AN EVALUATION OF THE USE OF THIOPENTAL AND DECAMETHONIUM BROMIDE FOR RAPID ENDOTRACHEAL INTUBATION *

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TECHNICS of anesthesia using drugs which permit rapid induction and greatly facilitate endotracheal intubation are currently receiving much attention. This has been prompted, in part, by the dissatisfaction of anesthesiologists with the older methods of inhalation anesthesia which were used in preparation for endotracheal intubation. Such methods were time consuming and often associated with various degrees of trauma, this being especially evident when intubation was hastily attempted in the lighter planes of anesthesia.

The need for a safe and effective method for rapid induction and intubation has also been significantly influenced by the recent improvements in surgical technic. For instance, the adoption of the routine use of detergents for the surgical scrub has deprived the anesthesiologist of the minimal ten minute period for induction and intubation which was previously available to him. At present, the interval of time which elapses from the time the surgeon sees his patient immediately preoperatively until he is ready to begin operating averages five minutes. It is a virtual impossibility to meet such time demands using the older methods of inhalation anesthesia for the induction and intubation of a patient.

The advent of the rapidly acting barbiturates and various curare preparations provided the anesthesiologist with agents which, when administered in combination intravenously, could produce immediate and rather profound effects. However, the acceptance of the routine use of these drugs by rapid intravenous injection, in dosages sufficient to permit endotracheal intubation, has been slow and guarded. This is perhaps explained by the lack of definite information concerning some of the effects of these drugs on the various body systems. Such information has evolved slowly through clinical investigations based on the use of these drugs on the human patient. Although it is suggestive

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TABLE 1

AGE DISTRIBUTION

	10–20	21–30	31–40	41–50	51–60	61–70	71–80	81–90
Patients with Normal Hearts	5	23	30	32	61	61	18	0
Patients with Heart Disease	0	0	6	7	23	28	23	1

from articles appearing in the literature that this method of induction and intubation produces no serious complications, nevertheless it is important to evaluate the method on the basis of some objective observations rather than on clinical impressions alone. The purpose of this study is to evaluate some of the changes effected by the rapid intravenous injection of a combination of thiopental (pentothal® sodium) and decamethonium (syncurine®) in sufficient dosage to permit rapid endotracheal intubation.

MATERIAL

The subjects of this study were 318 patients undergoing major surgical operations at the Graduate Hospital of the University of Pennsylvania. The age distribution of these patients was from 14 to 90 years, 67 per cent of them being over 51 years of age (table 1).

Complicating diseases were very common among these patients. Definite clinical and electrocardiographic evidence of cardiac disease was manifest in 88 of the patients in this group (table 2). In addition, almost all of the patients with cardiac disease gave evidence of complications of their cardiac disease such as decompensation, myocardial infarction, hypotension, cerebral hemorrhage or thrombosis, arterial embolism and pulmonary edema, either at the time of surgery or sometime in the past. Concomitant hepatic, renal and pulmonary diseases

TABLE 2

88 PATIENTS WITH HEART DISEASE

Cardiovascular Condition (Preoperative Diagnosis)	Cases with EKG Studies During Anesthesia	Cases with No EKG Studies During Anesthesia	Total
Arteriosclerotic Heart Disease	6	9	15
Myocardial Damage	1	9	10
Syphilitic Aortitis	1	0	1
Hypertension	14	21	35
Coronary Heart Disease	6	5	11
Ventricular Aneurysm	1	0	1
Auricular Fibrillation	1	4	5
Rheumatic Heart Disease	3	4	7
Bundle Branch Block	0	2	2
1st Degree Heart Block	1	0	1
Total	34	54	88

and metabolic derangements further complicated the physical status of many of these patients with cardiac disease. As a result of these physical findings, most of the patients in this group were poor candidates for major surgical procedures.

The remaining 230 patients of this study did not have clinical evidence of cardiac disease. However, the incidence of complicating hepatic, renal and pulmonary diseases was also quite high in these patients. Despite the absence of cardiac disease, the majority of them were classified as poor surgical risks (Classes III and IV).

Major thoracic or intra-abdominal operations were performed on 92 per cent of the patients studied. Table 3 lists the various operations that were performed. Most of these operations were of an elective nature. Many, however, were done as emergency procedures on patients who were acutely ill. Intestinal obstruction, massive gastrointestinal hemorrhage, gastrointestinal perforation and peritonitis were a few of the complications which necessitated immediate surgical intervention.

In general, the patients undergoing intra-abdominal operations included in this study comprised a group in whom the use of spinal anesthesia was thought to be contraindicated, based on the preoperative evaluation of the patient.

METHODS

All patients in this series received morphine sulfate, 8 mg. to 15 mg., and atropine sulfate or scopolamine hydrobromide, 0.4 mg. to 0.6 mg., by hypodermic injection one to one and one-half hours prior to the induction of anesthesia. Those patients undergoing emergency surgical procedures were given their premedication by intravenous injection five to ten minutes before the induction of anesthesia.

For each patient, a standard mixture of 400 mg. thiopental (8 cc of 5 per cent solution) and 4 mg. of decamethonium bromide (either 1 or 2 mg. per cubic centimeter) was prepared. The resulting total volume was either 10 cc. or 12 cc. depending on the concentration of decamethonium bromide in milligrams per cubic centimeter which was employed. Venipuncture was performed using an 18 gauge needle to permit rapid injection. The patient was then given 100 per cent oxygen by breathing bag and face mask for a period of about one minute. At the end of this interval, the total mixture of thiopental and decamethonium bromide was injected intravenously at a rapid rate, the entire injection requiring about five seconds. Oxygen administration was continued. After waiting twenty to twenty-five seconds following the completion of the injection, the patient was intubated by the direct oral route using a cuffed Magill endotracheal tube. Intubation usually required fifteen to twenty-five seconds. Following intubation, the endotracheal tube was attached by means of a flexible connector to a closed to-and-fro absorption system. The endotracheal cuff was inflated with

enough air to insure a completely closed system. The patient was immediately given 100 per cent oxygen following intubation and respiratory exchange was maintained by controlled respirations. All patients were apneic for varying periods of time.

Cyclopropane was employed as the primary anesthetic for the maintenance of anesthesia. Small quantities of diethyl ether were used as supplemental anesthesia. Further requirements for relaxation during the operation were satisfied by the use of *d*-tubocurarine chloride given intravenously in suitable dosage. Additional doses of decamethonium

TABLE 3

OPERATIVE PROCEDURES

(318 Cases)

Operations	Number of Patients with Normal Hearts	Heart Disease
Colectomy, Colostomy, Anterior Resection, Abdominoperineal Resection, Polypectomy	30	17
Hysterectomy, Salpingo-Oophorectomy, Appendectomy	30	10
Exploratory Laparotomy	34	14
Cholecystectomy, Choledochostomy, Choledochojejunostomy	29	12
Small Bowel Resection, Ileostomy	10	
Craniotomy, Laminectomy, Cordotomy	12	
Splenectomy	1	
Total and Subtotal Gastrectomy, Esophagectomy, Perforated Duodenal Ulcers, Bleeding Ulcers	54	21
Thoracolumbar Sympathectomy, Lumbar Sympathectomy	3	5
Fenestration, Mastoidectomy, Sinus Operations	5	
Pneumonectomy, Lobectomy, Thoracotomy, Diaphragmatic Hernia	11	1
Thyroidectomy	1	
Nephrectomy, Nephropexy	7	1
Inguinal Hernia, Incisional Hernia	3	5
Adrenalectomy		1
Ligation of Inferior Vena Cava		1
Totals	230	88

bromide for needed relaxation were not employed. All cases were terminated with an adequate washout by nitrous oxide-oxygen mixtures.

Electrocardiographic studies were done on 34 patients with a preoperative diagnosis of heart disease and on 30 patients without heart disease. Using a direct writing Viso-Cardiette, a control lead II tracing was recorded before induction. Continuous electrocardiographic tracings (lead II) were recorded during induction, laryngoscopy and endotracheal intubation, and for two minutes after intubation.

Blood pressure readings were taken on 22 patients with heart disease and 22 patients without heart disease by the indirect method of

Riva Rocci. Serial readings were obtained from the time of induction of anesthesia until two minutes after the completion of intubation. Recordings were taken as rapidly and as often as possible.

Continuous direct arterial blood pressure and pulse rate recordings were made in 10 cases using a strain gauge manometer and direct writing Poly-Viso recorder. Recordings were obtained from either a brachial or femoral artery.

Two arterial blood samples were drawn from each of 8 patients—one preoperatively before the injection of the drugs, the other seventy to eighty-five seconds following intravenous injection. Arterial carbon dioxide and oxygen analyses were carried out using the manometric

TABLE 4

ARRHYTHMIAS IN PATIENTS WITH NORMAL HEARTS

(30 Cases)

	Pentothal and Syncurine	Laryngoscopy	Intubation	Summary		
				Number	Per Cent of Total Arrhythmias	Per Cent of Total Cases
1st Degree A-V Block	1			1	25	3.3
Nodal Extrasystoles			3	3	75	10
Ventricular Extrasystoles						
Upper Nodal Tachycardia						
Multifocal Ventricular Extrasystoles						
Total Arrhythmias	1	0	3	4	100	13.3
Unaffected	29	30	27	26		86.7
Grand Total	30	30	30	30		

method of Van Slyke and Neill. Carbon dioxide tension was calculated. Blood hydrogen ion measurements were made anaerobically at 38 C. using a glass electrode.

OBSERVATIONS AND RESULTS

I. *Electrocardiographic Results*

A. *Patients without preoperative evidence of cardiac disease:*

In this group of 30 patients, the rapid injection of the thiopental-decamethonium mixture produced nodal extrasystoles in one patient (table 4). No new arrhythmias developed during laryngoscopy. During intubation, ventricular extrasystoles developed in 3 patients (10 per cent). Therefore, in a total of 13.3 per cent of the patients in this group cardiac arrhythmias developed sometime during induction, instrumentation and intubation.

Disturbances in rate were common. Sinus tachycardia developed in 3 patients following induction with thiopental-decamethonium, in 3 patients during exposure of the larynx and in 4 patients immediately after intubation.

B. *Patients with preoperative evidence of cardiac disease:*

In this group of 34 patients, the rapid injection of the drugs produced very transient, first degree heart block in one patient (table 5). During laryngoscopy, first degree heart block of very short duration developed in one patient, while ventricular extrasystoles appeared in 2 other patients. At the time of intubation, ventricular extrasystoles developed in 4 patients, upper nodal tachycardia in one patient, and multifocal ventricular extrasystoles in one patient. Ventricular extrasystoles were recorded in 20.6 per cent of the patients in this group during laryngoscopy and intubation. The total incidence of cardiac arrhythmias among these 34 patients was 29.4 per cent.

TABLE 5

ARRHYTHMIAS IN PATIENTS WITH HEART DISEASE
(34 Cases)

	Pentothal and Syncurine	Laryngoscopy	Intubation	Summary		
				Number	Per Cent of Total Arrhythmias	Per Cent of Total Cases
1st Degree A-V Block	1	1		2	20	5.9
Nodal Extrasystoles						
Ventricular Extrasystoles		2	4	6	60	17.7
Upper Nodal Tachycardia			1	1	10	2.9
Multifocal Ventricular Extrasystoles			1	1	10	2.9
Total Arrhythmias	1	3	6	10	100	29.4
Unaffected	33	31	28	24		70.6
Grand Total	34	34	34	34		

Sinus tachycardia developed in 7 patients following the injection of thiopental-decamethonium, in 5 patients incident to laryngoscopy and in 2 patients following endotracheal intubation.

Table 6 presents a summary of the total changes in cardiac rhythm which were observed in the 30 patients without heart disease and the 34 patients with heart disease; cardiac arrhythmias appeared in 21.5 per cent of the total number of patients. Of this number, 15.5 per cent were ventricular extrasystoles. All ventricular arrhythmias were associated with laryngoscopy and intubation, most of them appearing immediately after endotracheal intubation.

II. *Pulse Changes*

Some increase in heart rate was observed in 62 per cent of the patients following the injection of thiopental-decamethonium. In some instances this increase in rate was of sufficient magnitude to be classified as sinus tachycardia (rates over 100 per minute); in the others, the increase observed did not exceed 100 per minute.

Minimal or no change in pulse rate was observed in 31 per cent of the patients following the injection of the thiopental-decamethonium mixture; in 7 per cent of the patients, a decrease in pulse rate was noted.

Exposure of the larynx produced a slowing of the pulse in only two of the total number of patients studied. The pulse rate increased in all other patients.

TABLE 6

TOTAL ARRHYTHMIAS

(64 Cases)

	Pentothal and Syncurine	Laryngoscopy	Intubation	Summary		
				Number	Per Cent of Total Arrhythmias	Per Cent of Total Cases
1st Degree A-V Block	1	1	0	2	14.2	3
Nodal Extrasystoles	1	0	0	1	7.2	1.5
Ventricular Extrasystoles	0	2	7	9	64.2	14.0
Upper Nodal Tachycardia			1	1	7.2	1.5
Multifocal Ventricular Extrasystoles			1	1	7.2	1.5
Total Arrhythmias	2	3	9	14	100.0	21.5
Unaffected	62	61	55	50		
Grand Total	64	64	64	64		

During intubation, none of the patients showed a decrease in the pulse rate; *all* showed pulse increases of various magnitudes.

III. *Blood Pressure Recordings*

The effect of induction, laryngoscopy and intubation on the blood pressure was studied in 44 patients in this series using the indirect auscultatory method. In this group, 22 patients showed preoperative evidence of heart disease; the remaining 22 had normal hearts.

It is appreciated that the indirect method of recording blood pressures as used during the administration of an anesthetic is not accurate and is attended by errors of variable magnitude. However, these records were taken to reflect general trends of change in the blood pressure during the three procedures of induction, laryngoscopy and intubation rather than to record absolute values.

In order to substantiate the validity of the blood pressure recordings obtained by the indirect auscultatory method, and also to determine the magnitude of the errors associated with the method, direct arterial blood pressure tracings were taken on 10 patients chosen at random, subjected to the same factors of rapid injection, laryngoscopy and intubation. The results are recorded in table 7.

TABLE 7

AVERAGE FLUCTUATIONS OF SYSTOLIC AND DIASTOLIC BLOOD PRESSURE (B.P.) AND MEAN ARTERIAL BLOOD PRESSURE (M.A.B.P.) ACCOMPANYING INDUCTION WITH THIOPENTAL (400 MG.) AND DECAMETHONIUM BROMIDE (4 MG.), LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

Patient		Pre-induction	Lowest BP After Pentothal and Decamethonium	Average Laryngoscopy Range	Average Range After Intubation
1. C. E.	BP*	231/138	102/124	204/130	232/130
	MABP†	169	147	155	191
2. G. C.	BP	112/67	100/62	142/90	138/86
	MABP	89	81	116	112
3. H. N.	BP	204/98	150/76	150/78	200/117
	MABP	146	109	110	154
4. C. McN.	BP	132/75	97/60	116/73	153/92
	MABP	98	75	90	116
5. H. B.	BP	201/111	152/97	181/116	237/150
	MABP	154	123	147	191
6. C. D.	BP	127/73	97/60	103/67	129/85
	MABP	95	75	81	103
7. J. R.	BP	109/65	100/58	126/84	165/116
	MABP	83	74	101	136
8. M. G.	BP	134/74	90/48	110/62	155/86
	MABP	101	67	84	117
9. A. M.	BP	113/74	100/63	133/93	160/112
	MABP	90	78	109	131
10. J. S.	BP	142/71	110/65	120/62	153/86
	MABP	96	81	83	109

* Blood pressure
† Mean arterial blood pressure

A. *Effect of rapid induction with thiopental-decamethonium:*

1. Indirect blood pressure determination:

Sixty-four per cent of the 22 patients with abnormal hearts showed a decrease in systolic blood pressure (average fall 16 mm. of mercury) while 45 per cent of the patients in the same group showed a decrease

in diastolic blood pressure (average 13 mm. of mercury) following the rapid induction with these drugs.

In the group of 22 patients without heart disease, 90 per cent showed a decrease in systolic pressure averaging 11 mm. while 36 per cent of the patients showed decreases in diastolic pressure averaging 10 mm. following induction.

In the entire group of 44 patients, 77 per cent had a decrease in systolic blood pressure during induction, 7 per cent showed an increase and 16 per cent had no significant change.

2. Direct arterial blood pressure determinations:

In each of the 10 patients studied there was a decrease in both systolic and diastolic blood pressure following rapid induction. The average decrease in systolic pressure was 28 mm.—a 20 per cent reduction. The average decrease in diastolic pressure was 13.4 mm.—an 8 per cent reduction. The average decrease in mean arterial blood pressure was 18 per cent.

B. *Effect of laryngoscopy:*

1. Indirect blood pressure determination:

In the 22 patients with heart disease, laryngoscopy produced an average increase of 21 mm. of mercury in systolic pressure and an average increase of 20 mm. of mercury in diastolic pressure.

In the 22 patients without heart disease following laryngoscopy, an average increase of 61 mm. in systolic pressure and an average increase of 20 mm. in diastolic pressure were recorded.

These increases in blood pressure represent rises above the lowest recorded blood pressure following the administration of thiopental and decamethonium bromide.

2. Direct arterial blood pressure determination:

With laryngoscopy, there was an average increase of 19.6 mm. of mercury in systolic pressure and 14.5 mm. of mercury in diastolic pressure—above the lowest recorded pressures following the rapid induction with thiopental and decamethonium. If the preanesthetic blood pressure is used as the basis of comparison, then, following laryngoscopy, the systolic pressure was an average of 14.6 mm. of mercury lower than the starting pressure and the diastolic pressure unchanged.

C. *Effect of intubation:*

1. Indirect blood pressure determination:

Following intubation, the group of patients with heart disease showed an additional rise in systolic pressure averaging 21 mm. of

mercury. Diastolic pressure increased an additional 19 mm. of mercury in the same group. These increases represent rises above the highest recorded pressure following laryngoscopy.

Following intubation, those patients with normal hearts likewise showed an additional increase in systolic pressure (20 mm. average) and diastolic pressure (19 mm. average).

2. Direct arterial blood pressure determination:

In 9 of 10 patients following intubation, systolic pressure showed an average increase of 33.6 mm. of mercury while diastolic pressure increased an average of 16.2 mm. of mercury. These increases were over and above the highest pressures recorded following laryngoscopy.

If the preoperative blood pressure is taken as the basis of comparison, then, following intubation, systolic pressure increased only an average of 21.6 mm. while diastolic pressure showed an average increase of 17.4 mm.

IV. *Influence of Method on Ease of Intubation:*

Of the total of 318 patients intubated following the injection of thiopental-decamethonium mixture, only 10 patients (3.1 per cent) presented difficulties in exposure of the vocal cords and intubation. In these 10 cases, intubation required more than thirty seconds, the longest requiring ninety seconds. Two of the 10 patients required additional anesthesia for intubation—the initially injected dosages being inadequate for the physical habitus of these patients.

Anatomical abnormalities accounted for the difficulties in laryngeal exposure in 7 of the 10 patients in whom intubation was difficult. It should be stressed that the main difficulties encountered were associated with exposure of the larynx and not with spasm of the vocal cords. It is thought that these patients would have presented the same difficulties no matter what technic of induction and oral intubation was employed.

In 97 per cent of the cases, laryngoscopy and intubation were performed with facility. The profound muscular relaxation of the oral, pharyngeal and laryngeal structures which accompanied the rapid injection of the thiopental-decamethonium mixture almost completely obviated the use of force (with its risk of trauma) by the anesthetist during instrumentation and intubation.

In almost every patient, with exposure of the larynx, the vocal cords were found to be moderately to widely abducted. Mild adduction of the cords was observed occasionally but did not interfere with intubation since the endotracheal tube could be inserted readily with gentle pressure.

In 14 patients who began to cough immediately following the injection of the thiopental and decamethonium, moderate laryngeal spasm

developed initially, and subsided as the injected drugs exerted their effects more fully.

V. Effects of the Method on Respiration:

The rapid injection of these drugs produced an initial and very transient stimulation in rate and depth of respiration which appeared about fifteen seconds after start of injection and lasted about ten seconds. Progressive depression of respiration followed and subsequent apnea developed in all of the patients. The duration of the

TABLE 8

CHANGES OBSERVED FOLLOWING INJECTION OF THIOPENTAL (400 MG.) AND DECAMETHONIUM BROMIDE (4 MG.)*

(Oxygen content, hemoglobin saturation, carbon dioxide content and tension, and hydrogen ion concentration 70 to 85 seconds following injection.)

Patient	Time	Oxygen Capacity Vol. %	Oxygen Content Vol. %	% Saturation	CO_2 Content Vol. %	pCO_2 mm. Hg	pH 37 C
1. F. W.	Awake	20.09	19.39	96	49.44	54	7.28
	70 Sec.	20.09	18.53	92	52.07	66	7.21
2. D. S.	Awake	16.22	15.01	93	50.07	53	7.28
	85 Sec.	16.22	10.87	67	54.29	60	7.24
3. L. A.	Awake	17.24	16.15	94	46.08	46	7.31
	70 Sec.	17.24	14.61	85	48.42	48	7.29
4. C. S.	Awake	18.66	17.62	94	48.63	49	7.31
	75 Sec.	18.66	13.25	71	54.71	62	7.26
5. G. B.	Awake	16.22	15.16	94	52.23	56	7.28
	70 Sec.	16.22	13.33	82	55.00	64	7.23
6. C. H.	Awake	22.15	20.46	92	44.62	52	7.25
	70 Sec.	22.15	17.18	77	47.81	66	7.24
7. H. O.	Awake	16.92	15.95	94	48.91	45	7.35
	70 Sec.	16.92	13.41	79	52.13	52	7.32
8. M. R.	Awake	22.87	21.52	94	44.35	43	7.36
	85 Sec.	22.87	17.84	78	54.62	60	7.24

* Oxygen was not given before or after injection of the drugs.

apneic period was variable. Spontaneous respiratory efforts usually appeared eight to ten minutes after the injection but did not ensure an adequate respiratory exchange. Therefore, in all patients respiratory exchange was maintained by controlled respirations well beyond the point at which respiratory efficiency was restored. In many patients controlled respiration was purposely used throughout the entire surgical procedure. Nine patients failed to resume spontaneous respirations until twenty to twenty-five minutes had elapsed following en-

dotracheal intubation. It is realized that the estimation of the duration of the apneic period is unreliable because of the use of (1) controlled respiration and (2) the administration of anesthetic agents such as cyclopropane and ether shortly after intubation and during the period of controlled respiration. No patient in this series of 318 cases presented a persistent or prolonged period of respiratory paralysis which could be attributed to the initial injection of the thiopental and decamethonium bromide.

VI. Effect of the Method on Arterial Gases:

Seventy seconds following the injection of thiopental (400 mg.) and decamethonium bromide (4 mg.), there was a reduction in oxygen content, hemoglobin saturation (average decrease for 8 patients—94 to 81 per cent), and hydrogen ion concentration of arterial blood in each of the 8 patients. The carbon dioxide content and tension of arterial blood increased in each of the patients in the same interval (table 8).

DISCUSSION

A safe, reliable and efficient technic for rapid induction and immediate endotracheal intubation is available to the anesthesiologist and may be effected by the rapid intravenous injection of thiopental (400 mg.) and decamethonium bromide (4 mg.). This method, although extremely useful in the anesthetic management of the patient in good physical condition, is an invaluable asset in the anesthetic management of those patients of poor physical status. Patients with severe degrees of cardiac disease, in whom major surgical procedures are indicated or mandatory, can be safely managed by the use of this method. No fatality occurred in this group of patients.

A rapid intravenous injection of these agents produces certain general cardiovascular alterations; however, by clinical evaluation, these changes were not indicative of, nor did they precede the onset of dangerous cardiovascular depression or impaired circulatory efficiency. Even those patients with severe grades of cardiac disease did not show untoward circulatory effects following the use of this technic.

A decrease in both systolic and diastolic blood pressure, an increase in heart rate and a decrease in pulse pressure constituted the immediate characteristic circulatory response observed following induction in this manner. As would be expected, the indirect method of recording blood pressure did not give the true continuous quantitative variations which were obtained by the direct recording apparatus. However, the indirect method, which is employed routinely during the administration of most clinical anesthesias, did reflect an accurate parallelism with the fluctuations in blood pressure obtained by direct recording, and therefore is adequate for routine clinical use. It has been demonstrated that doses of decamethonium bromide comparable to those used in this

study, when administered alone, did not produce significant cardiovascular effects (1, 2). This finding was further confirmed by the present study. Therefore, the circulatory effects observed following induction were probably due to the thiopental. Analysis of the pressure-pulse curves obtained by direct intra-arterial recording did not conclusively demonstrate whether the decrease in blood pressure was the result primarily of a decrease in peripheral resistance or a reduction in cardiac output. A decrease in total peripheral resistance probably was the cause, judged by the decrease in the height of the dicrotic notch in many of the recordings. In other tracings, this alteration in the configuration of the pressure-pulse curve was not so prominent, yet decreases in blood pressure were recorded. Barbiturates administered in large doses are capable of decreasing total peripheral resistance by their depressant effect upon the arterioles and capillaries (3). The dose of thiopental as used in this study (400 mg.) is a comparatively large dose.

A decrease in cardiac output might also be a causative factor in the post-induction hypotension. Cardiac output could be reduced by a direct depressant effect of 400 mg. of thiopental on the myocardium. The electrocardiographic recordings of this study failed to indicate such a depressant effect on the conductive mechanism. Could a reduction in cardiac output be the result of a diminished venous return arising from the apnea which appeared in each of the patients following the injection of the mixture? This is unlikely, since the decrease in blood pressure was usually observed before the onset of the apnea.

Thus, from the presently available evidence, the decrease in blood pressure which occurs following the rapid injection of 400 mg. of thiopental is predominantly due to a decrease in total peripheral resistance. This hypotension, which averages a decrease of 28 mm. in systolic pressure and 13 mm. in diastolic pressure by direct recording, was not associated with any untoward over-all circulatory effects even in those patients with serious cardiovascular disease. Its duration was transient, lasting a few seconds until the initiation of laryngoscopy, at which time a pressor response was noted. This effect has been previously reported (4). This was the observed sequence in almost every patient on whom direct or indirect blood pressure recordings were taken. The very fact that such an active pressor response could be elicited immediately following the sudden initial circulatory depression, precludes the onset of deleterious and irreversible circulatory deterioration.

The increase in heart rate which was noted in 62 per cent of the patients following the injection of this combination of agents is not easily explained. A pressure static mechanism was considered—that is, cardiac acceleration following a decrease in blood pressure. However, the increase in heart rate was observed even when blood pressure decreases were not observed or when blood pressure was actually in-

creased by the pre-induction use of intravenous pressor drugs. In no instance was this increase in heart rate very marked or of any clinical significance. It probably represents a direct drug effect and occurs even when 100 per cent oxygen is administered before and during induction.

The rapid intravenous injection of thiopental and decamethonium bromide did not produce serious or significant derangement of the cardiac conducting mechanism as recorded by the electrocardiogram. Two minor arrhythmias appeared following injection, lasted a few seconds and subsided spontaneously. The incidence of cardiac arrhythmias was the same in the group of patients with and without cardiac disease. The intravenous injection of the combination of agents in the doses employed does not increase cardiac irritability nor does it produce any dominant electrocardiographic manifestations of parasympathomimetic cardiac effects as might be expected if the circulatory effects of thiopental were vagal in character. From these results, there was no evidence that thiopental produces parasympathomimetic effects on the circulatory system whether of a direct or reflex nature.

A constant respiratory response was obtained following the rapid injection of thiopental and decamethonium bromide. Within fifteen to twenty-five seconds following injection, a transient stimulation of respiration was noted with an increase in both rate and depth. The variation in the time of onset of this hyperpnea was probably dependent upon the individual circulation time. The cause of this response is obscure. It is not associated with a decrease in blood pressure since it appears before there is any change in pressure. A chemoreceptor reflex was considered, even though it has not been demonstrated that an increase in the hydrogen ion concentration of arterial blood will produce respiratory stimulation as occurs with a decrease in arterial hydrogen ion concentration. To rule out the alkaline factor as a cause, a solution of sodium carbonate with a pH of 10 was prepared corresponding to the hydrogen ion concentration of the thiopental. Eight cubic centimeters of this solution was injected intravenously at a rapid rate. No respiratory effect was noted. This same respiratory response is consistently obtained with the rapid injection of 8 cc. of thiopental (5 per cent) alone, indicating that this agent rather than the decamethonium bromide is the causative factor. The rapid intravenous injection of 4 mg. of decamethonium bromide produced no respiratory stimulation. This action of thiopental deserves further study.

Apnea developed in each patient in this series following the initial phase of respiratory stimulation. During the apneic interval, the oxygen content of arterial blood decreased while the carbon dioxide content increased. However, since intubation was accomplished within thirty to forty seconds following injection, these changes were not considered significant. The magnitude of the changes in arterial gas

content, as determined in this study, represented the changes during a seventy to eighty-five second interval—almost twice the length of time required for intubation. Likewise, if intubation was unsuccessful in a sixty second interval, the attempt was discontinued and oxygen was administered to the patient. Therefore, the degree of decrease of arterial oxygen as seen in this study was not permitted to occur. Prior to induction, oxygen was not administered to the 8 patients in whom arterial gas analyses were conducted. Such oxygen administration should be routine when this technic is employed and would decrease the degree of reduction in arterial oxygen content. It would be beneficial to study further the carbon dioxide and oxygen content of arterial blood at the moment of intubation. Clinical evidence of damage to the cardiovascular system resulting from the decrease in the arterial oxygen content which existed at the time of intubation was not encountered even in those patients with serious cardiac disease. It was thought that apnea, with its accompanying temporary reduction in arterial oxygen, was less hazardous to the patient than the anoxia which frequently occurs when laryngospasm develops incident to a prolonged induction and intubation when using technics of inhalation anesthesia.

The time required for induction and intubation using this technic was not permitted to exceed sixty seconds. If intubation was unsuccessful in this interval following induction, laryngoscopy was discontinued and 100 per cent oxygen was administered by face mask and breathing bag. Because of the extreme degree of muscular relaxation and hence the absence of laryngospasm, this maneuver could be accomplished with great ease. With the patient adequately oxygenated in this manner, a second immediate attempt at intubation could be made with complete safety. This is certainly not the case when intubation is attempted under various inhalation agents. Repeated unsuccessful attempts at intubation when using inhalation agents will frequently precipitate severe laryngospasm. The lack of relaxation of the cords makes inflation of the lungs difficult, if not impossible, and a second attempt at intubation can be made only after a protracted re-anesthetization of the patient. There is little question that the method which permits immediate oxygenation and a second attempt at intubation under conditions of ideal relaxation and safety to the patient, following an initial unsuccessful attempt at intubation, is to be highly desired in the patient with cardiac disease.

Immediately following intubation, controlled respiration was instituted using 100 per cent oxygen. The use of intermittent positive pressure in the apneic patient did not produce adverse effects either in the group of patients with or without cardiac disease. This technic of rapid intubation, therefore, is not contraindicated because of the respiratory depression which follows its use, providing the sixty second interval after induction is not exceeded by unsuccessful attempts at intubation.

Laryngoscopy, elevation of the epiglottis and endotracheal intubation produced a predominant sympathetic response in the majority of patients in this study. There was very minimal evidence of parasympathetic vagal stimulation following these manipulations. These observations have previously been reported (4). Characteristically, an increase in both systolic and diastolic blood pressure was noted which was initiated by laryngoscopy and further augmented by endotracheal intubation. Pulse rate, which increased following laryngoscopy, became more rapid with actual intubation. The cardiac arrhythmias which developed during instrumentation and intubation were those usually associated with sympathetic stimulation, being characterized by increased cardiac irritability (ventricular extrasystoles). All of the instances of arrhythmia were of short duration and subsided spontaneously. When they appeared, they were followed to their termination by continuous electrocardiographic tracings. The significance of these arrhythmias is obscure. Occasional cardiac irregularities occur frequently during the course of general anesthesia. Their deleterious effect on over-all circulatory efficiency is questionable. The onset of ventricular tachycardia, if allowed to persist untreated, might have a more serious implication. Such arrhythmias might predispose to the development of ventricular fibrillation. However, these arrhythmias were so infrequent and self-limited in duration that it was not thought an indication existed for their routine prophylaxis or treatment by drugs which decrease cardiac irritability. The arrhythmias appeared more frequently in the group of patients with cardiac disease. The incidence of arrhythmias in this group was 50 per cent greater.

A comparison of the incidence of cardiac arrhythmias which appeared during laryngoscopy and intubation following the injection of thiopental and decamethonium bromide was made with the incidence of arrhythmias which appeared in a comparable period when using other anesthetic agents. In a group of 32 patients without cardiac disease and 9 patients with cardiac disease who were given thiopental (250 mg.) for induction, followed by cyclopropane and ether in a closed circle, carbon dioxide absorbing system, continuous electrocardiographic tracings were taken. Direct oral intubation was performed in the lower second plane of surgical anesthesia. The results obtained showed that 33 per cent of the patients with heart disease and 21 per cent of the patients without heart disease developed ventricular arrhythmias during laryngoscopy and intubation. In the present study, using a combination of thiopental and decamethonium bromide, the incidence of ventricular arrhythmias during induction, laryngoscopy and intubation among the group of patients with heart disease was 20.6 per cent and only 10 per cent in the group without heart disease. If the development and persistence of ventricular arrhythmias, especially in the patient with cardiac disease, might be associated with serious derangement of cardiac function, then it is certainly desirable to reduce their

incidence, if this can be done with complete safety to the patient. From the results in this clinic, the incidence of cardiac arrhythmias which develop during laryngoscopy and intubation following the use of thiopental and decamethonium bromide is significantly lower than the number which appear when more orthodox and clinically proven inhalation anesthetics are used prior to endotracheal intubation.

Various investigators (4, 5) have demonstrated the lower incidence of cardiac arrhythmias associated with endotracheal intubation performed under deeper planes of surgical anesthesia. It has been suggested, therefore, that intubation should be performed under deeper planes of surgical anesthesia. However, the rationale of decreasing these arrhythmias in this manner can be questioned. The most common cardiac arrhythmias which develop during laryngoscopy and intubation are of a transient nature and of questionable clinical significance. The use of greater depth of anesthesia, especially in the cardiac patient, produces cardiac vascular depression with hypotension and minimizes but does not abolish the development of cardiac arrhythmias. The injection of the combination of thiopental and decamethonium bromide which probably produces first plane third stage anesthesia, permits intubation with ease at this light level and still results in a lower incidence of cardiac arrhythmias than is seen when deep second and upper third plane anesthesia, induced by other agents, is employed prior to intubation. By clinical evaluation, rapid intubation in this manner is superior to slower intubation under greater depth of anesthesia.

What is the over-all circulatory effect which is produced by the rapid intravenous injection of thiopental and decamethonium bromide as used in this study? In every instance, circulatory adequacy was maintained and evidence of dangerous cardiovascular deterioration was lacking. The circulatory changes associated with induction and intubation produced opposing effects which resulted in the maintenance of circulatory stability (fig. 1). The decrease in systolic and diastolic blood pressure which usually followed the injection of these agents was immediately counteracted by the pressor response, elicited by laryngoscopy, and further augmented by intubation. The duration of this pressor effect was between two and three minutes, with an immediate return toward preoperative levels. Thus the entire circulatory response to induction and intubation using these agents is brief and probably of no greater significance than the fluctuations in blood pressure which result from the routine daily activities of the individual patient.

It has been demonstrated, as with the cardiac arrhythmias, that this pressor reflex is less active under deeper planes of anesthesia and suggested that intubation should, therefore, be performed at such planes to avoid an increase in cardiac work (4). The results of this study failed to demonstrate any immediate adverse circulatory effects arising from an active pressor response when intubation was performed

in first plane third stage anesthesia. It is thought that no real justification exists for attempting to minimize this response by employing deeper anesthesia which itself could be detrimental to the cardiac patient.

Rapid methods of endotracheal intubation are a great asset in the management of many major anesthetic problems. The use of thiopental and decamethonium bromide offers a direct, rapid means of safely intubating a patient under optimal conditions of relaxation.

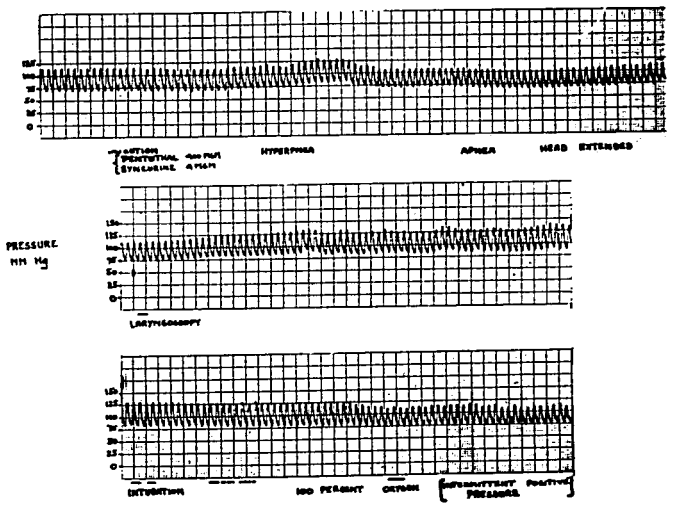

FIG. 1. Continuous arterial blood pressure tracing following induction with thiopental (400 mg.) and decamethonium bromide (4 mg.), laryngoscopy and intubation. Note return of blood pressure to preoperative level shortly after intubation and stability during intermittent positive pressure of 18 to 20 cm. of water. Pressure levels marked on left. Each block represents a 1 second interval.

Coughing, nausea and vomiting, retching, poor relaxation of the jaw and especially laryngospasm—complications so frequently accompanying induction and intubation when using inhalation agents—are extremely rare when using these agents. The use of this technic permits the rapid intubation of patients with advanced grades of pulmonary disease such as emphysema and edema. These conditions were frequently encountered in the cardiac patient in this series. Edentulous patients and those with various oral and nasal gastrointestinal drainage tubes in place, did not pose any problem concerning fitting of the

mask during induction and prior to intubation. Once intubation with a cuffed endotracheal tube was performed, a completely closed system could be established.

The injection of thiopental and decamethonium bromide permits extreme ease in laryngoscopy and intubation. The need for haste is abolished. The anesthesiologist need not fear inadequate relaxation, insufficient depth to permit intubation, or the development of laryngospasm. However, certain precautions must be observed in the use of this method. It should be reserved for the experienced, competent anesthesiologist. If used by inexperienced personnel, constant, close supervision by a qualified anesthesiologist must be maintained. The success of the method depends upon perfection of technic. With venipuncture, the needle must be well within the vein. Partial extravascular injection can lead to certain failure because of inadequate relaxation and laryngospasm. Immediately upon injection, some time notation should be made. This will permit accurate knowledge of the time consumed by laryngoscopy and intubation. If difficulty is encountered during intubation, the attempt should be discontinued after fifty-five to sixty seconds and the patient well oxygenated. After this maneuver, intubation can once again be attempted. Immediately upon intubation, the anesthesiologist must be certain that the endotracheal tube is in the trachea. Severe anoxia can result in the curarized, apneic patient in whom the endotracheal tube has been accidentally inserted into the esophagus.

Patients who present anatomical abnormalities of the mouth, jaw, teeth, larynx and neck usually are not good candidates for this method of intubation. A short, thick neck with limited extension, a receding mandible, prominent or protruding upper teeth, and edema of the floor of the mouth, neck or larynx could make laryngeal exposure and intubation extremely difficult. Under such circumstances difficulties of intubation should be anticipated and recognized before induction. These difficulties are unrelated to muscular relaxation and will be present no matter what technic for oral intubation is employed. By choice, such patients are intubated by the nasal route using light thiopental narcosis and topical anesthesia.

The use of thiopental and decamethonium bromide for rapid intubation is particularly valuable in the management of those patients in whom the tracheal aspiration of foreign material is a hazard. Patients with massive hematemesis, intestinal obstruction or acute dilatation of the stomach must be intubated before regurgitation and flooding of the bronchopulmonary tree can occur. This technic permits immediate intubation and, with other precautions such as positioning of the patient and preanesthetic use of intestinal drainage tubes, decreases the aspiration danger. It is recognized that when intubation is performed thirty to forty seconds after the injection of the drugs, the

maximal curarizing effect of the decamethonium bromide has not been established. The full curarizing effect of the drug does not appear for three to four minutes following the intravenous injection. In instances in which regurgitation of gastrointestinal content is a danger, it would be unwise to wait for full relaxation to be established. Too often regurgitation is precipitated by the onset of profound muscular relaxation. The ability of 4 mg. of decamethonium bromide and 400 mg. of thiopental to permit excellent laryngeal exposure and atraumatic intubation within thirty seconds following its injection is, therefore, a real advantage in the management of the patient in whom aspiration is a hazard. Further proof that decamethonium bromide exerts considerable muscle relaxation within thirty seconds after its injection is obtained by attempting to intubate, using 400 mg. of thiopental alone. Such attempts resulted in poor relaxation, with severe bouts of laryngospasm and traumatic intubations.

In an effort to compare the immediate effects of decamethonium bromide when injected intravenously with those of *d*-tubocurarine chloride, a large number of patients, not reported in this study, were given a combination of 400 mg. of thiopental and 15 mg. of *d*-tubocurarine chloride by rapid intravenous injection. It was found that the 15 mg. dose of *d*-tubocurarine chloride did not permit satisfactory laryngeal exposure and atraumatic intubation to be performed within the first thirty to forty-five seconds following its administration, as did the decamethonium bromide. It was concluded that *d*-tubocurarine chloride in 15 mg. doses was an inferior drug to decamethonium bromide for immediate endotracheal intubation as performed in this series. However, if the patient was oxygenated for one minute following the injection of the thiopental and *d*-tubocurarine chloride, allowing the curare to act, intubation could then be performed with equal ease. The curarizing effect of decamethonium bromide manifests itself more rapidly than does the action of *d*-tubocurarine chloride.

The use of the combination of thiopental and decamethonium bromide for rapid intubation is a distinct asset in the anesthetic management of the patient with cardiac disease. The results of this study demonstrated the safety of its use for those patients with severe grades of cardiac disease. The technic ideally fulfills the precautions which must be observed during the induction and intubation of these patients (6, 7). Induction is rapid and smooth, without excitement and struggling. Emotional and physical exertion is thus avoided. Intubation is accomplished with rapidity, with ease and with a minimum of trauma. A reliable and patent airway is thus immediately established, insuring excellent oxygenation of the patient. Serious deterioration of circulatory efficiency was not observed in any of the patients of this series. The lack of serious morbidity and mortality related to the method alone precludes any consistent interference with circulatory adequacy. Pa-

tients with advanced cardiac disease tolerated the injection of these agents well. Other investigators have confirmed the safety of employing rapid intubation in the poor risk cardiac patient (8, 9).

Electrocardiographic changes which developed during rapid intubation while using these agents in the group of patients with cardiac disease were less frequent than those associated with the use of cyclopropane and ether for induction and intubation. The ventricular arrhythmias, with a more serious possible implication in the cardiac patient, were transient and associated with the reflex stimulation by intubation rather than the injection of the drugs *per se*. There was no evidence that either thiopental or decamethonium bromide increased myocardial irritability even in patients who preoperatively had cardiac arrhythmias.

Caution should be observed with the use of this technic in patients with advanced aortic stenosis, recent myocardial infarction, surgical shock and cachexia. The fixed cardiac output which results from aortic stenosis does not permit adequate circulatory compensation to be initiated following the rapid injection of thiopental and decamethonium bromide. Serious and persistent hypotension results. The heart acutely damaged by a large infarction tolerates poorly the alterations in circulatory dynamics which attend the use of this technic. Cardiac failure could rapidly ensue in the heart with poor reserve. Advanced shock and cachexia reduce the need for the dosages used in this study.

It is interesting to compare the circulatory reactivity of the group of patients with cardiac disease with that of the group with normal hearts following rapid induction and intubation. In general, patients with cardiac disease displayed more stability and less reactivity than did the group of patients without cardiac disease. For instance, by indirect recording, a decrease in systolic blood pressure following the injection of the drugs developed in 64 per cent of the patients with cardiac disease, while 90 per cent of the patients with normal hearts showed a similar decrease. Likewise, the pressor response following laryngoscopy and intubation was of a lesser magnitude in the cardiac group. Transient electrocardiographic changes, such as inversion of the T waves, decreased amplitude of the P and T waves, depression of the ST segment, and so forth, were seven times as common in those patients *without* cardiac disease as they were in the cardiac group. What might this mean? Repeated exposures of the cardiac patient to various stress stimuli such as myocardial anoxia, associated with various organic changes in the cardiovascular system, may lead to decreased circulatory reactivity and lability. Circulatory stability may be the ultimate result of repeated stress situations. Therefore, when patients with and without heart disease were subjected to the same type of stress situation, that is, the injection of thiopental and decamethonium bromide, a greater response was observed in the absence of cir-

culatory disease. These findings are in accord with those of May (10) who found that in a group of patients subjected to gradually induced anoxemia, the degree of change in the T wave decreased strikingly with advancing age.

SUMMARY

A combination of thiopental (400 mg.) and decamethonium bromide (4 mg.) was administered by rapid intravenous injection to 318 unselected patients, varying in age from 14 to 90 years, for induction and immediate endotracheal intubation. The incidence of serious complicating diseases in this group was quite high. Eighty-eight patients had preoperative evidence of cardiac disease.

The use of this technic even in the poor risk cardiac patient did not produce significant deterioration of cardiac efficiency. A transient decrease in systolic and diastolic blood pressure with an increase in pulse rate usually followed injection of the drugs. Alarming decreases in blood pressure were not encountered. Laryngoscopy and induction elicited a significant pressor response. The incidence of cardiac arrhythmias during laryngoscopy and intubation was lower than results when using a standard, accepted technic of inhalation anesthesia. Serious ventricular arrhythmias were extremely rare in those patients with cardiac disease.

The rapid method of intubation described in this study presents many definite advantages to the anesthesiologist. These have been discussed. Mortality attributable to this method has not been encountered. From the results of this study, the use of thiopental and decamethonium bromide for induction of anesthesia and endotracheal intubation is, in our experience to date, the method of choice in the anesthetic management of the cardiac patient and other patients in poor physical condition who require major surgery.

Since the completion of this study, 720 additional patients have been intubated using this technic. The results were similar to those obtained in the original study.

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