Retrospective study of *Pneumocystis* pneumonia over half a century in mainland China

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A retrospective study was performed on case reports of *Pneumocystis* pneumonia (PCP) from 1959 to 2009 in mainland China. The epidemiological characteristics of PCP over half a century were investigated over two time spans. The first was from 1959, when the first incidence of PCP was reported, to 1984, before the emergence of AIDS in mainland China. The second was from 1985, when the first AIDS case was reported in mainland China, to the end of 2009. A total of 2351 PCP cases were reported during these two time spans, covering a 51-year period. Only seven PCP cases were reported during the first time span. Six were diagnosed by autopsy, accordingly without treatment, whilst the other was diagnosed by open lung biopsy in a living patient who eventually recovered following treatment with sulfadiazine and pyrimethamine. The other 2344 PCP cases were reported during the second time span (1985–2009) from 21 provinces, four municipalities and three autonomous regions. Among the 2344 PCP cases, 70.22 % (1646/2344) were identified together with human immunodeficiency virus (HIV) infection or were in AIDS patients. The remaining 698 non-HIV-infected patients had undergone organ transplantation, had other underlying diseases such as malignancy or hyp immunity, or had undetermined diagnosis. The results of statistical analysis indicated that AIDS was the most common underlying disease of PCP for patients <1 year and >14 years. For patients aged between 1 and 14 years, haematological malignancy was the most common underlying disease. The trend of the underlying diseases changed with time, showing that the number of PCP patients afflicted by HIV/AIDS increased dramatically, reaching almost threefold during the most recent 5 years compared with the level of the previous 10 years. The number of patients undergoing organ transplantation or with other underlying diseases rose constantly, but the number of malignancies tended to decline from 1995–2004 to 2005–2009. During the second time span (1995–2009), most of the patients (97.61 %) were diagnosed alive and only 56 cases (2.39 %) were identified by autopsy. The mortality of PCP patients treated with anti-*Pneumocystis* drugs was 14.61 % for those with HIV/AIDS and 15.84 % for those without HIV/AIDS. For the PCP patients without anti-*Pneumocystis* treatment, all (100 %) of the HIV/AIDS-associated PCP patients died, whilst 13.79 % (4/29) of non-HIV-infected PCP patients survived. These data from epidemiological investigation of PCP in China over a period of half a century may provide useful information for prevention and the development of treatment of PCP.

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INTRODUCTION

Pneumocystis pneumonia (PCP), which most commonly occurs in immunocompromised individuals, is a serious

and lethal opportunistic infection caused by *Pneumocystis jirovecii* (formerly *Pneumocystis carinii* f. sp. *hominis*). A number of factors can predispose people to PCP, such as AIDS, malignancies, congenital immunodeficiencies and immunosuppressive therapy for people who have undergone organ transplantation. During the early years of the AIDS epidemic, PCP was the AIDS-defining illness and the

Abbreviations: BALF, bronchoalveolar lavage fluid; HAART, highly active antiretroviral therapy; PCP, *Pneumocystis* pneumonia; TMP–SMZ, trimethoprim–sulfamethoxazole.

major cause of human immunodeficiency virus (HIV)/AIDS-associated morbidity and mortality. In developed countries, the incidence of PCP has declined as a result of the highly active antiretroviral therapy (HAART) administered to HIV-infected people and as a result of effective prophylaxis (Lian *et al.*, 2007), but PCP remains the leading cause of opportunistic infection in the AIDS population without any medication or with HIV drug resistance (Kaplan *et al.*, 2000; Morris *et al.*, 2004).

In developing countries, PCP occurs frequently (Fisk *et al.*, 2003) and has shown an increasing trend in recent years (Abouya *et al.*, 1992; Carme *et al.*, 1991; Fisk *et al.*, 2003; Machiels & Urban, 1992). In the HIV-negative population, the incidence of PCP was rare in history and limited mainly to those with congenital immunodeficiency, organ transplantation/immunosuppressive regimens and malignancy. The increased use of immunosuppressive agents for organ transplantation and the increased administration of chemotherapeutic regimens for malignancy have resulted in an increasing number of non-HIV-infected PCP cases (De Castro *et al.*, 2007).

The epidemiological characteristics and outcome of HIV/AIDS-associated PCP in developed countries have shifted multiple times over the course of the AIDS epidemic (Morris, 2008; Walzer *et al.*, 2008). However, epidemiological data on PCP are lacking in mainland China. The aim of this study was to review the history of PCP in mainland China from 1959 to 2009, and to investigate the geographical and periodic distribution from the following aspects: age, gender, underlying diseases, diagnostic methods, treatment procedures and prognosis. It is hoped that the data obtained from this study will be useful for developing a strategy for prevention and treatment of PCP in China and developing countries.

METHODS

The retrieval study was conducted by searching Medline, Pubmed and the China National Knowledge Infrastructure, WANFANG and VIP databases. PCP case reports that had occurred in mainland China up to the end of 2009 were collected by searching the databases for '*Pneumocystis carinii*', '*Pneumocystis jiroveci*', '*Pneumocystis pneumonia*' or 'PCP' within the full text. Two PCP cases reported in 1959 and 1979 were obtained manually because they were inaccessible online.

The reported PCP cases and articles were identified and filtered either by detecting *Pneumocystis* or *Pneumocystis*-specific DNA or by overall consideration of the clinical symptoms, physical signs and patients' response to anti-*Pneumocystis* treatments. Repeated cases were excluded.

We collected and sorted the features of the PCP cases considering the following aspects: age, gender, locality where PCP was diagnosed, underlying diseases, diagnostic methods, treatment procedure and prognosis. Outcomes were described either as survival with relief of symptoms after a regimen of PCP treatment or as death. We investigated the epidemic characteristics over two time spans: the first from 1959, when the first incidence of PCP was reported, to 1984, before the emergence of AIDS in mainland China, and the second

from 1985, when the first AIDS case was reported in mainland China, to the end of 2009. To gain insight into changes in PCP over time in terms of underlying diseases, diagnostic methods, treatment and prognosis, we further divided the second span into three time intervals. Each of the first two intervals (1985–1994 and 1995–2004) covered 10 years, whilst the last interval (2005–2009) covered the remaining 5 years. As underlying diseases are important predisposing factors for PCP, we investigated them within each of four age groups: <1 year, 1–14 years, 15–60 years and >60 years.

RESULTS

The history of PCP in mainland China

The earliest PCP cases in China were reported by Jirovec in 1959 (Chinese Academy of Medical Sciences, 1959). Jirovec investigated the lung tissue of children who had died of interstitial pneumonia in the hospital of Peking Union Medical College and found two cases of infection with *Pneumocystis*. The first adult PCP case was reported in Shanghai, China, by Xu *et al.* (1979), and involved a post-renal transplantation patient, identified by antemortem open-lung biopsy. The first HIV/AIDS-associated PCP case was determined in 1985 (Ministry of Health of the People's Republic of China, <http://www.moh.gov.cn/publicfiles/business/htmlfiles/mohbgt/s3582/200911/44754.htm>), and was that of a foreign AIDS patient who died of PCP while travelling in Beijing, China. Among tumour patients, 16 child cases of PCP were reported in 1987 (Yang *et al.*, 1987). All were diagnosed with acute leukaemia and complicated with PCP during leukaemic remission following chemotherapy in Peking Children's Hospital. Two of the cases were identified by the presence of *Pneumocystis* in the organs by autopsy, whilst the remaining 14 case patients were hospitalized in the same ward and diagnosed by clinical symptoms. The first detected *Pneumocystis* in bronchoalveolar lavage fluid (BALF) from renal transplant recipients was reported in Shenyang in 1996 by An & Tanabe (1996).

PCP cases from 1959 to 1984

Only seven PCP cases (five male, two female) were reported during the first time span: four in Beijing and three in Shanghai. Four *Pneumocystis* infections occurred in 1-year-olds, all of whom were born with immunodeficiencies and were diagnosed by autopsy, accordingly with no anti-*Pneumocystis* treatment. The other three were distributed in the age range 15–60 years, whose underlying diseases were renal transplantation/immunosuppressive regimens. One was diagnosed by open-lung biopsy and finally recovered following treatment with sulfadiazine and pyrimethamine, whilst the other two were diagnosed by autopsy and died left untreated (Table 1).

PCP cases from 1985 to 2009

There were 2344 cases in total reported during this second time span from 21 provinces, four municipalities and three

Table 1. Overall data on PCP cases occurring before 1985 ($n=7$)

Characteristic	Locality		Total
	Beijing	Shanghai	
Gender			
Male	3	2	5
Female	1	1	2
Age (years)			
<1	2	2	4
15–60	2	1	3
Underlying disease			
Congenital immunodeficiency	2	2	4
Kidney transplantation	2	1	3
Diagnostic methods			
Autopsy	4	2	6
Lung biopsy	0	1	1
Treatment			
Sulfadiazine and pyrimethamine	0	1	1
No corresponding treatment	4	2	6
Prognosis			
Survival	0	1	1
Death	4	2	6

autonomous regions in mainland China. There were no PCP case reports from Hainan province, Tibet and Neimenggu autonomous region (Fig. 1). We sorted these

cases according to six factors: gender, age, underlying diseases, diagnostic methods, treatment and prognosis.

Detailed information for these 2344 cases with regard to the distribution for locality, gender and age is shown in Fig. 1 and Table 2. The PCP cases reported in six regions – Guangxi (500 cases), Henan (370 cases), Beijing (352 cases), Guangdong (346 cases), Shanghai (108 cases) and Zhejiang (105 cases) – accounted for 76.40 % (1781/2344) of the total cases, with more than 100 cases in each region (Fig. 1). Analysis of gender distribution found that nearly two-thirds of the case patients were male, twice as many as the number of females (1561 and 753, respectively), with the gender in the remaining 30 cases unreported (Table 2). In terms of age distribution, 85.37 % (2001/2344) of the *Pneumocystis* infections were diagnosed in patients between the ages of 15 and 60 years. The age groups of 1–14 years and over 60 years comprised 5.20 and 4.27 % of the cases, respectively. For patients <1 year old, only 21 cases (0.90 %) were reported. The ages in the remaining 100 cases were unknown (Table 2).

The underlying diseases of PCP patients in China during the second time span (1985–2009) are shown in Tables 2 and 3 and Fig. 2. They were more varied compared with those during the first time span (1959–1984). We analysed the data from three aspects: the underlying disease of the PCP patients at different ages (Table 3), the occurrence of common underlying diseases in different time spans (Fig.

Fig. 1. Geographical distribution of PCP cases in mainland China. PCP cases were reported from 21 provinces, four municipalities and three autonomous regions in mainland China, but not from Hainan province, Tibet and Neimenggu autonomous region.

Table 2. Overall data on PCP cases occurring from 1985 to 2009 ($n=2344$)

Characteristic	No. PCP cases
Gender	
Male	1561
Female	753
Unknown	30
Age (years)	
<1	21
1–14	122
15–60	2001
>60	100
Unknown	100
Underlying disease	
AIDS	1646
Renal transplantation	411
Periosteum transplantation	1
Liver transplantation	12
Bone marrow stem cell transplantation	5
Antitumour therapy	116
Other immunocompromising diseases	143
No underlying disease	2
Unknown	8
Diagnostic method	
Sputum/BALF/biopsy	1146
Autopsy	56
PCR	38
Clinical diagnosis	1104
Treatment	
SMZ	1673
SMZ and caspofungin	10
SMZ and clindamycin	17
Caspofungin	6
Clindamycin	19
Pyrimethamine	2
Chinese drugs	1
No corresponding treatment	62
Unknown	554
Prognosis	
Survived	1447
Died	302
Unknown	595

2), and the gender ratio of male:female in patients with AIDS and in patients with organ transplantation (the most common underlying disease in non-HIV-infected PCP patients). For patients <1 year old, congenital diseases, including immunodeficiency, autoimmune diseases, trisomy 21 syndrome and cardiac abnormalities, accounted for up to 38.10% (8/21) of the cases, with AIDS comprising the largest percentage (11/21; 52.38%), whereas in other age groups, congenital diseases were negligible (Table 3). In patients aged 1–14 years, those with haematological malignancies accounted for the majority of cases (79/122; 64.75%), followed by AIDS (37/122; 30.33%). In the 15–60 years age group, AIDS was the leading disease underlying PCP, reaching 73.06% (1462/2001). After

AIDS came organ transplantation (418/2001; 20.89%), most of which was renal transplantation. Patients with malignancies comprised only a minor portion (28/2001; 1.40%). In the age group >60 years, AIDS remained the most common underlying disease at 36% of cases (36/100). However, gerontological diseases, such as long-term hospitalization or long-term mechanical ventilation because of pulmonary disease, severe pneumonia, coronary heart diseases and cardiac insufficiency, comprised up to 19% and became the second leading underlying disease in this group. Organ transplantation (11/100; 11%) was the third leading cause. Malignancies at 9% within this age group constituted another important risk factor (Table 3). The ratio of male:female patients was about 2.1:1 (1113:523), with the gender in the remaining ten cases unclear in the AIDS-associated PCP group. A gender ratio of 2.9:1 (319:110) was found in the organ transplantation group. During the three time intervals (1985–1994, 1995–2004 and 2005–2009), the number of PCP patients afflicted by HIV/AIDS rose dramatically with time, with the value during the last 5 years reaching threefold that of the previous 10 years. The number of patients undergoing organ transplantation and with other underlying diseases rose steadily, but the number of malignancies tended to decline from 1995–2004 to 2005–2009, as shown in Fig. 2.

The diagnostic methods applied in this study included microscopic diagnosis, involving detection of *Pneumocystis* by sputum test/BALF test/lung biopsy or autopsy, PCR and clinical diagnosis. Clinical diagnosis was made by overall consideration of the patients' clinical symptoms, physical signs, X-rays, CT scans and efficiency of anti-*Pneumocystis* treatment, rather than by detecting the pathogen directly. The data showed that most of the PCP cases (97.61%) were diagnosed while the patient was alive by detecting *Pneumocystis* from sputum/BALF/biopsy tissues or by clinical diagnosis. Only 56 cases (2.39%) were identified by autopsy (Table 2). Although the proportion diagnosed by microscopy did not differ much among the three time intervals (data not shown), the percentage of microscopic diagnosis made by detecting the pathogen by sputum/BALF/biopsy and the percentage of microscopic diagnosis made by autopsy generally changed reciprocally, with increasing numbers of cases being identified while the patient was alive (data not shown). This may have been the result of increasingly widespread use of newly developed diagnostic methods, such as Gömöri methenamine silver staining, or increased awareness of PCP by physicians. PCR tests used for the diagnosis of PCP began to appear after 2005 and only included a small proportion (1.62%) of all the cases (Table 2).

Trimethoprim–sulfamethoxazole (TMP–SMZ) was the drug predominantly used and was used for 71.37% (1673/2344) of the PCP patients. Other drugs, such as caspofungin, clindamycin, traditional Chinese medicine and pyrimethamine, were only used in 2.35% (55/2344) of the cases. The remaining 26.28% (616/2344) of patients were not treated or did not report the relevant information

Table 3. Underlying diseases of PCP patients in different age groups from 1985 to 2009

Underlying disease	Age (years)					Total
	<1	1–14	15–60	>60	Unknown	
AIDS	11	37	1462	36	100	1646
Renal transplantation	0	0	401	10	0	411
Liver transplantation	0	0	11	1	0	12
Periosteum transplantation	0	0	1	0	0	1
Bone marrow stem cell transplantation	0	0	5	0	0	5
Haematological malignancy	0	79	26	3	0	108
Lung cancer	0	0	2	5	0	7
Prostate cancer	0	0	0	1	0	1
Long-term hospitalization or long-term mechanical ventilation	0	0	0	11	0	11
Severe pneumonia	1	0	0	4	0	5
Chronic obstructive pulmonary disease	0	0	0	4	0	4
Congenital immunodeficiency	3	0	0	0	0	3
Thrombocytopenic purpura	3	0	0	0	0	3
Cardiac anomalies	1	0	0	0	0	1
Trisomy 21 syndrome	1	0	0	0	0	1
Congenital absence of the thymus	0	1	0	0	0	1
Other	1	5	93	25	0	124
Total	21	122	2001	100	100	2344

(Table 2). PCP cases in all three time intervals with both defined treatment and defined prognosis were analysed. The result demonstrated that drugs other than TMP–SMZ were reported to be initiated for the treatment of PCP from 1995 onwards, and the percentage continued to rise from

0.26 % (1/387) during 1995–2004 to 4.31 % (54/1253) during 2005–2009, regardless of the cases with unknown treatment regimen or prognosis. In the TMP–SMZ treatment group, 1377 patients survived and 242 patients died, and the overall mortality was 14.95 %, as shown in Table 4.

In the group with anti-*Pneumocystis* treatment, the mortality of PCP patients with HIV/AIDS and of the non-HIV-infected population was 14.61 and 15.84 %, respectively. In the group without anti-*Pneumocystis* treatment, all (100 %) of the HIV/AIDS-associated PCP patients died, and 13.79 % (4/29) of non-HIV-infected PCP patients survived (Table 5).

Fig. 2. Trends in the common underlying diseases of PCP cases in the different time spans. ◆, AIDS; ■, transplantation; ▲, cancer; ●, others. The number of HIV/AIDS-associated PCP patients was low during the period 1985–1994. After 1995, the number rose dramatically, and increased almost threefold during 2005–2009 compared with the period 1995–2004. The number of patients undergoing organ transplantation or with other diseases rose steadily, whilst the number of patients with malignancies appeared to decline from 1995–2004 to 2005–2009.

DISCUSSION

All the PCP cases (except two very early cases) included in this manuscript were diagnosed in hospital and were reported, and all of the case reports are accessible online. Some PCP cases may have been missed because of no hospitalization, misdiagnosis, no report after PCP diagnosis or because the reports could not be reached online.

During the first time span, only seven PCP cases were reported in Beijing and Shanghai, whilst after 1985, 2344 PCP cases were reported from nearly all regions in mainland China, which suggested that PCP had become widespread in China. This may have been partly a result of the increasing number of immunocompromised patients, especially as a result of the prevalence of AIDS after 1985 and the increasing number of organ transplants, and partly because of increased vigilance in the detection of PCP by medical staff. Among the six regions (Guangxi, Henan,

Table 4. Overall data on the treatment and prognosis of PCP patients during the three time intervals from 1985 to 2009

Time span	TMP-SMZ treatment			Treatment with other drugs		
	Total	Survived	Died	Total	Survived	Died
1985–1994	34	30 (88.24 %)	4 (11.76 %)	0	0	0
1995–2004	386	325 (84.20 %)	61 (15.80 %)	1	1 (100 %)	0
2005–2009	1199	1022 (85.24 %)	177 (14.76 %)	54	44 (81.48 %)	10 (18.52 %)
Total	1619	1377 (85.05 %)	242 (14.95 %)	55	45 (81.82 %)	10 (18.18 %)

Beijing, Guangdong, Shanghai and Zhejiang) with the highest number of PCP cases, Guangxi, Henan and Guangdong showed a severe situation with regard to the spread of AIDS (Gill & Okie, 2007; Sheng & Cao, 2008; Wang, 2007; Yin *et al.*, 2003), with accumulative numbers of HIV/AIDS patients lying in the top five in mainland China. Some big cities, such as Beijing and Shanghai, accumulate a large population of experienced, distinguished doctors, and thousands of patients converged from all over the country to the bigger cities in pursuit of better medication every year. Therefore, higher diagnostic accuracy and a larger number of patients may have led to more PCP cases being determined and reported there.

Analysis of the gender distribution of PCP cases showed that there were nearly twice as many male cases as female cases, both in terms of the overall numbers of PCP cases and of HIV/AIDS-associated PCP cases. This result is different from a study that demonstrated that male and female patients appeared to have an equivalent risk for PCP in the USA (Kaplan *et al.*, 1998), and is also different from a study conducted at the University College London Hospitals, UK, in which 94.3 % of the patients were male (Walzer *et al.*, 2008). This can be explained by gender distribution in patients with different underlying diseases. For PCP patients with AIDS, this may be due to the different ways of HIV transmission in different regions. In China, the main factors for HIV infection were drug addiction and illegal blood donation (Jia *et al.*, 2010; Li *et al.*, 2010; Sheng & Cao, 2008; Wang, 2007), whilst in the London study, researchers declared that the main risk factor was sex with other males (Walzer *et al.*, 2008).

We noticed that the diseases underlying PCP changed dramatically during the study period of half a century. During the first time span, congenital deficiency and renal transplantation comprised nearly equal proportions of the seven PCP cases. However, due to the limitation of the

small number of samples, it is hard for us to draw any reasonable conclusion. After 1985, when the first AIDS patient was discovered, HIV/AIDS predominated as the underlying disease and the number of HIV/AIDS-associated PCP cases increased very rapidly. This rise in number was especially obvious after 1995 when HIV/AIDS entered an intensive epidemic period in mainland China (Gill & Okie, 2007; Sheng & Cao, 2008; Wang, 2007). In non-HIV-infected PCP patients, organ transplantation was the most common underlying disease. Our data illustrated a different result when compared with a French retrospective study (Roblot *et al.*, 2002), which showed that only 8 % of non-HIV-infected PCP patients were organ transplant recipients, whilst 58 % of the patients had haematological malignancies. In our study, malignancies constituted the third most common underlying disease and appeared to decline in number from 1995–2004 to 2005–2009 (Fig. 2). However, this may be not the case, as the latter time period covered a time interval that was half as long as the former. However, this may have reflected how fast AIDS and organ transplantation rose as the leading underlying diseases of PCP. According to the trend showing a shift in the underlying diseases, we believe that the number of HIV/AIDS-associated PCP cases and the number of organ transplant-associated PCP cases will continue to increase in the near future.

We found that there was a difference in the underlying diseases of PCP patients at different ages. For infants (<1 year old), AIDS was the leading underlying disease followed by congenital diseases including congenital immunodeficiency. For children (1–14 years), haematological malignancies accounted for the highest number of underlying diseases. For the patients in the 15–60 years age group, in which 85.24 % (2004/2351) of the PCP cases lay due to the larger age interval and the patients' vulnerability to HIV infection, AIDS predominated as the underlying disease. For patients >60 years, AIDS was still

Table 5. Overall data on the treatment and prognosis of PCP patients with or without HIV/AIDS from 1985 to 2009

Underlying disease	With anti- <i>Pneumocystis</i> treatment			No anti- <i>Pneumocystis</i> treatment		
	Total	Survived	Died	Total	Survived	Died
HIV/AIDS-associated patients	1068	912 (85.39 %)	156 (14.61 %)	15	0	15 (100 %)
Non-HIV-infected patients	606	510 (84.16 %)	96 (15.84 %)	29	4 (13.79 %)	25 (86.21 %)

ranked first, but was less predominant compared with the 15–60 years age group. To our knowledge, this is the first time that differences in the underlying diseases of PCP patients in different age groups have been systemically investigated.

TMP–SMZ is well known for its effectiveness for the prophylaxis of PCP and the treatment of PCP patients who can tolerate it (Ioannidis *et al.*, 1996). It is relatively inexpensive and the risk of adverse effects is generally rare. In our study, the most common drug used for the PCP patients was TMP–SMZ. Up to 85 % of patients survived after administration of TMP–SMZ. Drug resistance has rarely been reported in China. In those who did not respond to TMP–SMZ efficiently, this was most likely because of either the delay in PCP diagnosis or complications with other diseases. There was one HIV/AIDS-associated PCP patient who was diagnosed by clinical diagnosis. She was hypersensitive to TMP–SMZ and was treated by traditional Chinese medicine (the components are as follows: 10 g mahuang, 12 g xingren, 50 g shengshigao, 50 g qinghao, 50 g xianhecao, 30 g danshen, 30 g chaihu, 15 g gancan, in 200 ml; administered orally twice a day). She survived well after the treatment for 2 weeks. As only one case was observed, it is hard for us to conclude that Chinese traditional medicine was effective against PCP, but it is an area that could be researched further to investigate its potential for the treatment of PCP. Some of the PCP patients were not treated for PCP because the diagnoses were made by autopsy, or they could not cover the cost, and some patients gave up treatment after their diagnosis of HIV infection.

Our data demonstrated that the mortality of PCP patients with AIDS in mainland China was 15.79 % (171/1083), regardless of those with unclear prognosis. It was a little higher than that (13.5 %) in a single-centre study conducted in the University College London Hospitals, UK, from June 1985 to June 2006 (Walzer *et al.*, 2008) and that (11.3 %) in a multicentre study by Arozullah *et al.* (2000). The reason might be the delayed or failed diagnosis of AIDS or PCP, insufficiency of the medical care services, or unavailability of HAART treatment, which has only been used for a minority of AIDS patients in recent years. It is uncertain whether the administration of HAART would affect the occurrence and the outcome of PCP. A study performed on patients admitted to the intensive care unit with PCP found that the mortality of PCP patients was substantially lower among those who continued or began HAART during hospitalization (Morris *et al.*, 2003). However, another study performed on non-intensive care unit PCP patients showed that there was no difference in mortality following application of a HAART regimen either before or during hospitalization (Radhi *et al.*, 2008). Information on the application of HAART to AIDS patients with PCP was rare up to the end of 2009. With the increased HAART regimen in mainland China, the impact of HAART administration on the prognosis in PCP patients with AIDS should be investigated.

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REFERENCES

- Abouya, Y. L., Beaumel, A., Lucas, S., Dago-Akribi, A., Coulibaly, G., N'Dhatz, M., Konan, J. B., Yapi, A. & De Cock, K. M. (1992). *Pneumocystis carinii* pneumonia. An uncommon cause of death in African patients with acquired immunodeficiency syndrome. *Am Rev Respir Dis* **145**, 617–620.
- An, C. L. & Tanabe, M. (1996). Four cases of *Pneumocystis carinii* pneumonia in Shengyang, Northeast China. *Kisechugaku Zasshi* **45**, 512–517.
- Arozullah, A. M., Yarnold, P. R., Weinstein, R. A., Nwadiaro, N., McIlraith, T. B., Chmiel, J. S., Sipler, A. M., Chan, C., Goetz, M. B. & other authors (2000). A new preadmission staging system for predicting inpatient mortality from HIV-associated *Pneumocystis carinii* pneumonia in the early highly active antiretroviral therapy (HAART) era. *Am J Respir Crit Care Med* **161**, 1081–1086.
- Carne, B., Mboussa, J., Andzin, M., Mbouni, E., Mpele, P. & Datry, A. (1991). *Pneumocystis carinii* is rare in AIDS in Central Africa. *Trans R Soc Trop Med Hyg* **85**, 80–85.
- Chinese Academy of Medical Sciences (1959). [Two cases of *Pneumocystis carinii* pneumonia]. *Zhonghua Er Ke Za Zhi* **4**, 354 (in Chinese).
- De Castro, N., Pavie, J., Lagrange-Xélot, M. & Molina, J. M. (2007). [*Pneumocystis jiroveci* pneumonia in patients with cancer: is it unavoidable?]. *Rev Mal Respir* **24**, 741–750 (in French).
- Fisk, D. T., Meshnick, S. & Kazanjian, P. H. (2003). *Pneumocystis carinii* pneumonia in patients in the developing world who have acquired immunodeficiency syndrome. *Clin Infect Dis* **36**, 70–78.
- Gill, B. & Okie, S. (2007). China and HIV – a window of opportunity. *N Engl J Med* **356**, 1801–1805.
- Ioannidis, J. P., Cappelleri, J. C., Skolnik, P. R., Lau, J. & Sacks, H. S. (1996). A meta-analysis of the relative efficacy and toxicity of *Pneumocystis carinii* prophylactic regimens. *Arch Intern Med* **156**, 177–188.
- Jia, M., Luo, H., Ma, Y., Wang, N., Smith, K., Mei, J., Lu, R., Lu, J., Fu, L. & other authors (2010). The HIV epidemic in Yunnan Province, China, 1989–2007. *J Acquir Immune Defic Syndr* **53** (Suppl. 1), S34–S40.
- Kaplan, J. E., Hanson, D. L., Navin, T. R. & Jones, J. L. (1998). Risk factors for primary *Pneumocystis carinii* pneumonia in human immunodeficiency virus-infected adolescents and adults in the United States: reassessment of indications for chemoprophylaxis. *J Infect Dis* **178**, 1126–1132.
- Kaplan, J. E., Hanson, D., Dworkin, M. S., Frederick, T., Bertolli, J., Lindegren, M. L., Holmberg, S. & Jones, J. L. (2000). Epidemiology of human immunodeficiency virus-associated opportunistic infections in the United States in the era of highly active antiretroviral therapy. *Clin Infect Dis* **30** (Suppl. 1), S5–S14.
- Li, N., Wang, Z., Sun, D., Zhu, Q., Sun, G., Yang, W., Wang, Q., Nie, Y. & Wu, Z. (2010). HIV among plasma donors and other high-risk groups in Henan, China. *J Acquir Immune Defic Syndr* **53** (Suppl. 1), S41–S47.

- Lian, Y. L., Heng, B. S., Nissapatorn, V. & Lee, C. (2007). AIDS-defining illnesses: a comparison between before and after commencement of highly active antiretroviral therapy (HAART). *Curr HIV Res* 5, 484–489.
- Machiels, G. & Urban, M. I. (1992). *Pneumocystis carinii* as a cause of pneumonia in HIV-infected patients in Lusaka, Zambia. *Trans R Soc Trop Med Hyg* 86, 399–400.
- Morris, A. (2008). Is there anything new in *Pneumocystis jirovecii* pneumonia? Changes in *P. jirovecii* pneumonia over the course of the AIDS epidemic. *Clin Infect Dis* 46, 634–636.
- Morris, A., Wachter, R. M., Luce, J., Turner, J. & Huang, L. (2003). Improved survival with highly active antiretroviral therapy in HIV-infected patients with severe *Pneumocystis carinii* pneumonia. *AIDS* 17, 73–80.
- Morris, A., Lundgren, J. D., Masur, H., Walzer, P. D., Hanson, D. L., Frederick, T., Huang, L., Beard, C. B. & Kaplan, J. E. (2004). Current epidemiology of *Pneumocystis* pneumonia. *Emerg Infect Dis* 10, 1713–1720.
- Radhi, S., Alexander, T., Ukwu, M., Saleh, S. & Morris, A. (2008). Outcome of HIV-associated *Pneumocystis* pneumonia in hospitalized patients from 2000 through 2003. *BMC Infect Dis* 8, 118–127.
- Roblot, F., Godet, C., Le Moal, G., Garo, B., Faouzi Souala, M., Dary, M., De Gentile, L., Gandji, J. A., Guimard, Y. & other authors (2002). Analysis of underlying diseases and prognosis factors associated with *Pneumocystis carinii* pneumonia in immunocompromised HIV-negative patients. *Eur J Clin Microbiol Infect Dis* 21, 523–531.
- Sheng, L. & Cao, W. K. (2008). HIV/AIDS epidemiology and prevention in China. *Chin Med J (Engl)* 121, 1230–1236.
- Walzer, P. D., Evans, H. E., Copas, A. J., Edwards, S. G., Grant, A. D. & Miller, R. F. (2008). Early predictors of mortality from *Pneumocystis jirovecii* pneumonia in HIV-infected patients: 1985–2006. *Clin Infect Dis* 46, 625–633.
- Wang, N. (2007). [The epidemic character of AIDS in China]. *Infect Dis Info* 20, 325–326 (in Chinese).
- Xu, Z. Y., Weng, X. H., Guo, M. Y., Ying, Y. Y., Wang, G. X., Huang, M. Y. & Dai, Z. Y. (1979). [One case report of renal transplant recipient co-infected with *Pneumocystis*, *Cytomegalovirus* and *Aspergillus*]. *Chin J Integr Med* 18, 293–295 (in Chinese).
- Yang, S. Y., Li, X. Q., Zhu, M. Z. & Wang, Q. S. (1987). [Sixteen acute leukemia cases complicated with PCP during the paracmasis of the leukaemia]. *Zhonghua Er Ke Za Zhi* 25, 264–267 (in Chinese).
- Yin, N., Mei, S., Li, L., Wei, F. L., Zhang, L. Q. & Cao, Y. Z. (2003). [Study on the epidemiology and distribution of human immunodeficiency virus-1 and hepatitis C virus infection among intravenous drug users and illegal blood donors in China]. *Zhonghua Liu Xing Bing Xue Za Zhi* 24, 962–965 (in Chinese).