Maternal hyperventilation and the fetus

Renate Huch

Department of Obstetrics, University of Zurich, Switzerland

1 Introduction

Pregnant women experience hyperventilation during pregnancy for several reasons: It occurs regularly and spontaneously during pregnancy, it occurs because of the type of ventilation practiced during the actual hours of labor and delivery, and sometimes it is induced by the anesthesiological technique during obstetrical operations. This often results in excessive hyperventilation and has significant effects on blood gases, the cardiovascular and neuro-psychomotorical systems of the female organism. One must assume that due to the physiological unity of the mother and fetus, there also exists, to a greater or lesser degree, a change in the fetal homeostasis. The extent to which this adversely affects the fetus is not agreed upon. Results and opinions of investigations vary considerably (ARNOUDSE et al. 1981 [2], COLEMAN 1967 [15], CRAWFORD 1966 [17], JAMES and INDYK 1976 [39], KUENZEL and WULF 1970 [41], LEDUC 1979 [43], LEVINSSEN et al. 1974 [46], LUMLEY et al. 1969 [50], MANTELL 1976 [53], MARSAI 1977 [54], MILLER et al. 1974 [57], MORISHIMA et al. 1964 [59], MOTOYAMA et al. 1966 [60], 1967 [61], 1978 [62], MOYA et al. 1965 [63], NAVOT et al. 1982 [64], PARER et al. 1970 [66], RALSTON et al. 1974 [69], SALING and LIGDAS 1969 [75]).

The following summary of acquired data intends to show what in general, and especially during pregnancy and labor, the reasons are for hyperventilation, and how extensively the pregnant woman hyperventilates during pregnancy and labor. It further attempts to review the effects of hyperventilation upon the human organism and how the fetus reacts to induced or spontaneous hyperventilation. This review is preceded by a definition of hyperventilation.

2 Definition of hyperventilation

Hyperventilation is defined as a condition in which the alveoli are ventilated at a greater extent than is necessary to maintain normal blood oxygen and carbon dioxide tensions (COMROE et al. 1968 [16]); it can be the result of an increase in the tidal volume or respiratory rate, or a combination of the two. According to definition, alveolar hyperventilation results in a decline in alveolar Pco2 (PAco2), and increase of alveolar Po2 (PAo2), leading to decrease and increase respectively in blood gases. Hyperventilation is not to be confused with the so called hyperpnea which is brought about by an increase in minute volume due to the greater oxygen requirement resulting from physical exertion. In the latter Pco2 remains unchanged, at least initially.

3 The causes of hyperventilation

The causes of hyperventilation are due to one or more of the following reasons (GIBSON 1979 [27]):
Physiological or environmental (reduced Fio₂ at altitude, increased Fico₂, thermal stress, vibrations)

Psychological (reaction to fear, anger, pain, extreme emotion — most probably stimulated by epinephrine secretion)

Pharmacological (salicylates, female sex hormones, catecholamines, all drugs which lead to an increase of H⁺ concentration), and

Pathological (e. g. metabolic acidosis, pyrexia, anemia).

Several authors have already grouped, under the heading “physiological reasons”, hyperventilation of the female in the luteal phase of the menstrual cycle (DOERING et al. 1950 [22], HASSELBALCH and GAMMELTOFT 1915 [30], HEERHABER 1948 [31], HEERHABER et al. 1948 [32], MACHIDA 1981 [51], WILBRANDT et al. 1959 [85]) and in the whole pregnancy (DOERING and LOESCHKE 1947 [21], HASSELBALCH 1912 [29], 1915 [30], MACHIDA 1981 [51]). It is not necessarily valid to call the hyperventilation of pregnancy a pathological phenomenon. However, it is undoubtedly true that hyperventilation by definition is present on the basis of blood gas alterations. Progesterone is held mainly accountable for hyperventilation both during the second cycle phase and during pregnancy.

Hyperventilation may also result in the male after progesterone administration (DOERING et al. 1950 [22], HEERHABER et al. 1948 [32]). Estrogens seem to have a culminating effect upon the condition (DOERING et al. 1950 [22], WILBRANDT 1959 [85]). What still remains unclear, despite more recent research, is the actual mode of action of the hormones. The claim, made by DOERING et al. 1950 [22], that progesterone changes the sensibility of the respiratory center, finds little support after more recent investigation (MACHIDA 1981 [51]). The hypothesis that progesterone has a local pulmonary effect was put forward by LEHMANN et al. 1974 [45]. LEHMANN et al. believe that H₂O retention in the lung can be accredited to progesterone, and this results in the need to hyperventilate to maintain Po₂. Their research shows a decrease in the lung diffusion capacity during pregnancy which would fit this concept. Also, our own measurements of the diffusion capacity (DLCO) in the normal pregnancy show quite positively a decrease of this variable (SPAETLING et al. 1984 [79]).

When considering hyperventilation during labor, more factors come into play. Fear, pain and emotional excitement are of major importance, and it will be shown later, quite conclusively, that pain during the contractions correlates with the extent of hyperventilation. Well meaning instruction to breathe deeply can lead to hyperventilation due to altered lung volumes during pregnancy. The psycho-prophylactic prenatal preparations, especially the technique of LAMAZE 1956 [42] can easily be misinterpreted and can lead to hyperventilation as well. Hyperventilation is practiced by certain anesthesists both intentionally and unintentionally (COLEMAN 1967 [15], MOYA 1965 [63]) during cesarian section.

4 The extent of maternal hyperventilation during pregnancy and during labor

The respiration of the mother changes quite markedly within the first weeks of pregnancy. The minute volume increases continuously. This increase is due mainly to the increase in tidal volume, while the respiratory rate remains relatively unchanged (BARTELS et al. 1972 [3], BONICA 1973 [7], CUGELL et al. 1953 [19], MARX and ORKIN 1958 [55]). The minute volume is 40 to 50% higher during pregnancy than in a non-pregnant state (BARTELS et al. 1972 [3], CUGELL et al. 1953 [19]). Because the dead space does not change significantly during pregnancy, an increase of 60 to 70% in alveolar ventilation results.

This rate of ventilation is beyond the increasing oxygen demand of the mother and fetus and is therefore hyperventilation. This change in respiration and the resultant low arterial Pco₂ value during pregnancy is, as has already been mentioned, a known factor which can be traced back to the influence of hormones. As can be
thus in the region of between 7.40—7.47 (reviewed in HUCH and HUCH 1984 [38]). During labor, especially in conjunction with the contractions, respiration is further increased, very often voluntarily on the basis of prenatal breathing exercises. Nearly all studies show that a large increase in respiration occurs, whether this has been measured either directly from variables of pulmonary ventilation or indirectly from resultant alterations in blood gas and acid-base status (table II). The increase becomes especially pronounced during contractions. The minute volume during labor increases as a result of both alterations in rate and tidal volume and can be, during a contraction, as high as 901 (COLE and NAINBY-LUXMOORE 1962 [14]). Pco2 — measured either end-expiratorily or in arterial blood — can drop down to 10 mm Hg (BONICA 1974 [8]). SALING’s investigation (SALING and LIGDAS 1969 [75]), involving 252 women during labor, showed that 40% of the parturients had values below 23 mm Hg of Pco2. Unphysiological alkaline pH values of up to 7.7 were observed (BONICA 1974 [8]).

### Table I. Mean values for arterial Pco2 in healthy pregnant women (late pregnancy); reviewed in HUCH and HUCH 1984 [38].

<table>
<thead>
<tr>
<th>Pco2 (mmHg)</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>32.8</td>
<td>Andersen and Walker (1970)</td>
</tr>
<tr>
<td>32.0</td>
<td>Blechner et al (1969)</td>
</tr>
<tr>
<td>31.0</td>
<td>Boutourline—Young and Boutourline—Young (1956)</td>
</tr>
<tr>
<td>27.3</td>
<td>Lim et al. (1976)</td>
</tr>
<tr>
<td>31.3</td>
<td>MacRae and Palavradji (1967)</td>
</tr>
<tr>
<td>26.4</td>
<td>Milewski and Schumann (1977)</td>
</tr>
<tr>
<td>30.8</td>
<td>Rooth and Sjöstedt (1962)</td>
</tr>
<tr>
<td>33.2</td>
<td>Rossier and Hotz (1953)</td>
</tr>
<tr>
<td>30.5</td>
<td>Schlick et al. (1977)</td>
</tr>
<tr>
<td>32.1</td>
<td>Sjöstedt (1962)</td>
</tr>
<tr>
<td>33.6</td>
<td>Stojanov (1972)</td>
</tr>
</tbody>
</table>

seen in table I, low Pco2 values during pregnancy were confirmed by all later studies. The resultant alkalosis is nearly or completely compensated; the blood pH during pregnancy being

### Table II. Indications for excessively increased ventilation during contractions during labor.

<table>
<thead>
<tr>
<th>uterine</th>
<th>relaxation</th>
<th>contraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>minute ventilation ↑</td>
<td>1974 Bonica Ø 10.51</td>
<td>22.41</td>
</tr>
<tr>
<td>tidal volume ↑</td>
<td>1972 Crawford 227–2258 ml</td>
<td>Ø 750 ml</td>
</tr>
<tr>
<td>resp. rate ↑</td>
<td>1962 Cole max. 72/min</td>
<td>max. 351</td>
</tr>
<tr>
<td>resp. rate ↑</td>
<td>1972 Crawford Ø 60/min</td>
<td>max. 901</td>
</tr>
<tr>
<td>alv. or art. Pco2 ↓</td>
<td>1966 Reid min. 13 mm Hg</td>
<td>1974 Bonica min. 10 mm Hg</td>
</tr>
<tr>
<td>alv. or art. Pco2 ↓</td>
<td>1969 Saling min. 11 mm Hg</td>
<td>1974 Bonica max. 7.7</td>
</tr>
<tr>
<td>pH ↑</td>
<td>1974 Bonica</td>
<td>1957 Hendricks 13 mg% 15 mg%</td>
</tr>
<tr>
<td>lactate ↑</td>
<td>1974 Huch</td>
<td>1982 Huch</td>
</tr>
<tr>
<td>transcut. Po2 ↑</td>
<td>1974 Huch</td>
<td>1982 Huch</td>
</tr>
<tr>
<td>transcut. Pco2 ↓</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

It can be assumed that the pain of contractions is one of the main causes of hyperventilation as hyperventilation and contractions occur together. This is also substantiated by research that shows the effects of the relief of pain or the absence of it (Bonica 1972 [6], Fisher and Prys-Roberts 1968 [25], Strasser et al. 1975 [81]).

Bonica 1972 [6] has shown, by measuring the minute volume and endexpiratory CO2, that the increase of minute volume and decrease of Pco2 together with the contractions, due to pain-induced hyperventilation — can be reduced by pethidine and can be totally eliminated by epidural anesthesia.

Fisher and Prys-Roberts 1968 [25] have investigated the changes of minute volume, tidal volume, Paco2 and the pH in the pause between and during the contraction, both with and without extradural blockage. Without analgesia, a significant hyperventilation has been measured during the contractions, whereas once the pain relief starts to take effect, no significant differences in respiration and blood gases have been observed when comparing the pause and the contraction.

Strasser, together with us [81], has shown that strong pain can lead to hyperventilation during contractions, and in the following pause a phase of hypoventilation or apnea results. The maternal apnea-related Paco2-decreases do not occur if complete pain relief has been achieved by epidural anesthesia.

Transcutaneous Paco2 measurements sub partu have shown that the extent of the Paco2 decrease due to hyperventilation during contraction increases more, the more intensive and prolonged the contraction is (Huch et al. 1982 [37]). It can be assumed that in the case of a more intensive and prolonged contraction, the pain is also more severe and persistent.

5 Physiological consequences and subjective symptoms of hyperventilation

When judging the effects of maternal hyperventilation, one has to distinguish between acute and chronic hyperventilation. The latter is present during pregnancy. In a chronic state of hyperventilation a compensatory or adaptive mechanism arises, as for example has already been described for the maternal pH value during pregnancy. The following review, therefore, deals mainly with the most important and relevant effects of acute hyperventilation.

The interested reader may refer to the detailed reviews on this subject by Brown 1953 [10], Engel et al. 1947 [23], Gibson 1979 [27], Missiri and Alexander 1978 [58], Richards 1964/65 [71].

5.1 Blood gases, acid-base balance and electrolytes

Excessive alveolar hyperventilation results in an increase of Po2 and decrease of Pco2 in the alveolar gas phase and consequently in arterial blood. Already one single deep breath can reduce the Pco2 by 7 — 16 mm Hg (Lewis 1953 [47]); continued voluntary hyperventilation can easily lower the Pco2 to 10 mm Hg (Gibson 1979 [27]). Under extreme conditions, for example on ascent of Mount Everest without oxygen, values close to 7 mm Hg for Pco2 have been determined (West 1984 [84]).

The Henderson-Hasselbalch equation

\[ \text{pH} = \text{pK} + \log \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]} \]

can be transformed to

\[ \text{pH} = \text{pK} + \log \frac{[\text{HCO}_3^-]}{\alpha \cdot \text{Pco}_2} \]

(\(\alpha\) = solubility factor)

It can be seen that with decreasing Pco2, the pH value becomes greater. A value above pH 7.43 is defined as alkalosis. Therefore, hyperventilation leads to alkalosis. If this is due exclusively to a decrease of Pco2, it is a so called respiratory alkalosis. Compensatory mechanisms result in a reduction of the bicarbonate concentration by increased renal excretion. This, for example, is the reason why the pH value is affected relatively little during pregnancy.
A decreasing Pco2, together with the resultant increase in pH have a significant effect on the position of oxygen dissociation curve. An increasing alkalosis results in an increase in the oxygen affinity of hemoglobin (Bohr effect). The ability for oxygen release in the tissue (fetus!) can thus be limited significantly.

When considering the multiple neuro-muscular symptoms related to hyperventilation, alterations in electrolytes, and in particular calcium must be mentioned. Tetanic symptoms occur with decreased calcium in the plasma. During hyperventilation, free calcium decreases as there are more ionized proteins in an alkaline state that can bind calcium.

5.2 Cardiovascular changes, organ perfusion

Many of the clinical symptoms of hyperventilation can be explained by significant changes in cardiac output, blood pressure and organ perfusion. Unfortunately, investigations into this subject in the human and animal do not agree uniformly. The latter is particularly true for the cardiac output investigations. Little and Smith 1964 [49], Zwillich et al. 1976 [87] and Buehlmann and Angehrn 1979 [11] describe a decrease, whereas most of investigators find an increase (Burnum et al. 1954 [12], Gibson 1979 [27], Gleason et al. 1958 [28], Richards 1964/65 [71], Rowe and Crumpion 1962 [74]).

In most of these studies a decrease in blood pressure is reported. Our own investigations during voluntary hyperventilation have confirmed this (Huch et al. 1975 [35]). In situations where the cardiac output remains constant or increases, this blood pressure decrease can only result from a net vasodilation. However, locally or in some organ systems (heart, skin, kidney, intestines, uterus [?]), a decreasing blood Pco2 is a recognized potent vasoconstrictor (Brown 1953 [10], Buehlmann and Angehrn 1979 [11], Little and Smith 1964 [49], Neill and Hattenhauer 1975 [65], Price 1960 [67]). Brain perfusion is significantly reduced (reviewed in Brown 1953 [10], Kety and Schmidt 1948 [40]), more pronounced in younger subjects (Yamaguchi et al. 1979 [86]), and responsible for many of the subjectively experienced symptoms of hyperventilation.

5.3 Respiration and respiratory control

Inevitably, with hyperventilation there is an increase in minute volume either due to an increase in respiratory rate or in tidal volume or a combination of both. Oxygen consumption increases concomitantly with the increased respiratory efforts. Of most importance, when discussing the effects of hyperventilation on the pregnant organism, is the physiological response of the peripheral and central chemoreceptors and the resulting changes of respiration to an acute phase of hyperventilation, bearing in mind the reduced chemoreceptor sensitivity in situations of chronic hyperventilation (Berger et al. 1977 [4], Brown 1953 [10]). As early as 1864 Rosenthal (cited by Brown 1953 [10]) noticed an apnea phase after a phase of hyperventilation, which he first attributed to the increased Pco2 after hyperventilation. Numerous following investigations have unequivocally identified the decreasing Pco2 as cause of the apneic phase following hyperventilation (reviewed in Brown 1953 [10]). Present day textbooks (Schmidt and Thews 1976 [77]) hold that the major part of the CO2 or pH effect on ventilation acts via CO2 and H ions on chemosensitive structures in the brainstem. Respiration, after a phase of hyperventilation is reduced, or arrested, as long as is necessary for the arterial Pco2 to reach the same level as it was prior to hyperventilation.

The so called CO2 response, i.e. the extent of ventilation as a response to increased inspiratory CO2, is weakened in situations of chronic hyperventilation (Berger et al. 1977 [4]).

5.4 Neurological and psychomotoric changes

Hyperventilation, either because of the alkaline pH or the decreased Pco2, has objective effects on muscle-, nerve- and on higher functions. It results in a strengthened patellar tendon reflex,
the occurrence of nystagmus, muscle hyperexcitability, muscle rigidity and muscle spasms. During voluntary and continued hyperventilation, generalized symptoms of tetany occur after 15 to 40 minutes (BROWN 1979 [10]). Muscular spasms of hands and feet (carpo-pedal spasms) are particularly pronounced (GIBSON 1979 [27]). Face and abdominal muscles are involved in extreme situations of hyperventilation (GIBSON 1979 [27]). The higher psychomotoric functions are easily affected. Touch, proprioception, cold, heat and pain perception are influenced, the audio-ability decreases. Visual performance is adversely affected (GIBSON 1979 [27]).

5.5 Summary — subjective and objective symptoms of hyperventilation

The described alterations of blood gases, acid-base-balance, and electrolyte metabolism, of the cardiovascular system, respiration and neuro-muscular functions explain nearly all subjective or clinical symptoms of hyperventilation. Table III summarizes these symptoms. Dependant on the extent and the duration of hyperventilation, they appear to a greater or lesser degree consistently. According to the investigations of WAYNE 1957 [83] for example, dizziness, lightheadedness and tingling sensations could be found in more of 60% of 165 investigated voluntary hyperventilating persons.

6 Relevance of the physiological changes and particular symptoms in the pregnant woman

This physiological hyperventilation, present in all pregnant women, is well compensated for in terms of blood gases and acid-base status and should have a far smaller effect on the mother than the changes caused by the growing fetus. It is unlikely, therefore, to account for symptoms related to pregnancy such as common fatigue, dyspnea or cramps in the calf muscles. One can also relate these symptoms to the great physical stress due to pregnancy and to the purely mechanical impairment of the respiratory excursions and electrolyte alterations.

However, without doubt the further increase in hyperventilation, often excessive during the hours of labor and delivery, may result in many

Table III. Symptoms of hyperventilation (in accordance with ENGEL 1947 [23], GIBSON 1979 [27], MISSRI 1978 [58] and WAITES 1978 [82]).

<table>
<thead>
<tr>
<th>General</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Dryness of the mouth</td>
</tr>
<tr>
<td>Weakness</td>
<td>Yawning</td>
</tr>
<tr>
<td>Exhaustion</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>Globus hystericus</td>
</tr>
<tr>
<td></td>
<td>Epigastric pain</td>
</tr>
<tr>
<td></td>
<td>Aerophagia</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Musculoskeletal</td>
</tr>
<tr>
<td>Palpitations</td>
<td>Muscle pains and cramps</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Muscular incoordination</td>
</tr>
<tr>
<td>Precordial pain</td>
<td>Tremors</td>
</tr>
<tr>
<td>Raynaud's phenomenon</td>
<td>Stiffness</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Carpopedal spasm</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Tetany</td>
</tr>
<tr>
<td>Lightheadedness</td>
<td>Psychologic</td>
</tr>
<tr>
<td>Disturbance of consciousness or vision</td>
<td>Tension</td>
</tr>
<tr>
<td>Sensation of unreality</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Numbness and tingling of the extremities</td>
<td>Apprehension</td>
</tr>
<tr>
<td>Tetany (rare)</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Paresthesias</td>
<td>Nightmares</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Confusion</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td></td>
</tr>
</tbody>
</table>
of the symptoms listed in table III. Whether they should only be interpreted as causing discomfort, or whether they are harmful to both the mother and the fetus, must depend on the extent of hyperventilation and the resulting symptoms.

Dizziness or psychological excitability, depression and an alteration in subjective time sense have been observed in women during labor, in general all conditions which interfere with the active cooperation of the parturient (PRILL 1981 [68]). Symptoms of tetany are well known to midwives and obstetricians. There is no question that the additional increase in physical work demanded for hyperventilation is disadvantageous to the maternal organism. Uncomplicated labor and delivery already implies medium physical work (LEHMANN et al. 1972 [44]). A further increase in oxygen consumption by intensive respiratory work is undesirable.

The described physiological fact of compensatory apnea following a phase of hyperventilation and CO₂ decrease, contains a further risk. The risk from this apnea phases is particularly marked in women during labor because the painful contractions occur periodically. The phases of hyperventilation are simultaneous with the contractions, and the apnea phases are synchronous with the contraction intervals. The latter’s effect on arterial PO₂ decrease is especially marked. This is caused, firstly, by the relatively increased oxygen consumption during labor and secondly, by the reduced functional residual capacity (FRC) of the pregnant woman who can not buffer breathing irregularities (BONICA 1972 [6]).

As has been shown with the results of continuous intravascular or transcutaneous PO₂ measurement in the woman during labor, maternal PO₂ during labor exhibits significant fluctuations parallel with the contractions (FABEL 1968 [24], HUCH et al. 1974 [34], HUCH et al. 1977 [36]). Apneic phases following excessive hyperventilation during contractions and/or the result of central sedation due to morphine drugs for pain relief occur in the pause between contractions and may result in PO₂ decreases down to hypoxemic values.

7 Effects of maternal hyperventilation on the fetus

Theoretically, one should expect on the basis of the described results of hyperventilation, the following effects on the uterus and the fetus:

a) as an advantage
- enlarged blood gas gradient between mother and fetus (if organ perfusion did not change as a consequence of hyperventilation).
b) as a disadvantage
- phasic decrease of maternal arterial oxygen tension as a consequence of apnea phases
- decrease of uterine and placental perfusion resulting from CO₂- or pH-induced local vasoconstriction, or from maternal blood pressure decrease, or from the appearance of shunts
- increase of oxygen affinity in maternal blood resulting in reduced oxygen transfer to the fetus
- increase of oxygen affinity also in fetal blood due to the occurrence of fetal alkalosis parallel to that of the mother, making oxygen release to the tissues more difficult (it may be that the latter effect is compensated for by the fetus by improved O₂ uptake of fetal blood in the placenta).

In table IV the results of the respective animal and human investigations have been listed. They are attempts to assess with indirect and direct variables fetal oxygen supply and its alterations due to maternal hyperventilation.

With one exception (PARE et al. 1970 [66]) the results from animal experiments are conclusive. The investigations agree on the fact that maternal hyperventilation endangers the fetus. The observed reduced fetal oxygenation had been attributed to the BOHR effect or to the measured decrease of utero-placental perfusion. As in the adult animal, blood pressure also decreases in the fetal circulation as a result of maternal hyperventilation (RALSTON et al. 1974 [69]). In favor of a dominant influence of the BOHR effect are the investigations of ARNOUSDE et al. 1981 [2], LEVINSON et al. 1974 [46], MOTOYAMA et al. 1967 [61]. The first study (ARNOUSDE et al. 1981 [2]) demonstrates, with
Table IV. Effects of maternal hyperventilation on the experimental animal (a) and the human fetus (b).

a) experimental animal

<table>
<thead>
<tr>
<th>Author</th>
<th>Species</th>
<th>measured fetal reaction</th>
</tr>
</thead>
</table>
| Aarnoudse et al, 1981   | ewe      | decrease fetal arterial $\text{So}_2$  
decrease fetal arterial $\text{Po}_2$  
decrease fetal subcut. $\text{Po}_2$  
decrease fetal transcut. $\text{Po}_2$  
increase fetal pH |
| James et al, 1976       | baboon   | reduced fetal breathing movements                                                      |
| Leduc, 1970             | rabbit   | decrease umbilical arterial blood flow                                                  |
| Levinson et al, 1974    | ewe      | decrease uterine blood flow  
decrease fetal arterial $\text{So}_2$  
decrease fetal arterial $\text{Po}_2$  
noc fetal acidosis |
| Morishima et al, 1964   | guinea pigs | increase fetal acidosis                                                                  |
| Motoyama et al, 1966    | ewe      | decrease fetal arterial $\text{Po}_2$  
decrease fetal umbilical arterial $\text{Po}_2$  
increase fetal acidosis |
| Motoyama et al, 1967    | ewe      | decrease fetal blood pressure  
decrease umbilical vein blood flow  
decrease fetal arterial $\text{Po}_2$  
decrease umbilical vein $\text{Po}_2$  
increase fetal alkalosis |
| Motoyama et al, 1978    | ewe      | increase fetoplacental vascular resistance                                             |
| Parer et al, 1970       | monkey   | no change uterine blood flow  
no change uterine oxygen consumption  
increase fetal alkalosis  
no change fetal blood pressure     |
| Ralston et al, 1974     | ewe      | decrease fetal blood pressure  
decrease fetal heart rate  
decrease uterine arterial flow  
decrease fetal arterial pH  
decrease fetal arterial $\text{Po}_2$  
decrease fetal arterial $\text{So}_2$ |

Simultaneous measurements of oxygen tension and saturation, that the major part in the reduction of oxygenation is attributable to the BOHR effect. Only a minor influence stems from vasoconstriction.

It is much more difficult to summarize the human data and to come to a satisfactory conclusion. The human studies — naturally — are not as systematic when compared with those of the animal, are contradictory (COLEMAN 1967 [15]) and are hindered by the fact that voluntary efforts to hyperventilate during labor may fail individually to produce significant changes in the mother and thus in the fetus. LUMLEY et al. 1969 [50] describe quite impressively that grouping patients according to the intention and protocol "quiet respiration" and "active respiration" turned out to be impossible. Only retrospective grouping on the basis of the $\text{Pco}_2$
Table IV. continued

b) human

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>measured fetal reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coleman, 1967</td>
<td>18 intentionally hyperventilated C.S. patients</td>
<td>relatively low fetal umbilical arterial SO(_2) and pH values*</td>
</tr>
<tr>
<td>Crawford, 1966</td>
<td>23 “clinically ideal cases”</td>
<td>no correlation between maternal Pco(_2) and fetal umbilical vein and umbilical arterial SO(_2)</td>
</tr>
<tr>
<td>Künzle et al, 1970</td>
<td>11 normal patients</td>
<td>decrease umbilical scalp blood PO(_2)</td>
</tr>
<tr>
<td>Lumley et al, 1969</td>
<td>86 patients with clinical indications for microblood analysis</td>
<td>no correlation between maternal Pco(_2) and fetal scalp blood PO(_2)</td>
</tr>
<tr>
<td>Mantell, 1976</td>
<td>7 patients</td>
<td>reduced fetal breathing movements</td>
</tr>
<tr>
<td>Marsal, 1977</td>
<td>?</td>
<td>reduced fetal breathing movements</td>
</tr>
<tr>
<td>Moya et al, 1965</td>
<td>85 patients (incl. 61 C.S.)</td>
<td>decrease umbilical vein pH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>decrease umbilical arterial pH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>decrease umbilical vein SO(_2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>decrease umbilical arterial SO(_2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>in cases with extremely low maternal Pco(_2) values</td>
</tr>
<tr>
<td>Miller et al, 1974</td>
<td>12 normal 8 high risk patients</td>
<td>decrease fetal scalp blood PO(_2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>increase fetal scalp blood Pco(_2)</td>
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<td></td>
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<td>increase fetal scalp blood pH</td>
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<td></td>
<td>increase fetal base deficit</td>
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<tr>
<td>Navot et al, 1982</td>
<td>50 normal and high risk cases</td>
<td>FHR acceleration and/or transient tachycardia</td>
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<tr>
<td>Saling et al, 1969</td>
<td>26 patients with clinical indications for microblood analysis</td>
<td>decrease fetal scalp blood pH (qu40)</td>
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</table>

* not in agreement with Coleman's interpretation

or pH values were realistic. Both the instruction to breathe normally as well as the instruction to hyperventilate could fail.

Crawford 1966 [17], who as well as Coleman 1967 [15] opposes Motoyama et al.'s 1966 [60] warning against maternal hyperventilation, describes for example the lack of relationship between maternal Pco\(_2\) and fetal saturation in a population of “23 clinically ideal cases” with a mean maternal arterial Pco\(_2\) of 31.9 mm Hg (range 24.7 — 39.5 mm Hg). It is questionable whether one should expect any negative effect on the fetus — and thus a correlation with maternal Pco\(_2\) values — from maternal Pco\(_2\) values within the physiological range of a pregnant woman. Studies of Moya et al. 1965 [63] show clearly that only in cases of extreme hyperventilation analogous to the animal studies can corresponding results be obtained. According to Moya’s investigation, maternal values have to be lower than 17 mm Hg to result in fetal acidosis. Coleman 1967 [15] attempts to prove with “normal umbilical vein

and arterial pH and blood gas values" that intentional hyperventilating during cesarean section anesthesia causes no disadvantage to the fetus. It is impossible to agree with Coleman's conclusion, and one wonders why no one queried the data when it was first published. Out of the given 18 umbilical arterial PO₂ values, two are 76 and 50 mm Hg — which is hardly possible before the onset of respiration — and eleven of the remaining 16 values range between 0 and 10 mm Hg.

It might be that the lack of uniformity in the results of the human fetus also has its origins in problems of correct interpretation. Figure 1, a description of a single case from an investigation by Lumley et al. 1969 [50], serves as an example. Simultaneous maternal and fetal scalp blood gas and pH measurements before, during and after intentional hyperventilation show a parallel decrease in maternal and fetal PCO₂ (more pronounced in the mother), a steep increase in maternal and fetal pH (here again the maternal rise more accentuated than the fetal one) and a significant increase in maternal PO₂. Fetal PO₂, however, decreases by a few mm Hg. This, albeit small decrease, has to be regarded as an impairment of fetal oxygenation. One would expect, as was found with the fetal PCO₂ and pH, an alteration in PO₂ at least in the same direction as the mother's, although this would be small in view of the existing full saturation of maternal blood. However, the absence of an increase and indeed a small decrease is proof of a decrease in fetal O₂ availability.

Miller's investigations 1974 [57] show more evidence of a clear fetal disadvantage with maternal hyperventilation. Figure 2 illustrates the mean maternal PCO₂ and mean fetal scalp PO₂ and PCO₂ before, during and after 5 minutes of maternal hyperventilation. Fetal PCO₂ increases concomitant with maternal PCO₂ whereas fetal PO₂ decreases. The mean fetal PO₂ decrease was 3.2 mm Hg. Miller was able to show that fetal PO₂ decreased more, the more pronounced was the maternal decrease in PCO₂ with hyperventilation. Mean fetal PO₂ decrease was 4.5 mm Hg in 5 cases where maternal PCO₂ was below 17 mm Hg. The investigations of Miller show in addition that fetal pH is an inappropriate variable to prove fetal impairment by maternal hyperventilation. The fact that maternal pH increase is reflected in fetal blood may well mask a fetal pH decrease due to a reduction in uterine blood flow or the occurrence of placental shunts. The resultant fetal pH may be the net result of two balancing influences. Only a decreasing fetal PO₂ can be interpreted as a significant impairment of fetal oxygenation due to maternal hyperventilation.

Other measurements of fetal wellbeing, such as heart rate and respiratory pattern, are not ideal methods of assessing oxygenation either (Mantell 1976 [53], Marsal 1977 [54], Navot et al. 1982 [64]). Alterations in heart rate, accelerations, the presence of tachycardia or reduced fetal breathing movements only allow to state that the fetus has been influenced. This may result from increased maternal breathing excursions or maternal heart rate accelerations fol-
allowing instructions to ventilate forcibly. However, if one compares the results from the animal and human studies where intensive hyperventilation has been achieved, one can draw the conclusion that significant maternal hyperventilation impairs the adequate supply of oxygen to the fetus. With acute maternal hyperventilation during labor, excessive enough to lower maternal Pco₂ down to 20 mm Hg and below, fetal P₀₂ decreases significantly and in relation to the severity of the fall in maternal Pco₂.

How relevant for the fetus slight hyperventilation is during labor — just above the limit that is considered physiological during pregnancy — is hard to answer. The data available are not substantial enough to allow one to draw definite conclusions. However, extreme hyperventilation should be avoided for the benefit of mother and fetus. Hyperventilation can be detected by observing the mother's breathing pattern during and between contractions, by the appearance of hyperventilation related clinical symptoms, or by direct respiratory or blood gas measurements. Hyperventilation can be avoided by correct instructions for slow, regular breathing. As pain during labor seems to be one of the major causes of extreme hyperventilation, one should consider measures for effective pain relief.

Keywords: Animal experiment, hyperventilation, labor, man, pregnancy, review.

Zusammenfassung

Mütterliche Hyperventilation und der Fet
Hyperventilation, eine Atmung, bei der die Alveolen stärker ventilierter werden als es zur Aufrechterhaltung der normalen Sauerstoff- und Kohlendioxidspannung im Blut erforderlich ist, wird bei der Frau in den Stunden der Geburt oft verstärkt gefunden. Definitionsgemäß resultiert eine derartige alveolaere Hyperventilation in einem Abfall des alveolaeren Pco₂ und Anstieg des alveolaeren P₀₂ und folglichem Abfall des arteriellen Pco₂ respektive P₀₂-Anstieg. Hyperventilation kann verschiedene Gründe haben. Man unterscheidet physiologische (z. B. erniedrigte FiO₂ in der Höhe), psychische (z. B. Angst, Schmerz, Erregung), pharmakologische (z. B. Sexualhormone) und pathologische Gründe (z. B. kompensatorisch bei meta-
L'hyperventilation maternelle et le fœtus

L'hyperventilation, respiration pendant laquelle les alvéoles sont ventilées plus que ne l'exige le maintien de la tension de l'oxygène et du dioxyde de carbonate sanguins, est fréquente en cours de grossesse. Elle est souvent marquée encore durant les heures de l'accouchement. Par définition une telle hyperventilation alvéolaire entraîne aussi bien une chute de la PCO₂ artérielle qu'une augmentation de la PO₂ alvéolaire et, par voie de conséquence, une chute de la PCO₂ artérielle, respectivement une augmentation de la PO₂ artérielle.

Diverses sont les causes de l'hyperventilation: causes physiologiques (par exemple FiO₂ basse, en altitude), psychiques (p. ex. peur, douleur, excitation), pharmacologiques (p. ex. hormones sexuelles) et pathologiques (p. ex. compensatoire en cas d'acidose métabolique). La progestérone est avant tout tenue pour responsable de l'hyperventilation dans la phase lutéale et durant toute la grossesse. Les œstrogènes semblent en augmenter l'effet. Plusieurs facteurs sont avancés comme cause de l'hyperventilation en cours d'accouchement. La peur, l'excitation et les douleurs sont les plus significatifs; l'intensité des douleurs durant les contractions ayant d'autre part une corrélation évidente avec l'intensité de l'hyperventilation.

Le degré d'hyperventilation durant la grossesse a fait l'objet de multiples études. Dans les premières semaines de grossesse on assiste à une baisse de 10 mm Hg de la PCO₂ artérielle. Pratiquement, l'alcalose qui en résulte est entièrement compensée. Pendant l'accouchement les volumes et les fréquences respiratoires dépassent plusieurs fois la norme. En cas d'hyperventilation excessive, la PCO₂ maternelle peut descendre jusqu'à 10 mm Hg. On peut voir des valeurs de pH alcalin non physiologiques atteindre 7,7. De nombreuses études ont montré que la douleur est la cause principale de cette hyperventilation. Une suppression ou l'apaisement des douleurs régulièrement en effet la respiration. L'hyperventilation conduit à de multiples symptômes, subjectifs et objectifs, touchant le système cardio-vasculaire, la perfusion viscérale, le contrôle respiratoire et les fonctions neuro-musculaires, troubles qui trouvent leur raison dans les altérations des gaz sanguins, de l'équilibre acide-base, et de l'équilibre des électrolytes. Ce qui est primordial pour la mère et l'enfant, ce sont modifications durant l'accouchement, l'hyperventilation étant alors beaucoup plus marquée. La plupart des symptômes observés comme la somnolence, l'excitation, les signes de tétanie, les phases d'apnée entre les contractions, le travail respiratoire excessif, sont considérés comme néfastes pour la parturiente.

Huch, Maternal hyperventilation
Opposés à l'avantage que représente le plus grand gradient de pression des gaz entre la mère et l'enfant, les désavantages pour l'enfant en particulier sont mis en évidence. On peut craindre, en se fondant surtout sur l'expérimentation animale une diminution de la perfusion placentaire par vasoconstriction, ou par une chute de la tension ou des shunts, une augmentation de l'affinité pour l'oxygène du sang maternel, et une diminution temporaire de la tension d'oxygène artérielle.

Les réactions du fœtus humain et la signification des résultats en cas d'hyperventilation spontanée et provoquée n'apparaissent pas aussi clairement que lors des expérimentations animales, peu systématiques étant les recherches sur l'homme, et très variables l'intensité des diverses hyperventilations. Seule une hyperventilation intense a des conséquences néfastes sur l'oxygénation fœtale: voilà le seul point sur lequel les chercheurs sont d'accord.

Mots-clés: Expérimentation animale, douleurs de l'accouchement, grossesse, l'homme, hyperventilation, revue.

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Prof. Dr. R. Huch, M. D.
Univ.-Frauenklinik
Frauenklinikstr. 10
CH-8091 Zürich
Seminars in Perinatology is a journal tailored to the interest of professionals who care for the mother, the fetus, and the newborn. It is a forum for the review of new information which serves as a base for the rapid development of neonatal/perinatal medicine. Evidence continues to mount that the provision of several levels of care for mother and baby has resulted in a decrease in maternal and perinatal mortality within recent years. Even more impressive is the growing support for the value of intensive neonatal care in reducing developmental morbidity in surviving infants.

Scheduled Topics for 1986: Congenital Anomalies, Frank Manning, Guest Editor. Genetics, Thomas K. Oliver, Guest Editor.