30 g, Xuanshen (Radix Scrophulariae) 30 g, Lianqiao (Fructus Forsythiae Suspensae) 15 g, Mudanpi (Rhizoma Coptidis) 15 g, Huanglian (Rhizoma Coptidis) 6 g, Zhiwu (Folium Phyllostachidis Henonis) 12 g, Yingzi (Semen Lepidii Apetalii) 15 g, Gancao (Radix Glycyrrhizae) 6 g.

Administration: one pack daily as a decoction (Shigao (Gypsum Fibrosum) and Shuniniujiao (Cornu Bubali) should be decocted first), 100-200 mL administered two to four times daily orally or via a nasal feeding tube.

Scope of application: this prescription is suitable for severe cases characterized by high fever, gasping, fatigue, respiratory distress, shortness of breath, and symptoms of obnubilation and hemorrhage, such as purpura, epistaxis, or hemoptysis.

Interpretation: this prescription is a modified form of Qingwen Baidu decoction, which has the functions of eliminating heat and detoxifying, cooling blood and hemostasis, purging the lung, relieving asthma, and inducing resuscitation. Qingwen Baidu decoction reduces the systemic inflammatory response in rabbits with sepsis via the TLR4/MyD88 signaling pathway, and downregulates the expression of IL-1β in the splenic tissue of rats with sepsis to protect the spleen function. This prescription also contains active ingredients with the potential to interfere with cytokine storms.

**Recommended Chinese patent medicines:** Xiyangping injection, Xuebijing injection, Reduning injection, Tanreqing injection, and Xingnaojing injection. Drugs with similar effects can be selected in accordance with individual conditions, or can be used in combination in accordance with clinical symptoms. TCM injections can be used together with TCM decoctions. Patients with severe COVID-19 may develop polyneuropathy, low blood oxygen saturation, progression of pulmonary lesions on imaging, and other clinical manifestations. In this severe stage, in addition to the various treatments based on TCM symptom pattern identification, the guidelines also recommend administering one or two TCM injections (Xiyangping injection, Xuebijing injection, Reduning injection, Tanreqing injection, and Xingnaojing injection) or administering a TCM injection in combination with a TCM decoction to treat the disease, slow the disease progression, and prevent complications.

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**TCM prescriptions for critical cases of COVID-19 (pattern of internal blockage and external desertion)**

Critical cases are defined as those meeting any of the following criteria: (a) respiratory failure requiring mechanical ventilation; (b) shock; (c) other organ failure that requires ICU admission.

Clinical manifestations: dyspnea, panting on exertion or a requirement for mechanical ventilation, unconsciousness and dysphoria, sweating, and cold extremities. The tongue is dark and purple with a thick greasy or dry coating. The pulse is floating and large without root.

Recommended prescription: Suhexiang Wān or Angong Niuhuang Wān with a decoction composed of Renshen (**Radix Ginseng**) 15 g, Fuzi (**Radix Aconiti Lateralis Preparata**) (decocted first) 10 g, and Shanzhuyu (**Fructus Macrocarpi**) 15 g.

Patients requiring mechanical ventilation and those with abdominal distension and constipation or difficult defecation may require 5-10 g of Dahuang (**Radix Et Rhizoma Rhei Palmati**). If patient-ventilator asynchrony occurs, clinicians should administer 5-10 g of Sheng Dahuang and 5-10 g of Mangxiaoyin (**Nalrii Sulfa**-**S**-**et-Rhizoma Rhei Palmati**). If patient-ventilator asynchrony occurs, clinicians should administer 5-10 g of Dahuang (**Radix Et Rhizoma Rhei Palmati**) and Mangxiaoyin (**Nalrii Sulfa**-**S**-**et-Rhizoma Rhei Palmati**) together with sedation and muscle relaxant medications.

Scope of application: this prescription is suitable for critical patients who have breathing difficulty, asthma, or require ventilation, have irritability, sweaty and cold limbs, or are in a coma.

Interpretation: this prescription is a modified combination of Shenfu decoction and Laifu decoction, and has the functions of reinforcing vital energy and restoring Yang to rescue collapse. In accordance with the hot or cold nature of disease, patients should be administered Suhexiang pill to warm or Angong Niuhuang pill to cool to open the epidemic toxin blockage of lung Qi. Shenfu decoction prolongs the hypoxia tolerance of animals, protects the myocardium, promotes coronary blood flow, immunoregulates, improves hemorheology, stimulates pituitary-adrenocortical function, and also has anti-arhythmia, anti-shock, and anti-lipid peroxidation functions.65

Patients who require mechanical ventilation may have symptoms such as abdominal distension, inhibited defecation, and even patient-ventilator desynchrony, owing to organ functional failure or the use of sedative and muscle relaxant medications. Such patients should immediately be administered Dahuang (**Radix Et Rhizoma Rhei Palmati**) and Mangxiaoyin (**Nalrii Sulfa**-**S**-**et-Rhizoma Rhei Palmati**) to expel harmful metabolites and toxins, maintain internal environment stability, and aid in ventilation.66

Recommended Chinese patent medicines: Xuebijing injection, Reduning injection, Tanreqing injection, Shenmai injection, Shenmai injection, and Shenmai injection. Drugs with similar effects can be selected based on individual conditions, or can be used in combination in accordance with the clinical symptoms. TCM injections can be used together with TCM decoctions.

The use of TCM injections follows the principle of starting from a small dose and modifying the prescription based on TCM pattern identification. The recommended usage of TCM injections for severe and critical cases is as follows. For viral infection or combined mild bacterial infection: 0.9% sodium chloride injection 250 mL with Xiyangping injection 100 mg (twice daily), or 0.9% sodium chloride injection 250 mL with Reduning injection 20 mL, or 0.9% sodium chloride injection with Tanreqing injection 40 mL (twice daily). For high fever with disturbance of consciousness: 0.9% sodium chloride injection 250 mL with Xuebijing injection 20 mL (twice daily). For systemic inflammatory response syndrome and/or multiple organ failure: 0.9% sodium chloride injection 250 mL with Xuebijing injection 100 mL (twice daily). For Immunosuppression: glucose injection 250 mL with Shenmai injection 100 mL or Shengmai injection 20-60 mL (twice daily).

Critical patients may have respiratory failure, shock, or concomitant failure of other organs because of the severe lung infection and complications. Aside from the first-aid decoction and oral Chinese patent medicines, critical patients should also receive intravenous injections of one or two kinds of Chinese medicines in accordance with the individual situation. The TCM protocol of the seventh version of the guidelines recommends Xuebijing injection, Reduning injection, Tanreqing injection, Xingnaojing injection, Shenfu Injection, Shengmai injection, and Shenmai injection. As well as the four recommended Chinese medicine injections, severe cases may be administered Shenfu injection, which originates from Shenfu decoction. The main components of Shenfu injection are Hongshen (**Radix Ginseng Rubra**) and Fuzi (**Radix Aconiti Lateralis Preparata**) extractions, which rescue collapse by restoring Yang, tonifying Qi, and preventing exhaustion. Shenfu injection also has the pharmacological actions of treating shock, improving hemorheology, regulating immune function, and improving cardiac function.67 Shenmai injection is based on Shengmai Powder, which contain extracts from Hongshen (**Radix Ginseng Rubra**), Maidong (**Radix Ophiopogonis Japonici**), and Wiweizi (**Fructus Schisandrae Chinensis**). Shenmai injection tonifies Qi and Yin, restores the pulse to relieve desertion, and has marked clinical effects on the cardiovascular system, immune system, and hemorheology.68 Shenmai injection is made from Hongshen (**Radix Ginseng Rubra**) and Maidong (**Radix Ophiopogonis Japonici**), and tonifies Qi, prevents exhaustion, nourishes Yin, and generates body fluid. Pharmacological studies indicate that Shenmai injection has anti-inflammatory, anti-ischemia-reperfusion injury, and anti-shock effects, and enhances the immune function.69 Application of Chinese medicine injections for severe...
and critical cases of COVID-19 must follow the principle of starting from a small dose and gradually adjusting the dosage in accordance with the manufacturer’s instructions.

**TCM prescriptions for use in convalescence**

This protocol is mainly aimed at patients who have already satisfied the discharge standards but still need quarantine and health monitoring, and patients who have completed the quarantine period but still have sequelae such as pulmonary function injury, pulmonary fibrosis, or fatigue. The following two types of clinical symptom patterns are displayed during the convalescence period.

**Pattern of lung and spleen Qi deficiency**

Clinical manifestations: shortness of breath, lassitude and fatigue, poor appetite with nausea and vomiting, abdominal fullness, a sense of incomplete evacuation, and sticky loose stools. The tongue is pale and enlarged with a white and greasy coating.

Recommended prescription: Banxia (Rhizoma Pinelliae) 9 g, Chenpi (Pericarpium Citri Reticulatae) 10 g, Danshen (Radix Codonopsis) 15 g, Huangqi (Radix Astragali Mongolici) 30 g, Baizhu (Rhizoma Atractylodis Macrocephalae) 10 g, Fuling (Poria) 15 g, Huoxiang (Herba Agastaches Rugosa) 10 g, Sharen (Fructus Amomi) (added later) 6 g, Gancao (Radix Glycyrrhizae) 6 g. Administration: one package daily, comprising 400 mL after decocting, divided into two equal portions, one of which is administered in the morning and one in the evening.

Scope of application: this prescription is suitable for convalescent patients with panting, fatigue, poor appetite, abdominal fullness, and poor bowel movement with loose stools.

Interpretation: this prescription is modified from Liujunzi decoction. It reinforces the spleen and strengthens Qi, expels phlegm, eliminates dampness and turbid pathogens, and improves the symptoms of patients with stable COPD. This prescription also improves quality of life and regulates the expression of inflammatory cytokines, helping patients recover from poor digestive function and fatigue. It might also help prevent disease recurrence.60

**Pattern of both Qi and Yin deficiency**

Clinical manifestations: fatigue, shortness of breath, dry mouth, thirst, heart palpitations, profuse sweating, poor appetite, low-grade or no fever, and dry cough with minimal sputum. The tongue is dry with scant fluid. The pulse is thready or weak and forceless.

Recommended prescription: Nanshashen (Radix Adenophorae Tetraphyllae) 10 g, Beishashen (Radix Glehniae) 10 g, Maidong (Radix Ophiopogonis Japonici) 15 g, Xiyangshen (Radix Panacis Quinquefolii) 6 g, Wuweizi (Fructus Schisandrae Chinensis) 6 g, Shigao (Gypsum Fibrosum) 15 g, Dazhuyue (Herba Lophatheri) 10 g, Sangye (Folium Mori) 10 g, Lugen (Rhizoma Phragmitis) 15 g, Danshen (Radix Salviae Miltiorrhizae) 15 g, Shigao (Gypsum Fibrosum) 6 g. Administration: one package daily, comprising 400 mL after decocting, divided into two equal portions, one of which is administered in the morning and one in the evening.

Scope of application: patients who are recovering but still have mild fatigue, coughing without phlegm, dry mouth, poor appetite, heart palpitations, and excess sweating.

Interpretation: this prescription is a combination of Shashen Maidong decoction, Shengmai decoction, and Zhuye Shigao decoction. It has the actions of benefitting Qi, nourishing Yin, eliminating heat, moistening dryness, and activating blood circulation to dissipate blood stasis. Shashen Maidong decoction improves symptoms such as cough variant asthma and chronic bronchitis, which might be related to its actions in the regulation of IL-6 and secretory IgA and the improvement of the damage caused by oxygen radicals.61, 62

Shengmai decoction prevents pulmonary fibrosis and injury of vascular endothelial cells.63

One of the major advantages of TCM is the prevention of disease relapse. To prevent COVID-19 recurrence in discharged patients and prevent pulmonary fibrosis and impaired lung function in severe cases, the Suggestive Guidance based on Chinese medicine for rehabilitation of COVID-19 was issued by the National Health Commission of the People’s Republic of China and National Administration of TCM on 22nd February 2020. This medical approach is the first a national standard specifically designed for discharged patients. Designed for use by both clinicians and patients, this document recommends a comprehensive strategy of interventions, including TCM, conventional non-pharmaceutical therapy, psychology, dietary management, and physical exercise.

**CONCLUSION**

China is currently in the critical stage of the COVID-19 epidemic. The number of newly confirmed and suspected cases is showing a tendency to continuously decline. However, the number of COVID-19 cases is rising globally. On 11th March 2020, the outbreak of COVID-19 was defined as a pandemic by the WHO.64 The number of cases outside China has increased by 13-fold, and the number of countries with cases of COVID-19 has tripled in the past 2 weeks. At 21: 00 on 3rd May 2020, a total of 3 349 786 cases had been confirmed worldwide, with 238 628 cases of death.65

During the control of the COVID-19 epidemic in China, TCM has played an important role in early intervention. The continuous updating of the clinical guidelines protocol has been achieved with the support of research data and the experiences reported by frontline clinicians at the forefront of the epidemic in China.
clinical practices. Under these circumstances, TCM offers a complement for the therapeutic approach in mild cases in the early stage, helping with immunity adjustment, and decreasing the progression from mild to severe disease. The combined approach of TCM and conventional medicine for severe cases not only relieves the disease symptoms, but also effectively lowers the fatality rate and stops disease progression. The latest version of the TCM clinical protocol for COVID-19 provides a practical and effective approach, and may be used as a reference by international societies.

REFERENCES


29 Zou L. The effects of Maxingshigan decoction on the levels of IL-6 and MCP-1 of mediated by type A influenza virus. Changsha: Hunan University of Chinese Medicine, 2017: 34.


31 Li JT, Liang HY, Su LF. Effect of Jiawei Shenzhu powder on the expression of NLRP3 inflammatory bodies and downstream inflammatory factors in FM1-infected mice. Shi Yong Zhong Yi Yao Za Zhi 2019; 35(10): 1180-1182.


38 Pan Y. Antagonism effects and signal transduction path of Hao Qin Qing Dan decoction on Damp-heat syndrome of pneumonia disease infected by influ-enza virus. Guangzhou: Southern Medical University, 2009: 42-52.

39 Qu J. Experimental research on the influence of Haoqin Qingdan decoction on the expression of NF-κBp65, IL-8 in mice gastritis caused by H.pylori infection. Chengdu: Chengdu University of Chinese Medicine, 2013: 28.

40 Yang FY. Experimental research on the influence of Haoqin Qingdan decoction on the expression of COX-2, TNF-α in gastric mucosa of mice model of chronic gastritis and spleen stomach damp heat syndrome caused by H. Pylori infection. Chengdu: Chengdu University of Chinese Medicine, 2015: 22-23.

41 Li L. Experimental research about Haoqin Qingdan decoction effecting the expression of IL-4, IFN-γ in serum of mice with chronic gastritis after infecting with H.Pylori. Chengdu: Chengdu University of Chinese Medicine, 2015: 28-29.

42 Xu JF, Chen CD, Tang MM. Therapeutic effects on tuberculous pleuritis and the impacts on immune function in the patients treated with the modified tingli daye xiefei decoction and anti-tuberculous drugs. Shi Jie Zhong Xi Yi Jie He Za Zhi 2018; 13(11): 1592-1595.

43 Zhou YX. The experimental study on Pingwei powder repair the damage of intestinal barrier the rats model of dampness obstructing spleen-stomach syndrome. Chengdu: Chengdu University of Traditional Chinese Medicine, 2009: 37.

44 Deng LP. The Mechanism research of aquaporin differentially expressed in a animal model on the syndrome of dampness incumbering middle energizer in stomach tissue by Pingwei dosage. Chengdu: Chengdu University of Traditional Chinese Medicine, 2011: 49-51.


51 Diao YF. Zhang SJ, Zhao WY, Sun FT, Zhang S, Sun L. Effect of Xuebijing injection on expression of interleu-kin-6 and tumor necrosis factor-α in patients with severe


60 Huang ZF, Lin HX, Wu MQ. A randomized controlled study of modified Liujunzi decoction on the "Qi deficien-
cy with phlegm" syndrome of COPD in the stable stage. Shen Zhen Zhong Yi Xi Jie He Za Zhi 2016; 26(21): 30-32.


62 Ji M, Wang ZC, Yang J. Efficacy of Shashen Maidong soup for the treatment of chronic bronchitis: a Meta-analy-


