

Human Infection with Hemoplasma in Mainland China

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Abstract: Human infection with hemoplasma has been extensively reported in China. The present study reviews prevalence and outbreaks of human hemoplasma in China. This type of disease may really exist in humans but it may be over-reported because of etiological mis-recognition and/or inadequate diagnostic tests in China. Molecular studies to re-assess the prevalence of human hemoplasma are warranted.

Key words: *Eperythrozoon*, *Hemobartonella*, hemoplasma, outbreak, extensively, China

INTRODUCTION

Hemoplasmas are a group of bacteria that infect animals and animals. They are small epicellular parasites that adhere to the host's erythrocytes which were originally classified as members of the two genera of order *Rickettsiales* namely *Eperythrozoon* and *Haemobartonella*.

There once have been sporadic reports of similar infections in man but these have been poorly characterized (Pitcher and Nicholas, 2005; Hoelzle, 2008). A recent study showed *Mycoplasma haemofelis* like infection in an HIV-positive patient which is the first molecular study to date documenting hemoplasmas infection in human beings (Santos *et al.*, 2008). However, outbreaks of human infection with hemoplasma have been extensively reported in China, this type of disease was called human eperythrosis in China.

PREVALENCE OF HUMAN HEMOPLASMA (HUMAN EPERYTHROOSIS) IN CHINA

In China, human infection with *Eperythrozoon* has been deemed as galactic hazardous to public health and extensive studies have been attempted to assess the prevalence of hemoplasma in selected human populations (Yang *et al.*, 2007; Ma *et al.*, 2005). Since 1991, this disease has been seen sporadically in Inner Mongolia, China (Yang *et al.*, 2007). The number of cases has increased sharply in recently years. Table 1 shows

epidemiological surveys of human hemoplasma carried out between 1992-2009 with 0-100% prevalence and an average of 44.8% (19,691/43,929) people in China were positive.

VISUAL IDENTIFICATION AS THE ONLY CRITERIA FOR HUMAN HEMOPLASMA

However, the lack of an adequate diagnostic test for *Eperythrozoon* hampers the identification of infected human. Although visual identification of hemoplasmas is a subjective way to detect those organisms (Messick, 2004), this approach has been widely used in China. Such diagnostic problem is likely to lead to over-reporting of the prevalence of human hemoplasma in China. At present, reported outbreaks of human eperythrosis in China used only visual identification as criteria for diagnosis but no molecular studies to assess the prevalence have been reported.

UNDEFINED CATEGORIZATION OF HUMAN INFECTION WITH HEMOPLASMA

Hemoplasmas are organisms that are obligated to attach to red blood cells of several mammalian species as well as human (Messick, 2004; Pitcher and Nicholas, 2005; Hoelzle, 2008). But a widely cited case report in China showed that suspected *Eperythrozoon* was able to exist in swollen lymph node of the neck from a patient (Puntaric *et al.*, 1986).

Additional studies have documented that bone marrow are the main location of generation of *Eperythrozoon* in human body (Tai *et al.*, 1998a) and

Table 1: Reported outbreaks of human hemoplasma, according to a range of national and provincial surveys in mainland China carried out between 1992-2009

| Years report | Location city, country, Province) | Number examined | Number infected | Prevalence (%) | References |
|--------------|-----------------------------------|-----------------|-----------------|----------------|-------------------------------|
| 1992 | Inner Mongolia | 79 | 69 | 87.34 | Shi ZB <i>et al.</i> (1992) |
| 1994 | Inner Mongolia | 473 | 412 | 87.00 | Du YF (1994) |
| 1994 | Inner Mongolia | 105 | 90 | 85.00 | Hou JF <i>et al.</i> (1994) |
| 1995 | Linshou, Hebei | 268 | 0 | 0.00 | Shang DQ <i>et al.</i> (1995) |
| 1995 | Inner Mongolia | 100 | 80 | 80.00 | Le FY <i>et al.</i> (1995) |
| 1995 | Nantong, Jiangsu | 82 | 0 | 0.00 | Shang DQ <i>et al.</i> (1995) |
| 1995 | Gaoning, Jiangsu | 396 | 315 | 79.50 | Shang DQ <i>et al.</i> (1995) |
| 1995 | Qing Tongxia, Ningxia | 96 | 16 | 16.70 | Shang DQ <i>et al.</i> (1995) |
| 1996 | Linshou, Hebei | 707 | 0 | 0.00 | Shang DQ <i>et al.</i> (1996) |
| 1996 | Gaoning, Jiangsu | 944 | 790 | 83.69 | Shang DQ <i>et al.</i> (1996) |
| 1996 | Xifeng, Liaoning | 105 | 0 | 0.00 | Shang DQ <i>et al.</i> (1996) |
| 1996 | Fushun, Liaoning | 19 | 0 | 0.00 | Shang DQ <i>et al.</i> (1996) |
| 1997 | Lanzhou, Gansu | 277 | 205 | 70.40 | Tian H <i>et al.</i> (1997) |
| 1997 | Lanzhou, Gansu | 98 | 98 | 100.00 | Li QJ <i>et al.</i> (1997) |
| 1997 | Nanhai, Guangdong | 219 | 113 | 51.60 | Shang DQ <i>et al.</i> (1997) |
| 1997 | Ningshan, Guangxi | 376 | 197 | 52.30 | Shang DQ <i>et al.</i> (1997) |
| 1997 | Nanning, Guangxi | 68 | 35 | 51.40 | Shang DQ <i>et al.</i> (1997) |
| 1997 | Inner Mongolia | 1529 | 540 | 35.32 | Yun X <i>et al.</i> (1997) |
| 1997 | Gaoning, Jiangsu | 463 | 378 | 81.60 | Shang DQ <i>et al.</i> (1997) |
| 1997 | Liaoning | 702 | 0 | 0.00 | Sun GM <i>et al.</i> (1997) |
| 1997 | Xingjiang | 200 | 90 | 45.00 | Shang DQ <i>et al.</i> (1997) |
| 1998 | Inner Mongolia | 1529 | 650 | 35.32 | Tai XZ <i>et al.</i> (1998b) |
| 1998 | Xingjiang | 200 | 90 | 45.00 | Li L <i>et al.</i> (1998) |
| 1998 | Yunnan | 700 | 513 | 73.29 | Huang ZM <i>et al.</i> (1998) |
| 1999 | Fuyang, Anhui | 1301 | 442 | 33.97 | Yang YZ <i>et al.</i> (1999) |
| 1999 | Fuyang, Anhui | 539 | 173 | 32.10 | Yang and Sun (1999) |
| 1995 | Saxian, Fujian | 517 | 218 | 42.17 | Yan WY <i>et al.</i> (1995) |
| 1999 | Yuxi, Yunnan | 4652 | 3470 | 74.59 | Huang ZM <i>et al.</i> (1999) |
| 2000 | Fuyang, Anhui | 624 | 235 | 37.66 | Guo <i>et al.</i> (2000) |
| 2000 | Xuzhou, Jiangsu | 400 | 55 | 7.50 | Yang XC <i>et al.</i> (2000) |
| 2000 | Inner Mangolia | 1529 | 540 | 35.30 | Yang DX <i>et al.</i> (2000) |
| 2000 | Huaipei, Anhui | 1115 | 397 | 35.60 | Li ZY <i>et al.</i> (2000) |
| 2000 | Saxian, Fujian | 986 | 485 | 49.19 | Dong <i>et al.</i> (2000) |
| 2000 | Yuxi, Yunnan | 1149 | 784 | 68.23 | Huang (2000) |
| 2001 | Fuyang, Anhui | 820 | 272 | 33.17 | Li ZY <i>et al.</i> (2001) |
| 2001 | Ningxia | 96 | 16 | 16.70 | Zhang RY <i>et al.</i> (2001) |
| 2001 | Shandong | 776 | 57 | 7.30 | Tao XR <i>et al.</i> (2001) |
| 2002 | Yingchuan, Ningxia | 300 | 123 | 41.00 | Zhang MJ <i>et al.</i> (2002) |
| 2003 | Xingshan, Hubei | 174 | 17 | 6.44 | Zhou CX <i>et al.</i> (2003) |
| 2003 | Dalian, Liaoning | 1051 | 982 | 93.00 | Chen <i>et al.</i> (2003) |
| 2006 | Fuyang, Anhui | 1301 | 442 | 33.97 | Li GL <i>et al.</i> (2006) |
| 2007 | Xingshan, Hubei | 5224 | 2931 | 56.11 | Zhou CX <i>et al.</i> (2007) |
| 2007 | Tibet | 3214 | 103 | 3.12 | Shi GQ <i>et al.</i> (2007) |
| 2007 | Inner, Mangolia | 1450 | 1421 | 98.00 | Du YF <i>et al.</i> (2007) |
| 2007 | Gongshan, Yunnan | 1408 | 960 | 68.18 | He TC <i>et al.</i> (2007) |
| 2008 | Shanghai, Shanghai | 997 | 129 | 12.94 | Zhu M <i>et al.</i> (2008a) |
| 2008 | Shanghai, Shanghai | 3003 | 516 | 17.18 | Zhu M <i>et al.</i> (2008b) |
| 2009 | Taian, Shangdong | 987 | 223 | 22.59 | Han <i>et al.</i> (2009) |
| | Total | 43348 | 19672 | 45.38 | |

bone marrow samples were also collected to assess the prevalence (Yang *et al.*, 2000). Actually, molecular studies should be carried out to clarify whether hemoplasma do exist in bone marrow or other organs and tissues in human body.

UNDEFINED TRANSMISSION MODES FOR THE HUMAN INFECTION WITH HEMOPLASMA

Many studies in China attempted to explain modes of transmission for hemoplasma but the exact modes of transmission are still unknown. Close contact with

infected individuals or insect bites, particularly by lice, fleas, mosquitoes, midges and stable flies are thought to be the principal modes of transmission between animals from animals to humans or transplacental transmission (Yang *et al.*, 2000).

However, hemoplasmas appear to show the same host specificity as other mycoplasmas as judged by their identification through 16S rRNA sequencing (Pitcher and Nicholas, 2005; Yang *et al.*, 2007). More strict animal experiments and molecular studies should be conducted to explain the mechanism of cross-species transmission. A recent report claimed that *Mycoplasma*

haemofelis DNA has been detected in HIV-positive patient, indicating that feline hemoplasma *M. haemofelis* may be a zoonotic causative organism that can infect human beings (Puntaric *et al.*, 1986).

CONCLUSION

Hemoplasma may really existed in humans in China but it may be over-reported because of etiological mis-recognition and/or inadequate diagnostic tests in China. Genomic sequencing of human hemoplasma is essential for future studies including reclassification of this organism, identification of virulence factors, protein antigens, etc. Molecular studies to re-assess the prevalence of human hemoplasma are warranted.

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