ANESTHESIA FOR THE ASTHMATIC PATIENT

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IT is estimated that two million Americans suffer from bronchial asthma, a disease characterized by recurrent attacks of ventilatory insufficiency due to narrowing of the bronchioles.[1] These paroxysms of bronchiolar spasm are clinically manifested by dyspnea and audible wheezing.[2] Inevitably every anesthesiologist must face the problem of choosing techniques or agents for patients with asthma who require operation. This investigation was undertaken to study the clinical experiences obtained in the anesthetic management of asthmatic patients at the Presbyterian Hospital in New York.

METHOD

A period of two and a half years was arbitrarily chosen for study. Of the 55,696 surgical procedures requiring anesthesia at Columbia-Presbyterian Medical Center during the 30-month period from January 1958 through June 1960, 687 (1.2 per cent) were performed on patients in whom a history of asthma was obtained preoperatively. These 687 unselected consecutive anesthesia records were reviewed in terms of the following data: age and sex of the patient, asthmatic status and treatment during the preoperative period, premedication, induction agent and dose, primary agent for maintenance of anesthesia, the method of its administration, endotracheal intubation, type and dose of relaxant, use of topical anesthesia, and type of operation. The anesthetic period was analyzed for persistence or onset of wheezing which was diagnosed clinically by the auscultation of asthmatically generated rales heard in the lung fields bilaterally, usually during both inspiration and expiration. When this complication occurred, its temporal relation to anesthesia and surgery was noted.

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The 687 records were divided into two main groups; those 638 patients in remission whose asthmatic symptoms were quiescent (group 1) and the remaining 49 who were wheezing prior to the induction of anesthesia (group 2).

RESULTS—GROUP 1

Of the 638 patients with clear chests, 42 (6.5 per cent) developed wheezing during anesthesia. These patients had a variety of gynecological, urological orthopedic, neurological, otolaryngological, ophthalmological, plastic, thoracic, and general surgical procedures. In these patients sex distribution showed no significant difference (according to chi-square test $P = > .05$): 7.0 per cent (25 of 354) females and 5.9 per cent (17 of 284) males wheezed during anesthesia (table 1-A). Comparison of age groups shows an increasing percentage of asthmatics who developed wheezing during anesthesia (with

TABLE 1

INCIDENCE OF WHEEZING DURING ANESTHESIA—GROUP 1

	Total Number of Patients	Wheezed During Anesthesia	
		Number	Per Cent
(A) Sex			
Female	354	25	7.0*
Male	284	17	5.9
(B) Age			
1–20 years	152	4	2.6†
21–50 years	298	18	6.0
51 and over	188	20	10.6
(C) Preoperative therapy			
No treatment	514	31	6.0‡
Treatment	124	11	8.8

According to chi-square test:
* $P = > .05$.
† $P = < .01$.
‡ $P = > .05$.

TABLE 2

INCIDENCE OF WHEEZING DURING INDUCTION—GROUP 1

Inductions	Number	Asthmatic Attacks	Per cent
Thiopental and intubation	195	12	6.7*
Thiopental, no intubation	135	2	1.4
Cyclopropane	43	2	4.6
Nitrous oxide-ether	31	1	3.2
Halothane	25	0	0.0
Tribromethanol	21	0	0.0
Divinyl ether	14	0	0.0
Diethyl ether (open drop)	6	0	0.0
Nitrous oxide	5	0	0.0
Meperidine (I.V.)	4	0	0.0
Total	479	17	3.5

* According to chi-square test using Yates adjustment for continuity comparison of thiopental with and without intubation $P = .05$.

advancing age (table 1-*B*). This finding is statistically significant (according to chi-square test $P = < .01$).

Approximately the same percentage of patients who received preoperative antiasthmatic therapy developed wheezing as those who received no specific treatment (table 1-*C*). The possible significance of this finding, as well as recommended regimens, will be discussed below.

Premedication. Almost all the patients (94.6 per cent) received intramuscular doses of meperidine, 50 to 100 mg.; secobarbital, 50 to 100 mg.; and atropine or scopolamine, 0.4 mg., either singly or in combination approximately one hour before induction of anesthesia.

Induction of Anesthesia. Table 2 itemizes the various agents used for induction. In 195 patients, anesthesia was induced with thiopental, their lungs were ventilated with 100 per cent oxygen, they were given 40 to 100 mg. of succinylcholine intravenously and their tracheas were intubated with an endotracheal airway. Before spontaneous respiration returned, 12 patients (6.7 per cent) developed wheezing during controlled respiration; one of these patients had spasmodic coughing following the administration of thiopental. In 135 patients in whom anesthesia was induced with thiopental, an endotracheal tube was not required. Of these, only 2 patients (1.4 per cent) developed asthma prior to the start of operation. The difference in the incidence of wheezing in these two groups is of borderline statistical significance (according to the chi-square test $P = .05$). Age distribution in the 2 groups was similar.

Cyclopropane was used as the induction agent for 43 patients; 2 (4.6 per cent) developed wheezing during this period, one immediately after endotracheal intubation. A nitrous oxide-oxygen-ether sequence was used to induce anesthesia in 31 patients; one patient wheezed approximately five minutes after the start of anesthesia. Halothane was used to induce anesthesia in 25 patients and none of these patients wheezed during this period. Tribromethanol (Avertin) was used as the induction agent for 21 patients; 13 were subsequently given a paralyzing dose of succinylcholine and their tracheas were intubated. No patient wheezed during this period of anesthesia. In the remaining 29 patients anesthesia was induced with a variety of agents including divinyl ether, nitrous-oxide, open drop ether and intravenous meperidine; none of these patients wheezed during the induction.

Maintenance of Anesthesia. The agents used for maintenance of anesthesia are listed in table 3. Nitrous oxide with small intermittent doses of thiopental was used in 133 patients; 5 of these (3.7 per cent) developed asthma during this period. Ether was used for maintenance in 140 patients, 6 (4.3 per

TABLE 3

INCIDENCE OF WHEEZING DURING MAINTENANCE—GROUP 1

Maintenance	Number	Asthmatic Attacks	Per Cent
N_2O and thiopental	133	5	3.7*
Diethyl ether	140	6	4.3
Halothane	129	5	3.9
Regional	159	3	1.9
Cyclopropane	42	2	4.8
Miscellaneous	35	4	Insufficient numbers
Total	638	25	3.9

* No statistically significant difference between any two anesthetics (according to chi-square test $P = >.05$).

TABLE 4

INCIDENCE OF WHEEZING DURING MAINTENANCE OF GENERAL ANESTHESIA AND REGIONAL ANESTHESIA—GROUP 1

Maintenance	Number	Asthmatic Attacks	Per Cent
(*1*) General anesthesia—intubated	296	19	6.4*
(*2*) General anesthesia—not intubated	183	3	1.6
(*3*) Regional anesthesia	159	3	1.9
Total	638	25	3.9

* According to chi-square test using Yates adjustment for continuity:

Comparison of *1* and *2*: $P = <.01$.
Comparison of *1* and *3*: $P = .03$.
Comparison of *2* and *3*: $P = >.05$.

cent) developed wheezing. Halothane was used in 129 patients. This agent was usually administered in concentrations of 0.5 to 2.0 per cent in a mixture of approximately 60 per cent nitrous oxide and oxygen. The systems used were either nonrebreathing or partial rebreathing with carbon dioxide absorption. Five of these patients (3.9 per cent) developed wheezing during operation. Regional anesthesia was used for 159 patients; of these 3 (1.9 per cent) wheezed during the procedure. Cyclopropane was used in 42 patients; 2 (4.8 per cent developed asthma during this period. A small number of patients were maintained with a variety of agents including trichlorethylene, ethylene, intravenous narcotics and barbiturates; 4 patients wheezed, 2 while receiving trichlorethylene and 2 while receiving ethylene. Age distribution in these groups was similar, with the exception of those patients who received regional anesthesia. There was a preponderance of patients over the age of 20 (93 per cent) in the group given regional anesthesia.

When the incidence of acute asthmatic attacks during maintenance with any two anesthetic methods is compared, a statistically significant difference is not seen (according to chi-square tests $P = > .05$). Table 4 compares the incidence of wheezing during the maintenance of general anesthesia with an endotracheal airway, general anesthesia without an endotracheal tube and regional anesthesia. There is no significant difference ($P = > .05$) between the groups given general anesthesia without an endotracheal airway and regional anesthesia. However the higher incidence of wheezing during general endotracheal anesthesia is statistically significant ($P = < .01$) when compared to general anesthesia without a tube. The age distribution in these 2 groups of patients was similar. The difference in wheezing between patients who received general anesthesia with an endotracheal airway and regional anesthesia is of borderline significance ($P = .03$). There was a preponderance of older patients in the regional anesthetic group which may have rendered the groups not quite comparable.

Lidocaine hydrochloride, 2 to 4 per cent, or hexylcaine hydrochloride, 5 per cent were applied topically to the trachea in 60 per cent of the patients who were intubated during general anesthesia. A Devilbiss atomizer no. 15 and/or a 5 ml. syringe with a no. 22 gauge needle were used to instill the topical anesthetic. There was no statistically significant difference ($P = > .05$) in the occurrence of wheezing in these patients and those who did not receive a topical anesthetic (table 5).

Curare was used for muscle relaxation in 51 patients. Five patients were wheezing before the administration of the drug; in none did the asthma worsen clinically. Four additional patients developed wheezing at variable periods of time but not less than 15 minutes after the injection of the relaxant.

Treatment. The majority of the 42 patients

TABLE 5

INCIDENCE OF WHEEZING DURING MAINTENANCE OF GENERAL ENDOTRACHEAL ANESTHESIA WITH AND WITHOUT TOPICAL ANESTHETIC—GROUP 1

Maintenance	Number	Asthmatic Attacks	Per Cent
General anesthesia intubated topical anesthesia	170	13	7.6*
General anesthesia intubated no topical anesthesia	126	6	4.8
Total	296	19	6.4

* According to chi-square test: $P = >.05$.

TABLE 6

PREANESTHETIC ASTHMA—49 PATIENTS—GROUP 2

Anesthesia	No.	Wheezing Cleared	Wheezing Moderately Cleared	Wheezing Unchanged	Wheezing Worsened
Thiopental: N_2O	5			4	1
Ethylene	3			1	2
Regional	14			13	1
Cyclopropane	2			1	1
Diethyl ether	10	1	3	6	
Halothane	15	10	4	1	

who developed wheezing during anesthesia were given either diethyl ether or halothane to stop the attack of asthma. Ether was administered to 20 patients; in 13 the wheezing cleared and in 7 no clinical change was noted. Halothane was given to 12 patients; in 9 the wheezing cleared, in one it improved moderately and in the other 2 there was no change. One of these two patients never received more than 0.5 per cent halothane. The disappearance of audible wheezing after halothane administration in the majority of patients was more rapid than with ether. Within 2 minutes of inhalation of 0.8 to 2.0 per cent halothane there was increased ease in assisting or controlling respiration with improved ventilation; within 5 minutes the wheezing was usually completely eliminated and auscultation of the lung fields revealed clear chests without rales.

Intravenous hydrocortisone 100 to 200 mg. was given to 6 patients; improvement was observed in 5. The remaining 4 patients did not receive therapy and recovery took place gradually. There were no deaths due to asthma.

RESULTS—GROUP 2

This group of 49 patients who had clinical evidence of asthma at the time of induction, were anesthetized with a variety of techniques (table 6) which reflected the differences in views held by the staff as to the preferred methods of anesthetizing actively wheezing patients. Nitrous oxide supplemented with thiopental was administered to 5 patients; the wheezing remained unchanged in 4 patients and worsened in 1. Ethylene was given to 3 patients; the wheezing was unchanged in 1 and worsened in 2. Spinal or epidural anesthesia was given to 14 patients; the wheezing was unchanged in 13 and worsened in 1. Cyclopropane was administered to 2 patients; the wheezing worsened in 1 and remained unchanged in the other. Ether was given to 10 patients; the wheezing cleared to varying degrees in 4 and remained unchanged in 6. Halothane was given to 15 patients; the wheezing cleared in 14 and did not improve in 1.

Table 7 compares the results of the treatment of bronchospasm with ether and halothane. This group included those patients who either wheezed preoperatively or developed asthma during the induction or maintenance of general anesthesia. Of the 30 patients given ether, 17 improved; of the 27 patients given halothane, 24 improved. The difference in the percentage of improvement with halothane is statistically significant (according to the chi-square test $P = < .01$).

DISCUSSION

Proper preparation of asthmatic patients for operation is most important. The patients reported in this communication were treated actively from this point of view.

Prickman and Whitcomb [3] observed a decreased incidence of postsurgical complications

TABLE 7

TREATMENT OF ASTHMA—57 PATIENTS—GROUPS 1 AND 2

	Cases	Improvement	Per Cent
Diethyl ether	30	17	56.7
Halothane	27	24	88.9*

* According to chi-square test using Yates adjustment for continuity: $P = <.01$.

in asthmatic patients who received theophylline, bronchodilator aerosols, steroids and antibiotics preoperatively. Beck[4] has recommended a course of preoperative and postoperative management which was used in 39 patients in this series, 35 of whom came to operation free of symptoms. This regimen is outlined below and consists of the administration of bronchodilators and steroids for a few days before and after operation.

Bronchodilators. Aerosol: 2 per cent phenylephrine HCl with 0.4 per cent isoproterenol or 2.25 per cent racemic epinephrine with 0.4 per cent isoproterenol. After inhalation of the aerosol, an asthmatic's vital capacity may increase three fold, his mid-expiratory flow rate double and his maximum breathing capacity increase significantly.[4] Oral: ephedrine 25 mg. q. i. d. and aminophylline 0.2 to 0.3 Gm. q. i. d. Intravenous or rectal: aminophylline may be administered intravenously preoperatively using 0.5 Gm. in 100 to 200 ml. of 5 per cent dextrose in water or rectally in 30 ml. of tap water.

Steroids. The object of steroid therapy is the elimination of bronchiolar muscle spasm and bronchial edema preoperatively, the prevention of acute respiratory insufficiency and asthma during anesthesia and the avoidance of postoperative adrenal insufficiency in chronically debilitated patients. Steroids are recommended for all patients with moderate to severe pulmonary insufficiency due to asthma in doses of oral prednisone 10 to 25 mg. q. i. d. for 4 days preoperatively, intravenously 50 to 100 mg. during operation and orally in gradually reduced dosages postoperatively. Antacids should always be given 2 hours after meals in order to reduce the acidity associated with steroid therapy. Beck emphasized added precautions: the patient with chronic pulmonary infection must be given antibiotics and patients with a history of arrested tuberculosis should receive streptomycin, para-aminosalicylic acid or salts or isoniazid.[4]

The observation that approximately the same percentage of patients in our series receiving preoperative anti-asthmatic therapy developed wheezing as those receiving no specific preoperative treatment is explained by the fact that only severe asthmatics received this care and asymptomatic patients did not. It is probable that effective preoperative preparation rendered wheezing patients as safe for anesthesia and operation as the asymptomatic milder cases not receiving treatment.

Selection of Techniques. The principles of selection of anesthesia for the asthmatic have not altered significantly in the last two decades. Conduction anesthesia when possible is the method of choice for many.[4] Unfortunately, regional techniques do not guarantee freedom from pulmonary complications: 1.9 per cent of the present series given regional anesthesia developed asthma during the procedure. Nonetheless, the well-managed regional anesthetic eliminates the use of irritant gases and the introduction into the airway of foreign bodies which also may provoke an asthmatic attack.

The choice of agent remains controversial when general anesthesia must be used. Intravenous barbiturates are considered by some to be absolutely[5] or relatively[6] contraindicated because of their parasympathomimetic properties. We have observed asthmatic attacks during a thiopental induction in only 1.4 per cent of patients whose tracheas were not intubated. Tribromethanol, in small doses for its amnesic effect does not cause undue respiratory depression and has bronchodilator activity which may be useful for asthmatic patients.[7]

Curare is said to cause asthma on occasion through its release of histamine.[8] However, Mongar and Whelan[9] injected 35 to 40 mg. of curare into the brachial artery of 5 anesthetized and 2 conscious nonasthmatic patients. In none did the plasma histamine rise significantly and local signs such as flaring and whealing were slight. It has always seemed unlikely that relaxant doses of *d*-tubocurarine given intravenously for clinical purposes produce side effects due to the release of histamine. Curare did not appear to precipitate or aggravate pre-existing asthma in this series.

Although cyclopropane is said to cause wheezing in asthmatics and in some apparently normal patients,[10] it has also been recommended as an efficient and safe mode of treatment for status asthmatics by others.[11] We noted wheezing during a cyclopropane induction in 2 of 43 patients, one of whom did not

begin to wheeze until after endotracheal intubation. An additional 42 patients were maintained on this agent; two (4.8 per cent) had asthmatic attacks during this period.

Diethyl ether is well known as a bronchodilator agent and has been used to terminate status asthmaticus where other forms of therapy have failed.[12, 13, 14] Our current experience in the treatment of asthma with ether is not significantly different from the previous report from this institution[14]: approximately 58 per cent of patients improved clinically when ether was administered. However, it was noted that wheezing and small tidal volumes usually persisted until relatively deep surgical anesthesia was reached when respiratory sounds become normal and tidal volume increased. This practice is not entirely safe because of the possibility of circulatory depression, easily produced by overdoses of ether in debilitated patients.

Little has been reported on the effect of halothane on the bronchial muscle or its use for anesthetizing patients with asthma. Brown[15] reported the use of this agent for bronchoscopy in 26 children. He noted that the bronchial musculature appeared always to be relaxed with a concentration of 1.5 to 2.0 per cent halothane and oxygen. Stephen and co-workers[16] reported that halothane was employed advantageously in 40 patients having a definite history of asthma; 8 of these patients were actively wheezing. In no patient did the asthmatic condition become worse clinically. Ausherman[17] reported that none of 8 symptom-free asthmatics exhibited stridor or wheezing during halothane anesthesia. Abajian[18] reported that asthmatics seemed to be improved on the inhalation of halothane as manifested by decreasing rales and a shortening of the expiratory phase.

Our experience with 144 patients who received halothane indicates that this agent administered in concentrations of 0.8 to 2.0 per cent is at least as satisfactory as ether and probably superior to it for the establishment of general anesthesia in an asthmatic patient and in the treatment of wheezing should it occur.

The most common single factor which precipitated an acute attack of asthma during operation on an asthmatic patient was *not* the anesthetic agent but the introduction or presence of an endotracheal tube regardless of the use of surface anesthesia. This finding was, in fact, no surprise and suggests that endotracheal airways be inserted during optimum conditions to avoid the pulmonary responses to the stimulation it causes. Furthermore, anesthesia must be maintained in a satisfactory depth with a suitable agent. Nothing in this finding suggests that endotracheal intubation is to be avoided. It simply points out the need for improvement in the use of a tube during general anesthesia in a patient with asthma.

The predilection of older asthmatics for clinical difficulties may be the results of the problems caused by the changes of emphysema in these patients. This finding needs further study.

Summary

During an 18 month period, anesthesia was administered to 638 symptom-free and 49 wheezing patients with bronchial asthma. These were consecutive patients unselected except for a history of asthma. In 6.5 per cent of the patients, with clear chests preoperatively, asthma developed during anesthesia; 2.6 per cent during the induction and 3.9 per cent during the maintenance of anesthesia.

Regional anesthesia was associated with the same incidence of wheezing as general anesthesia without an endotracheal airway. The most common single factor which precipitated an attack of wheezing during general anesthesia was the presence of an endotracheal tube. This finding does not contraindicate endotracheal intubation during operation on asthmatic patients but points out the need for better management of endotracheal airways in these patients.

Halothane is a valuable drug for anesthetizing patients with asthma and for treating asthmatic attacks should they occur during anesthesia. Cyclopropane, thiopental, and curare did not cause attacks of asthma out of proportion to the established over-all incidence during all forms of general anesthesia.

Older patients were more susceptible to asthmatic attacks during general anesthesia than younger patients.

Competent preoperative medical preparation and postoperative care of the asthmatic pa-

tient is important in holding pulmonary complications to a minimum.

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NORADRENALINE Noradrenaline uptake by heart and spleen after intravenous infusion was measured in the rat. Cocaine specifically prevented the uptake of noradrenaline by tissues, thus increasing the amount of noradrenaline available for combination by adrenergic receptors. Drugs related to cocaine, such as alpha-cocaine, amethocaine and atropine, did not alter the noradrenaline uptake or potentiate the blood pressure response to noradrenaline. (*Muscholl, E.: Effect of Cocaine and Related Drugs on Uptake of Noradrenaline by Heart and Spleen, Brit. J. Pharmacol. 16: 352 (June) 1961.*)

PHENOTHIAZINE Alveolar P_{CO_2} was artificially controlled in man to study the time course of changes in respiratory rate, depth and minute volume after intramuscular injection of saline, chlorpromazine (25 mg./70 kg.), meperidine (100 mg./70 kg.) and meperidine with chlorpromazine in the same doses. The results obtained indicated a prominent and persistent respiratory depression by meperidine; chlorpromazine alone produced no consistent respiratory depression; and the simultaneous administration of chlorpromazine with meperidine caused respiratory depression greater in degree and duration than that produced by meperidine alone. (*Lambertsen, C. J., Wendel, H., and Longenhagen, J. B.: Separate and Combined Respiratory Effects of Chlorpromazine and Meperidine in Normal Men Controlled at 46 Mm. Hg Alveolar P_{CO_2}, J. Pharmacol. Exp. Ther. 131: 381 (Mar.) 1961.*)