Biological indicators of sub-optimal health status

Limin Wang, Xin Zhao, Jiaxu Chen, Xiaoling Guo, Xin Liang, Danhui Yi, Huating Cui, Yueyun Liu

**Abstract**

**OBJECTIVE:** To investigate biological indicators of sub-optimal health status and provide means of objective assessment of sub-optimal health status.

**METHODS:** We set the unified standards for diagnosing a SHS. We tested various laboratory indicators in 407 cases that we selected randomly from 2807 subjects and collected 15 mL of fasting venous blood from each case. We measured serum immunoglobulin A (IgA) and immunoglobulin G (IgG) concentrations, serum beta endorphins (β-EP), cortisol (C), testosterone (T), plasma adrenocorticotropic hormone (ACTH) and serum T lymphocyte subsets CD3+ and CD4+.

**RESULTS:** Mean serum testosterone concentrations and their ratio to cortisol (C) concentrations were significantly higher in the healthy group than in those with sub-optimal health status (P<0.01). Mean serum CD3+ concentrations were significantly higher in those with sub-optimal health status than in the healthy group (P<0.05).

**CONCLUSION:** Decreased serum testosterone/cortisol ratio may be an objective indication of sub-optimal health status. Changes in neuroendocrine and immunological indicators may explain some of the symptoms, including malaise and poor work performance, attributable to persistent or relapsing fatigue in subjects with sub-optimal health status.

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**Key words:** Testosterone; Hydrocortisone; Sub-optimal health status; Biological indicator

**INTRODUCTION**

Sub-optimal health status (SHS) has become a new challenge to public health in China. An intermediate state between health and disease, SHS is mainly characterized by a general decline in health, non-specific weakness, and decreased energy. Manifesting as reduced strength and a decline in function and adaptability, this syndrome does not meet any current diagnostic criteria for disease. According to the theories of Traditional Chinese Medicine (TCM), the body’s *Yin* and *Yang*, *Qi* and blood are in an unbalanced state but no pathological changes have yet developed in patients with SHS.

Previous studies on SHS have mainly focused on the definition of this concept, differentiating it from the viewpoint of TCM, associated risk factors, and TCM-type interventions; there are few studies of its biological indicators. In this study, we investigated biological indicators of SHS extensively with the aim of identifying an objective means of assessing SHS.
OBJECTIVES

We conducted a cross-sectional study to identify biological indicators in healthy and poorly healthy women and men, in order to study the association between SHS and physical dysfunction in the nervous, endocrine, and immune systems induced by mental, emotional, and social factors, and to explore the causes of SHS.

METHODS

Subjects

Both the research protocol and written informed consent forms were reviewed and approved by the Ethics Committee of Beijing University of Chinese Medicine prior to initiation of this study. From October 2009 to May 2010, we conducted a cross-sectional study on sub-optimal health. We distributed a syndromes questionnaire to the following six medical/physical examination centers: Beijing Guanghua Hospital (Beijing, China), Shaanxi Hanzhong People’s Hospital (Hanzhong, Shaanxi, China), affiliated hospital of Jilin Changchun University of TCM (Changchun, Jilin, China), Jiangsu Zhenjiang People’s Hospital (Zhenjiang, Jiangsu, China), Second People’s Hospital of Shenzhen city of Guangdong province (Shenzhen, Guangdong, China), and the Huangshi Aikang Hospital (Huangshi, Hubei, China). From about 10,000 subjects who were attending for medical check-ups, we generated a random sample of 407 by using the RAND function of Excel. Of this sample, 365 were in good health and 42 had SHS according to the criteria described below.

Data and collection

We set the following uniform standards for diagnosing a SHS: (a) malaise and poor work performance lasting for more than three months; and (b) no major identifiable diseases or mental illnesses. The inclusion criteria were: (a) age range 18–49 years; (b) syndromes complying with the above two diagnostic criteria; and (c) having given written informed consent. The exclusion criteria were: (a) pregnancy, lactation or planning to be pregnant; (b) metabolic syndrome; (c) incomplete data collection.

We collected 15 mL of fasting venous blood from each participant: 8 mL with heparin anticoagulant, 2 mL with aprotinin and EDTA anticoagulant, and 5 mL without anticoagulant. The serum and plasma were separated and placed in a refrigerator at −80°C until measurement.

Reagents used for blood tests included radio-immune reagents produced by Beijing Kemei Dongya Biotechnology (Beijing, China) and enzyme-linked immunosorbent assay (ELISA) immunosorbent reagents purchased from Beijing, China. Instruments used for testing included a Hitachi 7080 automatic biochemistry analyzer (Tokyo, Japan) and a DFM-96 type γ radio-immunity counter (Nanjing Medical University, China). We measured serum immunoglobulin A (IgA) and immunoglobulin G (IgG) concentrations by a biochemical immune turbidity method; serum beta endorphins (β-EP), cortisol (C), testosterone (T), and plasma adrenocorticotropic hormone (ACTH) by a radio-immunity method; and serum T lymphocyte subsets CD3+ and CD4+ by an ELISA method.

RESULTS

Distribution of sex and health status in study subjects

Of the 407 subjects, 226 were men and 181 women. Of the men, 29 were healthy and 197 had SHS; of the women, 13 were healthy and 168 had SHS.

Biological indicators in men

As shown in Table 1, the mean T and CD3+ differed significantly between the two groups (P<0.01, t-test), the mean T concentration in the healthy group being far higher than that in the SHS group and the mean CD3+ concentration in the SHS group being higher than that in the healthy group.

Because the distribution of the T/C ratio was skewed, we performed a non-parametric test, which showed a significant difference between the two groups (Z=–2.683, P=0.007<0.01), the mean T/C ratio being significantly higher in the healthy group (42 cases, Mean=1.5009, Median=1.5808) than in the SHS group (364 cases, Mean=1.0456, Median=0.8109).

Biological indicators in women

As shown in Table 2, mean CD3+ and T concentrations differed significantly between healthy men and those with SHS groups (P<0.05, t-test), the mean T concentration in healthy men being higher than that in men with SHS and the mean CD3+ concentration being lower in healthy men than in those with SHS. Consistent with the results above, the non-parametric testing confirmed that the results of CD3+ and T concentrations differed significantly between healthy men and those with SHS (P<0.05, Table 3).

Biological indicators in women

As shown in Table 4, the mean CD3+ concentration in healthy women differed significantly from that in those with SHS (P<0.05), being lower in the former than in the latter.

As the distribution of both T concentration and T/C ratio were skewed, non-parametric testing was performed; this showed no significant differences in these variables between the two groups (P>0.05, Table 5).

DISCUSSION

SHS is caused by physical dysfunction in the nervous, endocrine, and immune systems induced by mental,
Table 1: Biological indicators in healthy subjects and those with SHS (±±)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>IgG (mg/dL)</th>
<th>IgA (mg/dL)</th>
<th>C (ng/mL)</th>
<th>T (ng/dL)</th>
<th>ACTH (pg/mL)</th>
<th>β-EP (ng/mL)</th>
<th>CD3+ (ng/mL)</th>
<th>CD4+ (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health status</td>
<td>42</td>
<td>1295.4±257.4</td>
<td>220.1±85.7</td>
<td>265.4±58.5</td>
<td>404.1±319.8</td>
<td>26.9±14.8</td>
<td>216.7±66.2</td>
<td>1.7±2.6</td>
<td>3.05±1.1</td>
</tr>
<tr>
<td>SHS</td>
<td>364</td>
<td>1264.4±264.5</td>
<td>225.2±104.6</td>
<td>251.2±74.5</td>
<td>245.0±239.9</td>
<td>28.1±11.0</td>
<td>204.8±50.3</td>
<td>5.1±3.2</td>
<td>2.48±1.3</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.470</td>
<td>0.763</td>
<td>0.235</td>
<td>0.003</td>
<td>0.622</td>
<td>0.264</td>
<td>0.178</td>
<td></td>
</tr>
</tbody>
</table>

Notes: SHS: sub-optimal health status; SD: standard deviation; IgG: immunoglobulin G; IgA: immunoglobulin A; C: cortisol; T: testosterone; ACTH: adrenocorticotropic hormone; β-EP: beta endorphins. Compared with healthy group, *P<0.001.

Table 2: Biological indicators in male subjects (±±)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>IgG (mg/dL)</th>
<th>IgA (mg/dL)</th>
<th>Cor (ng/mL)</th>
<th>T (ng/dL)</th>
<th>ACTH (pg/mL)</th>
<th>β-EP (pg/mL)</th>
<th>CD3+ (ng/mL)</th>
<th>CD4+ (ng/mL)</th>
<th>T/C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health status</td>
<td>29</td>
<td>1250.2±197.9</td>
<td>227.7±87.9</td>
<td>274.5±57.9</td>
<td>569.2±241.4</td>
<td>28.2±16.0</td>
<td>212.2±67.7</td>
<td>3.1±1.3</td>
<td>2.1±0.9</td>
<td>2.9</td>
</tr>
<tr>
<td>SHS</td>
<td>197</td>
<td>1188.9±238.8</td>
<td>220.4±102.4</td>
<td>255.3±78.2</td>
<td>426.6±185.1</td>
<td>28.5±11.9</td>
<td>204.8±50.0</td>
<td>5.1±2.8</td>
<td>2.5±1.3</td>
<td>1.8±0.9</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.189</td>
<td>0.717</td>
<td>0.205</td>
<td>0.004</td>
<td>0.576</td>
<td>0.000</td>
<td>0.233</td>
<td>0.12</td>
<td></td>
</tr>
</tbody>
</table>

Notes: SHS: sub-optimal health status; SD: standard deviation; IgG: immunoglobulin G; IgA: immunoglobulin A; C: cortisol; T: testosterone; ACTH: adrenocorticotropic hormone; β-EP: beta endorphins. Compared with healthy group of male subjects, *P<0.001.

Table 3: T and CD3+ findings in male subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Mean Rank</th>
<th>Sum of Ranks</th>
<th>Z</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>T (ng/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health status</td>
<td>29</td>
<td>261.56</td>
<td>10985.50</td>
<td>-3.349</td>
<td>6.341</td>
</tr>
<tr>
<td>SHS</td>
<td>197</td>
<td>197.38</td>
<td>72042.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD3+ (ng/mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health status</td>
<td>29</td>
<td>95.01</td>
<td>3990.50</td>
<td>0.001</td>
<td>0.000</td>
</tr>
<tr>
<td>SHS</td>
<td>197</td>
<td>216.54</td>
<td>79373.50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: T: testosterone.

Table 4: Biological indicators in female subjects (±±)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>IgG (mg/dL)</th>
<th>IgA (mg/dL)</th>
<th>C (ng/mL)</th>
<th>T (ng/dL)</th>
<th>ACTH (pg/mL)</th>
<th>β-EP (pg/mL)</th>
<th>CD3+ (ng/mL)</th>
<th>CD4+ (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health status</td>
<td>13</td>
<td>1396.3±345.1</td>
<td>203.2±81.4</td>
<td>244.9±56.9</td>
<td>35.1±22.4</td>
<td>24.1±11.8</td>
<td>226.8±64.1</td>
<td>2.0±2.9</td>
<td>3.0±0.8</td>
</tr>
<tr>
<td>SHS</td>
<td>168</td>
<td>1352.9±266.4</td>
<td>230.8±107.3</td>
<td>246.4±69.8</td>
<td>32.1±28.0</td>
<td>27.6±9.8</td>
<td>204.8±50.9</td>
<td>5.1±3.7</td>
<td>2.5±1.4</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.581</td>
<td>0.367</td>
<td>0.940</td>
<td>0.661</td>
<td>0.226</td>
<td>0.142</td>
<td>0.003</td>
<td>0.495</td>
</tr>
</tbody>
</table>

Notes: SHS: sub-optimal health status; IgG: immunoglobulin G; IgA: immunoglobulin A; C: cortisol; T: testosterone; ACTH: adrenocorticotropic hormone; β-EP: beta endorphins. Compared with healthy women, *P<0.001.

We have observed that, in most subjects with SHS, repeated physical discomfort and poor work performance are attributable to overwork. Assessment of biological indicators related to the nervous, endocrine, and immune systems in individuals with SHS may, to some extent, help to clarify the mechanisms underlying this condition.

The hormone testosterone promotes protein synthesis and the ability of the immune system to resist infection, strengthens muscle, stimulates red cell production through increasing erythropoietin concentrations, enhances sexual function. Generally speaking, serum T concentrations vary very little when the body is functioning well, but decline when it is in bad condition, such as in a state of fatigue. In comparison with the acceleration of anabolism induced by T in vivo, C accelerates catabolism, and maintains the normal glucose metabolism and relative stability of blood glucose concentrations. However, excessive C can cause negative emotions, such as those experienced with increasing psycho-logical stress, and suppress the immune system. Therefore, the level of T and C concentrations are the most sensitive indicators of SHS status currently available. In addition, the T/C ratio can help clarify the state of balance between anabolism and catabolism (building up and breaking down). When this ratio is high, anabolic processes are dominant, whereas when it is low, catabolism becomes predominant, which means that the organism is in an ongoing consumption-dominated status and cannot readily recover from fatigue. In our study, the mean T concentration and T/C ratio in the healthy group were significantly higher than in those with SHS, which indicates an imbalance between anabolism and catabolism in those with SHS. These findings confirm with previously study by Xu et al. That the body is in a state in which catabolism predominates is reflected by symptoms such as fatigue, difficulty in recovering from fatigue and poor adaptability. In men, the mean serum T concentration in the SHS group was significantly lower than that in the
healthy group. Among women, the mean serum T did not differ significantly between the two groups because the concentration of serum T is higher in men than in women.

The level of CD3+ and T concentrations differed significantly between healthy male subjects and those with male SHS, whereas mean CD3+ concentrations were significantly higher in those with female SHS group than in healthy female subjects. These findings indicate that the immune system functions abnormally in both male and female with SHS.

In conclusion, changes in biological indicators related to the nervous, endocrine, and immune systems in subjects with SHS may shed light on the physiological basis for the symptoms described above. The T/C ratio was significantly decreased in subjects with SHS, which implies that changes in this ratio T/C are associated with SHS. Thus, decreased serum T/C ratio might be helpful for the objective evaluation of SHS. This study suggests that SHS could be objectively evaluated by laboratory indicators (decreased serum T/C ratio), clinical symptoms and signs, and using our reported SHSQ-50 questionnaire with good reliability and validity.17

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REFERENCES