This article describes some of the problems encountered in measuring the prevalence of asthma and discusses ways these may be approached. It outlines some of the insights into the nature of asthma arising from epidemiologic studies and makes some suggestions for future studies based on questions which might be answered by appropriate population studies.

Problems Associated with Measuring the Prevalence of Asthma

Lack of Definition

There is no agreed clinical, physiologic or epidemiologic definition of asthma. Without a definition it is likely that different studies will measure different aspects of the disease, thus making comparisons between and within populations difficult.

Questionnaires

The words "wheezing," "chest tightness" and "breathlessness" mean different things to different people within and between given societies and also present problems in translation, leading to considerable difficulties in designing questionnaires. If the question, "Have you ever been diagnosed as having asthma?" is asked, the answer depends on many things including the subject's memory, the criteria used by the doctors concerned to diagnose asthma and, since asthma can have high or low status in different communities, on what the doctor decided to tell the subject.

Tests of Bronchial Responsiveness

Objective evidence of asthma requires measurements of lung function reflecting acute changes in bronchial lumen size. In clinical practice this involves measuring spirometric function or peak flow rate before and after a bronchodilator drug is given. In the population setting, relatively few people have abnormal lung function and, of these, very few have changes in function after bronchodilator aerosol inhalation. This means that a bronchoconstrictor test is necessary to detect abnormal bronchial responsiveness (BHR). Usually histamine or methacholine, the so-called "nonspecific" agents, are used to document the presence or absence of bronchial hyperresponsiveness (BHR). Inhalation tests with these agents are reproducible, safe, and can be rapidly and easily performed in the field. Furthermore, they correlate reasonably well with the severity of asthma as measured by symptoms or treatment requirements. However, they are nonspecific for asthma because a positive response is found in many people with chronic inflammation of the bronchi, including those with chronic obstructive pulmonary disease, as well as in some apparently healthy subjects who have never had symptoms of asthma.

The Changing Nature of Asthma

The severity of asthma varies in intensity with time in the individual, particularly in children with mild asthma. Some children appear to grow out of their asthma as they grow older; their symptoms or treatment requirements decrease. It is not known whether BHR decreases in these children, but data currently being analyzed in our laboratory suggest that this may be the case. In some individuals the degree of BHR decreases to the

Epidemiologic Methods for Measuring Prevalence of Asthma*

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Problems identified as associated with measuring the prevalence of asthma include the lack of an agreed definition, absence of standardization of questionnaires (both the content and the form in which questions are worded) the nonspecific nature of tests of bronchial responsiveness and the variation in the nature of asthma at different ages, seasonally and due to occupational exposures. Approaches to the resolution of these problems and outstanding questions are discussed.

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level where provocation in day-to-day life is never severe enough to produce airway narrowing and thus symptoms. Such a person may not have had symptoms for several years but the inhalation test remains positive, usually revealing mild but definite BHR. Also, since many subjects with previously diagnosed asthma have normal BR, it appears likely that increased BR can return to normal. Changes in the level of BR between the asthmatic and the normal range have been reported only in individuals with occupational and "seasonal allergic" asthma (see below). 8,9

Occupational and Seasonal Allergic Asthma

Although occupational asthma is relatively uncommon, it is possible that some people in a population sample have symptoms of asthma only in relation to a single agent—either a chemical used at work or a pollen. Subjects with "occupational" and "seasonal allergic" asthma are different from other asthmatic subjects because, at a time when they have not been exposed for several weeks or months to the agent or to the pollen, they have no BHR to histamine and methacholine. 8,9 Such persons in a survey would have questionnaire data consistent with asthma but normal BR.

Methods to Solve These Problems

Definition

The problem of defining asthma can be overcome in two ways. First, by having no definition and simply measuring the prevalence of the features known to be most characteristic of the disease (BHR and symptoms). Second, by acknowledging that there are several kinds of asthma and making some arbitrary definitions specifically for epidemiologic studies. Some suggested definitions follow.

Asthma. Asthma is defined as bronchial hyperresponsiveness (demonstrated by the response to either a bronchoconstrictor or bronchodilator) plus symptoms of asthma.

The symptoms are wheeze, chest tightness and, particularly in children, dry cough at night. Breathlessness is not particularly helpful since asthmatic subjects rarely have it as a solitary symptom without wheeze or chest tightness.

Asthma can be defined as "current" or "past" depending on the length of time since symptoms were experienced. An arbitrary period of 12 months is usually used.

Seasonal Allergic Asthma. Seasonal allergic asthma is defined as symptoms consistent with asthma during the season of a specific pollen and airway narrowing in response to challenge with the pollen, but normal bronchial responsiveness outside the pollen season.

Occupational Asthma. Occupational asthma is defined as symptoms consistent with asthma, related only to exposure to a specific substance at the work place and airway narrowing in response to challenge with the substance. Bronchial responsiveness may be normal or increased depending on a number of factors and is not part of the definition.

Chronic Obstructive Pulmonary Disease (COPD). Chronic obstructive pulmonary disease (COPD) can be defined as airflow limitation (low FEV/FVC ratio) in subjects having less than 15 percent increase in FEV, after bronchodilator aerosol administration. Breathlessness may or may not be present depending on the severity of the airflow obstruction.

It is likely that some subjects have both asthma and COPD while in others it is not possible to define the nature of the bronchial disease during an epidemiologic study.

Questionnaires

The construction of questionnaires, which are simple, specific, reliable and useful in different populations is extremely difficult. Ideally it would be useful to have a questionnaire which could be used by itself to document the prevalence of asthma. However, at present it appears that realistic information about bronchial diseases in a population cannot be obtained without the response to bronchoconstrictor and bronchodilator agents.

Tests of Bronchial Responsiveness

Resting Lung Function. A detailed description of the methods used to document resting lung function and BR are not necessary here. It is important to use a spirometer which is reliable, easily calibrated and prints a trace of the expirograph which can be easily seen by both the subject and the operator so that reproducible values for the forced expiratory volumes are obtained.

Measurement of Bronchial Hyperresponsiveness. The method of bronchoconstrictor testing which we described uses hand-operated nebulizers to administer increasing doses of histamine or methacholine in a cumulative manner. The bronchial response (BR) is measured using a spirometer to record the FEV,. The dose delivered from the nebulizer, expressed in μmol on a log scale, is plotted against the percentage of change in FEV, to give a dose-response curve. The degree of BR is expressed as the provoking dose which causes a 20 percent fall in the FEV,. (PD FEV,). The test takes between six and 15 min depending on the number of doses given and the facility with which the subject can perform the tests of lung function.

Other methods can be used to measure BHR in populations. It is possible to adapt the Wright nebulizer method to make it shorter for field studies. Weiss et al have shown that it is possible to use eucapnic hyperpnea with subfreezing air for population studies in children. Such studies may be more difficult in subjects unable to hyperventilate because of abnormal resting lung function, and are difficult to do in the isolated field setting. Others have used exercise, but this test is much more difficult to standardize for field use.

The bronchodilator test is a useful method for measuring BR in subjects whose resting lung function is too poor to allow a test with a bronchoconstricting agent. The test consists of measuring the FEV, after increasing doses of a bronchodilator aerosol until no further improvement occurs. The response time to the particular drug used must be taken into account. The maximum improvement is expressed as a percentage of the initial value.

Changing Nature of Asthma

Because the degree of BHR changes with time in some individuals within populations, small cross-sectional studies at one point in time may not give a true indication of the prevalence of asthma. In addition, care must be taken with longitudinal studies to follow the whole sample. However, it is possible to document and report changing levels of BR within populations by the latter type of study.
Different Kinds of Asthma

Occupational asthma is rare in most communities. Specific questions relating to the time of onset and periodic nature of symptoms may allow it to be suspected but specific documentation requires further studies. Asthmatic subjects whose symptoms are worse in the pollen season are common in most communities. Subjects with "seasonal allergic asthma" to ragweed, as defined above, have been well described. Skin tests, questions about rhinitis and studies done in and out of the pollen season can be used to define this group if they are present.

RESULTS OF EPIDEMIOLOGIC STUDIES USING TESTS OF BRONCHIAL RESPONSIVENESS

Bronchial Hyperresponsiveness

The distribution of BR within a population and the prevalence of BHR, defined as different levels of $PD_{20FEV_i}$, are relatively easy to measure. In children in Australia we have found that BHR, defined for this purpose as a $PD_{20FEV_i}$ to histamine of less than 8.0 $\mu$mol/ varies from 10 to 18 percent in different populations, is relatively easy to measure. In children aged eight to 12 years, this prevalence would be much higher, and the prevalence decreases as children grow. In adults the prevalence, using the same definition, in a rural population was 14.6 percent.

Bronchial Hyperresponsiveness in Relation to Symptoms

Some children and adults with past symptoms of asthma and some with a previous diagnosis of asthma do not have increased BR. However, most subjects with recent symptoms (within the last year) have BHR.

On the other hand, asymptomatic BHR is relatively common, although the BHR is usually of mild degree. Most subjects with a $PD_{20FEV_i}$ of less than 1.0 $\mu$mol of histamine have had recent symptoms although sometimes they deny symptoms when answering the questionnaire. When asked during the test, they frequently admit to wheeze and/or chest tightness. There are also some children with asthma according to the present definition who have never been diagnosed and have never sought treatment. The importance of this group, also found in other studies, in terms of risk for developing asthma or abnormal lung function, is unknown.

Factors affecting BHR

Children who are highly atopic, as judged by skin tests, are more likely to have BHR than mildly atopic children and are also more likely than non-atopic children to continue to have BHR as they grow. Both a parental history of asthma and a history of bronchitis before the age of two years correlate with asthma and, in our as yet unpublished studies, we have found that these factors correlate strongly with the prevalence of BHR.

Asthma in Australia

Using the definition suggested above, figures for the prevalence of current asthma in different populations in Australia can be given. In children aged eight to 12 years, this varies between 5 and 7 percent in different populations. Figure 1 shows a hypothetic model of the factors which may predispose to BHR in childhood. It is suggested that genetic factors may predispose to BHR, as may the diet early in life. A predisposed child may then develop wheezing during infancy, especially if a severe respiratory infection occurs. During childhood, some of this group have intermittent BHR (symptoms of wheezing and/or chest tightness occur on occasions). A small percentage of the wheezing infants continues to have persisting BHR and asthma. Many children can be categorized as past incidence of asthma on the basis of wheezing or a previous diagnosis, but by the age of ten years they have no BHR. Some of them may well develop attacks of asthma in later life.

SUGGESTED METHOD FOR FUTURE POPULATION STUDIES

Protocols

Present experience suggests that it is not possible to define the prevalence of bronchial abnormalities or of asthma in a population without tests of BR. The test for bronchoconstriction described here is simple, cheap, easily performed in remote areas and above all, extremely safe. It becomes progressively easier to obtain ethical approval for studies on the basis of thousands of tests performed without incident. Ideally the protocols for studies relating to prevalence of, or factors associated with, asthma should include a simple, reliable questionnaire; a test of lung function, a test of BR and skin tests to document atopic status.

Choice of Bronchoconstrictor Test

As yet there is no single test specific for asthma. Presently, the most useful test is probably a methacholine inhalation test.
When to use a Bronchoconstrictor Test?

It is now clear from studies in the community and in the laboratory that virtually all patients with airflow limitation have BHR and, in patients with COPD, BHR is roughly proportional to the degree of resting obstruction as measured by the FEV1. If, during an epidemiologic survey, it is possible to study each individual on one day only, more information can be gained from a bronchodilator test than from a bronchoconstrictor test in subjects whose FEV1/FVC ratio is less than two standard deviations of the predicted value. A response of greater than 20 percent in the FEV1 is usually regarded as BHR, but the response can be treated as a continuous variable. It must be recognized, however, that when the FEV1 is less than 1.5L these changes are greatly magnified and a 20 percent change may not reflect the responsiveness of asthma. Also, it is known that some asthmatic subjects may not respond to bronchodilator aerosol inhalation on a given occasion but these people are usually very sick and not likely to attend a survey. If the distribution of BR in the whole community is required, and it is possible for subjects to attend on two different days, a bronchoconstrictor test can also be done.

Presentation of Data

The level of BR (in terms of the PD50FEV1, in µmol of histamine or methacholine) should be expressed as a continuous variable. The ranges found in clinical asthma using the same methods should be given to help in the interpretation of the data by others. Data should be reported in such a way as to allow the current prevalence of BHR, asthma, and COPD (as defined above) to be determined by the reader.

Questions Which Might Be Asked

Many questions remain unanswered about the nature of asthma. Some of them can be answered by epidemiologic studies. On the basis of the model described, some are listed.

Is there a genetic factor which predisposes to BHR?

Is there a dietary factor? In particular, does sodium intake predispose and fish oil protect children from the development of BHR?

Is the natural history of BHR (its onset, subsequent variability and persistence) related to the allergic status of individuals within populations?

Does the highly variable or intermittent BHR found in some children have different characteristics from the BHR documented in children with persisting asthma?

What are the factors associated with persisting rather than improving BHR as children grow?

Are children with unrecognized and/or untreated BHR at risk of developing abnormal lung function or severe asthma at a later time?

References

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