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# Report 1

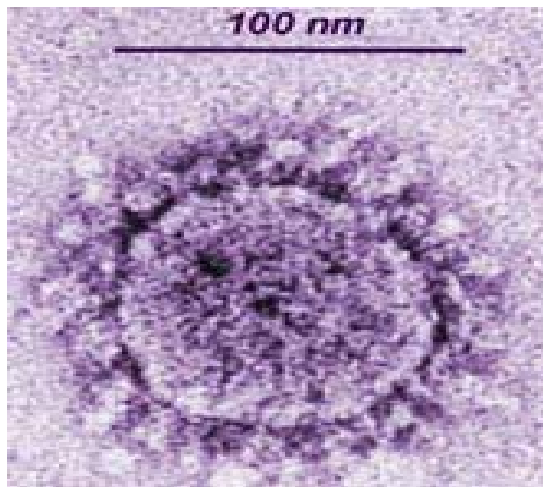
## Clinical research on treatment of SARS with integrated Traditional Chinese medicine and Western Medicine

Clinical Research Task Force for Treatment of SARS with Integrated TCM and Western Medicine <sup>1</sup>

### Background

In November 2002, cases of an atypical pneumonia with serious life-threatening respiratory symptoms and having an unknown cause appeared in the Guangdong province of China. The illness soon spread to over 30 countries and areas. In February 2003, the World Health Organization (WHO) named this illness "severe acute respiratory syndrome" (SARS). It was later discovered that the causative agent is a new variation of corona virus (1-6) (Fig. 1). The spread of SARS represented a tremendous threat to social life, the economy and public health. Various countries around the world took diverse measures in response to the threat of SARS and developed comprehensive prevention strategies based on Western medicine. The spread of the disease had been brought under control by July 2003.

*Fig. 1. The SARS virus*



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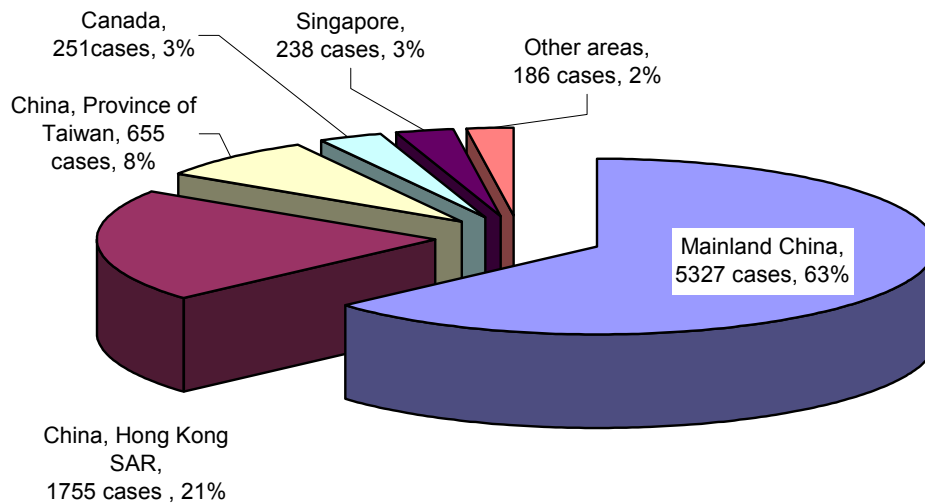
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## Epidemiology

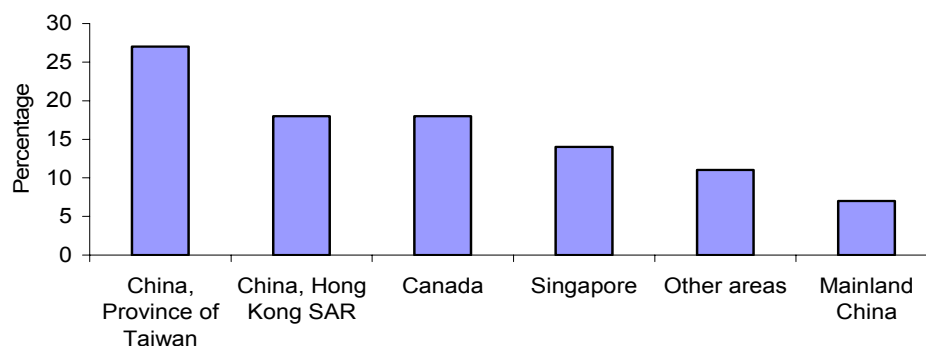
### Global picture

The first case of SARS outside China was reported in Viet Nam in November 2002; the epidemic had spread beyond mainland China to Canada, China, Hong Kong Special Administrative Region (SAR) and Singapore by March 2003. WHO issued a global warning for SARS on 12 March 2003. The global SARS epidemic peaked in April and May 2003. According to the statistics (7), during the outbreak of SARS from 1 November 2002 to 7 August 2003, there were 32 countries and areas in the world that had reported cases of SARS (a total of 8422 cases) (Fig. 2). The global case fatality rate was 11%, and Fig. 3 shows the case fatality rate for each country or area. The statistics produced by WHO indicated that SARS patients were predominantly middle-aged and young people, whereas there were fewer cases in the elderly and in children. The percentage of cases in health care workers was also high, but the percentages varied during the different epidemic periods.

*Fig. 2. Number of patients with SARS worldwide on 7 August 2003*



**Fig. 3. Case fatality rate of SARS in specific countries and areas on 7 August 2003**

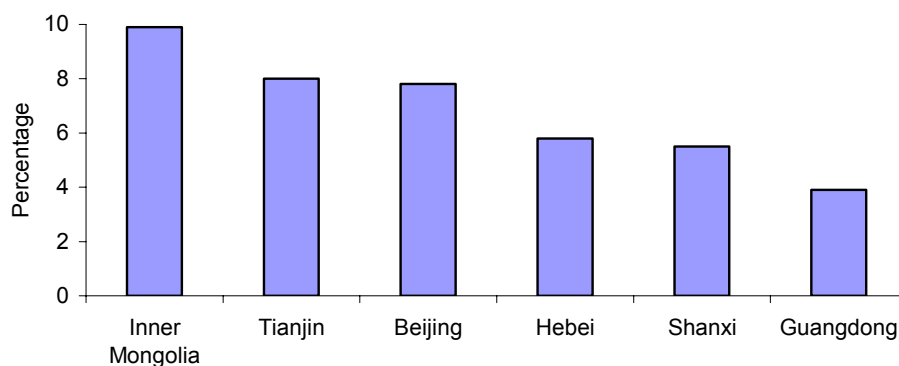


### *China*

Based on the statistics from the Ministry of Health of the People's Republic of China (8) and WHO, during the period between 1 November 2002 and 7 August 2003, in particular between the second half of April and the first half of May, SARS had shown a tendency to break out and flare up in mainland China. The cases were distributed as follows: 2521 in Beijing; 1512 in Guangzhou; 448 in Shanxi; 282 in Inner Mongolia; 215 in Hebei; and 175 in Tianjin.

By 14 July 2003, the SARS case fatality rate in mainland China was 7%, lower than that of the rest of the world (Fig. 3). Fig. 4 shows the case fatality rate in different areas of mainland China (8).

**Fig. 4. Case fatality rate from SARS in different areas of mainland China on 14 July 2003**



Most of the SARS patients in mainland China were middle-aged and young people. The numbers of elderly patients and children were relatively low. Patients had many different occupations. During part of the peak of the outbreak from 26 April to 30 April 2003, 19.6% of the SARS patients were health care workers whereas in Hong Kong SAR, the percentage was 22%.

## Clinical symptoms

### Symptoms and signs

The onset of the illness is sudden with fever as the primary symptom. The body temperature is usually higher than 38 °C, and the patients have headache, aching joints, muscle pains and fatigue. There are also symptoms of feeling chilly and diarrhoea, but there are no upper respiratory catarrhal symptoms. Often there is just dry cough, with a little phlegm, occasionally streaked with blood. There might be a feeling of tightness in the chest, with serious conditions such as rapid breathing or obvious respiratory distress. Some of the patients have some wet rale in breathing or signs of consolidation in the lungs. A few patients do not have fever as the primary symptom, especially those who have had operations or recent underlying disease.

### Laboratory examinations

The white blood cell count in the peripheral circulation is normal or even decreased. The numbers of lymphocytes often decrease.

### Chest X-ray examinations

The presence of different patch shapes, spots soakage shadow or net-shaped shadows is observed. The illness develops rapidly in some patients, and large areas of shadow are seen. There are usually changes in multiple lobes or bilateral changes, and the shadow shrinks and disperses slowly. The shadow in the lung may not be consistent with other symptoms.

### Pathological characteristics

#### *Pathological changes in the lungs*

Both lungs show substantial pathological changes, engorgement and congestion; they show spots and massive acute diffuse lobe interstitial inflammation. Alveoli are filled with proliferative epithelial cells and exudative protein, mononuclear cells, lymphocytes and plasmocytes. There are hyaline membranes. Some alveolar exudation shows glomerulus-like organized pneumonic changes. A virus can be found in alveolar epithelial cells and mononuclear macrophages which look like SARS virus in size and shape.

#### *Effects on the spleen and lymph nodes*

Massive necrosis is seen in spleen lymph tissue and spot necrosis in lymph nodes.

#### *Myelogenic haematopoietic tissue inhibition*

Myelogenic haematopoietic tissue proliferation is slowed down, karyocytes are obviously decreased, especially the numbers of granulocytes and lymphocytes. However, numbers of erythrocytes are increased, and plasmocytes, mononuclear and polynuclear giant cells proliferate.

**General effects**

Degeneration and necrosis of cells are observed in lungs, liver, kidney, heart and adrenal gland (9).

**Main challenges in the treatment of SARS****Difficulties in stopping the transmission and in early detection**

The results of research on SARS did not help to stop the transmission of the infection. The main reason for this is the difficulty of preventing and detecting SARS at an early stage. Clinically, the diagnosis of SARS depends mainly on virus antibody detection, rather than virus isolation. However, the appearance of virus antibodies usually occurs during the later stage of the illness. Furthermore, the transmission mechanism in nature is still unknown. All these factors lead to tremendous difficulty in the diagnosis of SARS at an early stage.

**Lack of safe and effective treatment**

The value of the treatment of SARS with high doses of antivirals and glucocorticoid is still uncertain. Furthermore, serious side-effects of using large doses of hormone have already been noted. Therefore, research into a safe and effective SARS treatment is a priority. As part of this research, summarizing and using the potential advantages and experience of treatment with Traditional Chinese medicine (TCM) might offer a shortcut to curing SARS.

**Influence of SARS on global health, tourism and the economy**

SARS has had a significant impact on the global public health system, and has revealed the fragility of the current public health system in dealing with the occurrence of a severe epidemic disease. As a result, all countries and regions, including China, will need to make adjustments and improvements to their current public health systems.

SARS had a significant influence on the global economic situation, especially on tourism. The tourist industry in the epidemic areas was almost paralysed, and that in nearby areas was also affected.

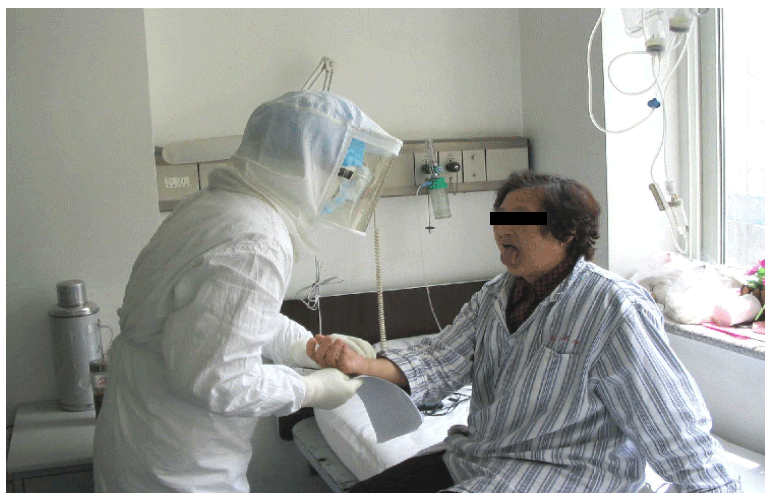
**Recognition of SARS from the point of view of Traditional Chinese medicine**

TCM is a complete systematic science based on the experience of disease prevention and treatment in China during the past several thousand years. It takes the holistic approach of "integration of nature and people", recognition of "testing and seeking for reasons", and diagnosis and treatment on the basis of an overall analysis of the illness and the patient's condition. Its core principles include the five-element theory and *yin* and *yang*, viscera-state doctrine, meridian doctrine, theory of the six exogenous factors causing illness, three-factor doctrine,

and four diagnoses and eight outlines. The theories of prevention are the essence of TCM, which advocates: "Sage doesn't treat but prevents disease, and doesn't solve disorder but prevents disorder" (*Plain questions/theories on four natures of adjustment*). As early as the sixteenth century, the method of human vaccination against smallpox was developed, which made a valuable contribution to vaccination worldwide. Chinese medicine considers that "health-qi inside the body can prevent the illness" (*Plain questions/theories on acupuncture*), and "if a person is sick, his qi must be weak" (*Plain questions/theories on fever*). Even when facing unknown causes, pathological changes and state of illness evolution principles, TCM is able to carry out a reasonable analysis on new epidemic diseases with difficult symptoms using its unique recognition theory systems. By taking the patient's pulse and knowing the characteristics of the illness, TCM could analyse the cause of disease and decide on an appropriate diagnosis and treatment.

SARS, despite being a new infectious disease, complies with the description that "epidemics of communicable diseases affect people irrespective of whether they are young or old, and the symptoms are similar", and is coincident with the symptoms of five infectious diseases illustrated in *Plain questions/theories on acupuncture*, as judged from the clinical symptoms of the disease and its evolution rules. It is characterized as a pestilence in TCM. There are many records about clinical diagnosis, treatment methods and experiences related to diseases such as pestilence, epidemic febrile diseases and enteric fever in the documentation on TCM. For instance, the *Treatise on pestilence* written by Wu Youke during the Ming Dynasty, *Treatise on epidemic febrile diseases* by Ye Tianshi during the Qing Dynasty, the *Treatise on differentiation and treatment of epidemic febrile diseases* written by Wu Jutong written during the Qing Dynasty and other such works are all monographs on the treatment of infectious diseases. Abundant details of medical cases and diagnosis and treatment experiences provide reference material and favourable conditions to facilitate studies on the diagnosis and treatment of SARS with TCM.

TCM states that pathogenic factors first invade lungs and then go upwards to the heart (See *Treatise on epidemic febrile diseases*). SARS is an epidemic disease. The cause is a virus, invading from the mouth or nose, with fever as the main symptom, accompanied by weakness, dry cough and difficulty in breathing. The pathogenicity comes from the virus gathering in the lung, phlegm blocking the qi of the lung and weakened qi and yin. The onset of the disease is rapid with serious symptoms; it spreads quickly, locates in lung, and affects the heart, kidney, stomach and other key organs. The illness is treated according to different stages and different symptoms, stressing that the illness is driven out and the body's resistance is strengthened, and on the basis that preventing transmission and deterioration can have worthwhile results.



## Treatment with integrated Traditional Chinese medicine and Western medicine

### General situation

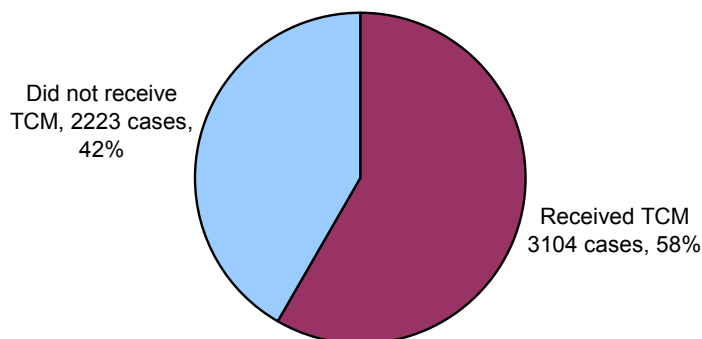
Since the outbreak of SARS began, the Chinese government has given unified orders and deployment of resources. The SATCM and various provincial and city TCM management departments have used the advantages of TCM in prevention, treatment, and aiding recovery from illness with unknown cause, and have participated in the clinical care and scientific research.

### *Medical treatment*

To strengthen the use of TCM to prevent SARS in various locations, the Administration organized a team of experts to develop the “*Technical Scheme on the prevention and treatment of SARS with TCM*” on 11 April 2003. They further revised the prevention component of the programme on 19 April and the treatment component on 11 May 2003. At the beginning of June 2003, they also published the *Recommendation on the treatment of SARS at the convalescence period with TCM* based on the symptoms of the patients. They also included acupuncture as part of the treatment plan. The publication of these regimens played an important role in encouraging and helping the TCM community to participate in the prevention and treatment of SARS.

On the basis of incomplete statistics, it is estimated that 195 hospitals in mainland China are designated for the treatment of SARS patients. Of these, 102 hospitals have professional staff in the field of TCM participating in the treatment of SARS patients, accounting for 52% of all the designated hospitals. Ninety-six Chinese medicine hospitals have sent out 2163 medical personnel to 93 designated hospitals. Of the 5327 patients diagnosed with SARS across the country, 3104 cases received TCM treatment (Fig. 5).

**Fig. 5. Percentage of 5327 patients with confirmed SARS in mainland China who received or did not receive treatment with traditional Chinese medicine**



The clinical results of integrated treatment with TCM and Western medicine have received the close attention of medical practitioners both in the People's Republic of China and elsewhere.

#### ***Scientific research***

After the outbreak of SARS, the SATCM initiated a research project that included basic research and clinical scientific investigation of SARS. At the same time, local government agencies at all levels also cooperated by setting up a number of research and development projects for the prevention and treatment of SARS with TCM. For instance, the Beijing area undertook 25 SARS-specific projects. Such projects have looked at clinical efficacy and safety evaluation, regimen optimization, basic features of the syndrome and so on, for both TCM and integrated Chinese and Western medicine in treating SARS.

#### **Method of clinical research on treatment of SARS with integrated Traditional Chinese medicine and Western medicine**

We reviewed nine representative studies, involving 777 cases, that evaluated the clinical effectiveness and safety of integrated treatment for SARS; the approaches taken are outlined below.

#### ***Study subjects***

All the study subjects were inpatients with clinically diagnosed SARS. The diagnosis was based on the diagnostic criteria for SARS issued by the Ministry of Public Health of the People's Republic of China (namely, *Clinical diagnosis criteria for infectious SARS* (trial) issued on 18 April 2003, and *Explanation of the revised edition of clinical diagnosis criteria for infectious SARS* (trial) issued on 3 May 2003). The clinical diagnosis was based mainly on the epidemiological history, clinical symptoms and physical signs, laboratory tests, chest X-ray examination and ineffectiveness of antibiotic treatment. In addition, the "atypical pneumonias" that might be caused by other pathogens were excluded and some of the cases were tested for serum antibodies.

#### ***Observation period***

The observations were made from November 2002 to July 2003 when SARS was prevalent. The studies started at the time the patients were included in the groups for observation and continued until the course of treatment ended. Some of the cases were followed up for a certain period of time after they had been

discharged from hospital, so as to monitor their convalescence. The criteria for discharge from hospital after 3 May 2003 followed the relevant reference criteria issued on 3 May 2003 by the Ministry of Public Health of the People's Republic of China.

### *Research design*

Two out of the nine studies were case-control studies using randomly allocated controls, and the remaining seven were prospective cohort studies or retrospective studies.

### *Therapeutic regimens*

Before 11 April 2003, therapeutic regimens of TCM and integrated treatment developed in individual hospitals were adopted. After this time, the "integrated treatment" used was the TCM regimen for SARS recommended by the SATCM on 11 April 2003. After 3 May 2003, the therapy with Western medicine for SARS refers to the therapeutic regimens recommended by the Ministry of Public Health of the People's Republic of China.

### *Organization of implementation and quality control*

Government agencies attached great importance to, and paid close attention to, the clinical studies of SARS by organizing researchers, integrating research resources and coordinating these studies. Importance was also attached to the study design and the establishment of the coordinated multicentre implementation network. Studies were coordinated through workshops and conferences. Multicentre facilities for quality control of clinical research data and real-time integrated analytical data were also set up. Appropriate standard operating procedures were developed for the studies; they covered the collection of clinical data, the collection of case report forms and data verification. By these means, the data management and quality control were strengthened.

## **Research results**

### **Clinical symptoms**

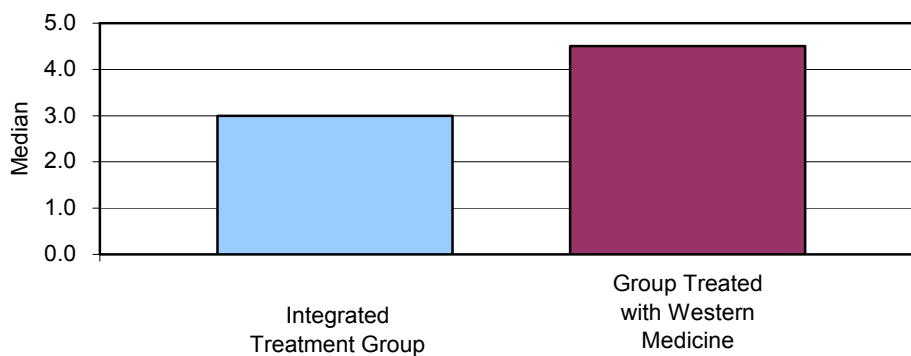
The analysis of the 524 SARS patients suffering from symptoms such as respiratory difficulty, is described in Report 2. The investigators made dynamic and longitudinal comparisons and analyses. They adopted the accumulative logistic model and the "mixed statistical process" using the SAS software package to study the difference in improvement of the symptoms between two therapeutic regimens. The regimens compared were integrated treatment with TCM and Western medicine, and treatment with Western medicine alone. The integrated treatment was found to be superior to the treatment with Western medicine alone in improving symptoms such as hypodynamia, shortness of breath and tachypnoea ( $p$ -values were 0.0343, 0.0457 and 0.0573, respectively). The observation on 63 SARS patients described in Report 7 showed that the severity of symptoms (headache, joint or muscular stiffness, cough, blood-tinged sputum, pectoralgia, poor appetite, nausea, vomiting, sweating, palpitations and some other symptoms) in the integrated treatment group in weeks 2 and 3, was obviously lower than that of the control group treated with Western medicine

alone. These findings show that treatment with integrated TCM and Western medicine was more effective than treatment with Western medicine alone.

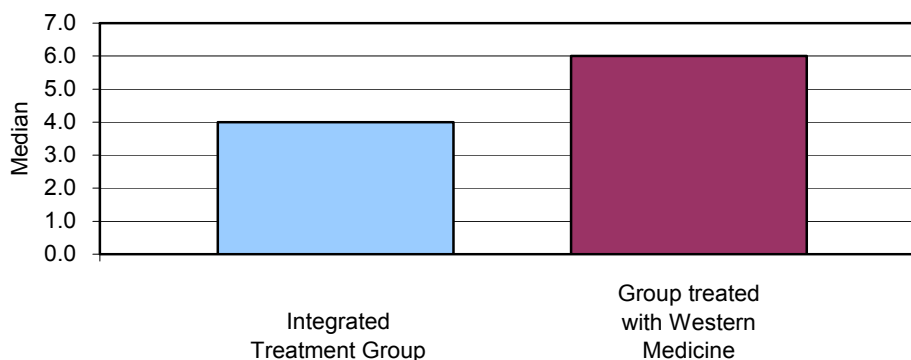
#### *Inflammation in the lungs*

The study described in Report 2 suggested that when integrated treatment was administered to patients in the early stage of the disease (within 7 days of onset), the total scores of lung inflammation shown on the chest radiographs ( $4.40 \pm 4.97$ , median 3.0) were significantly lower than those of the group treated with Western medicine alone ( $6.39 \pm 6.48$ , median 4.5), and the difference was statistically significant ( $Z = 3.32$ ;  $p = 0.0004$ ) (Fig. 6). In the comparison of patients with severe SARS between the two treatment groups, the score in the integrated treatment group ( $5.30 \pm 5.48$ , median 4.0) was also significantly lower than that ( $9.14 \pm 7.24$ , median 6.0,  $Z = 3.45$ ;  $p = 0.034$ ) of the group treated with Western medicine alone (Fig. 7). However, among the patients with normal SARS, the difference between the integrated treatment group ( $3.99 \pm 4.67$ , median 3.0) and the group treated with Western medicine alone ( $4.59 \pm 5.22$ , median 4.0) was not significant ( $Z = 1.17$ ;  $p = 0.12$ ), which suggested that intervention with integrated treatment in the early stage of disease can help reduce lung inflammation and that this tendency was more pronounced in the patients with severe SARS.

*Fig. 6. Total score (median) of lung inflammation on chest radiographs of patients within 7 days after onset of SARS*

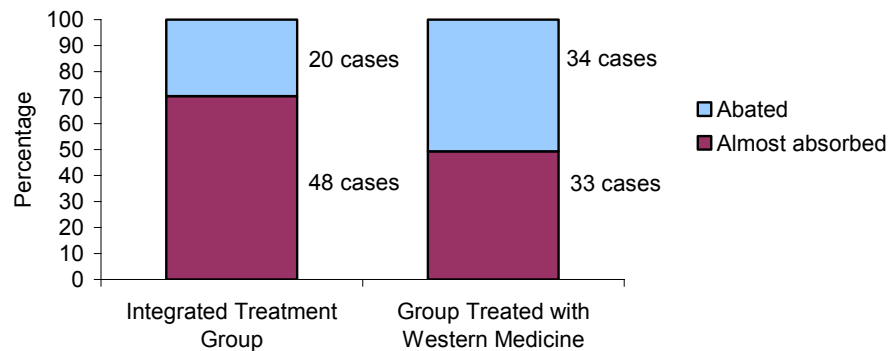


*Fig. 7. Total score (median) of lung inflammation on chest radiographs of patients with severe disease treated within 7 days after onset of SARS*



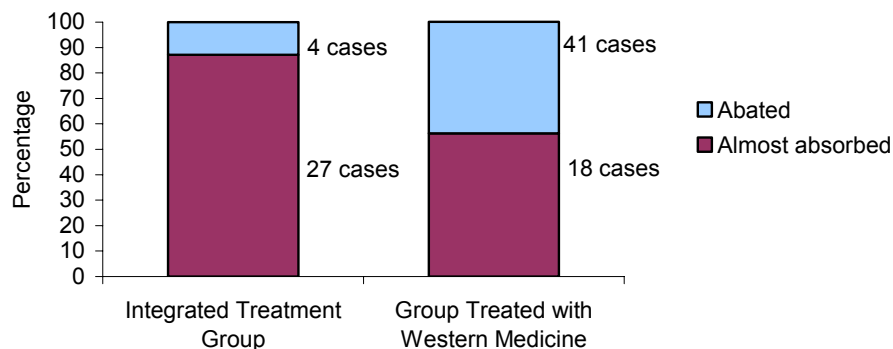
Report 9 described the observations on 135 SARS patients after a treatment period of 3 weeks. It was found that among the 68 patients included in the integrated treatment group, the inflammation in the lungs of 48 of the patients was almost absorbed and that of the remaining 20 patients was abated, whereas in the group treated with Western medicine alone, the inflammation in the lungs of 33 patients was almost absorbed and the remaining 34 patients showed no obvious improvement. The difference between the two groups was statistically significant ( $p = 0.014$ ) (Fig. 8).

**Fig. 8. Absorption of lung inflammation in 135 patients with SARS after 3 weeks of treatment (data from Report 9)**



Report 7 describes the observations on 63 SARS patients. After a treatment period of 3 weeks the lung inflammation of 27 (out of 31) cases in the integrated treatment group was almost absorbed, whereas the corresponding number in the group treated with Western medicine was 18 (out of 32 cases); the difference between the two treatment groups was statistically significant ( $p < 0.05$ ) (Fig. 9).

**Fig. 9. Absorption of lung inflammation in 63 patients with SARS after 3 weeks of treatment (data from Report 7)**



Report 5 described a study in which 11 patients with normal SARS were treated with TCM alone. The average absorption time for the lung shadows in nine of the patients was  $14.56 \pm 6.71$  days, indicating that the treatment with TCM facilitated the absorption of lung inflammation.

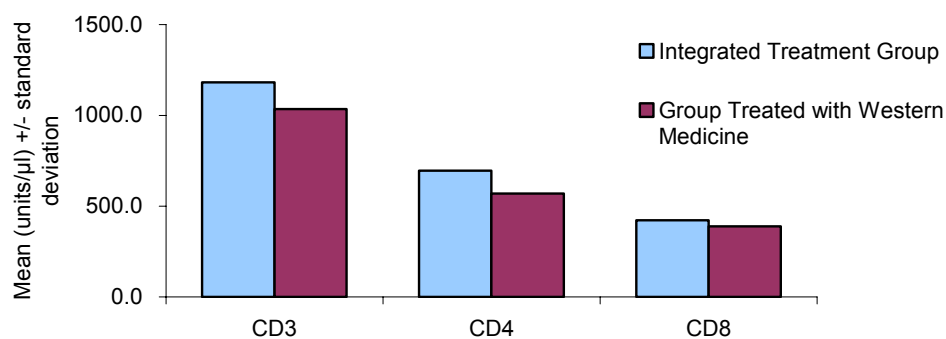
## Degree of blood oxygen saturation

The study described in Report 2 used the logistic regression model with SAS statistical software in a study of 447 SARS patients. An analysis of the difference in blood oxygen saturation between the two treatment groups found that there was no significant difference between the groups after 0–2 days of treatment ( $p = 0.4464$ ) when compared with that of the group treated with Western medicine alone. However, after a treatment period of 3–14 days, and after 15 days, the difference between the two groups was significant ( $p = 0.0038$  and  $p = 0.0007$ , respectively), which indicates that the integrated treatment can reduce the likelihood of reduced blood oxygen saturation. More specifically, from day 3 to day 14, the odds ratio (OR) of both groups was  $\exp(-0.6582) = 0.5178$ , and after day 15,  $\text{OR} = \exp(-1.4164) = 0.2426$ . After adjustment for age, for the patients with normal SARS, the results of the integrated treatment and the treatment with Western medicine alone were not significantly different ( $p = 0.4745$ ) in reducing the risk of low blood oxygen saturation. However, for the severely ill patients, the integrated treatment was superior to the treatment with Western medicine alone in reducing the risk of low blood oxygen saturation:  $\text{OR} = \exp(-1.7173) = 0.18$  ( $p = 0.0001$ ). The observations recorded in Report 3 and other reports on the blood oxygen saturation of 45 patients with severe SARS on day 7, day 13 and day 23 suggested that the integrated treatment can help stabilize the abnormal fluctuations in blood oxygen saturation.

## Immunological functions

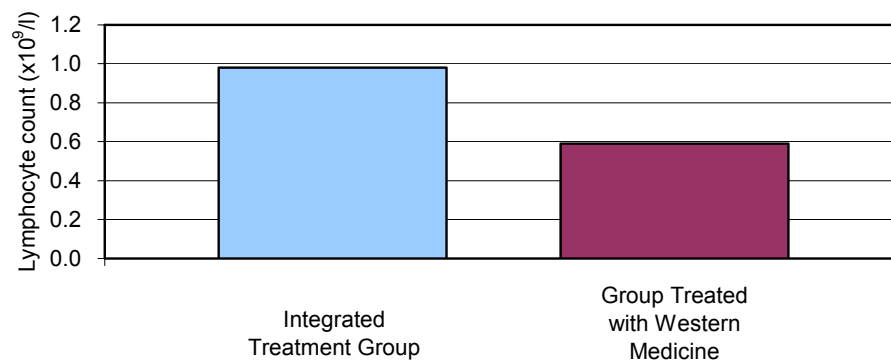
Report 9 was a study on the peripheral blood lymphocytes and T-lymphocyte subpopulations of 135 patients with SARS. The counts of peripheral blood lymphocytes and T-lymphocyte subpopulations in the integrated treatment group after 20 days of treatment (mean  $\pm$  standard error of blood lymphocytes, CD3, CD4 and CD8 were  $1.84 \pm 0.12 \times 10^9/l$ ,  $1182.48 \pm 67.24$  units/ $\mu l$ ,  $695.21 \pm 46.33$  units/ $\mu l$  and  $421.65 \pm 27.30$  units/ $\mu l$ ) exceeded those of the group treated with Western medicine alone (mean  $\pm$  standard error of blood lymphocytes, CD3, CD4 and CD8 were  $1.54 \pm 0.14 \times 10^9/l$ ,  $1034.38 \pm 70.94$  units/ $\mu l$ ,  $570.29 \pm 40.36$  units/ $\mu l$  and  $389.81 \pm 36.40$  units/ $\mu l$ ), and the  $p$  values were 0.458, 0.027, 0.034 and 0.006 respectively (Fig. 10).

**Fig. 10.** Peripheral blood T lymphocyte subpopulations (mean  $\pm$  standard error  $\times$  count/ $\mu l$ ) in 135 patients with SARS after 20 days of treatment (data from Report 9)



Report 8 compares the counts of lymphocytes before and after the treatment of 35 (out of 47) SARS patients who had abnormal counts of lymphocytes in peripheral blood before treatment. The results showed that the increase in the count of peripheral blood lymphocytes ( $0.98 \pm 0.65 \times 10^9/l$ ) in patients in the integrated treatment group before and after treatment was greater than that ( $0.59 \pm 0.34 \times 10^9/l$ ,  $p = 0.0332$ ) of the group treated with Western medicine alone. For the nine cases in the integrated treatment group and 10 in the group treated with Western medicine alone who had abnormally low CD3 levels before the treatment, after being treated for 3 weeks, the numbers of cases that had normalized were seven and two respectively ( $p = 0.023$ ). Fifteen patients in the integrated treatment group and 13 in the group treated with Western medicine alone had abnormally low CD4/CD8 counts before the treatment, the numbers that had returned to normal after the treatment were 10 and three, respectively ( $p = 0.03$ ) (Fig. 11). The number of patients in the integrated treatment group with T-lymphocyte subpopulations that had been normalized tended to be greater than that in the group treated with Western medicine alone.

**Fig. 11. Differential values ( $X \pm SD \times 10^9 / \mu l$ ) of peripheral blood lymphocytes in 47 patients with SARS before and after treatment**

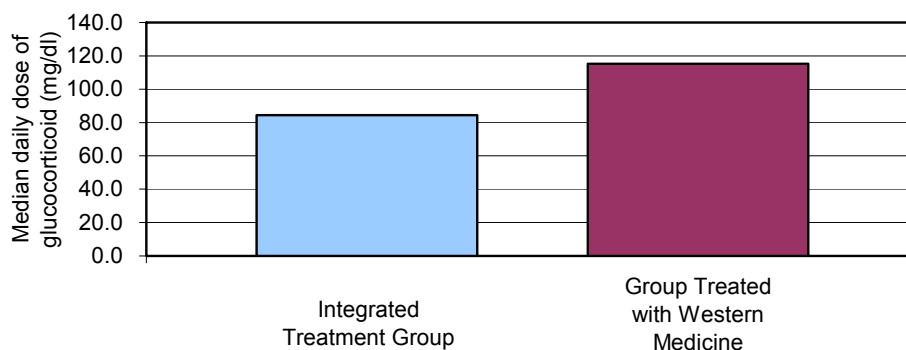


### Administration of glucocorticoid

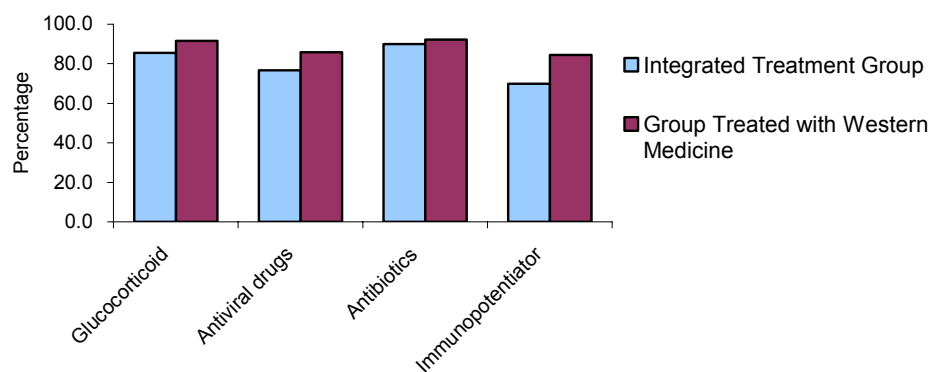
The analysis described in Report 2 on the dosage of glucocorticoid administered to 461 hospitalized SARS patients in the integrated treatment group showed that the average daily dosage of hormone (calculated on the basis of methylprednisolone) administered during the hospitalization period was  $115.78 \pm 87.51$  mg/day with a median of 84.40 mg/day. The average daily dose administered to patients in the group treated with Western medicine was  $130.78 \pm 85.63$  mg/day with a median of 115.33 mg/day. The dosage of hormone used in the integrated treatment group was obviously less than that in the Western medicine treatment group ( $p < 0001$ ) (Fig. 12). Report 2 also showed that, of the 318 patients in the integrated treatment group and 206 patients in the group treated with Western medicine, the numbers of patients who had received antiviral drugs were 244 (76.7%) and 177 (85.9%), the numbers who had received antibiotics were 286 (89.9%) and 190 (92.2%), the numbers treated with glucocorticoid were 272 (82.9%) and 189 (96.4%), and the numbers who had received an immunopotentiator were 222 (69.8%) and 174 (84.5%) (Fig. 13). Except for antibiotics ( $\chi^2 = 0.712$ ,  $p = 0.374$ ), the difference between the use of antiviral drugs ( $\chi^2 = 6.690$ ,  $p = 0.01$ ), hormone ( $\chi^2 = 4.529$ ,  $p = 0.033$ ) and

immunopotentiator ( $\chi^2 = 15.544$ ,  $p = 0.001$ ) for the two treatment groups was significantly different, suggesting that the use of antiviral drugs, glucocorticoid and immunopotentiator in the integrated treatment group was lower than that in the group treated with Western medicine.

**Fig. 12.** *The dosage of glucocorticoid administered to 461 patients with SARS during hospitalization (median mg/day)*



**Fig. 13.** *Percentage of patients treated with glucocorticoid, antiviral drugs, antibiotics and immunopotentiator (data from Report 2)*



Report 5 stated that 11 patients with normal SARS who were admitted to hospital and treated with TCM alone, without using hormone, recovered and were discharged from hospital. Report 4, describes how 34 SARS patients (including 20 severe cases and 14 normal cases) who received integrated treatment without hormone all recovered and were discharged from hospital.

#### **Case fatality rate**

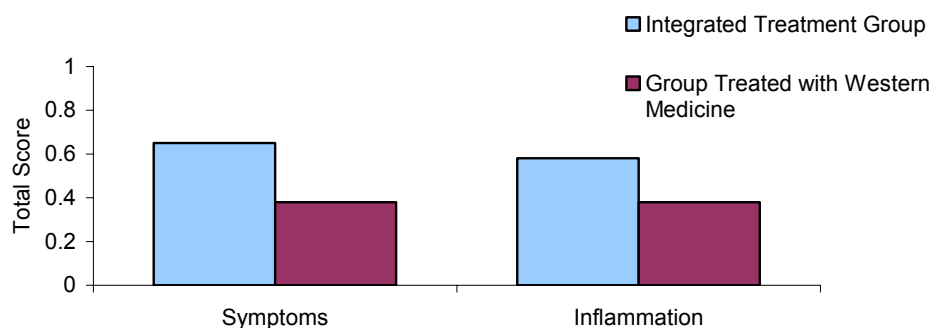
Report 2 gives details on the clinical outcome of 524 SARS patients. The investigators observed that there were no deaths in the group of 318 patients treated with integrated medicine, but seven out of the 206 patients in the group treated with Western medicine alone died (3.4%). The seven patients who died were 40 years old or more, and three of them had underlying diseases, three had none and the condition of the other was unclear. Report 9 described the final outcome of the treatment of 135 patients with SARS. It was reported that one of

the 68 patients in the integrated group died, and seven in the group treated with Western medicine alone died. Report 3 presented observations on 45 patients with severe SARS and showed that the case fatality rate was 20% (5/25) in the integrated treatment group and 30% (6/20) in the group treated with Western medicine alone. Report 7 followed 31 patients who received the integrated treatment, and the case fatality rate was 9.67% (3/31) after 3 weeks of treatment. The case fatality rate was 12.5% in the group treated with Western medicine alone: there were four deaths among the 32 cases).

### Treatment during the convalescent stage

Report 10 presents observations on 85 patients convalescing from SARS over a period of 2–3 weeks. The investigators reported that the scores for improvement in the patients' symptoms after treatment with TCM recipes were superior to those obtained in the control group. (The total scores (mean  $\pm$  standard error) for improvement of the symptoms in the TCM group and the control group before and after treatment were  $0.65 \pm 0.06$  and  $0.38 \pm 0.14$  respectively,  $p < 0.05$ ) and TCM treatment was also more effective in improving lung inflammation. (The scores for relieving inflammation as judged from chest X-rays of the group that received TCM and the control group before and after the treatment were  $0.58 \pm 0.05$  and  $0.38 \pm 0.08$  respectively.) (Fig. 14).

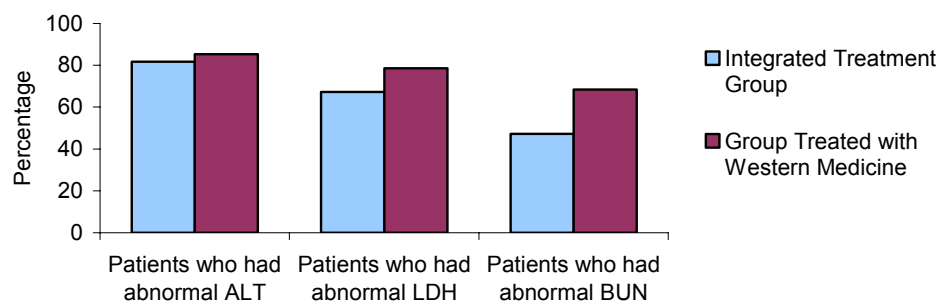
*Fig. 14. Comparison of scores for symptoms and inflammation in 85 patients convalescing from SARS (mean  $\pm$  standard deviation)*



### Alanine aminotransferase, lactate dehydrogenase and urea nitrogen

From observations conducted during the treatment of 524 SARS patients, the authors of Report 2 noted that the number and the incidence rate of patients whose alanine aminotransferase (ALT), lactate dehydrogenase (LDH) and blood urea nitrogen (BUN) levels were outside the normal range at least once in the group that received integrated treatment (318 cases) were 260 (81.8%), 214 (67.3%) and 150 (47.2%) respectively, whereas the number of cases and the incidence rate in the group treated with Western medicine alone were 176 (85.4%), 162 (78.6%) and 141 (68.4%), respectively (Fig. 15). These data show that the occurrence of abnormal increases in ALT, LDH and BUN in the group treated with Western medicine alone tended to be greater than that in patients in the integrated treatment group.

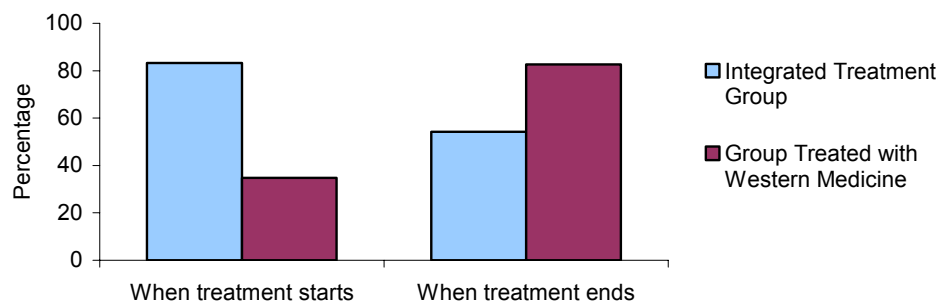
**Fig. 15. Incidence rate of abnormal alanine aminotransferase, lactate dehydrogenase and blood urea nitrogen in 524 patients with SARS (data from Report 2)**



ALT, alanine aminotransferase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen

The follow-up observation on 47 SARS patients described in Report 6 showed that, during the observation period, all the 47 patients showed an abnormal rise of ALT. The numbers of patients with abnormally elevated ALT in the integrated group and the group treated with Western medicine alone at the time when the treatment was started were 20 and eight respectively, and the numbers at the end of the course were 13 and 19 respectively (Fig. 16). The numbers of patients who had an abnormal rise in total bilirubin in the integrated treatment group and the group treated with Western medicine alone at the start of treatment were 11 and six respectively, and at the end of the course, only one patient in each group had an abnormally high concentration, which suggests that the integrated treatment for SARS is safe.

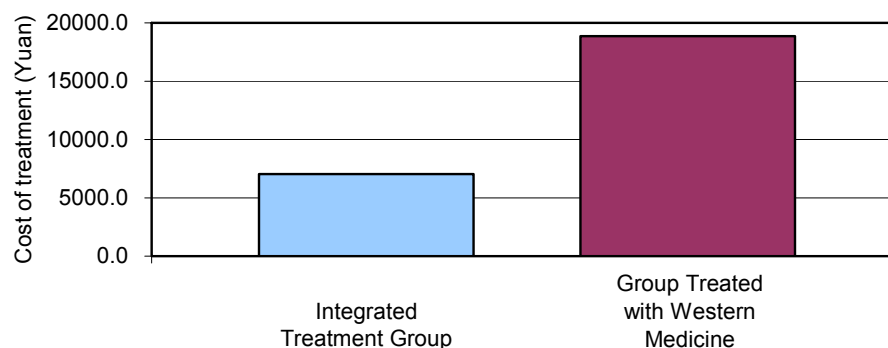
**Fig. 16. Incidence rate of abnormal alanine aminotransferase in 47 patients with SARS before and after treatment (data from Report 6)**



### **Cost of treatment**

Report 5 stated that the average cost for the treatment of 11 SARS patients with TCM was 7 024.41 Yuan, whereas that for the treatment with Western medicine of concurrent cases with an identical state of illness was 18 867.36 Yuan (Fig. 17).

*Fig. 17. Comparison of average cost (Yuan) for treating patients with SARS (data from Report 5)*



## Discussion

### Relative advantages of treatment with Traditional Chinese medicine

There are certain advantages in treatment with TCM.

- ◆ Firstly, TCM is not targeted only at a specific etiology or a certain pathological link, but also at the pathological status of the patients at that particular time. Therefore, comprehensive readjustment was made through various angles, targets and channels to restore the balance of the body.
- ◆ Secondly, there are advantages in the differentiation of disease and the treatment. Based on the different symptoms of the patient, TCM enables the physician to adopt the most suitable principle, provide individual treatment and to administer medicine in accordance with the actual process and nature of the illness.
- ◆ Thirdly, there are advantages in the results of the treatment; TCM can relieve symptoms, promote absorption of lung inflammation, improve the degree of blood oxygen saturation, regulate immunological functions, reduce the required dosage of glucocorticoid and other Western medicines, and reduce case fatality rate, in addition to lowering the cost of treatment.

### Problems with the research

Although the researchers tried their best to take measures to perfect the design and to reduce possible bias, the SARS studies were generally initiated urgently under the most severe conditions of the outbreak. A lack of medical resources meant the clinical workload was very heavy. The clinical research on SARS has encountered many difficulties that have not been met before in normal clinical research. These can be summarized as follows.

#### *Choice of control group and random allocation of study subjects*

In the clinical research on TCM, the choice of the control group and the testing group as well as the random allocation of cases to the different observation groups is always problematic. Some studies used random allocation of cases, but

most of the clinical studies were cohort studies or case-control studies. In the cohort and case-control studies, attention was paid to the choice of cases, to ensure the balance of factors other than the experimental factors in the different groups. Nevertheless, it is difficult to avoid potential bias when assigning patients to the different treatment groups and to ensure impartiality.

#### ***Loss to follow-up***

To guarantee the timely quarantine and treatment of SARS patients, the Government Departments coordinated the arrangements for the admission and transfer of the patients in a unified way. This caused difficulties in following up the patients, leading to loss of some cases in the observation period. Clinical research on therapy with integrated TCM and Western medicine for SARS patients requires improved study designs.

#### **Suggestions for further work**

*Improve understanding of, and scientifically evaluate the advantages of, TCM in treating acute and infectious diseases.*

TCM and integrated therapeutics are safe and they have shown advantages over Western medicine alone in treating SARS. Clinical research has shown that TCM should be applied early in the course of disease and used rationally taking patients' individual differences into consideration. The research has also suggested that in the case of an outbreak of an acute and infectious disease such as SARS, attention should be paid to the advantages of TCM, so that integrated therapy with TCM and Western medicine can be applied.

*Perfect emergency clinical treatment and the research network of TCM*

It is recommended that the relevant authorities should improve, as soon as possible, the rapid feedback network of clinical TCM practice and research for use in emergency situations. Preparations should be made for large sample studies in the future in case of another outbreak of SARS. Further evaluation of the effectiveness and safety of TCM in treating SARS is desirable.

*Share the experience of treating SARS with TCM*

TCM is the accumulation of thousands of years of experience of the Chinese nation in fighting disease. In the face of unknown reasons for, or complicated pathological causes of, disease, traditional Chinese medical theory and treatment principles have obvious advantages. It will also enable the whole world to share the fruits of Chinese medicine culture, resources and the related industry.

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