Discussion

From the results of skin testing, the authors and a consulting allergist concluded that the patient had manifested a severe allergic reaction to thiamylal (Surital). Although the patient had a similar but less marked reaction to *d*-tubocurarine (a known histamine liberator), the same reaction occurred in the control subjects. Subcutaneous injection of ten times the intradermal dose of *d*-tubocurarine caused no untoward response, excluding it as the causative drug. The patient showed no positive reaction to succinylcholine; however, prior to skin testing an allergy to succinylcholine could not be ruled out. Jerums[1] reported a case of anaphylaxis to succinylcholine and demonstrated skin sensitivity to this drug, but not to thiopental.

To our knowledge, a severe allergic reaction to thiamylal has not been reported. There are, however, several case reports of thiopental anaphylaxis. Davis[2] published a case report and referred to several others. We support the cautions that he cites: 1) anaphylaxis may occur without warning, and the possibility should be suspected in patients with an allergic history; 2) satisfactory use of barbiturates orally does not ensure that barbiturates will be tolerated intravenously; 3) anaphylactic treatment must be readily available to patients who receive barbiturates intravenously; 4) patients who sustain severe drug reactions should wear "Medic Alert" identification to avert future mishaps.

Reports of reactions to barbiturates given intravenously are rare, but their true incidence is not known. We suspect that severe anaphylactic reactions may be misdiagnosed and that mild allergic reactions may be unobserved or casually dismissed. It should be noted that barbiturates had been given several times in the past to this patient, not only orally but also intravenously, without report of ill effects other than the skin rash after his most recent anesthesia. This patient probably is also sensitive to thiopental; future skin tests are planned to determine this. Should he require an operation in the future, he has been given a warning, verbally and in writing, not to take barbiturates.

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The Effects of Innovar on Functional Residual Capacity and Total Chest Compliance in Man

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Innovar produces rigidity of the chest wall in some patients by enhancing skeletal muscle tone. Abdominal muscles may also contract after administration of this drug.[1,2] These are expiratory muscles, and an increase in their tone may result in active exhalation[3] and a decrease in functional residual capacity (FRC). The question we have tried to answer in this study, "Does Innovar decrease FRC?", is clinically important, since a decrease in FRC may impair arterial oxygenation.[4,5]

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Method

Six informed male patients, free of respiratory disease, consented to the study. They received Innovar intravenously at a rate of 1 ml/min (total dose 10 ml/70 kg body weight, or less if clinically noticeable muscle rigidity

or loss of consciousness occurred). Orotracheal intubation with a cuffed tube was carried out within 5 minutes after the Innovar administration, with the aid of topically applied lidocaine (as much as 5 ml of 2 per cent solution). Total static compliance was measured by inflating the lungs with 2 l of air in 0.5-l increments from a super-syringe and recording each pressure after 5 seconds. The patients then breathed into an oxygen-filled 9-liter Collins spirometer for 3 to 4 minutes. When the expiratory lung volume became stable, succinylcholine, 1 mg/kg, was given iv, to produce muscle paralysis. The change in the baseline of the spirogram was recorded for about 30 seconds (fig. 1). Immediately thereafter, total compliance was determined again, followed by direct measurement of FRC by a neon-rebreathing technique,[6,7] using the super-syringe to rebreathe the test gas in the apneic patient. This FRC value, less the change in lung volume produced by succinylcholine (*i.e.*, change in the baseline of the spirogram after relaxation), was considered to be the FRC after Innovar. Compliance curves were constructed from the absolute lung volumes and respective airway pressures, and examined in two ways. First, the airway pressures produced by increasing lung volume above actual FRC before and after muscle relaxation were compared. Second, the slopes of the near-linear portions of the compliance curves between relaxed FRC + 0.5 and 1.5 l of absolute lung volume before and after relaxation were compared. The airway pressure at relaxed FRC + 1.0 l lung volume was used as an estimate of the position change of the compliance curves after relaxation.

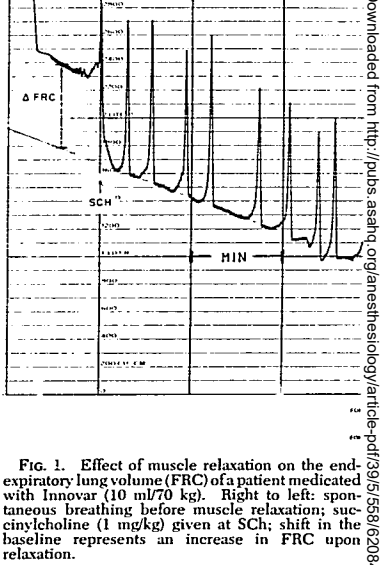

FIG. 1. Effect of muscle relaxation on the end-expiratory lung volume (FRC) of a patient medicated with Innovar (10 ml/70 kg). Right to left: spontaneous breathing before muscle relaxation; succinylcholine (1 mg/kg) given at SCh; shift in the baseline represents an increase in FRC upon relaxation.

Statistical analysis utilized paired t tests; $P < 0.05$ was accepted as significant.

TABLE 1. FRC's of Patients Receiving Innovar, before and after Muscle Relaxation with Succinylcholine

	Age (years)	Height (cm)	Weight (kg)	Dose of Innovar (ml)	Clinically Evident Chest-wall Rigidity	FRC (Liters)		
						Innovar	Innovar + Succinylcholine	Δ FRC
Patient 1	41	185	80	12	No	2.62	3.61	+0.99
Patient 2	39	178	84	8	No	1.99	2.52	+0.53
Patient 3	19	170	80	7	Yes	1.16	1.55	+0.39
Patient 4	25	183	77	9	No	1.30	1.53	+0.23
Patient 5	20	180	83	10	Yes	1.35	1.83	+0.48
Patient 6	19	193	89	11	No	0.99	0.99	0
MEAN						1.57	2.01*	0.44
SE						0.25	0.38	0.14

* $P < 0.05$.

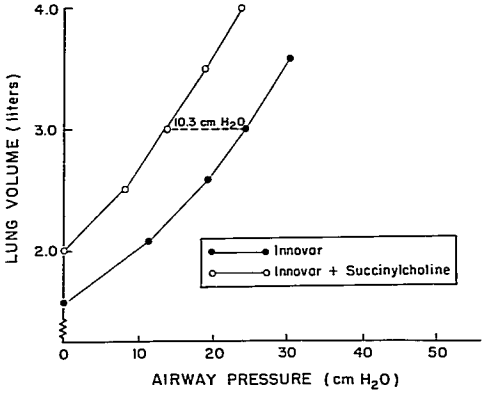

FIG. 2. Total compliance curves of six patients receiving Innovar before and after muscle paralysis. A shift of 10.3 cm H_2O to the left occurred after relaxation.

RESULTS

The mean FRC for the six patients after Innovar and succinylcholine was 2.01 ± 0.38 l (± SE). Muscle relaxation increased FRC by a mean value of 0.44 ± 0.14 l, as evidenced by the baseline shift of the spirogram (fig. 1). Calculation yielded a mean FRC after Innovar but before muscle relaxation of 1.57 ± 0.25 l ($P < 0.05$) (table 1).

Comparison of the pressure–volume curves with Innovar before and after muscle paralysis revealed that with Innovar alone, airway pressures were higher at every lung volume (table 2, fig. 2). A 2-liter inflation increased airway pressure by 30 cm H_2O before relaxation and by 24 cm H_2O after relaxation ($P < 0.05$). The slopes of the compliance curves determined between relaxed FRC + 0.5 and 1.5 l before and after succinylcholine were parallel, and

TABLE 2. Total Chest Compliances of Six Patients Receiving Innovar, before and after Muscle Relaxation with Succinylcholine

	Airway Pressure (cm H_2O)								Compliance between 0.5 and 1.5 Liters above Relaxed FRC (l/cm H_2O)		
	FRC + 0.5 Liters		FRC + 1.0 Liter		FRC + 1.5 Liters		FRC + 2 Liters				
	Innovar	Innovar + Succinylcholine	Innovar	Innovar + Succinylcholine	Innovar	Innovar + Succinylcholine	Innovar	Innovar + Succinylcholine	Innovar	Innovar + Succinylcholine	Shift after Relaxation (cm H_2O)
Patient 1	8	8	13	13	16.5	18	22	23	0.111	0.077	9.0
Patient 2	6.5	6	11.5	11	15.5	14	19.5	16	0.125	0.125	4.5
Patient 3	13.5	11.5	21.5	17.5	28.5	23.5	35.5	29.5	0.071	0.083	9.5
Patient 4	10.5	8.5	20	15.5	27.5	22.5	33	28.5	0.077	0.071	8.0
Patient 5	16.5	8.5	29.5	15	36.5	21	41	26	0.087	0.080	21.5
Patient 6	12.5	6.5	20	11	26.5	15	30.5	19	0.071	0.120	9.0
MEAN	11.25	8.17	19.25	13.83	25.17	19.0	30.25	23.67	0.090	0.093	10.3
SE	1.5	0.79	2.65	1.07	3.24	1.62	3.34	2.19	0.01	0.01	2.4
t	2.36		2.41		2.40		2.79		0.21		4.33
P	>0.05		>0.05		>0.05		<0.05		>0.08		<0.01

averaged 0.090 ± 0.01 and 0.093 ± 0.01 l/cm H_2O, respectively ($P > 0.8$). However, the airway pressures necessary to increase lung volume to relaxed FRC + 1.0 liter were, on the average, 10.3 ± 2.4 cm H_2O lower ($P < 0.01$) after muscle relaxation (fig. 2). Only two of the six patients (Patients 3 and 5) manifested clinically noticeable chest-wall rigidity; these patients also showed the greatest shifts in compliance curves upon relaxation (9.5 and 21.5 cm H_2O, respectively).

Discussion

Muscle rigidity after Innovar is usually attributed to large doses administered too rapidly. When rigidity occurs, it is usually treated with a muscle relaxant to facilitate positive-pressure ventilation.

Our finding of reduced total compliance and FRC after Innovar and its reversal by succinylcholine demonstrates that increased expiratory muscle activity was present even in the absence of clinically evident rigidity. Since Innovar[1] and fentanyl[2] are equally capable of increasing the EMG activity of the abdominal muscles, the changes we noted after administration of Innovar were probably produced by the opioid component, fentanyl.

Total compliance, measured from actual FRC, was lower in all patients after Innovar, explaining the clinical observation that higher airway pressures are necessary for controlled ventilation in patients who have been given Innovar. The reduction in total compliance may have resulted from decreases in both lung and chest wall compliance; the former by a decrease in lung volume and the latter by increased expiratory muscle tone.

When the compliance curves at equal higher lung volumes in each patient, *i.e.*, between 0.5 and 1.5 liters above the relaxed FRC, are compared, they are nearly parallel, and the relaxed compliance curve is shifted to the left. This suggests that the expiratory muscles with their reflexes resist inflation, acting as a constant load, rather than as an elastic load. Therefore, when sufficient airway pressures are applied to restore FRC and to overcome the increased muscle tone (the lower part of the compliance curve), additional increases in airway pressure will result in similar lung volume changes with or without muscle paralysis.

Measurement of FRC before Innovar administration would have been useful; however, it has been previously reported that FRC in awake man is slightly higher than that after succinylcholine paralysis[8,9] owing to inspiratory muscle tone.[9] Since injection of succinylcholine after Innovar produced an increase in FRC, we assume that FRC had been decreased after the administration of Innovar.

Decreased FRC has been associated with impaired arterial oxygenation;[5-7] Don *et al.*[4] suggest that decreases of FRC below closing volume (CV) would enhance venous admixture. We demonstrated that Innovar decreases FRC even when chest-wall rigidity is not clinically evident. This drug, therefore, should be administered with caution to patients in whom reduction of FRC may be undesirable.

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