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**Immediate ventilatory response to inspiratory elastic loads in newborn and adult rabbits**

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**Fisiologia.** — *Immediate ventilatory response to inspiratory elastic loads in newborn and adult rabbits* (\*). Nota di JOHN T. FISHER e JACOPO P. MORTOLA (\*\*), presentata (\*\*\*) dal Socio R. MARGARIA.

**RIASSUNTO.** — La risposta ventilatoria immediata (primo respiro) a carichi elastici inspiratori è stata studiata in 6 conigli neonati (N) ed in 6 conigli adulti (A) in anestesia barbiturica. Con carichi elastici corrispondenti a 2, 10 e 20 volte la elasticità dell'apparato respiratorio, il volume corrente ( $V_T$ ) scende al 60, 31 e 24% rispettivamente dei valori controllo in N, ed una simile riduzione si verifica nell'A. Anche la frequenza respiratoria ( $f$ ) diminuisce in maniera quasi simile nel N e nell'A. Tuttavia il calo di  $f$  in N è dovuto ad un simile aumento del tempo inspiratorio ( $T_I$ ) ed espiratorio ( $T_E$ ), mentre il caso di  $f$  nell'A è soprattutto dovuto ad un aumento del  $T_I$ . Di conseguenza, paragonando le funzione  $V_T/T_I$ , si osserva che, per lo stesso percentuale calo di  $V_T$ ,  $T_I$  aumenta meno nel N che nell'A. Questi risultati potrebbero indicare un minore contributo vagale alla ventilazione nel neonato.

## INTRODUCTION

The immediate reduction in tidal volume ( $V_T$ ) with inspiratory loading in adults has consistently been reported to be less than expected and consequently termed load compensation (Campbell, Dinnick and Howell, 1961; McClelland, Sproule and Lynne-Davies, 1972). In newborn rabbits airway occlusion (an infinite elastic load) has been used to assess the Hering-Breuer reflex by constructing the  $V_T$  vs. inspiratory time ( $T_I$ ) relationship before and after pentobarbital anaesthesia (Goldberg and Milic-Emili, 1977) and during ether induced apneusis (Thach, Wyszogrodski and Milic-Emili, 1976). However relatively little attention has been focussed on the comparison of ventilatory compensation in the newborn with respect to the adult. The purpose of the present study was to examine the immediate (first breath) ventilatory compensation to elastic loading in newborn rabbits and compare this response to the adult.

## METHODS

Experiments were performed on 6 newborn (1-9 days old) and 6 adult rabbits. Animals were anaesthetized with sodium pentobarbital (25-30 mg/kg i.p. or i.v.) and a tracheal cannula inserted below the larynx. The newborn

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animals were placed in a pressure plethysmograph previously described by Goldberg and Milic-Emili (1977). A pressure transducer connected to a port of the plethysmograph was calibrated to measure volume. Tidal volume in the adults was measured by a volume displacement body plethysmograph with a calibrated electrical output from a Krogh spirometer. Airway pressure ( $P_{ao}$ ) in both the newborn and adults was measured by a pressure transducer connected to one arm of the tracheal cannula. A three-way connector exterior to the plethysmograph was attached to the tracheal cannula so that the animal could inspire either from room air or from a syringe of variable volume representing elastic loads of different magnitude. Care was taken to apply the loads at end expiration. Passive elastance of the respiratory system ( $E_{rs}$ ) was measured by inflating the animals a known amount and measuring the subsequent  $P_{ao}$ . In order to compare the newborn to the adult the ventilatory response was examined at loads of 2–20 times the  $E_{rs}$  of each animal. All results refer to the analysis of the first loaded breath expressed as a percentage (%) of the mean of the 3 preceding control (unloaded) breaths.

#### RESULTS AND DISCUSSION

The mean response of ventilation ( $\dot{V}_E$ ) and its components tidal volume ( $V_T$ ) and frequency ( $f$ ) are illustrated in Figure 1 for one representative newborn and adult. The resultant  $V_T$  (mean  $\pm$  standard deviation) at loads of 2, 10 and  $20 \times E_{rs}$  for all the newborns pooled together was  $60 (\pm 9)$ ,  $31 (\pm 7)$ , and  $24 (\pm 6)$  % respectively of the control value while  $64 (\pm 3)$ ,  $33 (\pm 3)$ , and  $26 (\pm 5)$  % were the corresponding values in the adults. The immediate compensation of breathing rate was also not significantly different between the newborn and adult due to a large scatter though the mean values were higher in the newborns ( $92 \pm 5$ ,  $87 \pm 11$ , and  $82 \pm 17$  % in newborns and  $89 \pm 10$ ,  $77 \pm 7$ , and  $67 \pm 19$  % in adults for loads of 2, 10 and  $20 \times E_{rs}$  respectively). Consequently, there were no significant differences in the newborn and adult ventilatory ( $\dot{V}_E$ ) response ( $55 \pm 8$ ,  $27 \pm 8$ ,  $19.5 \pm 6$  % in newborns versus  $57 \pm 6$ ,  $25 \pm 3$  and  $17 \pm 3$  % in adults at the above loads).

The response of the timing components inspiratory time ( $T_I$ ) and expiratory time ( $T_E$ ) expressed as a percentage of the control values are shown in Figure 2 for a representative newborn and adult animal. The dashed line is the line of identity and the diagonals are iso-frequency lines which indicate all possible  $T_I$ – $T_E$  combinations that may exist at a given frequency. The newborn response to loading is a reduction in  $f$  with either  $T_I$ ,  $T_E$ , or both of the timing components increased. On the contrary the drop in  $f$  observed in the adult with loading is mediated primarily by an increase in  $T_I$  rather than  $T_E$  (Fig. 2). The  $V_T$  vs  $T_I$  relationship was obtained by adding progressively greater elastic loads. The mean response is shown in Figure 3 for 6 newborn and adult animals where  $V_T$  and  $T_I$  are expressed as a % of the control value. In general the  $V_T$  vs  $T_I$  curves were steeper in the newborn than in the adult. Since the duration of  $T_I$  is considered to be modulated by

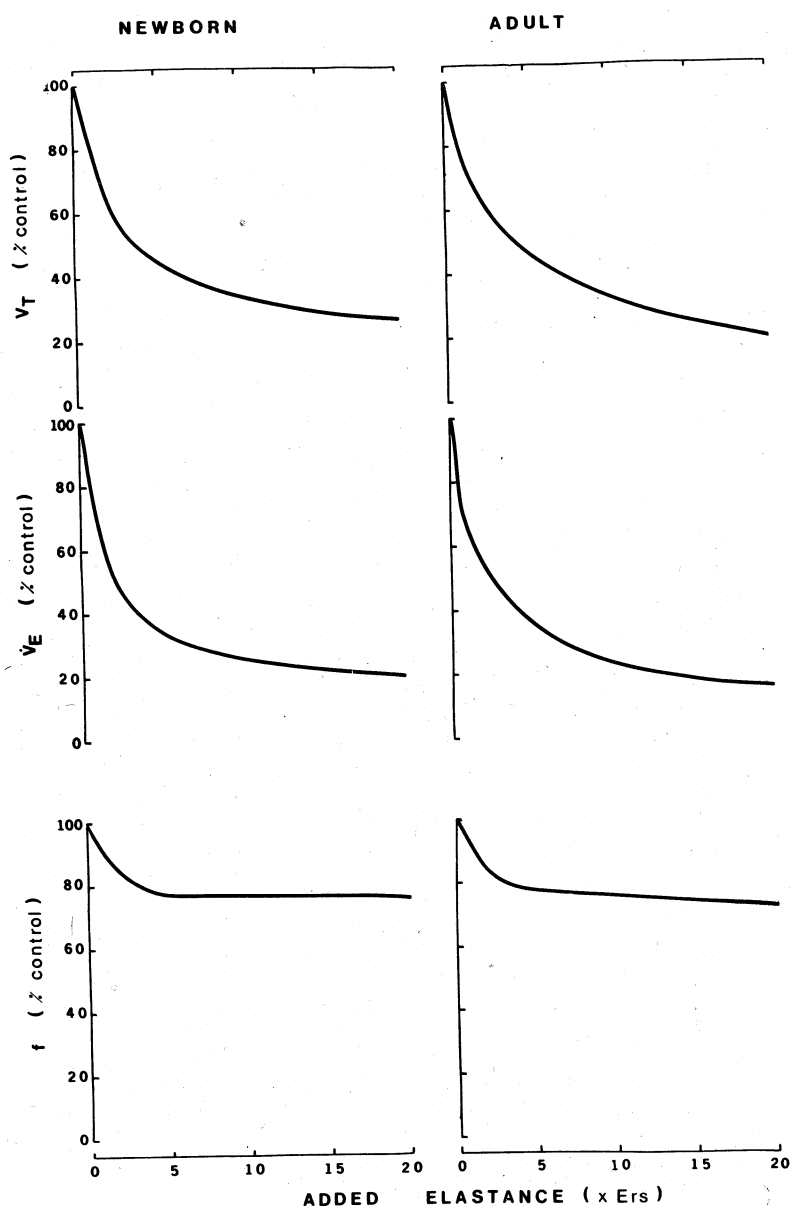


Fig. 1. - Immediate response of ventilation ( $\dot{V}_E$ ), tidal volume ( $V_T$ ) and frequency ( $f$ ) to elastic loading in a representative newborn and adult rabbit. Values are expressed as a percent of the control.

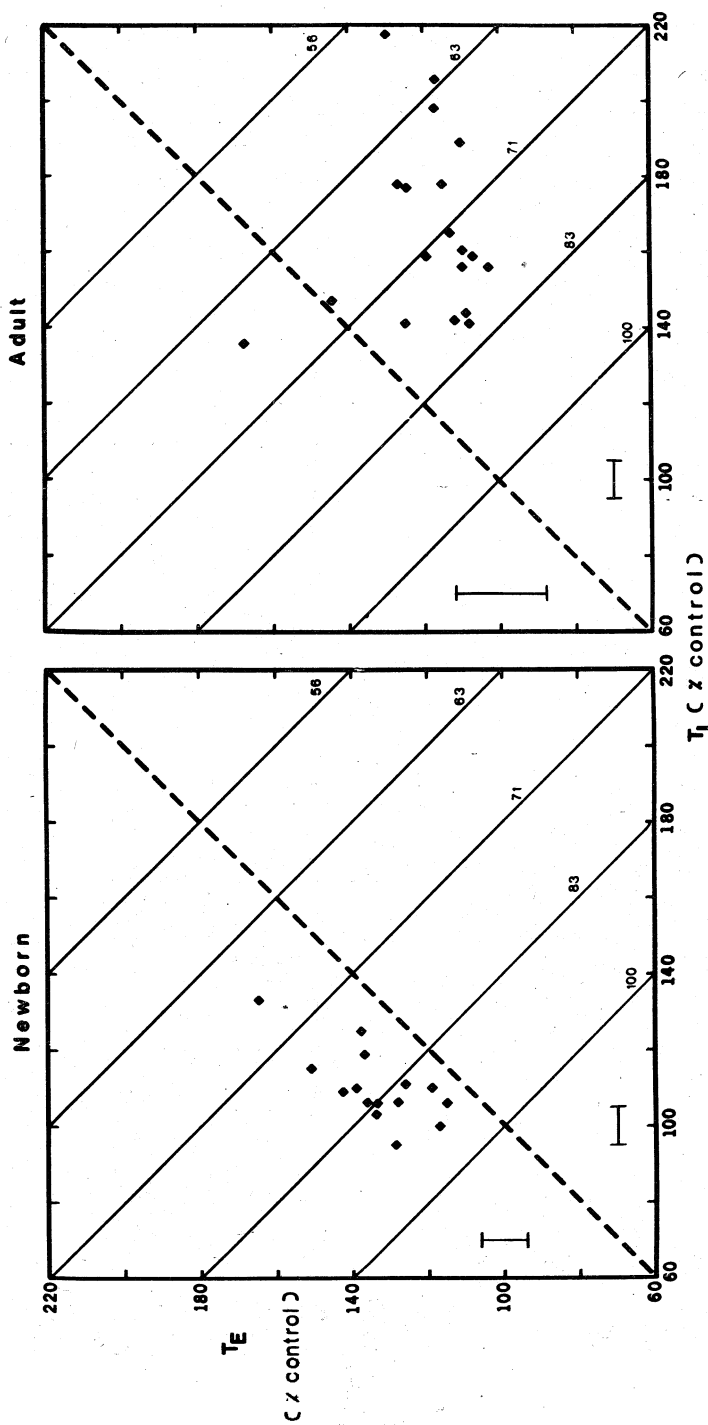


Fig. 2. - Immediate response of inspiratory ( $T_I$ ) and expiratory ( $T_E$ ) time to elastic loading in a representative newborn and adult rabbit. Diagonals are iso-frequency lines. All values are expressed as percent control.

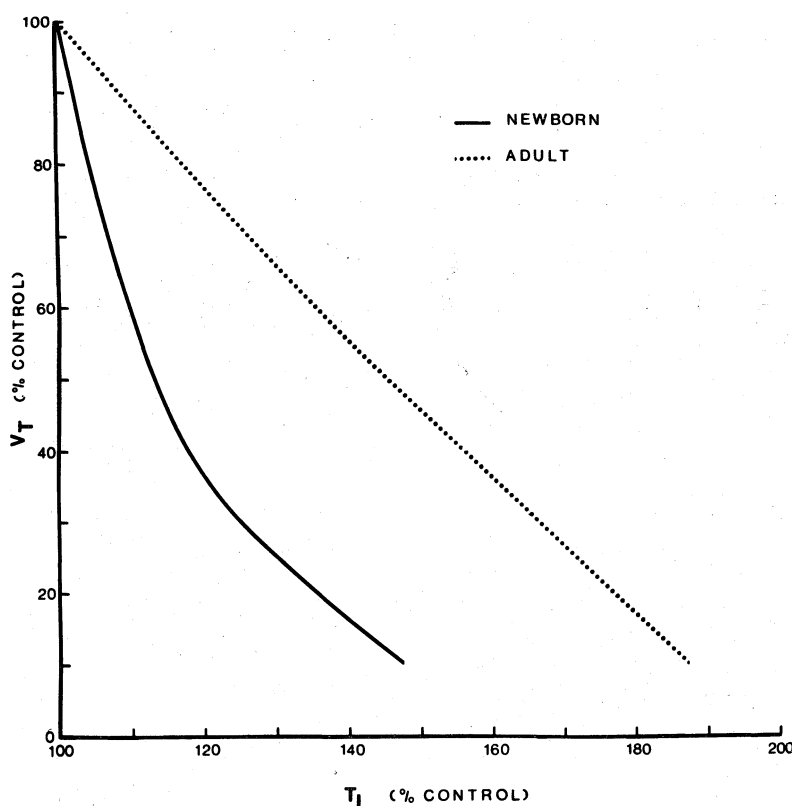


Fig. 3. — The mean  $V_T$  vs  $T_I$  curve for 6 newborn and adult rabbits obtained by applying elastic loads of different magnitude. Values are expressed as percent control.

$V_T$  via the pulmonary stretch receptors (Clark and von Euler, 1972) this finding might be interpreted as a lower sensitivity in the newborn to volume related vagal feedback (i.e. for a given reduction in  $V_T$ ,  $T_I$  is proportionately longer in the adult). However, this result must also be considered in the light of potential differences in the sensitivity to anaesthesia of the newborn and adult. In addition, the relative importance of the "background" chemical drive and its contribution to the  $V_T$  vs  $T_I$  curve in the newborn and adult is not known.

In summary, we have found that the compensation of  $V_T$ ,  $f$ , and  $\dot{V}_E$  to inspiratory elastic loading is similar in newborn and adult rabbits. However, the newborn adjusts  $f$  by modulating both  $T_I$  and  $T_E$  while the adult prolongs essentially  $T_I$  only. Consequently, the  $V_T$  vs  $T_I$  curve is steeper in the newborn than the adult although the exact cause of this difference is not clear at this time.

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