originally recommended by Mitenko and Ogilvie—namely, a 5.6 mg/kg loading dose followed by 0.9 mg/kg per hour for maintenance. It is disturbing to continue to see emphasis on and use made of this formula. Mitenko and Ogilvie studied nine asthmatic patients who were not acutely ill at the time of the study and who had stopped theophylline medication 15 hours before the theophylline pharmacokinetic studies were performed. Several investigators have subsequently shown that the clinical application of this formula in daily hospital practice often results in theophylline levels that are higher than desirable. Since the half-life of theophylline varies widely and is prolonged in many situations, this formula should not be relied upon. Others have modified the formula, recommending a smaller dose of aminophylline, particularly in patients with liver disease and congestive heart failure and in the elderly.

Seizures and death from theophylline toxicity have been reported. The theophylline levels in seven of the patients with seizures reported by Zwillich et al ranged from 47 to 70 μg/ml, with the dosage of intravenous aminophylline ranging from 27 to 51 mg/kg body weight per day. These dosages are higher than those usually used and were higher than those recommended by Mitenko and Ogilvie, whose maintenance schedule provides 21.6 mg/kg body weight per day. In one of the patients reported by Zwillich and co-workers, the highest theophylline level was only 25 μg/ml, and that patient received a dosage of 20 mg/kg body weight per day. The occurrence of seizures at a theophylline level of 25 μg/ml is uncommon, although others have reported seizures at similarly low levels.

When available, serum levels of theophylline are useful in guiding intravenous aminophylline therapy. Not everyone can readily obtain serum theophylline determinations, and the following guidelines are helpful. Because of the potential seriousness of theophylline toxicity, if one errs it should be in giving too little rather than too much. Bronchodilatation has been demonstrated even at serum levels as low as 2 and 5 μg/ml. I would concur with recommendations that the dosage of intravenous aminophylline in adults not exceed 1 gm in 24 hours or 0.5 mg/kg per hour, unless serum theophylline determinations are available. Toxicity may occur even at these dosages. The dosage should be reduced in patients who have congestive heart failure and liver disease, in the elderly, and in those who have other conditions in which the half-life of theophylline is prolonged. In children, dosage recommendations for maintenance aminophylline therapy range from 9 to 39.6 mg/kg per day.

Simons and associates found that 15 mg/kg per day was safe in 17 children. A similar figure has been given for the starting dose of oral theophylline. Lastly, it should be remembered that other measures in addition to theophylline must be used in treating severe asthma.

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Evaluation of Asthma

Physicians in the United States seem to be reluctant to perform and accept an objective measure of airway obstruction as the index of severity of asthma. Maybe they do not know that a test is available, or maybe they do not think it is necessary.

Such a test is available. The Wright peak flow meter, widely used in the United Kingdom and less so in this country, is now available as an inexpensive, accurate, lightweight and compact mini-Wright peak flow meter. Measurements of peak expiratory flow rate (PEFR) obtained with this instrument correspond closely to those obtained with the original peak flow meter and the instrument that we

calibrated with a pneumotachygraph was extremely accurate.

Why is it important to measure PEFR in asthma? There is a wealth of evidence that the severity of asthma is not reflected in the intensity of the patient's symptoms or in physical findings. It is generally agreed that severe asthma requires measurement of arterial blood gas levels, that a normal or increased Pco2 indicates severe asthma, and that this cannot always be predicted. However, lesser degrees of severity are not reflected in the level of Pco2 and one cannot or should not make this measurement as frequently as is needed to follow the sick patient carefully.

Asthma is a problem to the extent that the airways are obstructed, and airway obstruction is reflected both in increase of airway resistance and reduction of expiratory flow rates. In fact, there is close correlation between these measurements in asthma and it really does not matter which one is used to observe the patient's progress. PEFR is much the easiest. It does not require full expiration, which may itself provoke bronchoconstriction and worsening of symptoms, and it can be measured over and over again without difficulty.

The PEFR is an extremely useful indicator in the evaluation and treatment of asthma. If there is no improvement of PEFR after inhalation of a bronchodilator aerosol, epinephrine or terbutaline should be given by injection. In deciding whether or not a patient should be hospitalized, the finding of low PEFR after initial treatment has proven to be a very useful guide. In observing hospitalized patients, we have learned that if the PEFR rises it is not necessary to repeat arterial blood gas determinations because the Pco2 will not be higher. If the PEFR fails to rise, careful monitoring must be continued and therapy intensified.

We know that isoproterenol must be inhaled repeatedly, perhaps every 20 minutes, to produce maximal effect. Why should not each patient use the peak flow meter to learn how often to inhale bronchodilator drugs to obtain the optimal result? We know it is better to increase therapy, as with steroids, as asthma begins to worsen rather than to wait and try to reverse severe obstruction that has already developed. Why not have the patient measure PEFR every morning and use this to guide the intensity of therapy?

At this hospital, the PEFR has become synonymous with the severity of asthma in the emergency room, in the clinic and on the ward. I believe this has been very useful. We have identified and treated patients who were more sick than they thought and than we thought. We have not had to measure arterial blood gas composition so often. We have been able to make multiple measurements of drug response, so necessary in the evaluation of the treatment of a disease as variable as asthma, leading to knowledge of the dose-response curve of inhaled isoproterenol and the efficacy of use of aerosolized corticosteroids. Our patients have learned about their asthma and about the drugs they use. In an age when it is appropriate for a patient to know as much about his disease as his physician, his own performance and interpretation of a test is particularly appropriate.

At least the doctor treating the patient with asthma should measure PEFR and use the measurement as he uses the sphygmomanometer in treating hypertension. There is no reason why the patient participating in his own management cannot do the same.

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Has Impedance Plethysmography Come of Age?

Impedance plethysmography, lacking in credibility for many years, may have come of age, as exemplified in the article by Weng et al in this issue of Chest (see page 64). Forty years ago, due largely to the foresight and research of that article's senior author, Jan Nyboer, D.Sc., M.D.,¹ the utilization of impedance was expected to become one of the most significant innovations for the detection of disease in clinical medicine; it was extremely sensitive, yet totally noninvasive and safe.

Unfortunately, the world of clinical medicine still clung to its anatomic era, although the golden age of the great anatomist-physician had passed. There was little interest in a technique which could detect and measure changes in fluid in compartments of the...