A COMPARISON OF ATROPINE, OR SCOPOLAMINE, PLUS PENTOBARBITAL, MEPERIDINE, OR MORPHINE AS PEDIATRIC PREANESTHETIC MEDICATION

CAPTAIN EDMOND I. EGER, II, MC, MAJOR IDELLE D. KRAFT, ANC, HUGH H. KEASLING, PH.D.

APPROACHES to the problem of preanesthetic medication in children are infinite as may be inferred from the variety of drugs and dose schedules advocated. Few controlled studies have been done and these have failed to show any great differences in the effectiveness of any particular drug or drug combination. It is generally agreed that something is better than nothing, but something may vary from Jackson's artful psychological approach combined with minimal drug premedication [1] to minimal rapport and maximal drug premedication.

The importance of premedication in younger children has been shown.[2, 3] Eckenhoff found that stormy inductions in these patients were followed by untoward psychological repercussions.[2] He also found that the smoothness of induction was increased by the addition of barbiturate or of barbiturate plus a narcotic to atropine or to scopolamine, and concluded that a barbiturate should be administered to children preanesthetically.[3]

Freeman and Bachman [4] have recently published a study of premedication for pediatric patients using a double blind technique. The drugs used were atropine or scopolamine combined with pentobarbital, or morphine, or morphine plus pentobarbital, or various phenothiazines. Anesthesia in all patients was induced with cyclopropane to which ether was later added. The tracheae of all patients were intubated. They found that scopolamine plus pentobarbital or scopolamine with pentobarbital and morphine or atropine plus pentobarbital and morphine gave significantly greater sedation than atropine alone; no difference was found in other combinations. In addition to giving greater sedation, these combinations were associated with better inductions of anesthesia. The criteria used to determine excellence of induction were somewhat questionable since a comatose patient would be scored as best. These combinations also were related to less excitement postoperatively. Scopolamine was associated with less secretion than atropine both being given in the same dose (0.2 mg. per 30 pounds). Atropine was found to produce more cases of tachycardia than did scopolamine. No other significant differences were noted to occur between any of the other drug combinations.

Except for the above papers, little effort has been made by controlled study to distinguish the effectiveness of the drugs commonly used for premedication of children. At the United States Army Hospital, Fort Leavenworth, Kansas, an opportunity to undertake such a study offered itself and the following is a description of the work done.

METHODS

Subjects. Two hundred forty-eight children, who were to undergo tonsillectomy and/or adenoidectomy, were included in the study. Those weighing more than 80 pounds were not included.

Drugs and Administration. Atropine 0.0085 mg./pound, or scopolamine 0.0055 mg./pound was either given alone (control) or combined with pentobarbital 1 mg./pound, with meperidine 0.8 mg./pound, or with morphine 0.08 mg./pound. The actual milligram-dose of vagolytic given was the above calculated figure rounded to the nearest whole number after the decimal point. Similarly, the dose for pentobarbital and for meperidine was determined by rounding to the nearest whole figure ending in a 5 or a 0 while that for morphine was rounded to the nearest whole

Received from the Anesthesia Sub-Section, United States Army Hospital, Ft. Leavenworth, Kansas, and Department of Pharmacology, State University of Iowa College of Medicine, Iowa City, Iowa, and accepted for publication July 17, 1961. Dr. Eger is now in Department of Anesthesiology, University of California Medical Center, San Francisco 22, California. Dr. Keasling is now in Department of Pharmacology, Upjohn Co., Kalamazoo, Michigan.

figure. For example, a 40-pound child would receive either 0.3 mg. of atropine or 0.2 mg. of scopolamine, either alone or plus pentobarbital 40 mg., or meperidine 30 mg., or morphine 3.0 mg. There were 8 possible combinations: atropine, scopolamine, atropine-pentobarbital, scopolamine-pentobarbital, atropine-meperidine, scopolamine-meperidine, atropine-morphine, and scopolamine-morphine. The term depressant drug as used in the remainder of this paper will refer to morphine, meperidine or pentobarbital. The drug combinations were listed in a randomized fashion. In turn each patient's particular premedication was ordered from the succeeding combination of drugs in this list. The drugs were given 1 to 1½ hours before the induction of anesthesia.

Anesthesia. All anesthetics were administered and all observations were noted by one of us who was unaware at any time during the procedure of the premedication the patient had received. Anesthesia was induced with open drop divinyl ether and continued with open drop ether until tracheal intubation. After intubation an Ayre's T-piece (with a 20-ml. reservoir in larger children) was connected to the endotracheal catheter and anesthesia was maintained with nitrous oxide 6 liters per minute, oxygen 3 liters per minute, and ether. After operation the child remained in the recovery room for a minimum of 20 hours. Observations during this time were made by recovery room personnel as well as by one of us.

Method of Evaluation. A check sheet was prepared in which 5 periods of observation were defined and various qualities within these periods set down for evaluation. (1) PREOPERATIVE VISIT. On the sheet the patient's "age," "weight," and "sex" were noted. "Cooperation" was noted as "yes" or "no." It was divided into "passive" and "active" components: "passive cooperation" was defined as permissive inactivity; "active cooperation" was defined as positive responses to commands (such as "hold up your arm" or "take a deep breath"). "Fretfulness and irritableness" was noted as a minimal, moderate, or marked quality. Fretfulness and irritableness was defined as a tendency to overreact in an anxious or apprehensive fashion. The child who would cry, cling tenaciously or struggle, would be classified as "marked" in this quality. "Restlessness" was checked as "yes" or "no" and was defined by purposeless overactivity. This and the quality "fretfulness and irritableness" were thought related to apprehension. (2) PREANESTHESIA. This was the period 1 to 1½ hours after giving the premedicant but before the induction of anesthesia. "Cooperation" was evaluated as above. It was noted whether "fretfulness and irritableness" had increased, decreased, or remained the same. "Restlessness" and "flushing" were separately marked as "yes" or "no." "Drowsiness" and "depression of vital signs" were separately checked as minimal, moderate or marked. "Depression of vital signs" included the appearance of a markedly slowed respiratory rate (below 15) or a fall in blood pressure below 75-80 mm. of mercury systolic. (3) INDUCTION. Arbitrarily this was defined as the period from the start of anesthesia to the point of tracheal intubation. Here, "cooperation" was again noted as above. "Crying and/or struggling," "excitement during second stage," "mucous secretion," and "tendency to laryngospasm" were each noted separately as minimal, moderate, or marked. The number of minutes to intubation were noted. The over-all "impression of induction" was noted as being smooth, average, or stormy. Respiratory irregularities characterized either by "apnea or marked respiratory depression" or by "exhaustive and rapid ventilation" were noted separately as "yes" or "no." (4) MAINTENANCE. This was defined as the period from tracheal intubation to the end of the operative procedure. "Respiratory irregularities" were again noted as above. "Mucous secretion" was checked as minimal, moderate, or marked. The "maximum pulse during maintenance" was noted in beats per minute. "Perspiration" was marked as "yes" or "no." (5) RECOVERY. This was defined as the period from the end of the operative procedure to the following morning when the child left the recovery room. "Gag reflex at the end of procedure" and "movement at end of procedure" were noted separately as being present or absent. "Appropriate response to commands in the operating room," "airway to recovery room," "excitement in the recovery

TABLE 1

PREMEDICANTS, PERCENTAGE MALES, AVERAGE WEIGHTS, AGE AND TIME TO INTUBATION, AND MAXIMAL PULSE RATE

Drug Group*	Number	Males (%)	Average Weight	Average Age	Average Minute to Intubation	Average Maximum Pulse Rate
Age Group—5 Years and Younger						
S	15	47	41.7	4.60	9.73	129.2
A	16	40	39.6	4.00	10.00	141.0
S & M	15	47	37.1	3.87	7.80	125.7
A & M	18	50	39.2	3.67	7.56	137.4
S & D	16	69	43.1	4.31	10.31	131.8
A & D	17	71	37.9	4.00	10.24	146.4
S & N	13	69	41.1	4.08	8.15	133.2
A & N	20	65	39.6	4.00	9.90	137.0
Average	16	57	39.9	4.05	9.25	135.2
Age Group—6 Years and Older						
S	17	53	54.4	6.76	12.88	127.5
A	14	79	59.3	7.64	12.64	134.6
S & M	16	63	55.3	7.13	8.31	120.0
A & M	13	62	60.5	7.77	11.92	138.5
S & D	15	47	59.9	7.73	11.93	125.2
A & D	15	47	59.1	7.67	12.93	140.5
S & N	17	47	58.7	7.41	10.35	122.9
A & N	11	55	58.5	7.45	11.73	134.6
Average	15	57	58.2	7.43	11.59	130.5

* S = Scopolamine, A = Atropine, M = Morphine, D = Meperidine, N = Pentobarbital.

room," and "vomiting in the recovery room" were each noted separately as "yes" or "no." In addition "vomiting" was described as minimal, moderate, or marked. At the end of the procedure the question "Was the preanesthetic medication adequate?" was answered on the check sheet "yes" or "no" and was answered as to degree of adequacy: poor, fair, or good.

STATISTICAL METHODS

The values of age, weight, time to tracheal intubation and maximal pulse rate were submitted to separate analyses of variance.[5] The remaining items were submitted to chi-square analysis or in a few cases to the Fisher Exact Probability Test.[6]

RESULTS

Table 1 details the numbers in the groups receiving the various combinations of premedicants, the percentage of males and average values for weight, age, time to intubation and maximal pulse rate. The sex ratio in the various groups is not significantly different. As noted in the table the subjects were divided into two age groups, one 5 years or less (younger group) and the other 6 years or more (older group). The weights differ significantly between the two age groups but no other comparison reveals a difference. The analysis of age reveals that in addition to the obvious difference between the two groups, means 4.05 and 7.43 years, that the patients receiving atropine were significantly younger and older than those receiving scopolamine.

The analysis of time to tracheal intubation revealed that significant differences existed between the age groups, between atropine and scopolamine and between the various depressants. However, it seemed possible that these differences were correlated with age and/or weight. The Spearman rank correlation coefficient for the mean values of the 16 groups comparing time to intubation and

weight was 0.752, a highly significant value. Accordingly, the mean times to intubation were analyzed utilizing the mean weights in the various groups as a covariant. Time to intubation is significantly dependent on weight, the best estimate of this datum being that the intubation time increases 0.134 minutes/pound of body weight. Using this adjustment, there is no difference in time to intubation between the age groups nor between the anticholinergics. The latter difference just failed to be significant at the 5 per cent level (adjusted mean times atropine 10.85 minutes, scopolamine 9.95 minutes). The differences among depressants is, however, significant.* Premedication with morphine was associated* with more rapid inductions than meperidine or with a belladonna drug alone (control).

The mean values for maximum pulse rate also revealed significant differences. The younger the child the faster the maximum pulse (younger group mean 135, older group 130). In addition atropine was associated* with a faster rate than scopolamine.

In no form of comparison between the various drug combinations could any difference be found in the qualities "depression of vital signs" and "respiratory irregularities." Similarly, the gag reflex was universally present at the end of the procedure although 2 patients were returned to the recovery room with an airway in place. Gross movement was absent in only 15 patients (6.0 per cent). Appropriate response to commands in the operating room was present in 206 children (83 per cent).

Initially each of the remaining items was tested by pooling all values for the younger group and comparing this pool with the pooled values for the older. Where differences existed between the age groups, the effects of

* $P < 0.05$.

TABLE 2

COMPARISON BETWEEN PREMEDICANTS AND FACTORS STATISTICALLY SIGNIFICANT

Factor	Age Group	Atropine Alone or + Depressant	Scopolamine Alone or + Depressant
Maximum pulse rate*	Both	139.0	126.8
Decrease in fretfulness and irritability (%)†	Older	26	52
Drowsy (%)†	Both	19	39
Minimal mucous secretion during induction (%)†	Both	58	77
Minimal laryngospasm (%)*	Both	78	90
Minimal mucous secretion during maintenance (%)†	Both	62	81
Not perspiring (%)†	Both	69	86
Adjudged adequately premedicated (%)†	Both	81	93

* $P < 0.05$
† $P < 0.01$.

TABLE 3

COMPARISON BETWEEN PREMEDICANTS AND FACTORS STATISTICALLY SIGNIFICANT

Factor	Age Group	Vagolytic Alone	Meperidine +Vagolytic	Morphine +Vagolytic	Pentobarbital +Vagolytic
Time to intubation (minutes)*	Both	11.35	11.22	9.04	9.98
Active preanesthetic cooperation* Uncooperative (%)	5 & younger	29	12	36	45
Decrease in fretfulness and irritability (%)	5 & younger*	26	48	61	30
	6 & older	32	33	48	50
Minimal second stage excitement (%)*	Both	63	76	82	82
Minimal mucous secretion during induction (%)†	Both	52	78	85	57
Smooth induction (%)*	Both	56	65	79	61
Minimal laryngospasm (%)*	Both	73	87	94	82
Minimal mucous secretion during maintenance (%)*	Both	61	82	77	67
Not perspiring (%)†	Both	79	61	81	90
Excited in the recovery room (%)†	Both	34	17	9	26
Vomiting (%)†	Both	39	71	71	18
Moderate-marked vomiting (%)*	Both	16	38	33	0
Judged adequately premedicated (%)†	Both	76	90	98	83

* $P < 0.05$.
† $P < 0.01$.

TABLE 4

COMPARISON BETWEEN AGE GROUPS AND FACTORS STATISTICALLY SIGNIFICANT

Factor	Younger Group (5 Years and Younger)	Older Group (6 Years and Older)
Active cooperation at induction (%)†	54	83
Restless (%)		
Preoperatively*	28	15
Preanesthetic†	26	8
Moderate or marked crying or struggling during induction (%)*	50	24

* $P < 0.05$.
† $P < 0.01$.

the vagolytics and depressants were tested with each age group by appropriate combination values. In the absence of age difference, the total data for the item were combined in order to compare vagolytics and/or depressants. Tables 2 and 3 give the results of comparisons between premedicants which were found to be statistically significant. Table 4 gives the results of comparisons between the two age groups which were found to be statistically significant. The order of significance is also given.

Cooperation. The younger patients were consistently less cooperative than the older. In every case the difference was greater for active as opposed to passive cooperation and the cooperation decreased as the time for operation approached. Active cooperation evaluated at the time of induction indicated the least cooperation (children five and under 46 per cent "no," six and over 17 per cent "no").

Fretfulness and irritableness. In both preoperative and preanesthetic evaluation the younger children were more fretful and irritable,† and increased in this quality more than did the older children between the two evaluations. This change was not different for the two anticholinergics for the younger children but scopolamine was associated † with a greater decrease than atropine in the older group. The various depressants differed in both age groups in their ability to decrease fretfulness and irritableness. In the younger children, percentage decreases were: no depressant 26; morphine 61; meperidine 48 and pentobarbital 30.*

Younger children premedicated with narcotics decreased in fretfulness and irritableness more frequently * than younger children who did not receive a depressant or were given pentobarbital.

No difference could be found in the older group in the effect of morphine compared to pentobarbital or between meperidine and that group not given a depressant. However, the morphine or pentobarbital groups (average 49 per cent decrease in fretfulness and irritableness) were more effective than the control or meperidine groups (average 33 per cent decrease).*

Restlessness. The younger children also were more restless in both the preoperative * (28 per cent versus 15 per cent in the older group) and preanesthetic † (26 per cent versus 8 per cent) evaluations. When changes within the groups were tested, all were nonsignificant with the exception of pentobarbital in the older group which evidenced an increase in restlessness in the group treated with pentobarbital-atropine † (1 of 11 restless preoperative, 11 restless preanesthesia).

Flushing. No differences were found.

Drowsiness. There was slightly more drowsiness in the patients treated with scopolamine.† The differences among the various depressants failed to be significant ($0.10 > P > 0.05$) control 19 per cent, morphine 41 per cent, meperdine 25 per cent and pentobarbital 31 per cent moderate drowsiness).

Crying, Struggling and Excitement. During induction of anesthesia the younger patients exhibited significantly †more crying and struggling (50 per cent compared to 24 per cent in the older group). However no differences were apparent among the various premedicant groups. Few children were adjudged marked in the evaluation of second stage excitement and so for purposes of analysis moderate and marked were pooled. No differences were noted between the age groups or between the anticholinergics; however, the various depressants differed significantly.* The patients who received morphine and pentobarbital evidenced less

† $P < 0.01$.

excitement* than the control patients; those premedicated with meperidine were not significantly different from any group in this category.

Mucous Secretion, Laryngospasm and Smoothness of Induction. Mucous secretion during induction was not different for the two age groups (68 per cent minimal) but was significantly less in patients treated with scopolamine* and in patients treated with narcotics.* Induction was judged smoother in patients who had received depressant drugs*; however, age or vagolytic were apparently unimportant. The smoothness of the induction varied significantly among the depressants*; however, pentobarbital was not significantly different from the control group nor was morphine significantly different from meperidine. Pentobarbital and control group was significantly different from the narcotics* (narcotics 72 per cent smooth versus control and pentobarbital 59 per cent smooth). The tendency to laryngospasm was more frequently judged minimal in patients receiving scopolamine* or any of the depressant drugs.* However, the difference between the pentobarbital treated and control group was not significant while both narcotic treated groups demonstrated less laryngospasm than the control group,* but were not significantly different from each other.

Mucous Secretion and Perspiration During Maintenance. During anesthesia mucous secretion was less in patients who had received scopolamine.† The depressants also varied significantly. While pentobarbital was not significantly different from the control group, both narcotics were associated with less secretions than the other groups.* Those patients who received scopolamine had drier skin.† However, in the depressant groups those who received meperidine had the greatest tendency to perspire while those who received pentobarbital had the least.

Postoperative Excitement. There were significant variations* in postoperative excitement associated with the various drug groups. The opiates were associated with the least excitement as opposed to the pentobarbital or the control groups.† The differences between morphine and meperidine treated groups or between control and pentobarbital treated groups were not significant.

Postoperative Vomiting. Vomiting in the recovery room was not significantly different for the age groups or the anticholinergic groups (50 per cent vomited) but the depressants were significantly different.† The narcotics were associated with a high incidence of emesis while pentobarbital was associated with a low incidence. The control group fell between these two extremes. The difference between the narcotics was not significant but the difference between narcotics and control groups was highly significant † as was the difference between pentobarbital and control.* The intensity of vomiting showed a similar effect in that neither age nor anticholinergic was significant while the depressants exhibited highly significant differences. Pentobarbital premedicated patients exhibited *only* minimal vomiting, the remaining depressant groups varied significantly* with the percentage of minimal vomiting being respectively control 84, morphine 67 and meperidine 62.

Judgment of Adequacy. Adequacy did not vary between the age groups. However, scopolamine premedication was more often adequate than atropine.† Further, the depressant groups varied significantly † with control group 76 per cent; morphine 98 per cent; meperidine 90 per cent and pentobarbital 83 per cent adequate. Similarly, the degree of adequacy varied with anticholinergic* and depressant.*

Certain cross comparisons have been made to determine if certain of the variable were correlated. In these cases individuals were separately categorized with respect to the two variables. The change in fretfulness and irritableness (F + I), depended on the degree of drowsiness † in that decreases in F + I were associated with greater drowsiness (54 per cent) than increases (13 per cent) (or lack of change (12 per cent) percentage of moderate-marked drowsiness). The drowsier patients also had smoother inductions † (minimal drowsy 59 per cent smooth, moderate-marked drowsy 81 per cent). The change in fretfulness and irritability also varied significantly with relation to the impression of induction.† Those showing a decrease in F + I

having smoother inductions while those with increase in F + I tended to have stormier inductions. In addition, second stage excitement was also significantly different among the groups determined by change in fretfulness and irritability.* Minimal excitement was exhibited by 50 per cent of those increasing in F + I, 89 per cent of those decreasing and 75 per cent of those not changing in the quality.

Flushed patients tended to perspire.* However, flush and tendency to laryngospasm were not correlated nor were flush and degree of mucus during maintenance. The amount of mucus during induction was dependent on the amount of second stage excitement † in that greater excitement resulted in greater incidence of mucus. Increased mucus also evidenced a greater tendency to laryngospasm.* The degree of postoperative vomiting was not related to the degree of maintenance mucus.

Discussion

The drug effects noted in this study must be considered in the light of methodology ultilized in their evaluation. The circumstances of this study were such as to increase discrimination among the drugs if differences existed (*i.e.* limited patient type, operative procedure anesthetic agents, anesthetic system, and one anesthetist). Such a method, however, imposes limitations on the generality of the information obtained in that it is not possible to generalize from the present findings to situations in which these variables are grossly altered. Further, in the light of a single dose level of each of the drugs utilized it is possible that differences noted were not due to the drug but rather to the variations in drug effect with dose.

None of the drugs used caused significant depression either pre, during or postoperatively. This is also a reflection of the level of anesthesia maintained which was always as light as possible. There were no major anesthetic complications. Convulsions were not observed in this series although they might have been expected with the technique used.

In this study, scopolamine was consistently superior to atropine as a premedicant. Scopolmaine was associated with a more tranquil child. Anesthesia was less complicated following its use since with it there was less largyngospasm, tachycardia, mucous production and perspiration. The superiority in depressing mucous secretion has been previously noted.[4, 7]

The use of a depressant agent in combination with a vagolytic agent was found to be better than the use of a belladonna derivative alone. The child premedicated with only the vagolytic was frequently apprehensive. The course of the anesthesia in such a child was marred by greater excitement during induction, more laryngospasm, and more mucous secretion. Postoperatively this was the child most likely to be excited.

The effects of morphine and meperidine were usually similar qualitatively, with morphine being more satisfactory. One striking difference between the two drugs was their association with perspiration—the number who perspired after meperidine was double that of those given morphine. Morphine among all the depressants was associated with the greatest increase in tranquility, the most rapid and smoothest induction of anesthesia, the least mucous secretion and laryngospasm, and the least postoperative excitement. Many of these differences were not statistically significant.

Comparison of the narcotic and the pentobarbital group revealed that the latter usually was between the narcotic and control groups in effectiveness. This is probably in part a dose effect; if the dose of pentobarbital had been greater the difference between its effect and that of the narcotic might have been eliminated. In one respect pentobarbital was superior to morphine. The incidence and severity of postoperative vomiting was markedly diminished following pentobarbital. One disadvantage of pentobarbital was that when used in combination with atropine it appeared to increase preanesthetic restlessness in the older children.

A comparison of the different age groups shows that in general it is more difficult to adequately sedate the younger patient, and that he is less cooperative.

Correlations between qualities produced few surprising results. Direct correlation was

found between decrease in fretfulness and irritableness and drowsiness; between drowsiness and smoothness of induction, and between decrease in fretfulness and irritableness and excitement in the second stage. Flushing was unrelated to mucous secretion during maintenance or to laryngospasm, but was directly related to perspiration—those who were flushed tended to perspire. The amount of mucous secretion during induction was found to be directly related to excitement during the second stage of anesthesia and to a tendency to laryngospasm. The amount of mucous secretion during maintenance was not correlated with the incidence of vomiting. We had expected increased cooperation in the more sedated patient but could not demonstrate this. There was no statistically significant difference in the effect of the premedicants on the incidence of crying and/or struggling during induction although significant differences were found in excitement during the second stage where it is thought inhibitions are removed and latent anxieties may become more obvious. We had expected to see a difference between narcotics and pentobarbital in tendency to laryngospasm.[8] However, a difference was not found, either premedicant tending to reduce the incidence. This agrees with Freeman's observations.[4] Perspiration in the atropine and especially in the meperidine-atropine groups was unexpected as was the ability of pentobarbital to minimize this. More excitement postoperatively was expected in those patients who received scopolamine or pentobarbital or a combination of the two but this could not be demonstrated.

Summary

A blind comparison of the premedicating effects of atropine, scopolamine, atropine-pentobarbital, scopolamine-pentobarbital, atropine-meperidine, scopolamine-meperidine, atropine-morphine, and scopolamine-morphine was made in 248 children undergoing tonsillectomy and adenoidectomy. Anesthetic agents and technique were the same for all cases.

Scopolamine produced adequate sedation, drying and protection against laryngospasm, without appreciable tachycardia. Atropine, despite a larger dose (55 per cent greater) failed to produce comparable results.

Among the depressants (morphine, meperidine, and pentobarbital) morphine most frequently was associated with the greatest tranquility, smoothest induction, least mucous production and laryngospasm, and the least postoperative excitement. Pentobarbital afforded the greatest protection against postoperative vomiting. Differences between the drugs may be related to dose level and the circumstances of the study and not to particular drug effects.

References

1. Jackson, K.: Psychologic preparation as method of reducing emotional trauma of anesthesia in children, Anesthesiology 12: 293, 1951.
2. Eckenhoff, J. E.: Relationship of anesthesia to postoperative personality changes in children, A. M. A. J. Dis. Child. 86: 587, 1953.
3. Eckenhoff, J. E.: Sedation for children. Analysis of effects for tonsillectomy and adenoidectomy, A. M. A. Arch. Otolaryng. 57: 411, 1953.
4. Freeman, A., and Bachman, L.: Pediatric anesthesia: evaluation of preoperative medication, Anesth. Analg. 38: 429, 1959.
5. Snedecor, G. W.: Statistical Methods, ed. 5. Ames, Iowa, Iowa State Colleges Press, 1956.
6. Siegel, S.: Nonparametric Statistics for Behavioral Sciences. New York, McGraw Hill Book Co., Inc., 1956.
7. Wyant, G. M., and Dobkin, A. B.: Antisialogogue drugs in man, Anaesthesia 12: 203, 1957.
8. Eckenhoff, J. E., and Helrich, M.: Study of narcotics and sedatives for use in preanesthetic medication, J. A. M. A. 167: 415, 1958.