Increased airway resistance during xenon anaesthesia in pigs is attributed to physical properties of the gas


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Background. In this study we investigated the effects of the physical properties of xenon on respiratory mechanisms in pigs.

Methods. With institutional approval, 10 female pigs (mean 25.2 (SD 2.5) kg) were anaesthetized with thiopental, remifentanil, and pancuronium. Gas flow and pressure were recorded continuously at the proximal end of the tracheal tube during constant flow ventilation for control, with 100% oxygen (control), followed by 1.5% isoflurane in 70/30% nitrogen/oxygen, 1.0% isoflurane in 70/30% nitrous oxide/oxygen, and 70/30% xenon/oxygen in random order. Compliance (C) and resistance (R) were calculated using a single compartment model. Resistance was corrected for gas viscosities (η) and also for densities (ρ) and viscosities (η) as (ρ*η)^1/2 to compare assumptions of laminar and mixed flow in the airways.

Results. With constant flow ventilation, xenon increases inspiratory pressure compared with other gas mixtures. There were no significant differences in resistance, corrected for laminar or mixed flow, between the gas mixtures. Xenon anaesthesia did not affect compliance.

Conclusions. The increase in airway pressure observed with xenon anaesthesia is attributed completely to its higher density and viscosity. Therefore, determination of airway resistance must take into account the physical properties of the gas. Xenon does not exert any major effect on airway diameter.


Keywords: ventilation, respiratory mechanics; anaesthetic techniques, inhalation; anaesthetics gases, xenon

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At ambient temperature, pressure, and when water saturated, the density (ρ) and viscosity (η) of xenon is 5.44 g litre⁻¹ and 2.25 10⁻⁵ Pa s⁻¹, respectively.¹ These values are substantially higher than those of the other gases used in anaesthesia and may affect the determination of respiratory mechanics. An increase in airway resistance during xenon anaesthesia has been reported in previous investigations, for example in pigs² and in open-chest dogs.³ The question ‘is this attributable to physical properties of the gas or if xenon affects airway resistance as such?’ is yet to be answered.

When flow is laminar, viscosity is the only physical property of the inspired gas that has an influence on flow resistance. However, if flow is turbulent, resistance depends more on the density of the gas than its viscosity. The aim of this experimental study was to compare respiratory mechanics corrected for physical gas properties during xenon/oxygen anaesthesia to those with nitrogen/oxygen or nitrous oxide/oxygen, both with isoflurane, as the most frequently used inhaled anaesthetic. Two different, simplified assumptions of flow patterns, that are laminar, and mixed laminar and turbulent flow, were compared to determine if xenon affected airway resistance by a mechanism other than its physical properties.

Methods

The study was approved by the local Animal Care Committee as well as the governmental Animal Care Office and it was performed with 10 female German landrace pigs weighing 22–30 kg (mean 25.2 (SD 2.5) kg). Upon
Gas concentrations were monitored using thermo-conductotracheal intubation (using a 7.0 mm ID cannula percutaneous tracheotomy (because of difficulties on Ruesch Medical, Kernen, Germany) in six animals. Animals received azaperone 4 mg kg\(^{-1}\) and ketamine 10 mg kg\(^{-1}\) intramuscularly for premedication, which was followed by cannulation of an ear vein. Continuous infusion of Ringer’s solution 0.1 ml kg\(^{-1}\) min\(^{-1}\) was started, and general anaesthesia was induced by administration of thiopental 4 mg kg\(^{-1}\), continuous infusion of remifentanil 0.25 \(\mu\)g kg\(^{-1}\) min\(^{-1}\), and pancuronium 0.1 mg kg\(^{-1}\) followed by an infusion of 0.1 mg kg\(^{-1}\) h\(^{-1}\). Orotracheal intubation was performed using auffed 5.0 mm ID tube (Mallinckrodt Medical, Athone, Ireland) in four of the animals and percutaneous tracheotomy (because of difficulties on orotracheal intubation) using a 7.0 mm ID cannula (Ruesch Medical, Kernen, Germany) in six animals. Volume-controlled ventilation, using a closed circuit PhysioFlex anaesthesia ventilator (Draeger, Luebeck, Germany) was started using a tidal volume of 10 ml kg\(^{-1}\) with an inspiration:expiration ratio of 1:2, and a fixed ventilatory frequency of 24 breaths min\(^{-1}\) to maintain an end-tidal \(\mathrm{PCO}_2\) of 4.7–5.3 kPa. With this mode, the machine delivers a constant inspiratory flow (after a short period of exponential increase) by constantly moving the membrane of a membrane chamber within the circuit towards its outlet. The volume administered is measured by electronic detection of the membrane movement with an error of less than 10%. Thereby, the ventilator generates a ramp-like pressure. The ventilation pattern was kept constant throughout the experiment, which lasted 6–8 h.

**Animal preparation**

Animals received azaperone 4 mg kg\(^{-1}\) and ketamine 10 mg kg\(^{-1}\) intramuscularly for premedication, which was followed by cannulation of an ear vein. Continuous infusion of Ringer’s solution 0.1 ml kg\(^{-1}\) min\(^{-1}\) was started, and general anaesthesia was induced by administration of thiopental 4 mg kg\(^{-1}\), continuous infusion of remifentanil 0.25 \(\mu\)g kg\(^{-1}\) min\(^{-1}\), and pancuronium 0.1 mg kg\(^{-1}\) followed by an infusion of 0.1 mg kg\(^{-1}\) h\(^{-1}\). Orotracheal intubation was performed using auffed 5.0 mm ID tube (Mallinckrodt Medical, Athone, Ireland) in four of the animals and percutaneous tracheotomy (because of difficulties on orotracheal intubation) using a 7.0 mm ID cannula (Ruesch Medical, Kernen, Germany) in six animals. Volume-controlled ventilation, using a closed circuit PhysioFlex anaesthesia ventilator (Draeger, Luebeck, Germany) was started using a tidal volume of 10 ml kg\(^{-1}\) with an inspiration:expiration ratio of 1:2, and a fixed ventilatory frequency of 24 breaths min\(^{-1}\) to maintain an end-tidal \(\mathrm{PCO}_2\) of 4.7–5.3 kPa. With this mode, the machine delivers a constant inspiratory flow (after a short period of exponential increase) by constantly moving the membrane of a membrane chamber within the circuit towards its outlet. The volume administered is measured by electronic detection of the membrane movement with an error of less than 10%. Thereby, the ventilator generates a ramp-like pressure. The ventilation pattern was kept constant throughout the experiment, which lasted 6–8 h.

**Monitoring**

With general anaesthesia, a 20-gauge Teflon cannula was inserted in a femoral artery, a pulmonary artery catheter was placed via a femoral vein, and the urinary bladder was catheterized. ECG, ear pulse oximetry, and systemic and pulmonary arterial pressure were monitored by a Datex AS/3 anaesthesia monitor (Datex-Engstrom, Helsinki, Finland). Gas concentrations were monitored using thermo-conductive analysis for xenon and infrared spectroscopy for the others (including end-tidal carbon dioxide) by the PhysioFlex machine. Pressure and flow were recorded at the proximal end of the tracheal tube using a CP-100 Pulmonary Monitor (Bicore, Irvine, CA, USA) from which raw data were exported on-line to a PC for further processing. The CP-100 uses a variable orifice flow meter for which single-use flow probes, calibrated for air, were supplied by the manufacturer. A new calibrated flow probe was used for each animal, and the tidal volume was calculated by integration of the flow–time curve. As demonstrated recently by Goto and colleagues,\(^4\) readings of an orifice flow meter are dependent of gas composition. To allow for correction, tidal volume measured by the PhysioFlex ventilator, which is independent of gas composition, was divided by the value obtained from the CP-100 flow–time curve. This procedure revealed over-estimation of tidal volume by the CP-100 by 1.18 for oxygen, 1.09 for nitrogen/oxygen, 1.06 for nitrous oxide/oxygen, and 1.37 for xenon/oxygen. Thus, these factors were used for correction.

**Determination of respiratory mechanics**

Resistance (\(R\)) and compliance (\(C\)) were calculated according to the method published by Bates and co-workers using a single compartment model described by the equation:

\[
\frac{V(t)}{C} + \frac{V'(t)}{R} = a t
\]

where \(V(t)\) is volume, \(V'(t)\) is flow, \(C\) is compliance, \(R\) is resistance, \(a\) is the slope of the inspiratory pressure increase for a ramp-like pressure as applied by the ventilator during inspiration, and \(t\) is time. From the recorded flow data, a flow–time curve is obtained from which instantaneous volume (\(V\)) is calculated. This is plotted against inspiratory time (\(T_i\)) which is consequently replaced by applied pressure according to \(P(t) = a t\). The applied pressure is the sum of the pressure to overcome flow resistance (\(P_{\text{res}}(t) = V'(t) \times R\)) and the pressure to overcome elastic recoil forces (\(P_{\text{el}}(t) = V(t)/C\)). \(C\) is then derived from the linear part of the volume–time curve where flow is constant with \(V' = a \times C\), and \(R\) equals the point of the time axis intercept derived from back-extrapolating this linear portion (called the time constant \(\tau\) of the system), divided by the compliance.\(^5\)

If the flow is fully laminar, \(P_{\text{res}}\) is proportional to the viscosity, \(\eta\), while in turbulent flow it is mainly the density, \(\rho\), which determines pressure when all other parameters are held constant. In physiological conditions, laminar flow is

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**Table 1** Densities (\(\rho\)) and viscosities (\(\eta\)) at ambient temperature (20°C), pressure, and water saturated for various gas mixtures as used in this study

<table>
<thead>
<tr>
<th></th>
<th>(\text{O}_2\ 100%)</th>
<th>(\text{N}_2\text{O} / \text{O}_2\ 70/30%)</th>
<th>(\text{N}_2\text{O} / \text{O}_2\ 70/30%)</th>
<th>(\text{Xenon} / \text{O}_2\ 70/30%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\rho) (g litre(^{-1}))</td>
<td>1.32</td>
<td>1.21</td>
<td>1.67</td>
<td>4.20</td>
</tr>
<tr>
<td>(\eta) (10(^{-3}) Pa s(^{-1}))</td>
<td>2.00</td>
<td>1.81</td>
<td>1.61</td>
<td>2.18</td>
</tr>
</tbody>
</table>

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Xenon and airway resistance

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541
present in lower porcine as well as in human airways.\(^6\) In a tracheal tube, there is a considerable amount of turbulence caused by tube connectors and the increase in diameter at the tip of the tube within the trachea and, thus, gas density must be taken into account. Pedley and colleagues\(^7\) have suggested that the resistance ratio of two gas mixtures equals the ratio of their \((r^{*}\eta)^{1/2}\) under physiological mixed flow conditions. The viscosities, \(\eta\), and the densities, \(r\), for 100% oxygen, 70/30% nitrogen/oxygen, 70/30% nitrous oxide/oxygen, and 70/30% xenon/oxygen are shown in Table 1. Viscosities and the terms \((r^{*}\eta)^{1/2}\) were obtained and then normalized for those of 70/30% nitrogen/oxygen for better comparison. For example, the viscosity of xenon/oxygen \((2.18 \times 10^{-5}\text{ Pa s}^{-1})\) was divided by that of nitrogen/oxygen \((1.81 \times 10^{-5}\text{ Pa s}^{-1})\) to obtain a normalized \(\eta\) of 1.20 for xenon/oxygen. The results were compared with the ratios of the calculated, uncorrected resistances \(R_{uncorr}\) with the three gas mixtures to that with 70/30% nitrogen/oxygen to compare the assumptions on airway flow. Corrected resistance for laminar flow \(R_{corr}\) was obtained by dividing \(R_{uncorr}\) by normalized \(\eta\), and likewise, correction for mixed flow \(R_{corr:mixed}\) was achieved by dividing \(R_{uncorr}\) by normalized \((r^{*}\eta)^{1/2}\).

### Study procedure

While anaesthesia was maintained with thiopental, remifentanil, and pancuronium, control data (CON) during ventilation with oxygen 100% were collected. Afterwards, only remifentanil and pancuronium were continued and the animals received anaesthetic gas mixtures of 1.5% isoflurane in 70/30% nitrogen, 1.0% isoflurane in 70/30% nitrous oxide, or 70/30% xenon according to one of three different schedules to which they were randomly allocated (see Table 2). After each experimental mixture, gas washout was performed with 100% oxygen and after the next gas concentrations had been reached, 20 min were allowed for equilibration before data collection. As positive end-expiratory pressure (PEEP) is often used in clinical routine to maintain compliance by preventing partial collapse of alveoli during mechanical ventilation, each part of the experiment was repeated with PEEP set to 10 hPa (10 cm H\(_2\)O). Zero end-expiratory pressure (ZEEP) and PEEP were performed in random order for each gas.

### Data collection

When steady-state anaesthesia was established, pressure and flow data were collected as the mean values of three recordings during a 5-min period (taken at 0, 2.5, and 5 min) for each of the gas mixtures. From these recordings, compliance (\(C\)) and resistance (\(R\)) were calculated as described above.

<table>
<thead>
<tr>
<th>Control</th>
<th>Experiments</th>
<th>Part I</th>
<th>Part II</th>
<th>Part III</th>
</tr>
</thead>
<tbody>
<tr>
<td>100% O(_2)</td>
<td>Schedule I</td>
<td>Isoflurane/N(_2)/O(_2) (1.5% in 70/30%)</td>
<td>XEN/O(_2) (70/30%)</td>
<td>Isotflurane/N(_2)/O(_2) (1.0% in 70/30%)</td>
</tr>
<tr>
<td></td>
<td>Schedule II</td>
<td>Xenon/O(_2)</td>
<td>Isotflurane/N(_2)/O(_2)</td>
<td>Isotflurane/N(_2)/O(_2)</td>
</tr>
<tr>
<td></td>
<td>Schedule III</td>
<td>Isotflurane/N(_2)/O(_2)</td>
<td>Isotflurane/N(_2)/O(_2)</td>
<td>Xenon/O(_2)</td>
</tr>
</tbody>
</table>

### Table 2

Schedules with different orders of the three parts of the study to which the animals were randomly allocated. Four animals received schedule I, and three had schedules II and III, respectively.

### Table 3

Respiratory parameters: median (first line) and interquartile range (second line) for each gas mixture (CON, control with O\(_2\) 100%; N\(_2\)/O\(_2\), isoflurane in N\(_2\)/O\(_2\) 70/30%; N\(_2\)/O\(_2\), isoflurane in N\(_2\)/O\(_2\) 70/30%; XEN/O\(_2\), xenon/O\(_2\) 70/30%). \(V_t\), tidal volume calculated from flow data as control of preset value; \(P_{peak}\), peak inspiratory pressure; \(R_{uncorr}\), calculated, uncorrected resistance; \(C\), compliance. Upper part: end-expiratory pressure 0 (ZEEP); lower part: end-expiratory pressure 10 hPa (PEEP).

<table>
<thead>
<tr>
<th></th>
<th>CON</th>
<th>N(_2)/O(_2)</th>
<th>N(_2)/O(_2)</th>
<th>XEN/O(_2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZEEP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(V_t) (ml)</td>
<td>256 (241–262)</td>
<td>258 (235–268)</td>
<td>259 (244–273)</td>
<td>264 (239–275)</td>
</tr>
<tr>
<td>(P_{peak}) (hPa)</td>
<td>20.2 (17.2–22.8)</td>
<td>17.9 (16.0–20.3)</td>
<td>19.1 (16.5–21.1)</td>
<td>22.1 (17.0–30.0)</td>
</tr>
</tbody>
</table>
| \(R_{uncorr}\) (hPa s\(^{-1}\) litre\(^{-1}\)) | 18.4 | 17.1 | 23.1 | 27.0
| \(C\) (ml hPa\(^{-1}\)) | 20.5 (18.7–23.2) | 22.7 (20.0–24.3) | 25.0 (19.1–28.2) | 22.6 (18.6–30.0) |
| PEEP   |            |                |                |            |
| \(V_t\) (ml) | 258 (230–265) | 257 (240–266) | 251 (246–268) | 261 (232–267) |
| \(P_{peak}\) (hPa) | 26.5 (23.5–29.0) | 28.2 (27.3–32.4) | 26.9 (25.7–31.7) | 31.8 (26.6–38.7) |
| \(R_{uncorr}\) (hPa s\(^{-1}\) litre\(^{-1}\)) | 15.7 (10.7–20.6) | 17.4 (11.7–18.2) | 17.7 (14.4–25.0) | 28.6 (22.5–34.7) |
| \(C\) (ml hPa\(^{-1}\)) | 24.2 (22.1–28.8) | 21.3 (18.8–24.7) | 26.0 (19.0–30.2) | 22.1 (18.6–26.4) |
Xenon and airway resistance

Table 4 Uncorrected resistance ($R_{uncorr}$) at ZEEP (zero EEP) and PEEP (10 hPa EEP) and comparison of resistance ratios with viscosity ratios and ($\rho^*\eta$)$^{1/2}$ ratios. Ratios were obtained by dividing $R_{uncorr}$, $\eta$, and ($\rho^*\eta$)$^{1/2}$ of each gas mixture by the respective values for N$_2$/O$_2$. Note that resistance ratios are usually underestimated by $\eta$ ratios and closer to, although sometimes overestimated by ($\rho^*\eta$)$^{1/2}$ ratios as suggested by Pedley and colleagues. Corrected resistance ($R_{corr}$, assuming laminar flow) is obtained by dividing $R_{uncorr}$ by the respective $\eta$ ratio. Likewise, $R_{corr}$ (assuming mixed flow) is obtained by dividing $R_{uncorr}$ by the respective ($\rho^*\eta$)$^{1/2}$ ratio. Median values (interquartile range) from n=10

<table>
<thead>
<tr>
<th></th>
<th>$R_{uncorr}$ (hPa s$^{-1}$ litre$^{-1}$)</th>
<th>$R_{uncorr}$ ratio</th>
<th>$\eta$ ratio</th>
<th>$R_{corr}$ (hPa s$^{-1}$ litre$^{-1}$)</th>
<th>($\rho^*\eta$)$^{1/2}$ ratio</th>
<th>$R_{corr}$ (hPa s$^{-1}$ litre$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZEEP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CON</td>
<td>18.4 (11.5–21.7)</td>
<td>0.99</td>
<td>1.11</td>
<td>16.6 (10.4–19.5)</td>
<td>1.10</td>
<td>16.7 (10.5–19.7)</td>
</tr>
<tr>
<td>N$_2$/O$_2$</td>
<td>17.1 (12.4–22.8)</td>
<td>1</td>
<td>1</td>
<td>17.1 (12.4–22.8)</td>
<td>1</td>
<td>17.1 (12.4–22.8)</td>
</tr>
<tr>
<td>N$_2$O/O$_2$</td>
<td>23.1 (14.5–27.7)</td>
<td>1.22</td>
<td>0.89</td>
<td>26.0 (16.3–31.2)</td>
<td>1.11</td>
<td>20.8 (13.1–25.0)</td>
</tr>
<tr>
<td>XEN/O$_2$</td>
<td>27.0 (21.3–37.7)</td>
<td>1.76</td>
<td>1.20</td>
<td>22.5 (18.2–31.4)</td>
<td>2.04</td>
<td>15.2 (10.7–18.5)</td>
</tr>
<tr>
<td>PEEP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CON</td>
<td>15.7 (10.7–20.6)</td>
<td>0.97</td>
<td>1.11</td>
<td>14.2 (9.6–18.5)</td>
<td>1.10</td>
<td>14.3 (9.7–18.7)</td>
</tr>
<tr>
<td>N$_2$/O$_2$</td>
<td>17.4 (11.7–18.2)</td>
<td>1</td>
<td>1</td>
<td>17.4 (11.7–18.2)</td>
<td>1</td>
<td>17.4 (11.7–18.2)</td>
</tr>
<tr>
<td>N$_2$O/O$_2$</td>
<td>17.7 (14.4–24.9)</td>
<td>1.24</td>
<td>0.89</td>
<td>19.8 (16.2–28.0)</td>
<td>1.11</td>
<td>15.9 (13.0–22.5)</td>
</tr>
<tr>
<td>XEN/O$_2$</td>
<td>28.6 (22.5–34.7)</td>
<td>1.85</td>
<td>1.20</td>
<td>23.8 (18.8–28.9)</td>
<td>2.04</td>
<td>14.0 (11.0–17.0)</td>
</tr>
</tbody>
</table>

Statistics

All data are displayed as median and interquartile range. As there was no normal distribution, compliance and corrected airway resistance with each gas combination were compared with xenon values by Wilcoxon’s test for paired values, with Bonferroni’s correction for multiple testing. A $P$ level of <0.05 was regarded significant.

Results

With tidal volume, inspiratory flow, and ventilatory frequency maintained constant, inspiratory pressure and, thus, calculated resistance is increased with xenon whereas comparable for the other gases. These uncorrected values together with compliance, tidal volume (calculated from flow data as stated above), and peak pressure are shown in the upper part of Table 3. With PEEP set to 10 hPa (10 cm H$_2$O), values are not changed except for $P_{peak}$ (lower part of Table 3). There is, however, an increase in compliance close to significance after the introduction of PEEP with 100% oxygen ($P=0.07$).

Resistance with oxygen, nitrogen/oxygen, nitrous oxide/oxygen, and xenon/oxygen is opposed to normalized values for $\eta$ and ($\rho^*\eta$)$^{1/2}$ and resistance corrected for those factors in Table 4. This table shows resistance after correction for normalized $\eta$ ($R_{corr}$, assuming laminar flow) and for normalized ($\rho^*\eta$)$^{1/2}$ ($R_{corr}$, assuming mixed flow). Resistance corrected for laminar flow is very similar in all groups. When corrected for mixed flow, resistance tends to be lower with xenon compared with the other gases, but values are very close to each other and none of the differences are significant (however, xenon/oxygen compared with nitrous oxide/oxygen yielded $P<0.08$). There were no further differences in compliance (Table 3).

Systemic and pulmonary haemodynamics were within ±20% of control values, pulse oximetry saturation was between 97 and 100%, and end-tidal $PCO_2$ remained between 4.7 and 5.3 kPa throughout the study.

Discussion

Corrected resistance as shown in Table 4 is very similar for all the gas mixtures used in this study. When corrected for viscosity only, resistance is virtually the same in all groups, whilst following correction for ($\rho^*\eta$)$^{1/2}$, it tends to be lowest with xenon/oxygen. However, these differences are small and clinically irrelevant. When compliance is also unchanged, there is no evidence for a major effect of xenon anaesthesia on the respiratory system.

As haemodynamic and gas exchange parameters are completely stable, they should not have influenced the results.

There are some limitations to the results presented here: first, we determined the resistance of the whole respiratory system. Thus, resistance is slightly ‘over-corrected’ because the amount of tissue resistance and the influence of lung structure and the thorax (the so-called inertia), which are all independent of physical gas properties, were not subtracted. In order to do so, intrathoracic or oesophageal pressure would need to be measured. Nunn, however, pointed out that measuring oesophageal pressure in the supine position poses some difficulties and stated that tissue resistance amounted to less than 20% of airway resistance whereas the contribution of the inertance to flow resistance is ‘usually negligible’. Consequently, we decided to look at the respiratory system as a whole.

Secondly, assuming a uniformly laminar or mixed flow pattern is a simplification of the complex fluid mechanics within the airways. However, using xenon as an inhaled anaesthetic introduces a new problem: the gases used so far are very similar in their physical properties. Thus, a certain range of inspiratory pressure, in an anaesthetized individual, has been established as normal, and increased values correlated with a change in airway calibre, lung structure, or both.

With xenon anaesthesia, inspiratory pressure is increased to a level that may alert the clinical anaesthetist. Such increased airway pressures have already been reported even with lower concentrations of xenon inhaled for diagnostic
pneumonia. We find no evidence of decreased airway resistance with xenon as compared with nitrogen and nitrous oxide whereas there was no difference between the latter two. Similar results have been reported by Calzia and co-workers who studied respiratory mechanics with xenon anaesthesia in pigs. They described an increase in airway resistance with 70% xenon by a factor of 1.4 compared with 70% nitrous oxide and of 1.5 compared with 70% nitrogen with oxygen. These figures are close to our results before correction as we find an increase in calculated resistance by a factor of 1.4 for xenon compared with nitrous oxide and of 1.6 compared with nitrogen, each with 30% oxygen.

The influence of both density (p) and viscosity (η) on resistance depends on flow distribution: if flow is fully laminar, resistance at a given flow rate is determined by viscosity, and the influence of density increases with the development of turbulent flow. As the viscosity of xenon, in contrast to its density, is similar to that of the other gases, assuming laminar flow and correcting resistance for η would take into account only the smallest possible effect of xenon’s physical properties. Even with this correction, resistances become very similar for all gas mixtures (Table 4). However, there are important sources of turbulence, for example the tracheal tube and the sudden increase in diameter at its tip within the tracheal lumen, which has been reported by Ingram and Pedley to increase the calculated total resistance. Jaffrin and Kesic have stated that there is a varying level of change from turbulent to laminar flow within the lung and that their proportions are difficult to determine. The approach suggested by Pedley and colleagues, taking into account these sources of turbulence and, thus, assuming a mixed flow pattern rather than completely laminar flow, is a correction of the resistance for \((p+η)^{1/2}\). As the amount of turbulence in a certain airway at a given flow rate is again dependent on physical gas properties, it is likely to be different for the gas mixtures used in this study which adds to the complexity of the problem. Thus, correction of the resistance for \((p+η)^{1/2}\) is used as an approximation, which yields small differences of no clinical relevance. The surprising finding is that resistance tends to be lower with xenon than with the other gases but this difference is probably caused by failure to subtract tissue resistance prior to correction, which leads to some ‘over-correction’ and by inaccuracy of the correction factor.

Although dose-dependent bronchodilating effects of isoflurane on pre-constricted airways have been found in various species, it is still not clear if this also applies to unconstricted airways. Isoflurane at least, does not add to β2-adrenergic bronchodilation after tracheal intubation. We find no evidence of decreased airway resistance with isoflurane either 1.0% in nitrous oxide/oxygen or 1.5% in nitrogen/oxygen when compared with control in this study. A possible bronchodilation caused by ketamine premedication may be neglected because the experiments began a least 2 h later. An increase in bronchomotor tone caused by thiopental or remifentanil cannot be excluded. However, it is unlikely to be relevant because all animals received the same doses and airway resistance was not dependent on the order in which experiments were performed but rather on individual differences. Thus, the use of anaesthetics with possible effects on airway resistance may have added to the variability but not substantially changed our results.

A lack of increase in airway pressure with xenon has only been described once. Lachmann and co-workers did not find differences in expiratory resistance in patients with xenon as compared with nitrous oxide anaesthesia although they did not report corrections for density or viscosity. The reason for this finding is not clear whereas the increase in airway resistance reported in several experimental studies can be related to the lack of correction for physical properties of xenon. Calzia and colleagues also described that after correction for physical properties, resistance did not increase but they did not conclude that the uncorrected resistance to gas flow might not be relevant for determining the effects of xenon anaesthesia on respiratory mechanics.

For further studies using mechanical ventilation with xenon under clinical conditions, the simplified correction as suggested by Pedley and colleagues may be useful because determining the exact quantities of laminar and turbulent flow is very difficult.

The introduction of PEEP produced an effect only during ventilation with 100% oxygen. Here, 10 hPa of PEEP increased (approaching significance) compliance which may be because the fact that partial collapse of alveoli is more likely to occur with a high inspired fraction of oxygen and that this collapse may be resolved with PEEP. However, PEEP did not change respiratory mechanics with any of the other gases. This is surprising in view of the reciprocal relationship between lung volume and airway resistance but may be explained by the hypothesis that anaesthesia and paralysis did not induce relevant changes in lung volume. In contrast to adult humans and larger animals where functional residual capacity is reduced by supine positioning and anaesthesia, it was shown that this does not apply to smaller animals like dogs and small pigs. Thus, even before the introduction of PEEP, our animals may have been on the flat part of the volume–resistance curve where there are only minor effects of lung volume on airway resistance. Although we did not determine lung volume we can exclude relevant changes from the fact that ventilator settings and tidal volumes were identical and expiratory flow always returned to zero in all animals.

In conclusion, inspiratory pressure is increased with inhalation of a mixture of xenon and 30% oxygen when compared with 100% oxygen, isoflurane/nitrogen/oxygen (1.5% in 70/30%), and isoflurane/nitrous oxide/oxygen (1.0% in 70/30%) with no change in compliance, in anaesthetized pigs. This increase is not different between
PEEP levels at 0 and 10 hPa. It is produced solely by the physical properties of xenon. Xenon does not increase airway resistance when values calculated from pressure and flow, are corrected for its physical properties. Such a correction should be performed in any further investigations of respiratory mechanics during xenon anaesthesia.

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