长沙市第一医院大内科医学英语

讲 义

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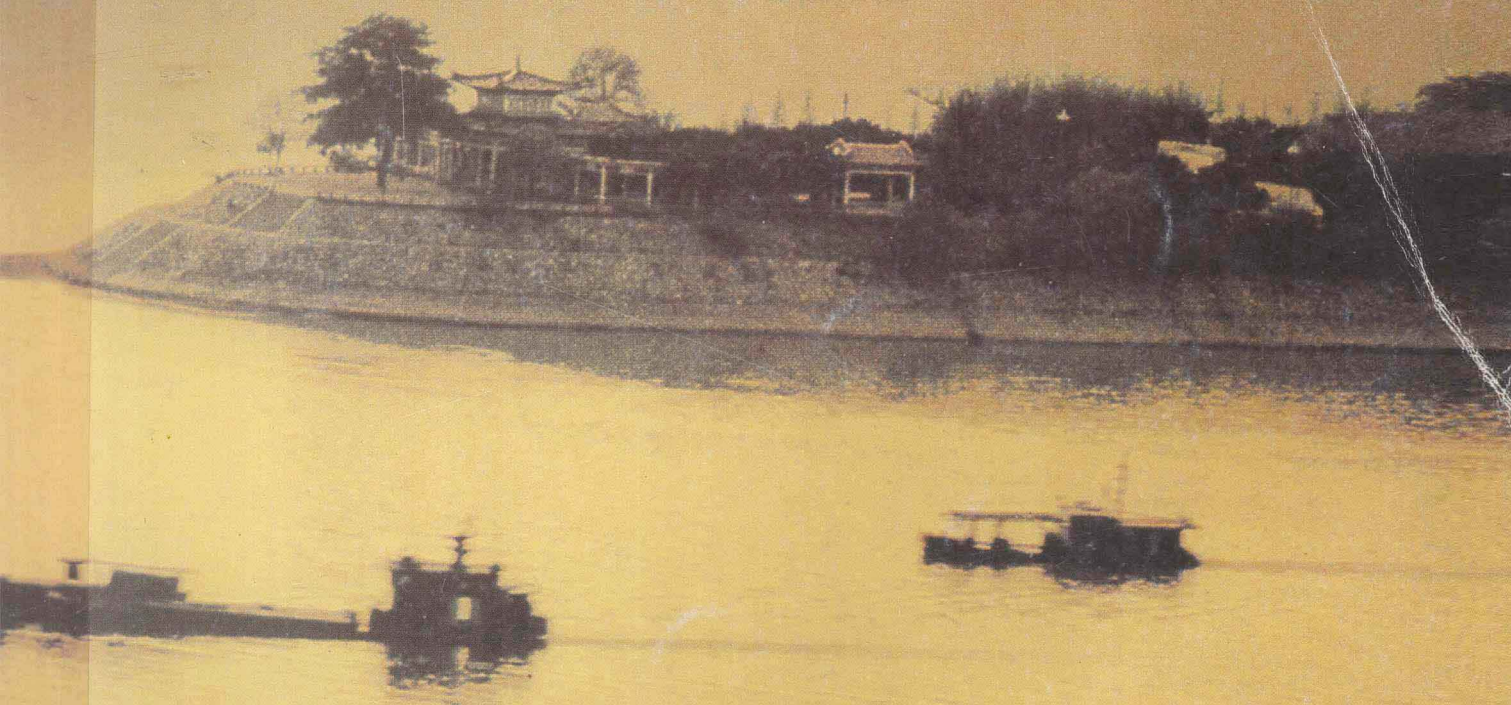

长沙市第一医院大内科
2005年2月

Preface

English is a universal language which is not replaced by other languages in the medical domain of world at present. As a medical student and doctor, if master English, he or she can read much more English literatures and English original articles about medicine successfully; he or she can gain advanced information about medicine from internet and enrich and increase medical knowledge constantly; he or she can publish one's own investigative outcome and experience; he or she can make an external and internal communication about medical speciality smoothly.

According to what scientific and teaching department in our hospital ask clinical physician to do in the medical English teaching and the need in bringing up post-graduates and medical students, medical department will make a plan to hold medical English lecture. Therefore, medical department invite teachers of postgraduates and medical post-graduates, who are better at English and have abundant clinical experience, to write this teaching material which is named《Medical English teaching materials of the NO 1 hospital in Changsha》. I believe this teaching material can not only help medical students、graduate students and young doctors to get medical knowledge, but also improve their abilities in reading medical English literatures and original articles. We hope medical students、post-graduates and young doctors in medical department will take part in the medical English lecture, and read this teaching material so that the level of medical English can be improved constantly.

In order to help medical students、post-graduates and young doctors to read this teaching material successfully, there is Chinese translation in the last part of this English teaching material. If some contents in this teaching material are different from something in our country, we should be based on domestic teaching materials in the course of clinical work.

We first time attempt to write this teaching material. In order to show this teaching material to readers as early as possible, we couldn't check it in detail after we finish it. Please correct the mistake when you read the teaching material and give us your precious advice so that we can revise the teaching material in future according to this.

Zhang Zhibo, Director of Internal Medicine, the First Hospital of Changsha

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前　言

英语是当今世界医学领域不可由其他语言替代的通用语言。作为医科学生和医学科技工作者，只有掌握英语，才能顺利阅读日益增多的医学英语文献和医学英语原著，才能从因特网上获取医学专业发展的前沿信息，才能不断充实和提高自己的医学专业知识，才能将自己的研究成果或经验和体会发表或报道出去，才能顺利地从事医学专业的对外交流和对内传播。

根据我院科教科对我院大内科临床医师的医学英语教学的要求和我院大内科培养研究生和七年制医科学生的需要，大内科将有计划地举办医学英语专题讲座。为此，大内科邀请了我院呼吸、心内、消化、肾内、血液、肿瘤、内分泌、代谢、风湿、神内、儿科等专业具有良好英语功底和丰富或较丰富临床工作经验的部分研究生导师和医学硕士编写和摘编了这本《长沙市第一医院大内科医学英语讲义》。我相信这本讲义在引导医科学生、研究生和青年医生获得医学知识的同时，对提高他们阅读医学英语文献和医学英语原著的能力将有较好的帮助。希望我院大内科的医科学生、研究生、青年医生积极参加大内科主办的医学英语专题讲座，认真阅读这本讲义的各篇讲稿，以不断提高自己的医学英语水平。

为了帮助我院大内科医科学生、研究生和青年医生顺利阅读这本讲义，在讲义后半部分编写了相对应的中文讲稿。讲义中的有关内容与我国情况有所不同，在临床工作中应以中文版教材为准。

这本讲义是首次尝试，为了尽快与大家见面，编写和摘编后没有详细校稿，望各位在使用过程中更正错误并提出宝贵意见，供今后修订时参考。

长沙市第一医院大内科主任　张智博

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Neurotrophins in Bronchial Asthma

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Introduction

BA is a complex disease with several clinically well defined pathogenic components, including recurrent reversible airway obstruction, chronic airway inflammation and development of airway hyperresponsiveness. Theconstituents of the inflammatory component have, in recent years, been relatively well characterized and defined. There is now overwhelming evidence that T cells play a central role in, particularly, allergic BA. Strong evidence supports the notion that T-helper 2 cells orchestrate allergic inflammation and control many important aspects of the effector phase response, including recruitment, activation and survival of eosinophils, activation of mast cells and IgE production. Reversible airway obstruction is pathogenetically related to mucus hypersecretion, development of local tissue edema as a consequence of acute inflammatory responses, and constriction of airway smooth muscle. Nonspecific bronchial hyperresponsiveness may be defined as an increase in the ease anddegree of airway narrowing in response to a wide range of bronchoconstrictor stimuli. The development of airway hyperresponsiveness is mediated by multiple independent and additive pathways working in concert, which can be clinically tested using stimuli such as methacholine, histamine, exercise, cold air, capsaicin, and so on. Constriction of airway smooth muscle is largely controlled by sensory and motor neurons innervating the airways and the lung. The autonomic nerves

that regulate many aspects of airway function, including airway smooth muscle tone,mucus secretion and bronchial microcirculation, can be functionally subdivided into cholinergic, adrenergic and nonadrenergic noncholinergic pathways.

Commentary

Abstract

Allergic bronchial asthma (BA) is characterized by chronic airway inflammation, development of airway hyperreactivity and recurrent reversible airway obstruction. T-helper 2 cells and their products have been shown to play an important role in this process. In contrast, the mechanisms by which immune cells interact with the cells residing in lung and airways, such as neurons, epithelial or smooth muscle cells, still remains uncertain. Sensory and motor neurons innervating the lung exhibit a great degree of functional plasticity in BA defined as 'neuronal plasticity'. These neurons control development of airway hyperresponsiveness and acute inflammatory responses, resulting in the concept of 'neurogenic inflammation'. Such quantitative and/or qualitative changes in neuronal functions are mediated to a great extent by a family of cytokines, the neurotrophins, which in turn are produced by activated immune cells, among others in BA. We have therefore developed the concept that neurotrophins such as nerve growth factor and brain-derived neurotrophic factor link pathogenic events in BA to dysfunctions of the immune and nervous system.

Neurogenic Inflammation and Neuronal Plasticity in BA

Sensory and motor neurons exhibit drastic functional changes in BA.

These changes are defined by the term 'neuronal plasticity'. Increased levels of neuropeptides including substance P have been detected in the lungs of asthmatic patients. Increased levels of Neurokinin A have been detected in bronchoalveolar lavage fluids of asthmatic patients following airway allergen challenge. Since cholinergic nerves represent the dominant bronchoconstrictor pathway, anticholinergic drugs are very effective bronchodilators in asthma therapy. This further underlines the importance of cholinergic mechanisms in the development of BA and airway hyperresponsiveness. The underlying mechanisms include enhanced reflex activity,increased mediator release, enhanced sensitivity of smooth muscle to neuropeptides and tachykinins, and increased density of receptor expression of both airway smooth muscle cells and neurons. In addition to qualitative changes in neuronal functions, debate still continues regarding whether quantitative changes in sensory and/or motor neurons also occur in this disease. Neuropeptides and tachykinins are involved in several key features of BA, including airway smooth muscle constriction, vascular dilatation, increased vascular permeability, mucus hypersecretion and acceleration of airway inflammation.These effects attributed to the function of neuropeptides and tachykinins lead to the concept of 'neurogenic inflammation' in BA .

Neurotrophins

The functional plasticity of sensory and motor neurons is under close control of neurotrophins. The neurotrophins nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophin-3 and neurotrophin-4/neurotrophin- 5 belong to a family of homologous proteins

that exert their effects primarily as target-derived paracrine or autocrine neurotrophic factors. The role of the neurotrophins in survival, differentiation and maintenance of neurons is defined well. They exhibit partially overlapping but distinct patterns of expression and cellular targets. In addition to the effects in the central nervous system, neurotrophins also effect peripheral afferent and efferent neurons. The biological effects of neurotrophins are mediated by binding either to the high affinity (KD10–11) tyrosine kinese receptors (trkA, trkB, trkC) or the low affinity (KD10–9) pan-neurotrophin receptor p75NTR. Substantial biological effects of neurotrophins are mediated by the high affinity kinese receptors. The high affinity effector for NGF is trkA, that for BDNF and neurotrophin-4 is trkB, and that for neurotrophin-3 is trkC.Neurotrophin receptors are widely expressed on the neurons of the peripheral and the central nervous system, both during development and in adults. However, trk receptors as well as p75NTR are also expressed on nonneuronal cells, including immune cells, muscle cells and epithelial cells.The traditional cellular sources of neurotrophins under physiological conditions are primarily nerve-associated cells such as glia cells, Schwann cells or fibroblasts and neurons themselves. NGF is also produced in inflammatory processes by a wide range of hematopoetic cells, including mast cells, macrophages, T cells and B cells. This has been shown in a well-characterized animal model system of allergic airway inflammation and airway hyperresponsiveness. In addition, airway epiphilium constitutively expresses BDNF but not NGF, and BDNF production is further enhanced during inflammatory responses. Further to animal model systems,enhanced neurotrophin production has also been shown in patients with several

allergic conditions. The initial report of enhanced NGF production was provided by Bonini *et al*, indicating that patients with severe allergic BA display high serum levels of NGF . Furthermore,increases in NGF serum levels have been demonstrated in patients with vernal ceratonconjunctivities and allergic rhinoconjunctivities. Together with the group of Virchow *et al*, we have more recently shown that neurotrophin production is increased in bronchoalveolar lavage fluids from patients undergoing segmental allergen provocation. BDNF and NGF levels were particularlyincreased 18 hours after provocation, whereas no increases were detected 20 min after provocation. These data again indicate local production and release of neurotrophins on stimulation, and increased levels of neurotrophins are associated with late-phase allergic responses, but not with the early-phase response. What are the functional effects of increased neurotrophin production during the allergic response? Based on the data provided by other workers and our group, we propose the concept that neurotrophins play an important role in the pathophysiology of asthma in several ways (Fig. 1). The predominant effect on peripheral nerves is described by the term 'neuronal plasticity', which is defined as qualitative and/or quantitative changes in the functional activity and capacity of peripheral neurons. Examples include increased production of neuropeptides and tachykinins, increased receptor expression, increases in the number of nerves producing certain neuropeptides and tachykinins, and lowering of the firing threshold ofnerves. For all these effects, there are ample examples provided by studies conducted either in animal model systems or using human cell cultures. Initialstudies were carried out by Undem *et al*, demonstrating allergen-induced sensory neuroplasticity in

guinea pig airways and NGF-induced phenotypic switch in airway sensory neurons . One result of these functional alterations is the development of airway hyperresponsiveness in BA. In parallel, neurotrophins also exhibit profound effects on immune cells residing in airways and lung tissue. These effects are described by the term 'immunological plasticity'. In this regard, neurotrophins act as amplifiers of the locally occurring immune dysbalance. This effect has so far exclusively been demonstrated for NGF, but not for BDNF. NGF augments the production of IL-4 and IL-5 but not IFN- . on activation of lymphocytes with allergen. Furthermore, these increases result in enhanced levels of IgE and IgG1 but not IgG2a antibodies.

Conclusion

It is important to note that the effects of neurotrophins are not immediate, but rather long acting. In this context, we propose the concept that neurotrophins act as intermediate or long-acting modulators of neuronal and immune functions in the pathogenesis of BA. Data on the kinetics of local neurotrophin production (manuscript in preparation) support this concept because peak levels of neurotrophin content in bronchoalveolar lavage fluid have been detected 7–10 days following local allergen challenges, and these levels return to baseline level no sooner than 3 weeks after allergen provocation. Further experiments are certainly required to further evaluate this concept. Treatment modalities particularly need to be explored, aimed to locally antagonize increased neurotrophin production. Neurotrophins may, however, represent the 'common' trunk of immune and nerve cell modulators. This may lead to similar clinical signs

and symptoms (e.g. airway hyperresponsiveness and airway obstruction owing to enhanced airway smooth muscle contractility, mucus hypersecretion and edema) observed in asthma patients, regardless of the underlying cause (e.g. allergen-induced asthma, airway hyperresponsiveness in association with viral infections, exercise-induced asthma, etc.).

Management of stable angina

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Abstract

Ischaemic heart disease may present as a wide variety of clinical entities including unstable or stable angina pectoris, acute myocardial infarction, and occasionally heart failure. Chronic stable angina is a common condition and results in a considerable burden for both the individual and society. The goals in management are (1) treatment of other conditions that may worsen angina; (2) modification of risk factors and treatment with medications for coronary artery disease to improve outcome; and (3) effective relief of anginal symptoms. There are limitations to the methods available to risk-stratify patients, and the optimal treatment strategy remains unclear. The benefits of lifestyle modification cannot be over-emphasised, and appropriate attention to modifiable risk factors is paramount. The mortality benefit of lipid lowering treatment and antiplatelet therapy is well proved. However the evidence base for anti-ischaemic therapy is less rigorous, being based mainly on extrapolations from studies of acute coronary syndromes. Angioplasty has been shown to be more effective in relief of symptoms than medical therapy alone, but provides no mortality benefit. Coronary artery bypass surgery, however, has been shown to reduce mortality in patients with severe proximal coronary disease when compared with medical management alone.

Keywords: stable angina; angina

Abbreviations: ACE, angiotensin converting enzyme; CABG, coronary artery bypass grafting; ECG, electrocardiogram; HOPE (study), Heart Outcomes Prevention Evaluation (study); PCI, percutaneous intervention

Epidemiology

The epidemiology of ischaemic heart disease is changing. The population is growing older and patients are now more frequently surviving myocardial infarction. The prevalence of risk factors such as diabetes mellitus and hypertension has also been seen to increase. As chronic stable angina may be the initial manifestation of coronary artery disease in about 50% of patients, its prevalence is also increasing, and it is possible that this condition affects 4%–5% of Western populations. This increase in both morbidity and mortality has important socioeconomic implications.

Diagnosis

History

Angina is a clinical diagnosis that may be established by obtaining a careful history. Typical angina presents as chest tightness or heaviness brought on by exertion and relieved by rest. The discomfort is frequently felt in the left arm and jaw also. More atypical presentations such as epigastric or hypochondrial pain occur rarely. The discomfort may be exacerbated by cold weather, heavy meals, or states of high emotion.

The Canadian Cardiovascular Society has produced guidelines relating to the grading of severity of angina (see box 1).

Box 1: Canadian Cardiac Society classification of angina

Class I: ordinary physical activity does not cause angina.

Class II: angina causes slight limitation of day to day activity.

Class III: symptoms cause marked limitation of ordinary activity.

Class IV: symptoms occur when undertaking any physical activity or at rest.

Examination

Clinical examination of patients with stable angina is often normal. However during episodes of chest pain features associated with autonomic nervous system over-activity or left ventricular dysfunction may be present. Clinical examination should also include assessment of conditions known to be associated with ischaemic heart disease, for example, xanthelasma, hypertension, or peripheral vascular disease. Conditions known to exacerbate pre-existing coronary artery disease, for example, hyperthyroidism, anaemia, or aortic stenosis should also be sought.

Investigation and Risk Assessment

Successful management of the patient with chronic stable angina requires correct stratification by assessing the risk of future coronary events. Patients at low risk for such events have a relatively good prognosis; revascularisation procedures (balloon angioplasty or surgery) offer no benefit over medical management. Such patients should be offered medical treatment as their first option.

Non-invasive

Electrocardiography

A rest 12 lead electrocardiogram (ECG) should be recorded in all patients with symptoms suggestive of angina pectoris, however this may be normal in approximately 50% of patients with chronic stable angina. Normal appearances of a 12 lead ECG do not exclude severe coronary artery disease. Evidence of left ventricular hypertrophy or ischaemic ST-T segment changes increase the probability of underlying coronary artery disease; the presence of Q waves suggestive of previous myocardial infarction makes coronary artery disease very likely. The presence of arrhythmia on a rest ECG does make the presence of coronary artery disease more likely, however other underlying causes must also be sought. An ECG obtained during an episode of chest pain will be abnormal in 50% of patients with angina who have a normal rest ECG. Dynamic ST-T segment changes with chest pain are highly suggestive of coronary artery disease, and carry a worse prognosis. If these changes are unequivocal and at low workloads these patients may require no further non-invasive testing. "Pseudonormalisation" of the ECG in patients with abnormal ST-T segments at rest may occur during episodes of chest pain. This too is a sign of underlying coronary artery disease.

Chest radiography

The chest radiograph is often normal in patients with coronary artery disease, and its usefulness in routine investigation of these patients is not well established. It is more likely to be abnormal in patients with previous or acute myocardial infarction, and non-cardiac causes of chest pain. Chest radiography may also reveal complications of coronary artery disease such as pulmonary oedema in congestive heart failure.

Stress testing

(1) Exercise ECG

By far the most available form of stress testing is the exercise ECG. First described in 1932, this procedure has been in widespread clinical use for many decades. Exercise ECG testing is safe, however both myocardial infarction and death occur at a rate of approximately 1/2500 tests. The absolute contraindications to exercise testing are shown in box 2.

Box 2: Absolute contraindications to exercise ECG testing

Acute myocardial infarction within the last two days.

Severe or symptomatic aortic stenosis.

Symptomatic heart failure.

Acute pulmonary embolism.

Acute myocarditis or pericarditis.

Acute aortic dissection.

Resting blood pressure >200/120 mm Hg.

Acute systemic illness.

Other contraindications are relative and include left main coronary artery disease, moderate aortic stenosis, hypertrophic obstructive cardiomyopathy or other outflow tract obstruction, and high degree atrioventricular block. Some studies have shown exercise ECG testing to be less specific and sensitive in women than men.

(2) Stress imaging

Both nuclear and echocardiographic imaging modalities can be utilised in the diagnostic and prognostic assessment in patients with suspected

coronary artery disease in whom an exercise ECG is likely to be unreliable. A variety of techniques can be employed to introduce stress and these include exercise, vasodilators (for example, adenosine), and inotropes (for example, dobutamine). Not only do they provide additional information for risk stratification but also functional information in coronary artery disease.

Newer technologies

Both electrobeam computed tomography and magnetic resonance angiography provide information regarding the severity of coronary artery disease. However neither of these techniques is currently widely available and hence their precise role in risk assessment of patients with coronary artery disease will not be discussed here.

Invasive Investigations

Coronary angiography

Coronary angiography remains the most accurate method for the diagnosis of clinically important obstructive coronary artery atherosclerosis. The technique involves the insertion of a catheter into the heart via a peripheral artery. Left heart catheterisation is usually performed via the right femoral artery and involves selective cannulation of the left and right coronary arteries, and ventriculography.

Minor complications occur in approximately 5% of patients. Such complications include localised bruising around the arteriotomy, allergy to contrast agents, and vasovagal reaction. Major complications, for example, death, myocardial infarction and stroke, are rare affecting approximately 0.25% of patients. Major complications are more common in those with advanced cardiac disease.