Review article

J. Perinat. Med.
14 (1986) 3

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 neuropsychomotorical 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], LEVINSEN et al. 1974 [46], LUMLEY et al. 1969 [50],MANTELL 1976 [53], MARSAL 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 preceeded 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 P_{CO_2} (PA_{CO_2}), and increase of alveolar P_{O_2} (PA_{O_2}), 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 P_{CO_2} 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 Fio_2 at altitude, increased $Fico_2$, 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], WILBRAND 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 culminative 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 H_2O retention in the lung can be accredited to progesterone, and this results in the need to hyperventilate to maintain Po_2. 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.

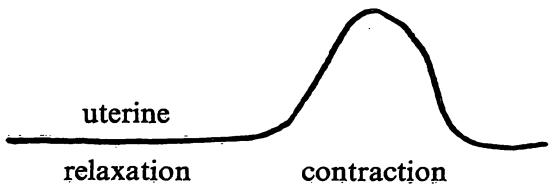
This rate of ventilation is beyond the increasing oxygen demand of the mother and fetus and is therefore hyperventilation. This change in respiration and the resultant low arterial Pco_2 value during pregnancy is, as has already been mentioned, a known factor which can be traced back to the influence of hormones. As can be

Table I. Mean values for arterial Pco_2 in healthy pregnant women (late pregnancy); reviewed in HUCH and HUCH 1984 [38].

Pco_2	31.9	Andersen and Walker (1970)
(mmHg)	28.7	Blechner et al (1969)
	30.9 ($PAco_2$)	Boutourline–Young and Boutourline–Young (1956)
	32.8	Cohen et al. (1970)
	32.0	Derom (1969)
	31.0	Friedberg (1980)
	27.3	Lim et al. (1976)
	31.3	MacRae and Palavradji (1967)
	26.4	Milewski and Schumann (1977)
	30.8	Rooth and Sjöstedt (1962)
	33.2	Rossier and Hotz (1953)
	30.5	Schlick et al. (1977)
	32.1	Sjöstedt (1962)
	33.6	Stojanov (1972)

seen in table I, low Pco_2 values during pregnancy were confirmed by all later studies. The resultant alkalosis is nearly or completely compensated; the blood pH during pregnancy being 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 90 l (COLE and NAINBY-LUXMOORE 1962 [14]). Pco_2 – measured either endexpiratorily 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 Pco_2. Unphysiological alkaline pH values of up to 7.7 were observed (BONICA 1974 [8]).

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



minute ventilation ↑	1974	Bonica	Ø 10.51	22.41
				max. 351
	1962	Cole		max. 901
tidal volume ↑	1972	Crawford		227–2258 ml
				Ø 750 ml
resp. rate ↑	1962	Cole		max. 72/min
	1972	Crawford		Ø 60/min
alv. or art. co_2 ↓	1966	Reid		min. 13 mm Hg
	1974	Bonica		min. 10 mm Hg
	1969	Saling		min. 11 mm Hg
pH ↑	1974	Bonica		max. 7.7
lactate ↑	1957	Hendricks	13 mg%	15 mg%
transcut. Po_2	1974	Huch	↓	↑
transcut. Pco_2	1982	Huch	↑	↓

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 CO_2, that the increase of minute volume and decrease of Pco_2 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, $Paco_2$ 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 Po_2-decreases do not occur if complete pain relief has been achieved by epidural anesthesia.

Transcutaneous Pco_2 measurements sub partu have shown that the extent of the Pco_2 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], MISSRI 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 Po_2 and decrease of Pco_2 in the alveolar gas phase and consequently in arterial blood. Already one single deep breath can reduce the Pco_2 by 7 — 16 mm Hg (LEWIS 1953 [47]); continued voluntary hyperventilation can easily lower the Pco_2 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 Pco_2 have been determined (WEST 1984 [84]).

The HENDERSON-HASSELBALCH equation

$$pH = pK + \log \frac{[HCO_3^-]}{[H_2CO_3]}$$

can be transformed to

$$pH = pK + \log \frac{[HCO_3^-]}{\alpha \cdot Pco_2} \quad (\alpha = \text{solubility factor})$$

It can be seen that with decreasing Pco_2, 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 Pco_2, 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 Pco_2, 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 uniformally. 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 CRUMPTON 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 Pco_2 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 Po_2 after hyperventilation. Numerous following investigations have unequivocally identified the decreasing Pco_2 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 CO_2 or pH effect on ventilation acts via CO_2 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 Pco_2 to reach the same level as it was prior to hyperventilation.

The so called CO_2 response, i. e. the extent of ventilation as a response to increased inspiratory CO_2, 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 Pco_2, has objective effects on muscle-, nerve- and on higher functions. It results in a strengthened patellar tendon reflex,

the occurence of nystagmus, muscle hyperexitability, 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]).

- General
  - Fatigue
  - Weakness
  - Exhaustion
  - Sleep disturbances
- Cardiovascular
  - Palpitations
  - Tachycardia
  - Precordial pain
  - Raynaud's phenomenon
- Neurologic
  - Dizziness
  - Lightheadedness
  - Disturbance of consciousness or vision
  - Sensation of unreality
  - Numbness and tingling of the extremities
  - Tetany (rare)
  - Paresthesias
- Respiratory
  - Shortness of breath
  - Chest pain
  - Dryness of the mouth
  - Yawning
- Gastrointestinal
  - Globus hystericus
  - Epigastric pain
  - Aerophagia
- Musculoskeletal
  - Muscle pains and cramps
  - Muscular incoordination
  - Tremors
  - Stiffness
  - Carpopedal spasm
  - Tetany
- Psychologic
  - Tension
  - Anxiety
  - Apprehension
  - Insomnia
  - Nightmares
  - Confusion

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 midwifes 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 CO_2 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 Po_2 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 Po_2 measurement in the woman during labor, maternal Po_2 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 Po_2 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 CO_2- 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 occurence 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 O_2 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 (PARER 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 ARNOUDSE et al. 1981 [2], LEVINSON et al. 1974 [46], MOTOYAMA et al. 1967 [61]. The first study (ARNOUDSE 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

Author	Species	measured fetal reaction
Aarnoudse et al, 1981	ewe	decrease fetal arterial So_2 decrease fetal arterial Po_2 decrease fetal subcut. Po_2 decrease fetal transcut. 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 So_2 decrease fetal arterial Po_2 no fetal acidosis
Morishima et al, 1964	guinea pigs	increase fetal acidosis
Motoyama et al, 1966	ewe	decrease fetal arterial Po_2 decrease fetal umbilical arterial Po_2 increase fetal acidosis
Motoyama et al, 1967	ewe	decrease fetal blood pressure decrease umbilical vein blood flow decrease fetal arterial Po_2 decrease umbilical vein 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 Po_2 decrease fetal arterial 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 Pco_2

Table IV. continued

b) human

Author	Patients	measured fetal reaction
Coleman, 1967	18 intentionally hyperventilated C.S. patients	relatively low fetal umbilical arterial So_2 and pH values*
Crawford, 1966	23 "clinically ideal cases"	no correlation between maternal Pco_2 and fetal umbilical vein and umbilical arterial So_2
Künzel et al, 1970	11 normal patients	decrease umbilical scalp blood Po_2
Lumley et al, 1969	86 patients with clinical indications for microblood analysis	no correlation between maternal Pco_2 and fetal scalp blood Po_2
Mantell, 1976	7 patients	reduced fetal breathing movements
Marsal, 1977	?	reduced fetal breathing movements
Moya et al, 1965	85 patients (incl. 61 C.S.)	decrease umbilical vein pH decrease umbilical arterial pH decrease umbilical vein So_2 decrease umbilical arterial So_2 in cases with extremely low maternal Pco_2 values
Miller et al, 1974	12 normal 8 high risk patients	decrease fetal scalp blood Po_2 increase fetal scalp blood Pco_2 increase fetal scalp blood pH increase fetal base deficit
Navot et al, 1982	50 normal and high risk cases	FHR acceleration and/or transient tachycardia
Saling et al, 1969	26 patients with clinical indications for microblood analysis	decrease fetal scalp blood pH (qu40)

* 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 Po_2 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 Pco_2 (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 Po_2. Fetal Po_2, 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 Pco_2 and pH, an alteration in Po_2 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 O_2 availability.

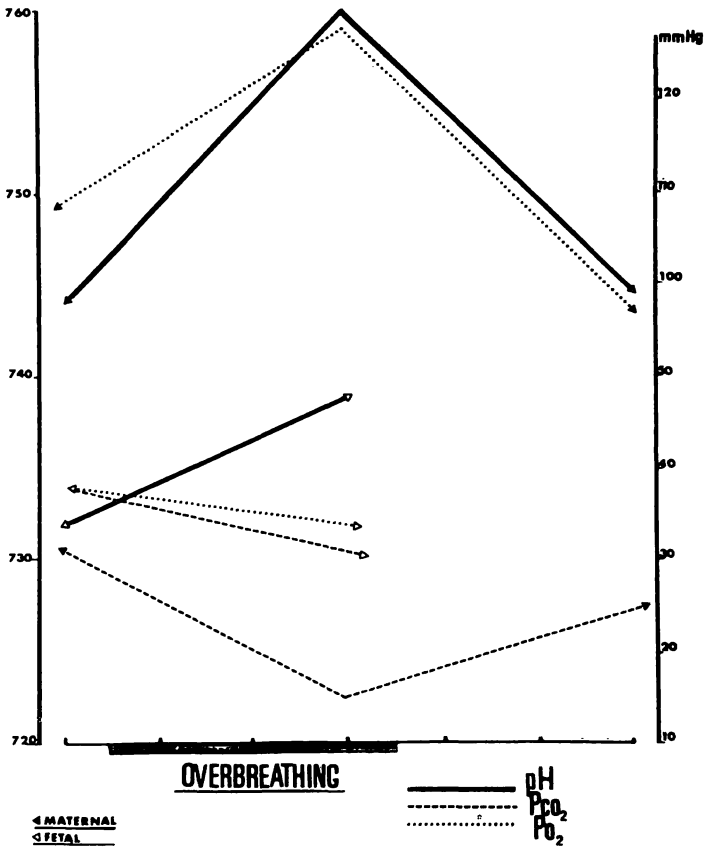


Figure 1. Effect of maternal voluntary hyperventilation on maternal and fetal pH, Pco_2 and Po_2 (from LUMLEY et al. 1969 [50]).

MILLER's investigations 1974 [57] show more evidence of a clear fetal disadvantage with maternal hyperventilation. Figure 2 illustrates the mean maternal Pco_2 and mean fetal scalp Po_2 and Pco_2 before, during and after 5 minutes of maternal hyperventilation. Fetal Pco_2 increases concomitant with maternal Pco_2 whereas fetal Po_2 decreases. The mean fetal Po_2 decrease was 3.2 mm Hg. MILLER was able to show that fetal Po_2 decreased more, the more pronounced was the maternal decrease in Pco_2 with hyperventilation. Mean fetal Po_2 decrease was 4.5 mm Hg in 5 cases where maternal Pco_2 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 occurence of placental shunts. The resultant fetal pH may be the net result of two balancing influences. Only a decreasing fetal Po_2 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-

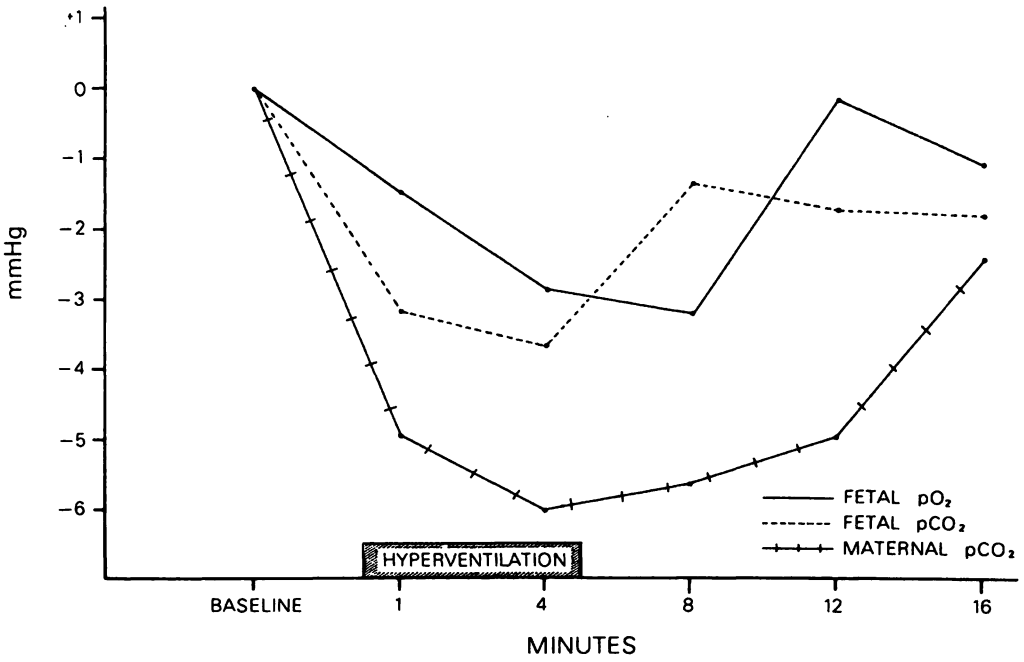


Figure 2. Mean maternal Pco_2 and fetal Po_2 and Pco_2 before, during and after voluntary maternal hyperventilation (from MILLER et al. 1974 [57]).

lowing 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 Pco_2 down to 20 mm Hg and below, fetal Po_2 decreases significantly and in relation to the severity of the fall in maternal Pco_2.

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 ventiliert werden als es zur Aufrechterhaltung der normalen Sauerstoff- und Kohlendioxidspannung im Blut erforderlich ist, wird bei der Frau in der Schwangerschaft regelmäßig angetroffen. Dieser Atemtypus wird in den Stunden der Geburt oft verstärkt gefunden. Definitionsgemäß resultiert eine derartige alveolaere Hyperventilation in einem Abfall des alveolaeren Pco_2.und Anstieg des alveolaeren Po_2 und folglichem Abfall des arteriellen Pco_2 respektive Po_2-Anstieg.

Hyperventilation kann verschiedene Gründe haben. Man unterscheidet physiologische (z. B. erniedrigte FiO_2 in der Höhe), psychische (z. B. Angst, Schmerz, Erregung), pharmakologische (z. B. Sexualhormone) und pathologische Gründe (z. B. kompensatorisch bei meta-

bolischer Azidose). Für die Hyperventilation der Frau in der Lutealphase des weiblichen Zyklus und in der gesamten Schwangerschaft wird vor allen Dingen Progesteron verantwortlich gemacht. Oestrogene scheinen eine additive Wirkung zu haben. Für die Hyperventilation während der Geburt kommen mehrere Gründe in Frage. Angst, Erregung und Schmerzen sind wohl am bedeutendsten, wobei die Schmerzintensität während der Kontraktion eindeutig mit dem Ausmaß der Hyperventilation korreliert.

Das Ausmaß der Hyperventilation während der Schwangerschaft wurde in zahlreichen Studien untersucht. Es kommt bereits in den ersten Wochen der Schwangerschaft zu einer Abnahme des arteriellen P_{CO_2} um ca. 10 mm Hg. Die resultierende Alkalose wird nahezu oder vollständig kompensiert. Während der Geburt, insbesondere im Zusammenhang mit schmerzhaften Kontraktionen, werden Atemvolumina und -frequenzen mehrfach über das Normale gesteigert. Bei exzessiver Hyperventilation kann der mütterliche arterielle P_{CO_2} bis auf 10 mm Hg abfallen. Unphysiologisch alkalische pH-Werte bis zu 7.7 Einheiten wurden dabei beobachtet. Es konnte in zahlreichen Untersuchungen gezeigt werden, daß Schmerz die Hauptursache dieser Hyperventilation ist. Schmerzlinderung oder Schmerzbefreiung resultiert in einer Normalisierung der Atmung.

Hyperventilation resultiert in zahlreichen subjektiven und objektiven Symptomen im cardiovaskulären System, bei der Organdurchblutung, der Atemkontrolle und der neuromuskulären Funktionen, die überwiegend in den Veränderungen der Blutgase, des Säurebasen- und Elektrolythaushalt ihre Erklärung finden. Relevant für Mutter und Fet dürften besonders die Veränderungen während der Geburt sein, da hier sehr häufig die Hyperventilation ausgeprägt ist. Viele der beobachteten Symptome wie Benommenheit, psychische Erregung, Tetaniezeichen, Apnoephasen in der Wehenpause und die exzessive Atemarbeit werden für die Gebärende als nachteilig angesehen.

Mit Ausnahme des Vorteils größerer Gasdruckgradienten zwischen Mutter und Fet werden besonders für den Feten Nachteile aus mütterlicher Hyperventilation diskutiert. Basierend auf überwiegend tierexperimentellen Befunden werden die Abnahme der uterinen und placentaren Durchblutung durch Vasokonstriktion, Blutdruckabfall oder Shunts, die Zunahme der O_2-Affinität des mütterlichen Blutes und der phasenhafte Abfall der arteriellen Sauerstoffspannung gefürchtet.

Die Reaktion des menschlichen Feten und die Deutung der Befunde bei spontaner und induzierter Hyperventilation sind uneinheitlicher als die Ergebnisse aus tierexperimentellen Studien. Die mangelnde Systematik der Untersuchungen beim Menschen und die unterschiedliche Intensität der Hyperventilation werden hierfür verantwortlich gemacht. Erst bei sehr ausgeprägter mütterlicher Hyperventilation stimmen die Untersucher überein, daß diese Form der mütterlichen Atmung eindeutig nachteilige Folgen für die fetale Oxygenierung hat.

Schlüsselwörter: Hyperventilation, Mensch, Review, Schwangerschaft, Tierexperiment, Wehentätigkeit.

Résumé

L'hyperventilation maternelle et le fœtus

L'hyperventilation, respiration pendant laquelle les alveoles sont ventilées plus que ne l'exige le maintien de la tension de l'oxygène et du dioxyde de carbone sanguins, est fréquente en cours de grossesse. Elle est souvent plus marquée encore durant les heures de l'accouchement. Par définition une telle hyperventilation alvéolaire entraîne aussi bien une chute de la P_{CO_2} alvéolaire qu'une augmentation de la P_{O_2} alvéolaire et, par voie de conséquence, une chute de la P_{CO_2} artérielle, respectivement une augmentation de la P_{O_2} artérielle.

Diverses sont les causes de l'hyperventilation: causes physiologiques (par exemple FiO_2 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 P_{CO_2} 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 P_{CO_2} 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 principle de cette hyperventilation. Une suppression ou l'apaisement des douleurs régularisent 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.

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 résultes 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.

References

[1] ANDERSEN, G. J., J. WALKER: Effect of labour on the maternal blood-gas and acid-base status. J. Obstet. Gynaecol. Brit. Cwlth. 77 (1970) 289

[2] ARNOUDSE, J. G., B. OESEBURG, G. KWANT, A. ZWART, W. G. ZIJLSTRA, H. J. HUISJES: Influence of variations in pH and Pco_2 on scalp tissue oxygen tension and carotid arterial oxygen tension in the fetal lamb. Biol. Neonate 40 (1981) 252

[3] BARTELS, H., K. RIEGEL, J. WENNER, H. WULF: Perinatale Atmung. Springer Verlag, Berlin 1972

[4] BERGER, A. J., R. A. MITCHELL, J. W. SEVERINGHAUS: Regulation of Respiration. N. Engl. J. Med. 297 (1977) 92

[5] BLECHNER, J. N., J. R. COTTER, V. G. STENGER, C. M. HINKLEY, H. PRYSTOWSKY: Oxygen, carbon dioxide and hydrogen ion concentrations in arterial blood during pregnancy. Am. J. Obstet. Gynecol. 100 (1969) 1

[6] BONICA, J. J.: Obstetric Analgesia and Anesthesia, Springer Verlag, Berlin 1972

[7] BONICA, J. J.: Maternal Respiratory Changes During Pregnancy and Parturition. In: MARX, G. F. (ed.): Clinical Anesthesia Parturition and Perinatology 10, F. A. Davis Company, Philadelphia 1973

[8] BONICA, J. J.: Maternal physiologic changes during pregnancy and anesthesia. In: SHNIDER, S. M. and F. MOYA (eds.): The Anesthesiologist, Mother and Newborn. Williams and Wilkins, Baltimore 1974

[9] BOUTOURLINE-YOUNG, H., E. BOUTOURLINE-YOUNG: Alveolar carbon dioxide levels in pregnant, parturient and lactating subjects. J. Obstet. Gynecol. 63 (1956) 509

[10] BROWN, E. B.: Physiological Effects of Hyperventilation. Physiol. Rev. 33 (1953) 445

[11] BUEHLMANN, A. A., W. ANGEHRN: Hyperventilation and Oxygen Supply of the Myocardium. Schweiz. Med. Wochenschr. 109 (1979) 908

[12] BURNUM, J. F., J. B. HICKAM, H. D. MCINTOSH: Effect of hypocapnia on arterial blood pressure. Circulation 9 (1954) 89

[13] COHEN, A. V., H. SCHULMAN, S. L. ROMNEY: Maternal acid-base metabolism in normal human parturition. Am. J. Obstet. Gynecol. 107 (1970) 933

[14] COLE, P. V., R. C. NAINBY-LUXMOORE: Respiratory volumes in labour. Br. Med. J. I (1962) 1118

[15] COLEMAN, A. J.: Absence of harmful effect of maternal hypocapnia in babies delivered at caesarean section. Lancet 1 (1967) 813

[16] COMROE, J. H., R. E. FORSTER, A. B. DUBOIS, W. A. BRISCOE, E. CARLSEN: Die Lunge. Klinische Physiologie und Lungenfunktionsprüfungen. F. K. Schattauer-Verlag, Stuttgart 1968

[17] CRAWFORD, J. S.: Maternal Hyperventilation and the Foetus. Letters to the Editor. Lancet (1966) 430

[18] CRAWFORD, J. S.: Principles and Practice of Obstetric Anaesthesia. Blackwell Scientific Publ., Oxford 1972

[19] CUGELL, D. W., R. FRANK, E. A. GAENSLER, T. L. BADGER: Pulmonary function in pregnancy. I. Serial observations in normal women. Am. Rev. Tuber. 67 (1953) 568

[20] DEROM, R. M.: Maternal acid-base balance during labor. Clin. Obstet. Gynecol. 11 (1968) 110

[21] DOERING, G. K., H. H. LOESCHKE: Atmung und Säure-Basengleichgewicht in der Schwangerschaft. Pflueg. Archiv ges. Physiol. 249 (1947) 433

[22] DOERING, G. K., H. H. LOESCHKE, B. OCHWADT: Weitere Untersuchungen über die Wirkung der Sexualhormone auf die Atmung. Pflueg. Archiv ges. Physiol. 252 (1950) 216

[23] ENGEL, G. L., E. B. FERRIS, M. LOGAN: Hyperventilation. Analysis of Clinical Symptomatology. Ann. Intern. Med. 27 (1947) 683

[24] FABEL, F.: Die fortlaufende Messung des arteriellen Sauerstoffdruckes beim Menschen. Arch. Kreislaufforsch. 3 (1968) 145

[25] FISHER, A., C. PRYS-ROBERTS: Maternal pulmonary gas exchange. A study during normal labour and extradural blockade. Anaesthesia 23 (1968) 350

[26] FRIEDBERG, V.: Nierenfunktion. In: FRIEDBERG, V. and G. H. RATHGEN (Eds.): Physiologie der Schwangerschaft. Georg Thieme-Verlag, Stuttgart 1980

[27] GIBSON, T. M.: Hyperventilation in Aircrew: A Review. Aviat. Space Environ. Med. 50 (1979) 725

[28] GLEASON, W. L., J. N. BERRY, F. M. MAUNEY, H. D. MCINTOSH: The hemodynamic effects of hyperventilation. Clin. Res. 6 (1958) 127

[29] HASSELBALCH, K. A.: Ein Beitrag zur Respirationsphysiologie der Gravidität. Skand. Arch. Physiol. 27 (1912) 1
[30] HASSELBALCH, K. A., S. A. GAMMELTOFT: Die Neutralitätsregulation des graviden Organismus. Biochem. Z. 68 (1915) 206
[31] HEERHABER, I.: Über die Atmung im mensuellen Zyklus der Frau. Pflueg. Archiv ges. Physiol. 250 (1948) 385
[32] HEERHABER, I., H. H. LOESCHKE, U. WESTPHAL: Eine Wirkung des Progesterons auf die Atmung. Pflueg. Archiv ges. Physiol. 250 (1948) 42
[33] HENDRICKS, C. H.: Studies on lactic acid metabolism in pregnancy and labor. Am. J. Obstet. Gynecol. 73 (1957) 492
[34] HUCH, A., R. HUCH, G. LINDMARK: Maternal hypoxaemia after pethidine. J. Obstet. Gynaecol. Brit. Cwlth. 81 (1974) 608
[35] HUCH, A., R. HUCH, D. W. LUEBBERS: Der periphere Perfusionsdruck: Eine neue nicht-invasive Meßgröße zur Kreislaufüberwachung von Patienten. Anaesthesist 24 (1975) 39
[36] HUCH, A., R. HUCH, H. SCHNEIDER, G. ROOTH: Continuous transcutaneous monitoring of fetal oxygen during labour. Br. J. Obstet. Gynaecol. Suppl. 1 (1977) 1
[37] HUCH, R., A. LYSIKIEWICZ, K. VETTER, A. HUCH: Fetal transcutaneous carbon dioxide tension — promising experiences. J. Perinat. Med. 10 (1982) 103
[38] HUCH, R., A. HUCH: Maternal and Fetal Acid-Base Balance and Blood Gas Measurement. Fetal Physiology and Medicine. Marcel Dekker, Inc., New York 1984
[39] JAMES, S. L., L. INDYK: Observations on Fetal Breathing in Baboons and Lambs. In: GENNSER, G., K. MARSAL, T. WHEELER (eds.): Proceedings of the Third Conference on Fetal Breathing, Malmoe 1976
[40] KETY, S. S., C. F. SCHMIDT: The effects of altered arterial tensions of carbon dioxide and oxygen on cerebral blood flow and cerebral oxygen consumption of normal young men. J. Clin. Invest. 27 (1948) 484
[41] KUENZEL, W., H. WULF: Der Einfluß der maternen Ventilation auf die aktuellen Blutgase und den Säure-Basen-Status des Feten. Geburtshilfe Frauenheilkd. 172 (1970) 1
[42] LAMAZE, D. F.: Qu'est-ce que l'Accouchement sans Douleur par la Methode Psycho-Prophylactique. Savoir et Connaitre, Paris 1956
[43] LEDUC, B.: The effect of acute hypocapnia on maternal placental blood flow in rabbits (abs.). J. Physiol. (Lond.) 210 (1970) 165
[44] LEHMANN, V., R. WETTENGEL, G. HEMPELMANN: Energieumsatz und Haemodynamik unter der Geburt. In: SALING, E. and F. J. SCHULTE (eds.): Perinatale Medizin 2. Georg Thieme-Verlag, Stuttgart 1972
[45] LEHMANN, V.: Veränderungen der Lungendiffusionskapazität als mögliche Ursache der Hyperventilation in der Schwangerschaft. In: DUDENHAUSEN, J. W. and E. SALING (eds.): Perinatale Medizin 5. Georg Thieme-Verlag, Stuttgart 1974
[46] LEVINSON, G., S. M. SHNIDER, A. A. DELORIMIER et al.: Effects of maternal hyperventilation on uterine blood flow and fetal oxygenation and acid-base status. Anesthesiology 40 (1974) 340
[47] LEWIS, B. I.: The hyperventilation syndrome. Ann. Intern. Med. 38 (1953) 918
[48] LIM, V. S., A. I. KATZ, M. D. LINDHEIMER: Acid-base regulation in pregnancy. Am. J. Physiol. 231 (1976) 1764
[49] LITTLE, R. C., C. W. SMITH: Cardiovascular response to acute hypocapnia due to overbreathing. Am. J. Physiol. 206 (1964) 1025
[50] LUMLEY, J., P. RENOU, W. NEWMAN, C. WOOD: Hyperventilation obstetrics. Am. J. Obstet. Gynecol. 6 (1969) 847
[51] MACHIDA, H.: Influence of Progesterone on arterial blood and CSF acid-base balance in women. J. Appl. Physiol. 51 (1981) 1433
[52] MACRAE, D. J., D. PALAVRADJI: Maternal acid-base changes in pregnancy. J. Obstet. Gynaecol. Brit. Cwlth. 74 (1967) 11
[53] MANTELL, C.: Human Fetal Breathing. The Effect of Altering Maternal CO_2 Level. In: Proceedings of the Third Conference on Fetal Breathing, Malmoe 1976
[54] MARSAL, K.: Ultrasonic measurements of fetal breathing movements in man. Thesis presented to the University of Lund. Malmoe 1977
[55] MARX, G. F., L. R. ORKIN: Physiological changes during pregnancy: A review. Anesthesiology 19 (1958) 258
[56] MILEWSKI, P., R. SCHUMANN: Besonderheiten der Substitution mit Wasser und Elektrolyten in Schwangerschaft und Geburt. In: AHNEFELD, F. W., H. BERGMANN, C. BURRI, W. DICK, M. HALMAGYI, E. RAEGHEIMER (eds.): Wasser-, Elektrolyt- und Säure-Basen Haushalt. Springer-Verlag, Berlin 1977
[57] MILLER, F. C., R. H. P. PETRIE, J. J. ARCE, R. H. PAUL, E. H. HON: Hyperventilation during labor. Am. J. Obstet. Gynecol. 120 (1974) 489
[58] MISSRI, J. C., S. ALEXANDER: Hyperventilation syndrome. A brief review. JAMA 19 (1978) 2093
[59] MORISHIMA, H. O., F. MOYA, A. C. BOSSERS, S. S. DANIEL: Adverse effects of maternal hypocapnea on the newborn guinea pig. Am. J. Obstet. Gynecol. 4 (1964) 524
[60] MOTOYAMA, E. K., G. RIVARD, F. ACHESON, C. D. COOK: Adverse effects of maternal hyperventilation on the fetus. Lancet I (1966) 286
[61] MOTOYAMA, E. K., G. RIVARD, F. ACHESON, C. D. COOK: The effect of changes in maternal pH and P_{CO_2} on the P_{O_2} of fetal lambs. Anesthesiology 28 (1967) 891

[62] MOTOYAMA, E. K., T. FUCHIGAMI, H. GOTO, D. R. COOK: Response of Fetal Placental Vascular Bed to Changes in P_{CO_2} in Sheep. In: LONGO, L. D., D. R. RENEAU (eds.): Fetal and Newborn Cardiovascular Physiology 2, Garland STPM Press, New York & London 1978

[63] MOYA, F., H. O. MORISHIMA, S. M. SHNYDER, L. S. JAMES: Influence of maternal hyperventilation on the newborn infant. Am. J. Obstet. Gynecol. 91 (1965) 76

[64] NAVOT, D., Y. DONCHIN, E. SADOVSKY: Fetal response to voluntary maternal hyperventilation. Acta Obstet. Gynecol. Scand. 61 (1982) 205

[65] NEILL, W. A., M. HATTENHAUER: Impairment of myocardial O_2 supply due to hyperventilation. Circulation 52 (1975) 854

[66] PARER, J. T., M. ENG, H. AOBA, K. UELAND: Uterine Blood Flow and Oxygen Uptake during Maternal Hyperventilation in Monkeys at Cesarean Section. Anesthesiology 32 (1970) 130

[67] PRICE, H. L.: Effects of carbon dioxide on the cardiovascular system. Anesthesiology 21 (1960) 652

[68] PRILL, H. J.: Methoden der Geburtserleichterung. Psychologische bzw. nichtmedikamentöse Methoden. In: KAESER, O., V. FRIEDBERG (eds.): Schwangerschaft und Geburt. 2. Georg Thieme-Verlag, Stuttgart 1981

[69] RALSTON, D. H., S. M. SHNIDER, A. A. DE LORIMIER: Uterine Blood Flow and Fetal Acid-Base Changes after Bicarbonate Administration to the Pregnant Ewe. Anesthesiology 40 (1974) 348

[70] REID, D. H. S.: Respiratory changes in labour. Lancet I (1966) 784

[71] RICHARDS, D. W.: Circulatory Effects of Hyperventilation and Hypoventilation. Handbook of Physiology III (1964/65) 1887

[72] ROOTH, G., S. SJOESTEDT: The placental transfer of gases and fixed acids. Arch. Dis. Child. 194 (1962) 366

[73] ROSSIER, P. H., M. HOTZ: Respiratorische Funktion und Säure-Basen-Gleichheit in der Schwangerschaft. Schweiz. Med. Wochenschr. 83 (1953) 897

[74] ROWE, G. C., G. W. CRUMPTON: Effects of hyperventilation on systemic and coronary hemodynamics. Am. Heart J. 63 (1962) 67

[75] SALING, E., P. LIGDAS: The effect on the fetus of maternal hyperventilation during labour. J. Obstet. Gynaecol. Brit. Cwlth. 10 (1969) 877

[76] SCHLICK, W., E. MUELLER-TYL, H. SALZER, P. SCHMID: Lungenfunktion und Säure-Basenhaushalt im Verlaufe der Schwangerschaft. Prax. Klin. Pneumol. 31 (1977) 635

[77] SCHMIDT, R. F., G. THEWS (eds.): Einführung in die Physiologie des Menschen. Springer Verlag, Berlin 1976

[78] SJOESTEDT, S.: Acid-base balance of arterial blood during pregnancy, at delivery and in the puerperium. Am. J. Obstet. Gynecol. 84 (1962) 775

[79] SPAETLING, L., R. HUCH, A. HUCH: unpublished data

[80] STOJANOV, S.: Untersuchungen über das Säure-Basen-Verhältnis im Blut von Schwangeren. In: SALING, E. and J. W. DUDENHAUSEN (eds.): Perinatale Medizin 3. Georg Thieme-Verlag, Stuttgart 1972

[81] STRASSER, K., A. HUCH, R. HUCH: Der Einfluß der lumbalen Epiduralanaesthesie unter der Geburt auf die Atmung und den kontinuierlich transcutan gemessenen P_{O_2} der Mutter. In: DUDENHAUSEN, J. W., E. SALING, E. SCHMIDT (eds.): Perinatale Medizin 6. Georg Thieme-Verlag, Stuttgart 1975

[82] WAITES, T. F.: Hyperventilation — Chronic and Acute. Arch. Intern. Med. 138 (1978) 1700

[83] WAYNE, H. H.: A clinical comparison of the symptoms of hypoxia and hyperventilation. USAF SAM Report 1957

[84] WEST, J. B.: Human Physiology at Extreme Altitudes on Mount Everest. Science 224 (1984) 784

[85] WILBRAND, U., CH. PORATH, P. MATTHAES, R. JASTER: Der Einfluß der Ovarialsteroide auf die Funktion des Atemzentrums. Arch. Gynaekol. 191 (1959) 507

[86] YAMAGUCHI, F., J. MEYER, F. SAKAI, M. YAMAMOTO: Normal human aging and cerebral vasoconstrictive responses to hypocapnia. J. Neurol. Sci. 44 (1979) 87

[87] ZWILLICH, C. W., D. J. PIERSON, E. M. CREAGH, J. V. WEIL: Effects of hypocapnia and hypocapnic alkalosis on cardiovascular function. J. Appl. Physiol. 40 (1976) 333

Prof. Dr. R. Huch, M. D.
Univ.-Frauenklinik
Frauenklinikstr. 10
CH-8091 Zürich