gas exchange and noninvasive spirometry employing a canopy-computer-spirometry system. Following baseline determinations, the subjects were given, at intervals of at least 1 week, an i.v. dose of curare sufficient to decrease (and maintain) peak static inspiratory pressure (PI_{max}) at −45 cm. H_2O (moderate weakness) or at −70 cm. H_2O (mild weakness). Data were collected during a 15-minute period of steady state muscle weakness at either weakness level.

In a second phase of the study, the response to a CO_2 challenge with 5 minutes of 3 per cent CO_2 was determined at a moderate level of weakness (−40 to −50 cm. H_2O).

Partial curarization to a mild level of muscle weakness did not produce significant changes in the respiratory functions studied. Increasing the level of muscle weakness, increased tidal volume from 166 to 186 ml. per M^2 and time of inspiration from 1.51 to 1.71 seconds. Minute ventilation did not change, nor was there a change in mean inspiratory flow (V_T/V_I).

The administration of 3 per cent CO_2 produced similar responses both normal and curarized subjects. Minute ventilation increased more than twice, chiefly on the basis of a marked increase in tidal volume, although there was an associated small increase in respiratory frequency in the curarized subjects.

Studies of patients with muscle weakness due to primary muscle disease have shown an increased respiratory rate and decreased tidal volume, in contrast with the current results, which showed an increased tidal volume and increased inspiratory time.

The present results indicate that, in situations with moderate muscle weakness, there was preservation of diaphragmatic strength. Since the diaphragm is the prime generator of respiration at rest, these findings are consistent with the observation that minute ventilation is preserved in partially curarized normal subjects. In the face of basically unaltered lung function, the response to CO_2 would be as observed.

It is suggested that rapid analysis of breathing patterns may serve to distinguish alterations in ventilation due to mild or moderate muscle weakness from the effects due to severe muscle weakness and/or disease of the pulmonary parenchyma.

Comment: This interesting scientific paper focuses our attention on the fact that partial curarization to a "mild" or "moderate" degree in awake volunteers is not associated necessarily with any reduction in tidal volume, and that a challenge with 3 per cent CO_2 produces a response similar to that in a normal subject. The respiratory sparing effect of low doses of nondepolarizing[1] and depolarizing[2] muscle relaxants has been documented. A functional diaphragm and an unobstructed airway are fundamental to these findings.

Rosenbaum and his colleagues did not study patients recovering from general anesthesia as opposed to awake volunteers: it might be supposed that the implications would then be different as chemoreceptor responses to hypoxia, which are those responsible for maintaining ventilation, are impaired or ablated by even small amounts of the volatile anesthetic agents. Studies of this kind[3] were performed in the acute situation, and we do not know whether the same responses would be obtained in a chronic situation in man. Nevertheless, Rosenbaum and his colleagues have provided data that help to document how so many patients throughout the world manage to survive in the recovery period despite some degree of residual muscle paralysis, which has often not been fully appreciated by the anesthesiologist.

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Clinical Evaluation of Atracurium Besylate Requirement for a Stable Muscle Relaxation During Surgery: Lack of Age-Related Effects

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A series of 24 patients scheduled for elective surgery, and free of any evidence of hepatorenal disorder, were divided into 3 groups by age: 1 (26 ± 3 yr.); 2 (53 ± 2 yr.); and 3 (76 ± 2 yr.). All were

premedicated with oral diazepam, and anesthesia was induced with methohexital-fentanyl-N_2O-O_2. Ventilation was maintained to produce normocapnia. A force-displacement transducer and tension attenuator were installed on the left upper extremity to permit determination of isometric contraction of the adductor pollicis (twitch height (TH)).

Tracheal intubation was performed at a minimum TH after injection of 0.3 mg. per kg. of atracurium, and thereafter the TH was maintained constant at 10 per cent of baseline values by continuous infusion of atracurium. Determination was made of atracurium dose requirements every 10 minutes, the time which elapsed between the end of atracurium administration and recovery to 25 per cent of control TH, and the time from 25 to 75 per cent TH recovery.

The amount of atracurium required to maintain stable TH values became nearly constant after 30 minutes of administration, and the dose requirements for steady state blockade were not significantly different between the 3 age groups. Recovery rates also were not age related.

This technique indicated that the amount of drug administered, once a steady state TH was attained, was a measure of total plasma clearance. The results indicated that the rate of elimination or inactivation of atracurium was independent of patient age. In addition, TH recovery rates were independent of age. Aging did not appear to affect the mechanisms of inactivation of atracurium.

Comment: It is a pleasure to see an increasing number of papers in the literature that address the special problems posed by anesthesia in elderly patients. The vast majority of these reports have shown that the "aged" behave somewhat differently from the "young." One exception relates to atracurium, which is shown here to be inactivated at similar rates in young and elderly patients alike, presumably by way of the nonenzymatic Hofmann elimination mechanism. From this consideration alone, atracurium may hold some advantage over vecuronium.

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Bradycardia After the Use of Atracurium

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Four patients undergoing general anesthesia in which neuromuscular blockade was produced by atracurium developed significant episodes of sinus or nodal bradycardia following one of the following surgical maneuvers: gallbladder traction, retinal manipulation, and traction on the peritoneum or uterus. Each was successfully treated by the injection of atropine 0.6 mg. i.v. without further incident.

Atracurium in clinical doses is believed to have minimal effects on the vagal or sympathetic systems. However, at the author's institution, several instances of profound bradycardia requiring treatment with atropine have occurred since the introduction of this new muscle relaxant.

It is speculated that 2 mechanisms may be involved: (1) the lack of cardiovascular effects by atracurium permits other substances with cholinergic actions to act unopposed; and/or (2) an atracurium metabolite may be exerting an action.

It is suggested that patients given atracurium in operations in which patent vagal stimulation is expected be monitored with an ECG and be fully atropinized at the time of induction of anesthesia.

Comment: It is extremely doubtful and most likely impossible that the instances of bradycardia described here can be fairly attributed to the use of atracurium; no clinical trial so far, and there have been several good ones published, has demonstrated any significant influence of atracurium on heart rate. The slowing of the heart in the 4 case reports described did not occur directly after the atracurium was given, but much later during the anesthetic. The bradycardia could be ascribed to the use of fentanyl, morphine, or halothane, the intrinsic effects of these drugs on heart rate being unmasked in the absence of any concomitant drugs that increase heart rate (e.g., atropine, pancuronium), and/or to surgical procedures that are noted to be associated with vagal responses to tissue traction. Cholecystectomy is notorious as an operation that can lead to hypotension, bradycardia, or both; such cardiovascu-