ASTHMA is among the serious manifestations of allergic disease for which patients require immediate relief. Because of its chronicity and tendency to recur there has been a continuous search for more effective symptomatic treatment.

A large number of drugs have been developed which are purported to relieve the symptoms of asthma. They are used and often abused to an extent which may actually endanger the life of the patient.

For some diseases, in which only one effective remedy is available, a calculated risk is justified to save the life of an individual. Under these circumstances the value of such treatment outweighs its danger. This situation should not often arise with asthma, for which the choice of remedies is wide enough to make it possible to avoid any one which may be hazardous in a particular patient. Let us, therefore, take stock of the measures used in the treatment of asthma and evaluate their respective merits.

We will begin with an example of a child who died from bronchial asthma after a surgical operation and whose case was presented at a hospital conference:

Post-mortem examination disclosed that the entire bronchial tree was completely filled with thick, gelatinous fluid. A discusser at the conference quite rightly criticized the use of atropine and stated that bronchoscopic aspiration, postural drainage and nasotracheal intubation should have been instituted. He added that adrenal steroids had also been indicated. To my astonishment he went on to recommend antihistaminics, aminophylline and epinephrine before, during and after anesthesia.

This discussion leaves one dismayed, for with a plugged bronchial tree many of the drugs suggested by the critic are as contraindicated as was the atropine. Antihistaminics, for example, with their drying, atropine-like action, are specifically contraindicated.

The abuse of drugs is further exemplified by the following fatal case of asthma, occurring in a 3-year-old girl; the evidence pointed to death being due in part or wholly to the medication used:

This young child was brought to a hospital because of respiratory distress with wheezing of 9 hours duration.

Except for two brief asthmatic attacks 2 months prior to admission, she had been ostensibly well. There was no history of recent infection. The morning of the day of admission she suddenly developed wheezing, becoming rapidly and progressively worse, so that within a few hours she was having severe dyspnea. A local physician gave an injection of epinephrine, without relief, and she was brought to the hospital a few hours later.

Physical examination revealed a fairly well-developed, undernourished, female, Negro child, critically ill, restless but exhausted, moderately dyspneic and cyanotic. Temperature was 38.8°C, pulse 130, rapid and weak, and respirations 50. Thoracic excursions were rapid and very shallow; there was marked suprasternal retraction, and abdominal breathing was prominent. The thorax was moderately hyperresonant and there were numerous sibilant and sonorous rales throughout both lung fields.

The child was placed in an oxygen tent and given 4 minims of epinephrine subcutaneously. Because there was no relief, 1 ml of 1:1000

* Posthumously submitted.
Presented at the Annual Meeting of the American Academy of Pediatrics, October 6, 1957.

ADDRESS FOR REPRINTS: M. Dworetzky, M.D., 50 East 78th Street, New York 21, New York.

PEDiATRICS, April 1959

781
782 ASTHMA

epinephrine in oil was given intramuscularly, shortly followed by 100 mg phenobarbital subcutaneously.

Subsequent therapy included $\frac{3}{4}$ tablet of Tedral® orally, repeated twice in 8 hours. A croup tent was substituted for the oxygen tent. One dram of Elixir of Benadryl® was given and twice repeated. An additional 0.75 grains of phenobarbital was given subcutaneously.

The temperature rose to 39.7°C, the pulse to 195 and the respirations to 68. Dyspnea and cyanosis increased and the patient finally expired from asphyxia 15 hours after admission.

At necropsy the pathologic diagnosis included: asphyxia due to generalized bronchial obstruction from excess bronchial mucus; pulmonary emphysema; right heart failure, as evidenced by dilatation of the right heart and marked engorgement of the great veins.

If this child did not die directly from overmedication of improperly chosen drugs and lack of proper physiologic therapy, it is likely that the medication used contributed to her death.

Having brought the problem of the use and abuse of drugs into focus with these two cases, let us now consider the value and the danger of each of the important drugs used in the treatment of asthma.

ANTIHISTAMINICS

Although these drugs do alleviate symptoms of excess nasal and lachrymal secretions, they generally fail to relieve asthma. As a matter of fact, they produce drowsiness and tend to dry the secretions, resulting in greater bronchial obstruction. Such adverse effects might conceivably cause or contribute to the death of a patient in status asthmaticus.

The toxicity of these drugs is high, especially for infants and young children. Patients given antihistaminics may develop severe drowsiness or insomnia, difficulty of co-ordination, muscular twitching, convulsions, vertigo, mental disorientation and even shock. Accidental deaths have ensued because of disorientation or in-co-ordination after taking such a drug.

Were these drugs of real value in alleviating asthma, they might be used under controlled conditions. However, because they so often aggravate asthma, they are contraindicated, as is exemplified in the case of the child previously cited.

Shortly after benadryl appeared on the market, we gave one dose of 50 mg to a 5-year-old child during an attack of asthma. This was followed by a striking aggravation of obstructed breathing and cyanosis. Epinephrine, oxygen and steam relieved this episode. Following this experience we have never used antihistaminics for asthmatic attacks. Numerous reports in the literature since that time have shown antihistaminics to be contraindicated in the treatment of asthma.¹

AMINOPHYLLINE

Aminophylline U.S.P. (theophylline ethylenediamine), one of the xanthine group of drugs, contains approximately 78% theophylline and 12% ethylenediamine. It is readily absorbed from the gastrointestinal tract. It is a stimulant to the central nervous system and gastric mucosa, a mild diuretic and smooth muscle relaxant. These effects are all accentuated with overdose.

Toxic symptoms are often seen in children as a result of accidental ingestion and excessive therapeutic doses. A series of alarming reports of severe toxicity and death have appeared since 1954.²⁻⁸ The toxic effects are irritability, dehydration, severe vomiting, hematemesis, albuminunia, stupor, convulsions and death.

In all reported cases of severe toxicity in children aminophylline medication by rectal suppository had been given repeatedly despite progressive development of alarming symptoms. This is illustrated by the following case of death cited by Nolke:⁴

A 3½-year-old boy with congenital stenosis of the trachea was admitted to the hospital for the tenth time for respiratory difficulty with

---

¹ Each tablet contains: Theophylline, 130 mg; ephedrine HCl, 25 mg; phenobarbital, 8 mg.
² Each 4 ml contains 10 mg benadryl hydrochloride.
infection of the upper respiratory tract. The child was placed in a steam room, and was given penicillin and sulfadiazine.

An aminophylline suppository (3% grains) was administered every 6 hours. The following events ensued after this repetition of aminophylline:

After the fourth suppository he refused all food except milk, which he was unable to retain. He urinated frequently in bed.

After the fifth suppository he became extremely restless and required restraints.

After the seventh suppository he vomited "brownish mucus shreds" that shortly became "reddish fluid." He perspired profusely and constantly asked for water.

After the ninth suppository, he was listless. Temperature rose to 38.4°C and he vomited a large amount of "brownish fluid."

After the eleventh suppository his vomitus was described as "coffee grounds with mucus" and he again became restless.

After the twelfth suppository his vomiting became continuous, his temperature rose to 40.0°C and he began to have convulsions. The temperature rose further to 41.1°C. The skin became cold and mottled, his peripheral veins collapsed and death followed shortly thereafter.

McKee and Haggerty cite another case of death in a 3-year-old child with recurrent attacks of asthma:

This child was admitted to the hospital because of vomiting and increasing lethargy of 18 hours duration.

Prior to entrance into the hospital he had been given full strength Aminet suppositories every 8 hours for three doses (32 mg/kg body weight per dose). Vomiting began 5 hours after the first suppository. It initially contained food and clear fluids and later coffee-ground material that was guaiac-positive. Initially restless, he became more and more lethargic until at the time of entry into the hospital he was stuporous.

Despite all efforts to save this child, his temperature rose to 41.7°C, the pulse was 200, respiration 30 and Kussmaul in type. The blood pressure finally became unobtainable and the patient died.

McKee and Haggerty reviewed a total of 35 patients from 8 weeks to 6 years of age with aminophylline poisoning (8 from their hospital records and 27 from the literature).

They found the earliest signs of toxicity to be irritability and restlessness which may progress to tremors, convulsions and finally coma. In this series, 29 of 30 showed irritability, 14 of 35 had convulsions, and 14 of 32 were stuporous. Approximately 20% died. Death in most cases was thought most probably due to medullary failure.

Vomiting occurred in practically all cases, accompanied by "coffee-ground" emesis. This persistent vomiting is probably due to central action. Diuresis and vomiting account for the dehydration which is seen in practically all the cases.

Nolke reports on the necropsy findings in four cases. Prominent among these are esophageal ulceration with perforation in two cases, pulmonary inflammatory changes in all, slight edema, and minimal vascular engorgement of the nervous system. Petechiae were seen in the gastric mucosa as well as central lobular congestion of the liver.

All who have reported on these toxic effects suggest that the pediatric-size suppository which contains 250 mg aminophylline is entirely too large a dose for a 3-year-old child and should be reduced to at least one-half. Preparations containing ephedrine are even more toxic, since this drug enhances the action of aminophylline.

Aminophylline can be used in the treatment of asthma when it is given sparingly in one or two small doses, 100 mg for infants and 250 mg for older children. Under no circumstances should an order be left to repeat it every 6 to 8 hours, for all the deaths occurring in young children resulted from this type of repeated medication. Aminophylline has proved highly toxic to children under 3 years of age. There are reports of deaths after intravenous injections in adults. The safest method of administration is orally or rectally. It should not be combined with ephedrine.

SEDATIVES AND OPIATES

Huber and Koessler in their classic paper
on the pathology of asthma, reported the outstanding finding to be complete obstruction of the middle and smaller bronchi and bronchioles by mucus secretions.

Walton et al., in a study of 13 patients with asthma who died and had necropsy performed, corroborated this observation and further correlated these asthmatic deaths with therapy used prior to death. They concluded that death may occur from asthma at any age. Heavy sedation preceded death in 9 of the 13 cases. They incriminated morphine, Demerol® (meperidine HCl), barbiturates, intravenous anesthetics and curare. Barbiturates, for example, are useful drugs to allay anxiety, but large doses are dangerous, as was shown in two of the cases.

Opiates

I should like to go on record with my opinion that the use of morphine in asthma is little short of criminal. Besides its inhibitory effect on the respiratory center, it also causes bronchoconstriction. I can see no reason for its use and believe that many deaths from asthma have been directly or indirectly due to its use. This is supported by the study of Huber and Koessler.9

Demerol®

This synthetic drug has gained popularity in the treatment of asthma. Its antispasmodic effect is thought to be atropine-like in quality, while the analgesic effect resembles that of morphine. Even though there is no unanimity of opinion about this, there is evidence supporting its depressant effect on respiration.11

There are two instances of death from Demerol® cited by Walton et al.10 In one instance a 31-year-old asthmatic took 300 mg of Demerol® by mouth and died during the night. Another 39-year-old asthmatic was given 100 mg of Demerol® for an attack of asthma and died 25 minutes later. In both instances the lungs at necropsy were voluminous and were occluded by thick tenacious mucus.

We are familiar with a case of a 12-year-old girl who died in a hospital shortly after receiving several doses of Demerol® for asthma.

Finally, Demerol®, as morphine, is a narcotic, and the danger of addiction from its use in a disease characterized by repeated exacerbations should be obvious to all. Therefore, Demerol® should not be used in the treatment of asthma.

Barbiturates

Phenobarbital is extremely valuable for mild sedation when given in ¼ or ½ grain doses. When given in excess, it may be a sole or contributory cause of death in asthma.

A striking case was that of a 14-month-old infant suffering from a severe asthmatic attack who was given 1 grain of phenobarbital at midnight and a second 1 grain dose 3 hours later. This infant died 2 hours after the second dose. The nurse recorded that the child’s labored breathing became quieter ½ hour before death. The authors state: “It is difficult to escape the impression that the heavy sedation, 2 grains of Luminal® (phenobarbital) in 3 hours, given to an exhausted, cyanotic baby, contributed to its death.” At necropsy the trachea and bronchi were found plugged with tenacious exudate.

In the first case we cited at the beginning of this paper, phenobarbital in excessive amounts may well have contributed to the death of the infant.

Walton et al. describe two cases, a 58-year-old patient who received 6 grains of sodium amytal intravenously and the other, a 44-year-old patient given 3 grains of sodium amytal by mouth. Both died within 2 and 1 hours, respectively, after medication was given. Post-mortem examination disclosed voluminous lungs with bronchi obstructed by mucous plugs. It was concluded that these patients died of acute asphyxia due to respiratory failure and that heavy sedation might well have contributed to death.

Therefore, while barbiturates in small quantities are beneficial in the treatment of asthma, excessive amounts may contribute to death.
Sedation in Preparation for Bronchoscopy

Although bronchoscopy is a valuable aid in the removal of foreign bodies in the trachea and bronchi, and is a useful diagnostic procedure in bronchial obstruction other than asthma, it should be avoided if possible in asthma. Two instances may be cited:

A 25-year-old war veteran had a severe attack of asthma and was completely refractory to the antispasmodics used. Bronchoscopy was attempted. One hour before this procedure he was given 50 mg of Demerol subcutaneously with intravenous Pentothal (thiopental) and curare as an anesthetic. His condition deteriorated rapidly and he died shortly thereafter.

A housewife, 44 years old, had an intractable attack of asthma and bronchoscopy was attempted. She was given 3 grain morphine and 1/150 grain atropine. Pontocaine 1% (tetra-caine) was applied to her pharynx and the patient expired suddenly, before the bronchoscope was passed.

Both post-mortem examinations revealed voluminous lungs with diffusely obstructed bronchi.

In one case of ours in which bronchoscopy was attempted, the child almost died. We have never since had the courage to subject an asthmatic child to this procedure.

If bronchoscopy is to be used at all, it should be done with ether anesthesia, avoiding barbiturates and opiates. Instead of using the bronchoscope to remove mucous plugs, we have accomplished the same purpose by the administration of syrup of ipecac, as will be discussed.

OXYGEN

Placing an asthmatic child in an oxygen tent is not as advisable as it might appear. Although the child may suffer from air hunger, the increased oxygen is relatively ineffective in severe status asthmaticus, where the bronchi are plugged. Moreover, oxygen therapy tends to further dry the bronchial secretions. An oxygen tent may be psychologically detrimental, causing claustrophobia and panic.

Prolonged oxygen therapy may be dangerous to patients who suffer from chronic hypoxemia and carbon dioxide retention due to any cause. The further administration of oxygen in such a situation causes decreased pulmonary ventilation which in turn leads to increased retention of carbon dioxide and lowering of the pH of the arterial blood, or respiratory acidosis.

Clinically the manifestations of respiratory acidosis are delirium, stupor and coma, and these are relieved by the withdrawal of the patient from tent or mask, and by increasing respiratory excursions by mechanical means, if necessary.

If oxygen is judged necessary, it is better practice to give it by nasal catheter, combining it with steam inhalation.

Helium-oxygen mixtures have been thought to pass the narrower bronchi with greater ease than oxygen alone. Schiller et al. subjected this hypothesis to study to determine whether there was any definite difference between air and a mixture of 80% helium and 20% oxygen. They found that in severely ill patients there was no significant difference between air and helium-oxygen mixtures in the expiratory reserve volume, the inspiratory and vital capacities or the speed of flow during the performance of vital capacity.

ADRENAL CORTICOSTEROIDS

Dworetzky et al. found that neither cortisone nor adrenocorticotropic (ACTH) had any effect on the degree of anaphylactic shock produced in sensitized guinea pigs. Arbesman et al. and Johnstone et al. reported that ACTH and cortisone afford a moderate protection against reversed anaphylaxis in the guinea pig, while Arbesman was unable to demonstrate protection by these hormones against direct active or passive anaphylaxis. Neither did they demonstrate any influence on antibody formation in the rabbit or guinea pig during sensitization, nor any influence on the reaginic titer in the sera of man.

Feinberg and Malkiel showed only a partial protective effect in inhibiting or de-
laying the symptoms of asthma induced by aerosolized antigens in passively sensitized guinea pigs.

We have long felt that any drug that does not prevent anaphylaxis in the guinea pig is unlikely to be efficacious in the treatment of clinical asthma. This has been generally true with the antihistaminics, which were shown to prevent anaphylaxis-like symptoms induced by the inhalation of histamine but failed to prevent or relieve true anaphylactic reactions. We have subsequently found that antihistaminics do not prevent or relieve asthma in the human being.

However, although the exact mechanism of adrenal steroid therapy is not known, it does afford symptomatic improvement in asthma, which is accompanied by a decrease in asthmatic paroxysms, dyspnea and wheezing, and an increase in vital capacity, appetite, sense of well-being and physical activity.

The warning stated by Thomas should be heeded, namely, that with prolonged use of these hormones there is a threat of death, of prolonged or permanent incapacitation, or of irreversible damage to vital tissues and organs.

Good and his associates have shown that significant danger exists when ACTH, cortisone, or related hormones are employed in pediatric practice. This danger is greatest with large doses and prolonged therapy, although patients treated with even relatively small doses over short periods of time have occasionally shown ill effects. The ill effects may include: disturbance of the electrolytic balance, with retention of sodium chloride and water and loss of potassium; disturbance of glucose metabolism, with occurrence of convulsive seizures; development of hypertensive encephalopathy, status epilepticus, permanent brain damage; gastrointestinal disturbances, such as intestinal perforation; lowered resistance to infection, with a tendency to the production of widespread staphylococcal infections; thrombembolic phenomena; emotional disturbances; osteoporosis; pathologic fractures and others.

Because status asthmaticus is so often associated with secondary pulmonary infections, hormonal therapy without antibiotics is hazardous. We also view with alarm the report of Haggerty and Eley in which was pointed out a greatly increased fatality rate from chickenpox in children who had been under treatment with adrenal corticosteroids. Two children receiving adrenal steroid therapy succumbed to fatal shock within a few days after vesicles appeared, and a third died of encephalitis 3 weeks after onset of varicella. Ten more fatal cases were discovered in the files of 65 physicians to whom they wrote.

To quote Good and his associates: "the best method of reducing the frequency of serious untoward side reactions to cortisone and ACTH is for every physician to recognize these hormones as the potent pharmacological agents which they are, and to use them only where they are clearly indicated after having evaluated the potential hazard as well as the potential benefit to be derived from their clinical application."

Therefore, we would state that adrenal steroids may be used to good advantage in status asthmaticus, but only after traditional therapy has been tried and found wanting. However, because of the potentially serious consequences of prolonged administration of these hormones in children, they should be discontinued as soon as the immediate symptoms have subsided.

**EPINEPHRINE (ADRENALIN®)**

A child should never be given an injection of more than 0.1 or 0.2 ml of epinephrine 1:1000 at a time. It should be given subcutaneously or intradermally and never intravenously or intramuscularly. There is no objection to the repetition of the same small dose at intervals of 20 to 30 minutes. If the aim is to produce relief of bronchiolar spasm, small amounts produce the desired effect, whereas large amounts may actually cause a further bronchiolar constriction.

Other ill effects of large doses, such as 0.5 to 1.0 ml, are apprehension, tachycardia,
pallor, headache, rise in blood pressure and syncope. These result in the superimposition of a greater feeling of disaster than the patient is already experiencing from the asthma.

**Epinephrine in Oil**

This has been advocated to overcome the undesired effects of large doses and for prolonged action. We do not believe it should be used in children. Unless Adrenalin® in oil has been thoroughly emulsified by warming in the hand and shaking vigorously, severe reactions to overdosage may occur.

Epinephrine is not a medication that can be used for a long-continued effect. It either works promptly or not at all. Since it retains potency only in an acid pH, it is probably effective in the alkaline pH of the blood for a short time.

Another undesirable effect that occasionally follows an injection of epinephrine in oil is the development of an oleoma, which may require excision, because sometimes it grows quite large.

**Epinephrine (1:100) by Inhalation**

If it is correct to assume that the action of epinephrine is immediate, one or two series of inhalations should be sufficient for relief of an attack of asthma.

Patients given nebulizers generally tend to use them excessively. The simplicity of inhalation therapy tempts the patient to reach for the nebulizer at the slightest provocation and its use may become habit-forming. The term “habit-forming” is not used in the same sense as addiction to morphine, but rather to indicate that the patient is tempted to administer it to himself for its stimulating effect when it may not be altogether necessary. It gives the patient a “lift.” I recently had a child 12 years of age who was so dependent upon it that she inhaled epinephrine every night before retiring for fear that she might otherwise suffocate. It took 4 months to rid her of the habit. She now states that at times she still misses the exciting stimulus it gave her.

We have also had the experience of substituting water for epinephrine solution in a nebulizer. The fact that relief was obtained demonstrates the psychologic dependence that had been established.

For these reasons I generally forbid the use of the nebulizer.

**EPHEDRINE**

What has been said about the undesirable effects of epinephrine holds for ephedrine as well, though to a lesser degree. Thoughtless and excessive use of ephedrine, orally or in nose drops, may result in the adsorption of large amounts. Ephedrine sulfate should be prescribed for a given attack and only several doses be advised. Nose drops should also be prescribed in small amounts and limitation put upon their use.

**SYRUP OF IPECAC**

In asthma due predominantly to bronchiolar spasm, the antigen reaches the bronchioles through the blood stream, and epinephrine will work most effectively. We find this type of reaction in food-sensitive cases, and it is the one often encountered in early childhood. The same type of reaction occurs in serum-sensitive patients following an injection of specific serum, and it is relieved by epinephrine if the shock is not too profound.

What about the child who is given injection after injection of epinephrine without the slightest relief and who may have been in status asthmaticus for several days? Why doesn’t the epinephrine help? In such cases it is not the bronchiolar spasm that is predominant, but edema with marked plugging of the bronchi. We learned this from guinea-pig experiments. When animals inhale antigenic dusts, the allergen, coming in direct contact with the lining and vessels of the larger air passages, produces predominantly edema and increased secretion which result in obstructive symptoms. On the other hand, in anaphylaxis after intravenous injection, the allergen, coming in contact with the smooth muscle of the terminal bronchioles, produces bronchiolar
spasm. If bronchiolar spasm is the main cause of the symptoms, the administration of epinephrine will bring about relief. Therefore, if no relief ensues from repeated injections of epinephrine or other anti-spasmodics and bronchodilators, we are more likely dealing with obstructive bronchial asthma, due in all probability to some inhalant allergen which has entered the air passages directly. Then, cease epinephrine administration and order some syrup of ipecac!

For infants and young children give % to 1 teaspoonful of syrup of ipecac; if this does not induce emesis, give 2 teaspoonfuls. For older children and young adults, repeated doses may be given until the desired effect is produced. Follow the ipecac with a half glass of lukewarm water to further its emetic action. If this therapy is used, the result is effective because relief from distress follows quickly upon the release of the mucous plugs in the bronchial tree.

What is the mechanism of action of emesis in raising sputum? Small particles, or even quite large objects may gain access to the respiratory tract. Macklin has pointed out three mechanisms by which such foreign substances, including secretions, are expelled: the cough reflex, the action of cilia and a wave motion said to resemble peristalsis. These three often work together.

According to Gunn, the cough reflex functions in the upper airway, the cilia act as far down as the finer bronchioles, while peristaltic-like movements evacuate the entire tract, including the terminal airway. Thus, these activities overlap: the upper part of the airway having all three available, the intermediate part two, while the terminal portion would have only one mechanism for evacuation, namely, that of “peristaltic” motion. The peristaltic movements are brought into play only under abnormal conditions, such as ejection of masses of thick exudate from the respiratory lumina. The peristaltic wave in the bronchial tree is said to resemble the reverse peristaltic wave in the digestive tract, and the speed is too rapid to be accounted for by ciliary action. Reinberg describes it as “tracheal vomiting” and Bullowa and Gottlieb as “bellows-like.”

Thus, ipecac, which causes nausea, retching and vomiting, and the irritation caused by the presence of foreign material in the air passages, hasten and increase peristaltis-like action. This tracheal vomiting releases the obstruction which under ordinary circumstances might not be released for days.

I have used this therapy for many years and have never had any untoward effects. I recall being called in consultation for a 2-year-old infant who was receiving the last rites. The child was in a semistuporous state from excessive amounts of phenobarbital and other therapy. I removed the infant from the oxygen tent, donned a rubber apron and gave him 2 teaspoonfuls of syrup of ipecac. Intensive retching ensued, followed by the release of large plugs of mucus. After he came out of the stuporous state, he was given some acetylsalicylic acid, steam inhalation and glucose solution intravenously, and made an uneventful recovery from an acute episode. This child might have died had the therapeutic approach employed during the critical status asthmaticus not been instituted.

DISCUSSION

The symptomatic treatment of asthma in children should be physiologic and mild in approach.

Perhaps the greatest handicap in the treatment of an asthmatic child is the intense apprehension of the parents, which is more often than we would like to admit, shared by the physician. This terror engendered in both parents and physician may impair the latter’s judgment so that he strikes out aimlessly to stop the child’s severe air hunger by any means at hand. As a result there have no doubt been many more needless deaths from asthma than the
literature reveals, since uncomplicated asthma, per se, seldom causes death.

Recall the description already given of the needless death of the child given 12 suppositories of aminophylline. Surely this child, who came to the hospital for respiratory distress due to congenital stenosis of the trachea, developed symptoms completely unrelated to the respiratory distress. Vomiting, hematemesis, irritability, stupor and convulsions were brought on solely by the 12 doses of aminophylline. One wonders how a physician could have given aminophylline 12 successive times in the face of these toxic complications unrelated to the respiratory system.

The infant who developed stupor and unconsciousness after excessive doses of phenobarbital and Benadryl® succumbed in part or wholly as a result of this ill-advised therapy.

The child with simple asthma who is given large doses of epinephrine develops a totally new group of cardiovascular symptoms, such as pallor, palpitation, high blood pressure, rapid pulse and cardiac syncope, which have nothing to do with the original disease. Large doses of epinephrine actually may increase bronchospasm.

We have cited the unfortunate instances in which permanent mental disturbances, gastrointestinal hemorrhage and death followed adrenal corticosteroid therapy.

Finally, antihistaminics, atropine or opiates, by depressing respiratory excursions and drying secretions, often produce effects opposite to those desired.

Therefore, we should concern ourselves with a rational physiologic approach in the management of asthma. All true bronchial asthma is initiated by a spasm of the terminal bronchioles and edema; either may be predominant. To overcome the former, one should administer two or three small doses of epinephrine, not over 0.1 or 0.2 ml each, spaced at half-hour intervals. If immediate relief is not obtained, no amount of antispasmodic will be of any further help, and therefore this medication should be stopped.

Aminophylline, which is a vasodilator as well as bronchodilator, should be given in one or two doses at an interval of several hours; if given by rectum, 100 mg for an infant, 250 mg for an older child. If good results are not achieved after two or three such doses, no further amount of aminophylline will be effective. The same holds true with ephedrine alone or in combination with other antispasmodics. Such medications should be discontinued if relief is not obtained after one or two doses.

If antispasmodics do not relieve the condition, then the asthma is probably not responding because the dyspnea is due predominantly to edema, secretion and bronchial plugging. As practically all deaths in asthma are due to complete plugging of the bronchial tree, it becomes urgently necessary to loosen and release these plugs. Bronchoscopy is dangerous because of the sedation necessary for this procedure. Oxygen is contraindicated because little actually gets into the alveoli and because it tends to further dry the mucous plugs.

What have we left in this desperate situation? Two remedies are at hand. One is to subject the child to steam inhalation, preferably in a steaming bathroom with a shower pouring hot water into the tub. This steam inhalation may help to liquefy the thick tenacious secretions. Fluids should be given orally. If the child is removed to the hospital, he should also be given 5% glucose in distilled water, intravenously, in order to restore fluids lost through sweat and hyper-ventilation. The second effective remedy is the administration of emetic doses of syrup of ipecac (1 or 2 teaspoonfuls) which may result in raising mucous plugs when nothing else has succeeded. Following emesis, the child is given ¼ to ½ grain of phenobarbital by mouth, usually combined with acetylsalicylic acid. This may be repeated every 4 hours for several doses.

Few patients in status asthmaticus can be relieved readily without the addition of antibiotic therapy, for the majority have secondary infections of the upper respiratory tract or lungs.

A remarkable adjuvant maneuver is the
admission of a child with severe asthma to a hospital ward. Taking the child out of the stressful, and perhaps antigen-laden, home environment may of itself produce beneficial effects. Cortisone, antispasmodics and sedatives should not be employed until the effects of the change to the hospital environment are observed. Too often, credit is given to medication when removal to a clean hospital environment is really responsible for the relief of asthma.

In conclusion, if the approach discussed seems nihilistic, such has not been my intention. With so many truly remarkable drugs available, we tend to accept their virtues and to overlook their dangers. I have tried to recall some of the dangers. Drugs, however valuable, must be used with discretion, not routinely. There is still no substitute for good judgment.

REFERENCES

THE USE AND ABUSE OF DRUGS IN THE TREATMENT OF ASTHMA IN CHILDREN

Bret Ratner

Pediatrics 1959;23;781

Updated Information & Services
including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/23/4/781

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
https://shop.aap.org/licensing-permissions/

Reprints
Information about ordering reprints can be found online:
http://classic.pediatrics.aappublications.org/content/reprints
THE USE AND ABUSE OF DRUGS IN THE TREATMENT OF ASTHMA IN CHILDREN
Bret Ratner
Pediatrics 1959;23;781

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/23/4/781