was given to maintain maternal arterial pressure, ephedrine was associated with fetal metabolic acidosis. The mean UABE was $-4.4$ mEq litre$^{-1}$ (SE 0.8, IQR $-1.4$ to $-6.5$) with ephedrine, compared with $-0.7$ mEq litre$^{-1}$ (SE 0.4, IQR 0.5 to $-1.9$) with phenylephrine ($P<0.001$) (t-test).

To assess the net effect of ephedrine on metabolic acid addition to/removal from the fetal circulation by the placenta, we used a regression model to predict umbilical venous base excess from umbilical venous base excess and patient group. There was a strong association between UABE and umbilical venous base excess, but this was not affected by patient group: UABE (mEq litre$^{-1}$) $= 0.66 + (1.13$ times umbilical venous base excess) ($r^2 = 0.87$, $t = 17.3$, $F = 301$, $P < 0.0001$). To assess the net effect of ephedrine on metabolic acid addition to/removal from the fetal circulation by the placenta, we used a regression model to predict umbilical venous base excess from UABE and patient group. There was a strong association between umbilical venous base excess and UABE. Interestingly, this was affected by patient group, with umbilical venous base excess being lower in the ephedrine group (Table 1).

To explain our observations, we suggest that ephedrine may increase placental lactate production: if a proportion of the additional lactate produced by the placenta is not metabolized by the fetus, hydrogen ions could accumulate within the fetal circulation, causing fetal metabolic acidosis. The possible influence of ephedrine on placental lactate production warrants further investigation.

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New use of a laryngectomy tube for management of mechanical ventilation in patients with anatomical abnormalities

Editor—It is sometimes difficult to manage airways in morbidly obese patients with a thick neck using standard tracheostomy tubes. So far, only a few techniques using tracheostomy tubes or tracheal tubes to manage artificial airways have been reported. We report successful use of reinforced laryngectomy tubes (LaryngoFlex®, Willy Rusch, Kernen, Germany) with flanges from tracheostomy tubes (ULTRA TracheoFlex®, Willy Rusch, Kernen, Germany) to secure a tracheostomy airway in a patient with serious anatomical abnormalities and severe systemic oedema.

A 72-yr-old male (height, 166 cm; weight, 90 kg), who had undergone laryngectomy for laryngeal carcinoma, was transferred to our intensive care unit (ICU) because of respiratory failure. His trachea was intubated through tracheostomy and his lungs were mechanically ventilated. At first, standard tracheostomy tubes (Portex®, Blue Line®, Smith Medical, Kent, UK) 8.0, 9.0, and 10.0 mm ID were used. However, the shape and size of the cuff and the tube length outside the stoma were not appropriate for the patient with a funnel-shape stoma and severe systemic oedema. Then, we tried a laryngectomy tube LaringoFlex® (11.0 mm ID) with a flange derived from a tracheostomy tube ULTRA TracheoFlex® of the same size to place at the optimal depth (Fig. 1). This sealed his trachea and his lungs could be ventilated properly.

The second patient was a 69-yr-old female (estimated height, 150 cm; weight, 67 kg) with rheumatoid arthritis and its complications. Since she had been intubated oroatra-chally over a long period, tracheostomy was done.

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Table 1 Regression model to predict umbilical venous base excess (mEq litre$^{-1}$) from UABE and ephedrine or phenylephrine group. Adjusted $r^2 = 0.88$

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient $b$</th>
<th>Standard error (SE) ($b$)</th>
<th>$t$</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>$-1.44$</td>
<td>0.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UABE (mEq litre$^{-1}$)</td>
<td>0.71</td>
<td>0.05</td>
<td>14.6</td>
<td>&lt;0.0001</td>
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<tr>
<td>Ephedrine group</td>
<td>$-0.85$</td>
<td>0.36</td>
<td>$-2.3$</td>
<td>0.024</td>
</tr>
</tbody>
</table>

**Source of variation**

<table>
<thead>
<tr>
<th>Analysis of variance</th>
<th>Degrees of freedom</th>
<th>Sum of squares</th>
<th>Mean squares</th>
<th>$F$</th>
<th>$P$-value</th>
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<tbody>
<tr>
<td>Regression</td>
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<td>402</td>
<td>201</td>
<td>167</td>
<td>&lt;0.0001</td>
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<tr>
<td>Residual</td>
<td>45</td>
<td>54</td>
<td></td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

**Table 1** Regression model to predict umbilical venous base excess (mEq litre$^{-1}$) from UABE and ephedrine or phenylephrine group. Adjusted $r^2 = 0.88$
However, the orifice of the stoma could not be accessed easily because of a severe systemic oedema due to chronic cardiac and renal failure. Therefore, as in the first case, we chose LaryngoFlex 9.0 mm ID with the flange and she was ventilated successfully.

To the best of our knowledge, this is the first report describing the use of a laryngectomy tube with a flange derived from a tracheostomy tube. Standard tracheal tubes are often chosen when tracheostomy tubes are not long enough to access the stoma. 1 The laryngectomy tube may overcome several drawbacks, such as proneness to kinking, short cuff length. For example, cuff lengths of LaryngoFlex® and Portex® of 9.0 mm ID are 36 and 26 mm, respectively (Fig. 1). This difference of 10 mm may also be an advantage to seal the trachea properly. Laryngectomy tubes are designed to be used during laryngectomy in the operating room, not during long-term mechanical ventilation in the ICU settings and therefore have no flange. It is usually fixed by an adhesive tape or a suture. This drawback can be overcome by using a flange from TracheoFlex® of the appropriate outer diameter.

In conclusion, we found that a laryngectomy tube with an adapted flange may provide a secure airway during mechanical ventilation via the stoma. We believe that this method is a good alternative to a standard tracheostomy tube for tracheostomized patients with severe anatomical abnormalities.

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S. Takahashi  
T. Hoshi  
M. Tanaka

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Subcutaneous tetrodotoxin and inflammatory pain

Peripheral tetrodotoxin (TTX) has been proposed for the treatment of several types of pain, and thus i.m. TTX is currently being evaluated in patients with severe cancer pain. 1 In some animal studies, it appears that inflammatory pain may also be responsive to the antinociceptive effect of TTX, but the potency of the drug after systemic injection is not clear. Thus, the subcutaneous injection of TTX attenuated pain behaviour in the inflammatory phase of the rat formalin test, 2 but one study reported lack of activity in the carrageenan model, where the drug only seemed effective when injected in the sciatic nerve. 3

We have studied the potential anti-hyperalgesic effect of subcutaneous TTX in the rat carrageenan model by using an analgesiometer (Ugo-Basile, Italy) to determine the threshold pressure needed to elicit a paw withdrawal reaction (Randall–Selitto test). After baseline determinations, the rats (SD, male, 250–350 g) were injected with TTX (2.5 mg kg⁻¹, s.c.) or vehicle and 1 h later with 0.1 ml of 1% lambda carrageenan into the surface of the right hind paw. The effects on withdrawal reaction were studied 3 h post-injection. TTX reduced hyperalgesia slightly but significantly in the animals treated with this drug (Fig. 1). This finding further supports the antinociceptive properties of systemic TTX in the rat carrageenan model by using an analgesiometer (Ugo-Basile, Italy) to determine the threshold pressure needed to elicit a paw withdrawal reaction (Randall–Selitto test). After baseline determinations, the rats (SD, male, 250–350 g) were injected with TTX (2.5 mg kg⁻¹, s.c.) or vehicle and 1 h later with 0.1 ml of 1% lambda carrageenan into the surface of the right hind paw. The effects on withdrawal reaction were studied 3 h post-injection. TTX reduced hyperalgesia slightly but significantly in the animals treated with this drug (Fig. 1). This finding further supports the antinociceptive properties of systemic TTX in the rat carrageenan model by using an analgesiometer (Ugo-Basile, Italy) to determine the threshold pressure needed to elicit a paw withdrawal reaction (Randall–Selitto test). After baseline determinations, the rats (SD, male, 250–350 g) were injected with TTX (2.5 mg kg⁻¹, s.c.) or vehicle and 1 h later with 0.1 ml of 1% lambda carrageenan into the surface of the right hind paw. The effects on withdrawal reaction were studied 3 h post-injection. TTX reduced hyperalgesia slightly but significantly in the animals treated with this drug (Fig. 1).

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This finding further supports the antinociceptive properties of systemic TTX in inflammatory hyperalgesia, which is in agreement with the prominent changes of TTX-sensitive channels associated with inflammation 4,5 and the reported analgesic effect in the formalin test. 2 The small decrease in pain that we have detected suggests that single doses of TTX would not be very effective in acute, severe inflammatory conditions like the one elicited in this study. However, we think that this activity is enough to suggest that the drug could provide significant relief in milder, chronic inflammation, but it must be tested accordingly. This is appropriate, as some reports have expressed concern about the safety of TTX. Thus, we have presented preliminary results showing that repeated subcutaneous injections of TTX are well tolerated in rodent models able...