normal in more than half of our asymptomatic ectopic trophoblast's viability and the interpretation of TVS is useful for the assessment and follow-up of the early in many such pregnancies. Nevertheless, hCG assay does supplement TVS in screening for ectopic pregnancy by vaginal ultrasonography in combination with a discriminatory serum hCG level of 1000 IU/L (IRP). Br J Obstet Gynaecol 1990; 97: 904-08.

Autoinhalation of nitric oxide after endogenous synthesis in nasopharynx

Herwig Gerlach, Rolf Rossaint, Dirk Pappert, Michael Knorr, Konrad J Falke

Exogenous nitric oxide (NO) reduces pulmonary vascular resistance after low-dose inhalation in patients. To estimate endogenous NO synthesis in the upper respiratory tract, we measured inhaled and exhaled NO in volunteers and patients during spontaneous or controlled ventilation, respectively. 20,3 nmol per min NO was synthesised in the nasopharynx of non-smoking volunteers, leading to autoinhalation of 0.07-0.13 NO parts per million during inspiration; smokers had reduced NO synthesis. In volunteers, 50-70% of the NO was resorbed by the lungs; ventilated patients were deprived of NO autoinhalation. Bacteria in the nose may take part in endogenous NO synthesis.

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In patients with adult respiratory distress syndrome (ARDS), inhaled nitric oxide (NO) induced selective vasodilation in ventilated areas, thus improving arterial oxygenation. Dose-response studies and early trials revealed that low doses of NO (similar to atmospheric concentrations) were successful in ARDS. Animal studies proved that endogenous NO is exhaled after synthesis in the respiratory tract. Here we describe the localisation of NO synthesis in the upper respiratory tract.

The studies were approved by the hospital ethics committee. In healthy volunteers (male, aged 25-41, 10 smokers and 10 non-smokers) breathing spontaneously with a mask through a ventilator, samples were taken from the inspiratory and expiratory limb of the ventilator and from the lower oropharynx. After intubation, samples were also taken from the trachea near the bifurcation. Nasopharyngeal NO synthesis were measured as in the volunteers. Samples from long-term ventilated patients (11 male, 7 female, aged 19-49 years, 13 smokers) were taken similarly.

NO/NO2 concentrations were measured with chemiluminesimeters (ECO Physics, Duernten); to reduce sample volume, a mass flow-controlled gas-diluter (TECAN, Hombrechtikon) was used. The system was calibrated according to the National Institute of Standards.

Measurements in volunteers during nose-breathing yielded maximum values of NO in the nasopharynx (table); only low concentrations were measured in the mouth (data not shown). Expiratory prelaryngeal and tracheal NO concentrations were lower than inspiratory data; 50-70% of the inhaled NO was resorbed by the lower respiratory tract. Hence, NO from the expiratory limb did not come from pulmonary NO synthesis, although a pulmonary portion cannot be excluded. Mean nasopharyngeal NO concentrations during mouth-breathing were 649 parts per billion (ppb) for non-smokers and 494 ppb for smokers—ie, 20-3 nmol NO was synthesised per min in the nasopharynx of non-smokers, and 15-4 nmol per min in that of smokers.

<table>
<thead>
<tr>
<th></th>
<th>Inspiration</th>
<th>Expiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-smokers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilator</td>
<td>2 (0-3 3)</td>
<td>63 (58-1 47 9)</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>109 (99 8-118 3)</td>
<td>79 (72 4-85 6)</td>
</tr>
<tr>
<td>Trachea</td>
<td>89 (72 2-10 8)</td>
<td>42 (28 4-55 6)</td>
</tr>
<tr>
<td>Smokers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilator</td>
<td>2 (0-3 3 7)</td>
<td>49 (43 7-54 3)</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>84 (75 6-92 4)</td>
<td>53 (48 6-57 4)</td>
</tr>
<tr>
<td>Trachea</td>
<td>72 (51 6-92 4)</td>
<td>31 (9 8-52 2)</td>
</tr>
</tbody>
</table>

*Mean (95% CI) in parts per billion (ppb); tracheal concentrations could not be measured in one subject.

Table: NO concentrations from healthy volunteers during nose breathing
nasopharyngeal NO is inhaled and resorbed by the lower respiratory tract, because the sum of NO and NO2 was mostly synthesised in the nasopharynx. The volunteers (19-6 nmol per min). All these patients were on antibiotics. 3 carried high NO synthesis (86-128 nmol per min). The inspiratory NO concentration in the trachea was slightly higher than that during expiration or from the inspiratory limb of the ventilator. Thus NO may also be produced in the trachea. Total nasopharyngeal NO synthesis was similar to that in volunteers (19-6 nmol per min).

In long-term ventilated patients, there was less nasopharyngeal NO synthesis, sometimes under 0.5 nmol per min. All these patients were on antibiotics. 3 carried multiresistant Staphylococcus aureus in the nose; these patients had the highest NO synthesis (86-128 nmol per min). We presume that the endogenous NO in the respiratory tract was mostly synthesised in the nasopharynx. The nasopharyngeal NO is inhaled and resorbed by the lower respiratory tract, because the sum of NO and NO2 was reduced in the inspiratory fraction and the NO/NO2 ratio changed only slightly—ie, the expiratory reduction of NO was not because of conversion of NO to NO2. Smokers had reduced nasopharyngeal NO concentrations, probably because the NO in cigarette smoke causes feedback inhibition of endogenous NO synthesis. Orotracheal intubation disrupts natural NO autoinhalation from the upper respiratory tract. Low-dose NO inhalation in ARDS patients might be considered as NO replacement, since the inspiratory NO concentrations in volunteers are similar to those that are effective in ARDS.2,3

Long-term ventilated patients on antimicrobial therapy synthesised less NO, and contamination of the nose was associated with enhanced NO synthesis. Thus bacteria or bacterial toxins might stimulate the nasal mucosa to synthesise NO, as in other cells,2 possibly to support antimicrobial mechanisms.4 Bacteria can, however, synthesise NO by themselves.5

NO autoinhalation, which is reduced in smokers and interrupted in ventilated patients, could regulate the ventilation/perfusion ratio in the lung. Our data are based on a non-random selection of a small number of subjects; however, the correlation between NO synthesis in the nose and the presence of bacteria suggests symbiosis, which merits further attention.

The studies were supported by the Deutsch Forschungsgesellschaft grants Fa 139/1-3 and Fa 139/2-3.

References

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Ultrasonic indicators of ureteric reflux in the newborn

Masahiro Hiraoka, Kenkou Kasuga, Chikahide Hori, Masakatsu Sudo

There is controversy over the value of ultrasonic screening for detection of vesicoureteric reflux (VUR) in babies. We scanned 300 newborn babies and identified 53 with a dilated renal pelvis or other minor abnormalities. Eventually, 9 of these were investigated by voiding cystourethrography and 3 (5 kidneys) proved to have VUR exceeding grade II. In 3 babies the reason for cystourethrography was persistent renal pelvis dilation; in 3 it was urinary tract infection; and in 3 it was a new ultrasonic sign observed early in the series—ballooning of the renal pelvis during voiding. Whereas persistent dilation of the renal pelvis was a non-specific indicator (absent in 2 of the 5 affected kidneys and present in 5 of those unaffected), ballooning was consistently seen in all 5 affected renal pelvises. This sign, easily obtained in a baby who has been sleeping, deserves prospective assessment for its value in screening.

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Vesicoureteric reflux (VUR) in early childhood predisposes to urinary tract infection and renal damage.1–3 Early detection allows preventive treatment,4 and several groups have explored the use of ultrasonic screening. Some conclude that the investigation is of value;5–6 others that it is too inaccurate to be useful.7 When assessing ultrasonic indices in a series of newborn babies we came upon a new sign that may improve the accuracy of screening.

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