GBZ

OCCUPATIONAL HEALTH STANDARD

OF THE PEOPLE'S REPUBLIC OF CHINA

ICS 13.100
C60

GBZ 57-2008

Replacing GBZ 57-2002

Diagnostic criteria of occupational asthma

职业性哮喘诊断标准

Issued on: June 06, 2008 **Implemented on: December 01, 2008**

Issued by: Ministry of Health of PRC

Table of Contents

Diagnostic criteria of occupational asthma

1 Scope

This standard specifies the diagnostic criteria and principles of treatment for occupational asthma.

This standard applies to the diagnosis and treatment of asthma caused by occupational allergens.

2 Normative references

The provisions in following documents become the provisions of this standard through reference in this standard. For the dated references, the subsequent amendments (excluding corrections) or revisions do not apply to this standard; however, parties who reach an agreement based on this standard are encouraged to study if the latest versions of these documents are applicable. For undated references, the latest edition of the referenced document applies.

GBZ 188 Technical specifications for occupational health surveillance

GB/T 16180 Standard for identify work ability - Gradation of disability caused by work-related injuries and occupational diseases

3 Principles of diagnosis

According to the exact occupational allergen exposure history, asthma history, clinical manifestations, combined with the results of specific allergen test, with reference to the survey data of on-site occupational hygiene, perform comprehensive analysis to exclude asthma or respiratory diseases which are due to other causes, then make diagnosis.

4 Specific allergen test

The specific allergen tests referred to in this standard include:

a) Bronchial provocation test at the work site (see Appendix D);

b) Bronchial provocation test of laboratory allergen (see Appendix D);

c) Allergen-specific IgE antibody testing (see Appendix E or Appendix F);

c) Concurrent pneumothorax, mediastinal emphysema or pulmonary heart disease, etc.

6 Principles of treatment

6.1 Principles of treatment

6.1.1 After the confirmation of occupational asthma through diagnosis, the corresponding person shall be removed from the original occupational activity environment as soon as possible, to avoid and prevent the recurrence of asthma.

6.1.2 The effectiveness of treatment for an acute asthma attack depends on the severity of the attack and the response to the treatment. The purpose of treatment is to relieve symptoms as soon as possible, to relieve airflow limitation and hypoxemia. Drugs and usage are mainly the repeated inhalation of fast-acting β_2-receptor agonists, oral taking or intravenous glucocorticoids, inhalation of anticholinergic drugs, intravenous aminophylline. For those with severe asthma attacks with acute respiratory failure, use the mechanical ventilation treatment if necessary.

6.1.3 For the treatment of asthma of chronic duration, it shall select appropriate treatment plan according to the severity of the disease, the main principle is anti-inflammatory and symptomatic treatment. It emphasizes the long-term use of one or more asthma control drugs, such as inhaled corticosteroids, long-acting β_2-receptor agonists, oral cysteinyl leukotriene receptor antagonists, sustained-release theophylline, etc. It may use the oral glucocorticoids of minimum controlled dosage if necessary.

6.1.4 The treatment in the relieving period is mainly based on anti-inflammatory. The purpose of treatment is to control chronic inflammation of the airway and to prevent acute attacks of asthma. The drugs inhaled are mainly inhaled glucocorticoids.

6.2 Other treatment

6.2.1 After relieving the asthma, it may arrange other work. For patients of severe asthma, it may assign work appropriately according to their health status.

6.2.2 If labor capacity assessment is required, it shall be handled in accordance with GB/T 16180.

7 Instructions for correct use of this standard

See Appendix A.

relieved naturally after leaving the occupational allergen or relieved quickly through treatment, but it can recur after re-exposure.

A.5 Diagnostic grading is judged comprehensively based on the frequency of asthma attacks (wheezing, shortness of breath, chest tightness, coughing, etc.) after separation from allergens and standardized treatments, the effects on activities and sleep, the laboratory tests such as increased airway resistance. Acute asthma attacks can occur at all grades, but acute attacks only represent the severity of the disease at a certain episode. Therefore, the severity of the acute attacks of asthma cannot be used as a grading index.

A.6 The atypical clinical manifestation of asthma means that there is no obvious wheezing or signs at the time of attack. Chronic cough is the main or only clinical manifestation, which is mostly irritating cough. It is a special form of asthma, called “cough variant asthma”. Its case physiological changes, like asthma, are also persistent airway inflammation and airway hyperresponsiveness.

A.7 Refractory asthma has a broad meaning, which is characterized by clinically uncontrollable chronic symptoms, paroxysmal aggravation, persistent variable airway obstruction. Currently, refractory asthma is divided into three types: acute severe asthma (mainly including severe asthma and fatal asthma), unstable asthma (mainly including fragile asthma and nocturnal asthma), chronic persistent asthma (mainly including glucocorticoid-dependent asthma and glucocorticoid-resistant asthma).

A.8 For those personnel that is exposed to occupational allergens, if the non-specific airway responsiveness test is characterized by airway hyperresponsiveness, with frequent episodes of rhinitis, nasal itching, runny sputum, continuous sneezing and other symptoms, it shall make close observation according to GBZ 188, to track the likelihood of occupational asthma.

A.9 Diagnosis of this disease shall exclude the history of bronchial asthma which exists before work, meanwhile identify it together with upper respiratory tract infection, chronic obstructive pulmonary disease, cardiogenic asthma, exogenous allergic alveolitis and other diseases.

A.10 Diagnostic naming of occupational asthma and its writing format

Standardizing the naming format for diagnosis of occupational asthma is conducive to accumulating clinical data, determining the treatment effect, and is more conducive to comprehensive assessment of the illness status in the identification of disability grading of occupational disease. The standardizing principle of naming is, after diagnosis, indicating the grading of the severity of illness status, wherein the XX refers to the name of the exposed allergen. Its

Appendix B

(Normative)

Non-specific bronchial provocation test (Determination of responsiveness after airway inhalation of acetylcholine/histamine)

Histamine is the main inflammatory medium of asthma, which can stimulate contraction of bronchial smooth muscle, increase the permeability of microvascular. Acetylcholine is a synthetic derivative of acetylcholine in the neural medium, which can be combined with the cholinergic receptor on the bronchial smooth muscle, to stimulate the contraction of smooth muscle. The degree of response of the smooth muscle for the same dose of the two reagents is consistent; however, in some cases, it is not exactly the same. The response of patients of mild chronic obstructive pulmonary disease to histamine is stronger than acetylcholine; the response of the patients of bronchial asthma is same to both. In the use of larger doses, the side effects of acetylcholine is smaller than that of histamine.

B.1 Adaptation disease

B.1.1 Diagnosis to exclude or determine asthma: for patients with existing asthma symptoms, where the regular lung function is normal or close to normal, meanwhile the presence of asthma cannot be determined by other methods, if the result of this test is negative, the asthma can be ruled out. For other patients who have atypical symptoms, are mainly featured by cough or chest tightness, but the conventional lung function is normal, if the result of this test is positive, after ruling out the causes which may cause similar symptoms, it can be confirmed as the cough variant asthma.

B.1.2 Differential diagnosis for asthma: The increased airway responsiveness is a more reliable indicator for diagnosis of asthma. Because the airway of patients of asthma is several or even dozens of times more responsive to certain drugs or irritants than normal personnel or patients who suffered from other lung and bronchial diseases, the results are more reliable.

B.1.3 It can be used for epidemiological investigation of asthma and study of the pathogenesis of asthma.

B.1.4 Evaluate the efficacy of asthma drugs.

B.2 Conditions and requirements of subject

B.2.1 The symptoms have been relieved during the test and there is no wheezing sound in the hearing.

a power source, the pressure of compressed gas is 3.5 kg/cm^2, the flow rate is 5 L/min, the nebulizer is loaded with 3 mL of saline, histamine or acetylcholine saline solution.

b) Concentration of histamine (His) or acetylcholine (Mch): It can be prepared to the solution of the following concentration (mg/ml) to prepare for use: 0.03, 0.06, 0.125, 0.25, 0.50, 1.00, 2.00, 4.00, 8.00, 16.00, 32.00, in double increments.

c) Determination steps:

1) The subjects rest for 15 min, take the sitting position, clamp the nose, determine FEV_1 for 2 times, take the higher value as the base value.

2) First inhale saline; wear a hole mask or mouth-piece which is connected to the nebulizer; turn on the gas source to start atomization, the nebulizer must be upright, otherwise it will affect the amount of atomization. Use the natural frequency to conduct tidal breathing for 2 min; stop breathing, afterwards make FEV_1 once at 30 s and 60 s, respectively. If the maximum value of FEV_1 reduces 10% or more as compared with the base value of FEV_1, the concentration of inhaled drugs shall start from low dose of 0.03 mg/min and cannot be simplified. The determination time of all FEV_1 shall be completed within 3 min.

3) Inhalation of drugs: the method is same as above, starting from the low dose, in double increments. Determine the FEV_1 once at 30 s and 60 s, respectively after each inhalation. Take the higher value. The interval of starting inhalation of adjacent two doses is 5 min, until the FEV_1 drop value is ≥ 20% of the base value of FEV_1 or the inhalation of the highest concentration.

4) At the end of the test, inhale the β_2-receptor agonist for two sprays.

5) Calculation of test results: The threshold of high responsiveness of airway is expressed in $PC_{20}FEV_1$ or $PD_{20}FEV_1$, abbreviated as PC_{20} and PD_{20}, wherein PC_{20} is the drug excitation concentration when the drop value of FEV_1 is equal to the 20% of the base value of FEV_1; PD_{20} is the cumulative dose of the drug excitation when the drop value of FEV_1 is equal to 20% of the base value of FEV_1.

PC_{20} = Cologarithm [logC_1 + (logC_2 - logC_1) (20 - R_1) / (R_2 - R_1)]

C_2 = The last drug concentration inhaled

C_1 = The penultimate drug concentration.

equivalent products have the same effect, it can use these equivalent products.

the startup of instrument. First inhale the saline. Afterwards after inhaling the atomization agent of each concentration for 1 min, automatically turn to the next dose, meanwhile automatically draw the response curve of dose. After inhaling the saline, the determined Rrs is the control value. The cumulative dose of inhaled drugs when the Rrs after inhaling drug increases 2 times higher than the control value is defined as the threshold of high responsiveness of airway, which represents the sensitivity of airway's reaction. The rising slope of curve represents the responsiveness. In addition, it may also use the airway conductivity (Grs) as an indicator of airway responsiveness, Grs = 1/Rrs. It can draw the Grs curve on the coordinate graph of the dose response curve. For the Grs, the inflection point at the startup of drop of the horizontal line which represents the control value is D minutes, which is the threshold of high responsiveness of the airway, represents the minimum dose of acetylcholine when this threshold is reached, indicates the sensitivity of the airway's reaction; the descending slope SGrs of the Grs represents the responsiveness, SGrs = ΔGrs / Δt, wherein t is the time. The unit of calculation of dose is as below: in case of tidal breathing, the inhalation of atomization solution of 1 mg/mL concentration for 1 min is equal to 1 U. For normal person, in case of inhalation of the solution of the above range of concentration, even it reaches the highest concentration, it will not result in reaction, which can be distinguished from the high airway responsiveness.

B.4 Precautions

B.4.1 Although the excitation test of histamine and acetylcholine is relatively safe, there is still a potential danger. The concentration of allergens inhaled shall not be too high, so as not to produce stimulating reaction. At the same time, it shall master the indications and contraindications, operate strictly in accordance with the operating norms. The technicians who implement operations must be familiar with the operating norms, meanwhile check the laboratory, where there must be equipped with bronchodilators, oxygen and other emergency drugs.

B.4.2 The normal value and abnormal value of the drug test may overlap, so the test results shall not be treated too mechanically. If His PC_{20} or Mch PC_{20} is ≤ 4 mg, the reliability of the diagnosis is very high; if 4 mg < Mch PC_{20} ≤ 16 mg, there may be false positive or false negative in this range. The clinical manifestation of the patient can be referred to when making judgement, for example, the more clinical basis of asthma, even if the PC_{20} value is relatively larger, the higher the reliability of diagnosing asthma.

B.4.3 In view of the need for certain equipment and technical conditions in this test, in the test process, an overreaction may occur in individual cases, so this test shall be carried out in a hospital with conditions.

B.4.4 It should not provide hints before or during the test, the subject shall not

puncture test, or the allergen infusion concentration of skin ridge (+) in the skin ridge test, or the 200 protein nitrogen units/mL, or the allergen concentration of 10^{-5} ~ 10^{-3} (W/V) can be used as a reference for the concentration of inhaled allergen, which is incremented by 10 times proportion based on this concentration, the time interval of inhalation is above 10 min.

D.1.2.3 Before the test, determine the index of the lung function. The determination of FEV_1 has been widely used in clinical practice and is the best reproducible index in lung function tests. Therefore, FEV_1 is the most commonly-used index for assessing the specific bronchial provocation test. As the base value, the difference between the two results of FEV_1 is not more than 5%; if a certain dilution is added into the allergen, before inhaling the allergen, it shall also perform the test after inhaling the dilution, as the control value, the change of which shall not exceed 10% of the base value.

D.1.2.4 The time interval between observations shall not be longer than 15 min ~ 30 min within the first 1 hour after inhalation. In addition to closely observing the response within 2 h after inhalation of allergens, it shall also pay attention to the observation of delayed or bidirectional reactions which occur within 4 h ~ 6 h. Therefore, the total observation time shall reach to 24 h.

D.1.3 Positive reaction criteria

D.1.3.1 The result is judged not PC_{20} but PC_{15}, that is, the concentration of allergen infusion (extraction) which causes a 15% drop in FEV_1 is used to indicate the airway responsiveness.

D.1.3.2 If there are obvious symptoms and signs after the stimulation, such as chest tightness, shortness of breath, cough, lung wheezing, etc., the upper value shall be relaxed, more than 10% can be judged as positive.

D.1.4 Precautions: Same as B.4.

D.2 Bronchial provocation test at work site

D.2.1 Pre-test preparation and basic conditions: Same as B.2.

D.2.2 Methods

D.2.2.1 Within 1 hour after entering the work site, determine the ventilation function (FEV_1) once every 15 minutes; after 1 h, determine the ventilation function once every 0.5 hour. According to the situation, it can stay at the site for 1 h ~ 2 h.

D.2.2.2 After keeping away from exposure, determine the lung function once every 1 h, pay attention to record the clinical symptoms and signs. Make continuous observation for at least 8 h. It shall make determination again at 24

Appendix E

(Normative)

Testing of allergen-specific IgE antibody - Fluorescent enzyme immunoassay (FEIA)

E.1 Principles

The allergen is covalently bound to the solid phase carrier of ImmunoCAP, a three-dimensional poly-cellulose plate. Add the patient's serum to cause specific binding of the antigen-antibody. After washing away the free IgE, add the enzyme-labeled anti-IgE antibody. After incubation, wash away the unbound enzyme-labeled anti-IgE, then incubate the ImmunoCAP together with the substrate. After the reaction is terminated, test the fluorescence intensity. The stronger the fluorescence intensity, the higher the content of specific IgE in the sample. Based on the World Health Organization (WHO)'s IgE reference 75/502, draw the standard curve. From the and the fluorescence intensity, it can derive the IgE concentration in the sample.

E.2 Instruments

Fully automatic in-vitro immunodiagnostic instrument ImmunoCAP 100/ImmunoCAP 250[4]. The instrument can automatically perform all steps of the testing analysis, meanwhile automatically print the results of the test after the analysis is completed.

E.3 Reagents

E.3.1 Dedicated testing reagents

Total IgE, specific IgE (about 600 species of allergens in more than 10 categories such as pollen, dust mites, food, microorganisms);

E.3.2 Dedicated system reagents

Enzyme, calibration solution, curve control solution, CAP for calibration, etc.;

E.3.3 General system reagents

Substrate solution (development solution), stop buffer, wash solution, etc.

[4] Note: Fully-automatic in-vitro immunodiagnostic instrument ImmunoCAP 100/ImmunoCAP 250 is the trade name of the product supplied by the supplier. This information is given to facilitate users of this standard and does not imply recognition of the product. If other equivalent products have the same effect, it can use these equivalent products.

Appendix F

(Normative)

Testing of allergen-specific IgE antibody - Enzyme-linked immunosorbent assay (ELISA)

F.1 Principles

The known specific antigen is first immobilized on the surface of the solid-phase carrier, to form a fixed-phase antigen. Add the sample to be tested, then add the enzyme-labeled antibody, to form an antigen-tested antibody-labeled antibody complex on the solid-phase carrier. After adding the enzyme substrate and the chromogen, it develops color and the degree of coloration is expressed by the absorbance (A), the measured A value is correlated with the level of the allergen to be tested.

F.2 Equipment

Porous polystyrene plate (the commonly-used plate is 96-hole plate, 12 × 8 holes), micro-pipette, enzyme-labeled immunoassay instrument, pH test paper, incubator, refrigerator, washing bottle, wet box, commonly-used glass instruments, etc.

F.3 Reagents

Currently, various ELISA tests have commercial dedicated kits, including the coated goat anti-human IgE reaction plate, series of standard substances (0 U/mL, 10 U/mL, 100 U/mL, 500 U/mL) and quality control serum; enzyme (HRP) labeled anti-human IgE monoclonal antibody; buffer solution, stop buffer, etc.

F.3.1 Enzyme dedicated for labeling: The horse-radish peroxidase (HRP) is most commonly-used to label various antibodies.

F.3.2 Commonly-used enzyme substrates and chromogens: The substrate of HRP is H_2O_2 (or hydrogen peroxide), which requires hydrogen donors to participate in the catalysis. The latter are mostly reducing dyes. Through reaction, it produces dark or fluorescent oxidizing dyes. There are many chromogens (hydrogen donors) available for HRP. The commonly-used chromogens are o-phenylenediamine (OPD), 3,3',5,5'-tetramethylbenzidine (TMB), tetramethylbenzidine sulfate (TMBS), etc. H_2O_2 (or hydrogen peroxide) and chromogen are often mixed prior to testing.

F.3.3 Coating buffer (pH 9.6 carbonate buffer solution): Add distilled water into 0.16 g of Na_2CO_3 and 0.29 g of $NaHCO_3$ to dissolve it, add water to 100 mL,

Appendix G

(Normative)

Specific-allergen skin test

G.1 Intracutaneous test

G.1.1 Selection of skin test solution

G.1.1.1 Test solution of allergen skin

It shall select the standardized skin test solution.

G.1.1.2 Control solution and purpose for skin test

In order to obtain an accurate skin test result, when performing the skin test, it shall establish the positive and negative controls at the same time. The positive control solution uses the histamine dihydrochloride at a concentration of 0.017 mg/mL or the histamine diphosphate at a concentration of 0.028 mg/mL, which is equivalent to a 0.01 mg/mL histamine substrate.

The purpose of using a positive control solution:

1) Judge the positive degree of the allergen skin test: Use the papule which is caused by the positive control solution as the standard “scale” to judge the positive degree of the allergen skin test;

2) Determine the intensity of the skin responsiveness of the skin tester: Due to different age, physical condition and geographical area, the skin responsiveness is not always the same. For example, the skin responsiveness of the elderly is poor, the responsiveness of the positive control is also weak.

3) Observe the inhibitory effect of the drug: When the positive control solution presents negative reaction, it indicates that the skin test result is likely to be inhibited by certain drugs, such as antihistamines, thus the skin test result is invalid. Only when the positive control solution presents positive reaction, it indicates that the skin test is not affected by drug inhibition or other factors, thus the skin test result is valid. The negative control solution is usually selected from physiological saline or allergen diluted preservation solution. The negative control solution presents negative reaction. If the patient is highly sensitive, it is possible to have a false positive reaction. At this time, the positive reaction of skin test as produced by the allergen is not clinically significant.

This is an excerpt of the PDF (Some pages are marked off intentionally)

------ The End ------