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The oxygen status of fetal blood

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Objective: To estimate the acid-base and oxygen status of fetal blood and compare with maternal placental venous blood.
Data sources and calculations: We selected pH and blood gas data from the literature pertaining to umbilical vein and artery blood obtained by cordocentesis and estimated values for the 30th and 40th gestational week. Average values for maternal venous blood leaving the placenta were estimated on the assumption of equal maternal arterio-venous and umbilical veno-arterial total oxygen concentration differences.
Results: pH and pCO_2 of maternal blood leaving the placenta and umbilical vein blood are almost identical at week 30. A small pCO_2 and pH difference may exist at week 40. The pO_2 of the maternal placental venous blood and umbilical vein blood are almost identical at week 30, but at week 40 a pO_2 difference indicates an umbilical arterio-venous shunting of as much as 30 %. The fetal mixed venous pO_2 falls from 2.6 kPa to 2.2 kPa from the 30th to the 40th gestational week.
Conclusion: More accurate measurements are needed to confirm our results. Future measurements should be performed with a combined pH-blood gas analyzer and haemoximeter to allow determination of the complete oxygen status of the blood.

Key words: acid-base status; blood gases; blood pH; carbon dioxide; cordocentesis; oxygen; physiology; umbilical cord.

Guidelines for measurement of pH and blood gas values in fetal blood have recently been published (1), describing prenatal sampling of blood from the umbilical vessels in conjunction with cordocentesis, intra partum sampling of fetal capillary blood by skin puncture of the presenting part, and post partum sampling of blood from a clamped section of the umbilical cord. Cordocentesis refers to ultrasound guided puncture of the fetal umbilical cord through the maternal abdomen during pregnancy with aspiration of blood samples for diagnostic purposes. An increasing number of pH and blood gas data have accumulated, allowing an estimation of reference values for blood from the umbilical vein and artery from the 20th gestational week and onwards. The purpose of the present study was to analyse the cordocentesis data more closely to synthesize a set of consistent values for blood from the umbilical vein and artery and compare these with values for maternal arterial blood and a hypothetical mixture of maternal venous blood draining the placental sinuses. The study was presented in part at a workshop in Zürich in 1993 in connection with the preparation of the Guidelines.

pH and blood gas regulation is quite different in the adult and the fetus. In the adult the lungs are coupled *in series* with the tissues; in the fetus the gas exchanger is the placenta, which is coupled *in parallel* with the tissues. This means that only half of the blood is oxygenated during one circulation in the fetus. The fetal circulation is shown schematically in Fig. 1. Values for blood flow are extracted from textbooks of physiology, where most of the data refers to fetal lamb. We prefer the terms umbilical vein blood and umbilical artery blood rather than umbilical venous and arterial blood to avoid any confusion arising from the fact that the umbilical vein blood is the "arterialized" or oxygenated blood in relation to the umbilical artery blood.

Blood from the umbilical vein mixes with fetal venous blood from the lower body and the hepatic vein and reaches the right atrium. Here most of it continues through the foramen ovale to the left atrium, the left ventricle and the upper aorta. A smaller part of the blood flows from the right atrium into the right ventricle, and due to a special anatomical structure (the crista terminalis), venous blood from the upper body tends to follow this blood stream. Most of the blood from the pulmonary artery is shunted into the aorta via the ductus arteriosus, a smaller part flows through the lungs. Due to the special flow arrangement in the heart the oxygen saturation in the blood to the upper body and brain is slightly higher than in the blood to the lower body, 67 % versus 64 %.

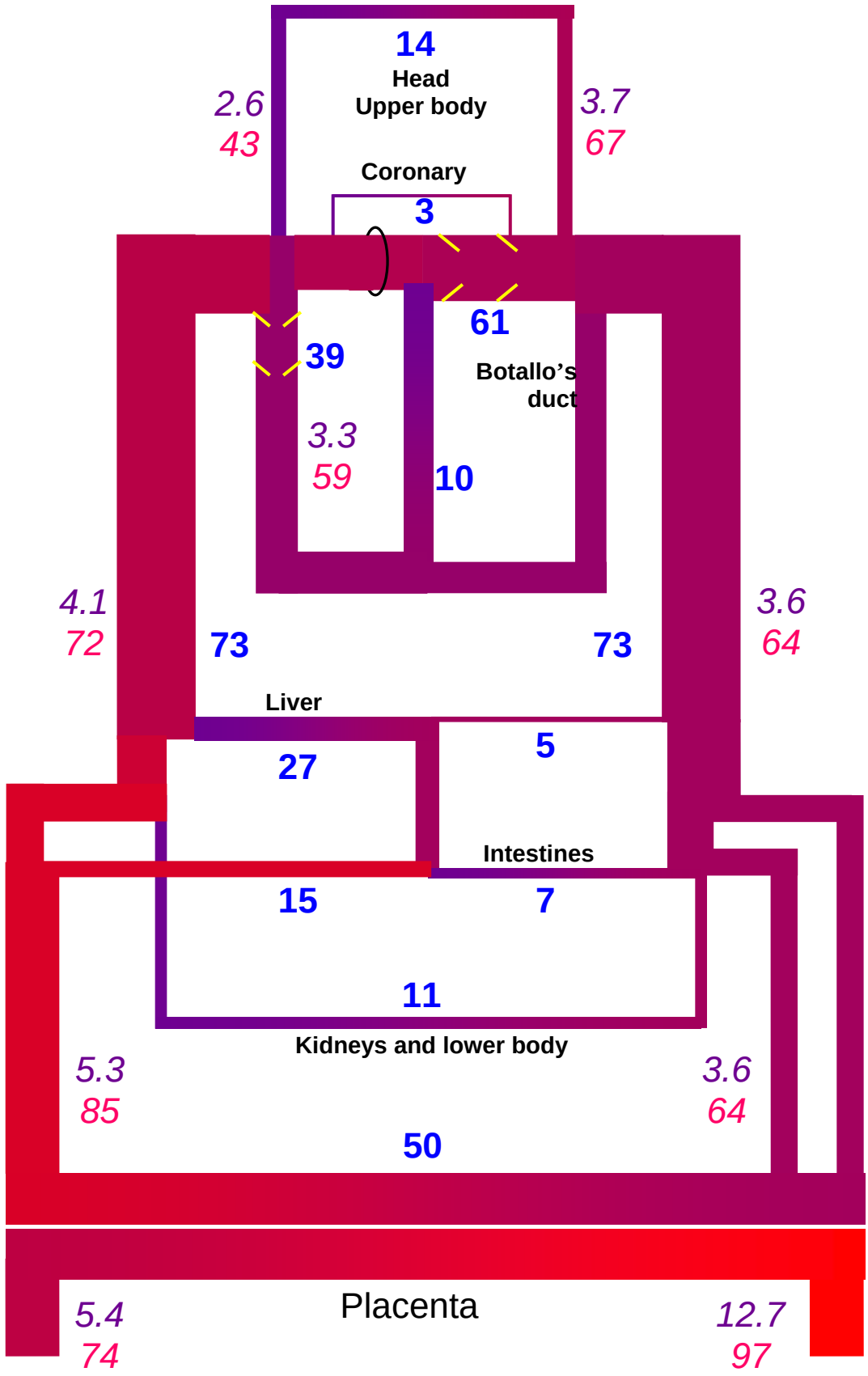

Fig. 1. Scheme of fetal circulation. Blood flow is indicated by the diameter of the vessel, and values printed in blue upright type indicate the flow relative to the total cardiac output, i.e. the flow through the pulmonary artery (39 %) and the aorta (61 %) adds up to 100 %. 50 % of the cardiac output goes to the placenta, and 50 % to the fetal tissues. Tissue flow from head and down is: 14 % (head and upper body), 3 % (coronary flow), 10 % (lungs), 5 % (liver), 7 % (intestines), 11 % (kidneys and lower body), all adding up to 50 %. Lilac values in sloping type are oxygen tensions (kPa) with percentage haemoglobin oxygen saturations in pink. Values refer to the 30th gestational week.

DATA SOURCES AND CALCULATIONS

We plotted data published by Nicolaides, Soothill and co-workers (2) and Weiner and co-workers (3) for the umbilical vein and the umbilical artery as a function of gestational age. Most of the data refers to week 20 to 35 with a few data from week 35 to 38. By visual interpolation, extrapolation, and averaging we obtained values for week 30 and week 40 (Table 1). Values for maternal blood sampled simultaneously with the cordocentesis are not available. We therefore calculated values for the arterial blood of a 20 year old mother, using a slightly lower pCO_2 (4.1 kPa), a slightly lower effective haemoglobin concentration (7.5 mmol/L), and a slightly higher erythrocyte 2,3-diphosphoglycerate concentration (6.0 mmol/L) than for a non-pregnant woman (4).

Direct measurement on placental venous blood is not possible. Uterine venous blood contains a mixture of blood from the placenta and the uterine wall. We therefore calculated values for placental venous blood on the assumption that the arterio-venous oxygen concentration difference of the maternal blood is the same as the umbilical veno-arterial oxygen concentration difference. The implications of this assumption are discussed later.

All calculations were performed with the Oxygen Status Algorithm, a computer program for calculation of the oxygen status and the acid-base status of the blood (5).

Table 1. Mean values for blood from the umbilical vein and artery, maternal artery and maternal placental venous blood at the 30th and 40th gestational week. The values were subjectively averaged from literature data. Values marked (c) were calculated. Temperature 37 °C.

Gestational age	week	30	40	30	40
		Umbilical vein		*Maternal artery:*	
Haemoglobin oxygen saturation		0.853	0.724	0.972[c]	0.971[c]
Oxygen tension	kPa	5.30	4.20	12.67[c]	12.64[c]
Total oxygen concentration	mmol/L	7.2[c]	6.7[c]	7.4[c]	7.4[c]
Carboxyhaemoglobin fraction		0.007	0.007	0.005	0.005
Methaemoglobin fraction		0.005	0.005	0.005	0.005
Effective haemoglobin concentration	mmol/L	8.4	9.2	7.5	7.5
Fetal haemoglobin fraction		0.929	0.800	0.005	0.005
2,3-diphosphoglycerate concentration	mmol/L	5.3[c]	5.3[c]	6.0	6.0
Halfsaturation tension	kPa	2.7[c]	2.9[c]	3.6[c]	3.6[c]
Oxygen extraction tension	kPa	3.1[c]	2.8[c]	4.7[c]	4.8[c]
pH	7.401	7.380	7.439	7.430	
Carbon dioxide tension	kPa	4.75	5.08	4.10	4.20
Ecf-Base excess concentration	mmol/L	-2.4[c]	-2.3[c]	-3.2[c]	-3.2[c]
		Umbilical artery:		*Placental venous:*	
Haemoglobin oxygen saturation		0.640	0.508	0.737[c]	0.705[c]
Oxygen tension	kPa	3.55	3.05	5.40[c]	5.18[c]
Total oxygen concentration	mmol/L	5.4[c]	4.7[c]	5.6	5.4
pH	7.370	7.353	7.411[c]	7.399[c]	
Carbon dioxide tension	kPa	5.46	5.75	4.65[c]	4.84[c]
		Veno-arterial:		*Arterio-venous:*	
Total oxygen concentration difference	mmol/L	1.8[c]	2.0[c]	1.8	2.0

pH AND pCO_2 VALUES OF MOTHER AND FETUS

At week 30 the pCO_2 and pH of placental venous blood and blood from the umbilical vein are almost identical indicating almost complete diffusion equilibrium (Fig 2). At week 40 the umbilical vein pCO_2 is slightly higher and pH slightly lower, suggesting a minor disequilibrium at term.

THE pO_2 DIFFERENCE BETWEEN PLACENTAL VENOUS AND UMBILICAL VEIN BLOOD

The oxygen status of mother and fetus at the 30th and 40th gestational weeks are illustrated in Fig. 3. Notice that the fetal pO_2 falls considerably with increasing gestational age.

Values for the placental venous blood were calculated on the assumption that the arterio-venous oxygen concentration difference on the maternal side of the placenta equals the veno-arterial oxygen concentration difference on the fetal side, i.e. the vertical distance between the points ma and pv should equal the distance between points uv and ua. The latter difference was found to be 1.8 mmol/L at the 30th gestational week and 2.0 mmol/L at the 40th week (Table 1). The implication of this assumption is that the blood flow on the maternal side equals the blood flow on the fetal side, because the amount of oxygen given off from the maternal blood must equal the amount taken up by the fetal blood, and the amount of oxygen is the product of blood flow and a-v (or v-a) oxygen concentration difference.

On the basis of this assumption we find that at the 30th week the pO_2 of placental venous blood almost equals the pO_2 of the umbilical vein, indicating almost complete diffusion equilibrium for oxygen. At the 40th week, however, we find the pO_2 of the umbilical vein significantly lower than the estimated pO_2 of placental venous blood, indicating a lack of oxygen diffusion equilibrium or a shunting of blood through inefficient sections of the placenta. The total "shunting" may be calculated to be about 30 %. This suggests that a gradual decline in the efficiency of the placenta as an oxygenator might be the explanation of the fall in fetal pO_2 during pregnancy.

At the 30th week, our data indicate that the blood flow on the maternal side of the placenta cannot be lower than the flow on the fetal side, because then the placental venous pO_2 would be lower than the umbilical venous pO_2, which is

impossible. At week 30 the maternal flow must equal or surpass the fetal flow. If the maternal flow is in fact higher than the fetal, then the point representing placental venous blood (pv) would move upwards towards the maternal arterial point (ma) and we would have a pO_2 difference between placental venous blood and the umbilical vein indicating non-equilibrium for oxygen diffusion or shunting of blood through inefficient sections of the placenta.

At the 40th week, the blood flow on the maternal side of the placenta could be somewhat lower than the fetal. If the flow is 30 % lower, then the point representing placental venous blood slides down along the oxygen binding curve to the same pO_2 level as the point representing the umbilical vein. The explanation of the decline in fetal pO_2 with gestational age would then be a gradual relative decrease in maternal blood flow through the placenta, rather than increasing "shunting" of blood.

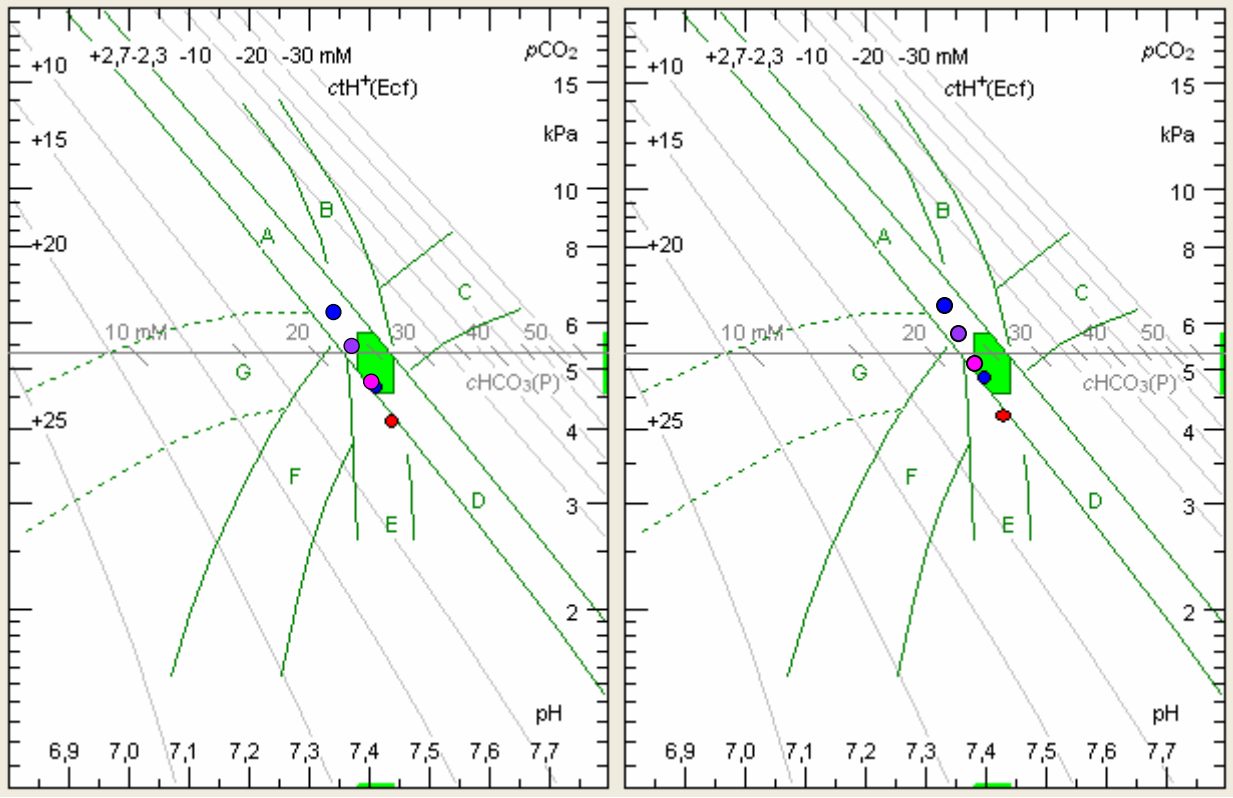

Fig. 2. pH and pCO_2 values of mother and fetus at the 30th and 40th gestational week, plotted in the acid-base chart (6). The points represent the pH and pCO_2 values of the maternal artery (red), placental venous (lower blue), umbilical artery (lilac), umbilical vein (pink), and fetal mixed venous blood (upper blue). The arterial point of the mother falls below the normal green area in the area of chronic hypocapnia (E), indicating that the mother hyperventilates slightly during pregnancy. At week 30 the points representing the maternal placental vein and the umbilical vein almost coincide.

THE pO_2 OF FETAL MIXED VENOUS BLOOD

In the fetus, venous blood does not mix in the right ventricle or pulmonary artery as it does in the adult. Nevertheless, it is possible to calculate the composition of a hypothetical mixture of all the venous blood draining the fetal tissues. The point representing fetal mixed venous blood (fv, in Figs. 3 and 4) was calculated on the assumption that the average arterio-venous oxygen concentration difference through the fetal tissues equals the umbilical veno-arterial oxygen concentration difference through the placenta. This means that the vertical distance between the pink point (umbilican vein) and the lilac point (umbilical artery) should be the same as the vertical distance between the lilac point and the blue point (fetal mixed venous blood). The implication is that the fetal cardiac output is distributed 50/50 to the fetal tissues and the placenta. On the basis of this assumption we find the fetal mixed venous pO_2 (or the average end capillary pO_2) to be 2.6 kPa at the 30th week, falling to 2.2 kPa at the 40th week.

The fetus possesses the same compensation mechanism towards a low mixed venous pO_2 as the adult: increasing the *cardiac output*. In a way this is twice as efficient in the fetus as in the adult. A doubling of the cardiac output in the adult causes a halving of the arterio-venous oxygen concentration difference and the mixed venous pO_2 increases approximately halfway towards the arterial. In the fetus the "mixed venous pO_2 increases all the way to the arterial because the pO_2 of the umbilical artery at the same time rises halfway towards the pO_2 of the umbilical vein .

It does not help the fetus, however, to increase the tissue perfusion by *changing the flow distribution* between fetus and placenta. Increasing the fetal flow would diminish the oxygen concentration difference between the arterial and the "fetal mixed venous blood" but at the same time the gap between the umbilical artery and vein would increase. And the result would be a fall in mixed venous pO_2. For example, if the fetus gets 75% and the placenta only 25% of the cardiac output, then the point representing the umbilical artery would drop to the position the fetal mixed venous blood had before and the fetal mixed venous pO_2 would drop from 2.6 to 2.0 kPa (Fig. 4). The opposite does not help either.

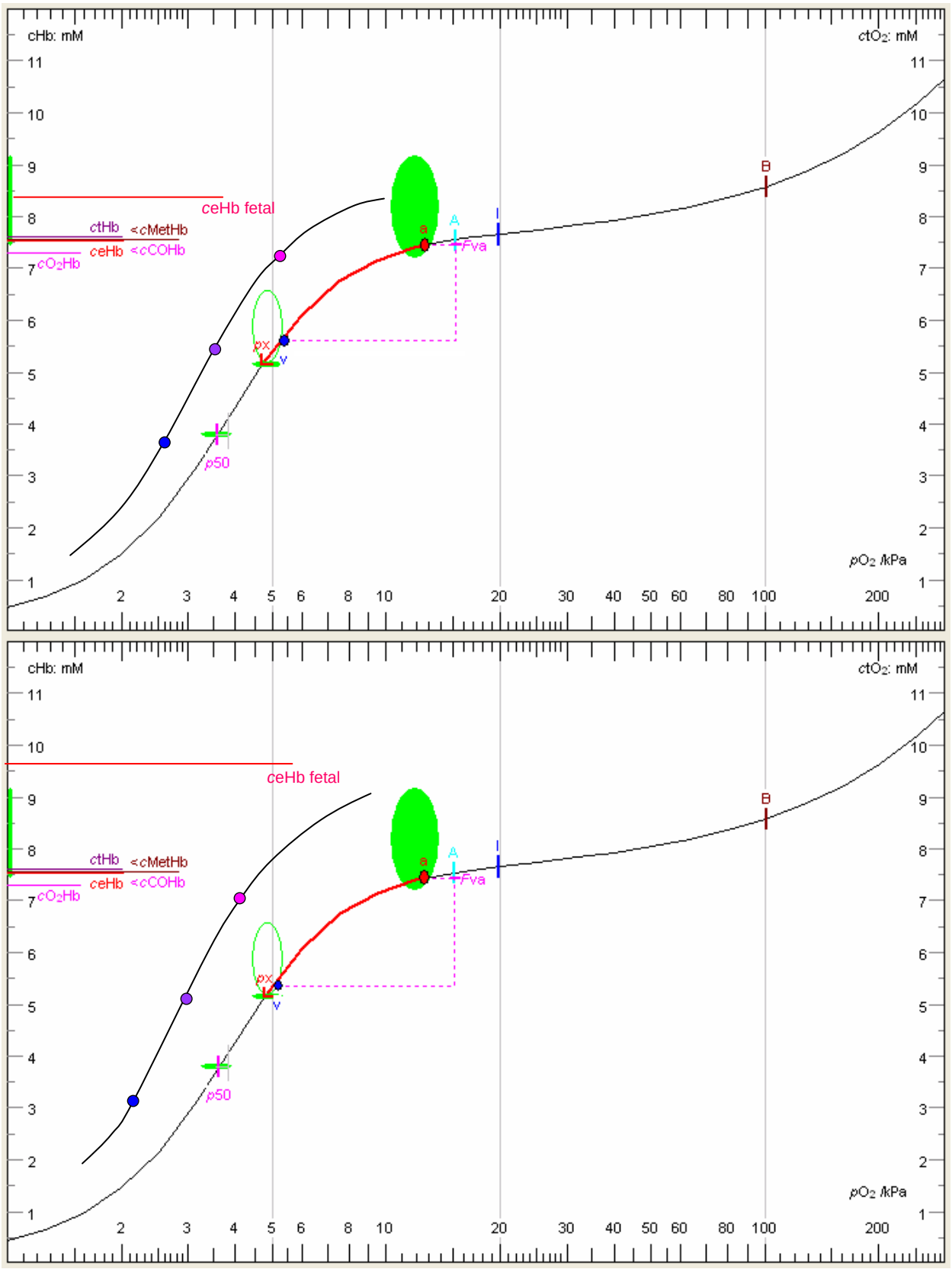

Fig. 3. The oxygen status of mother and fetus at the 30th gestational week (upper graph) and 40th gestational week (lower graph). As in Fig. 2, the points represent maternal, umbilical, and fetal mixed venous blood. The oxygen binding curve of the fetal blood is displaced upwards and to the left due to the higher haemoglobin concentration and the higher haemoglobin oxygen binding affinity caused by the fetal haemoglobin. Notice that the fall in total oxygen concentration from artery to vein on the maternal side equals the rise from artery to vein on the fetal side.

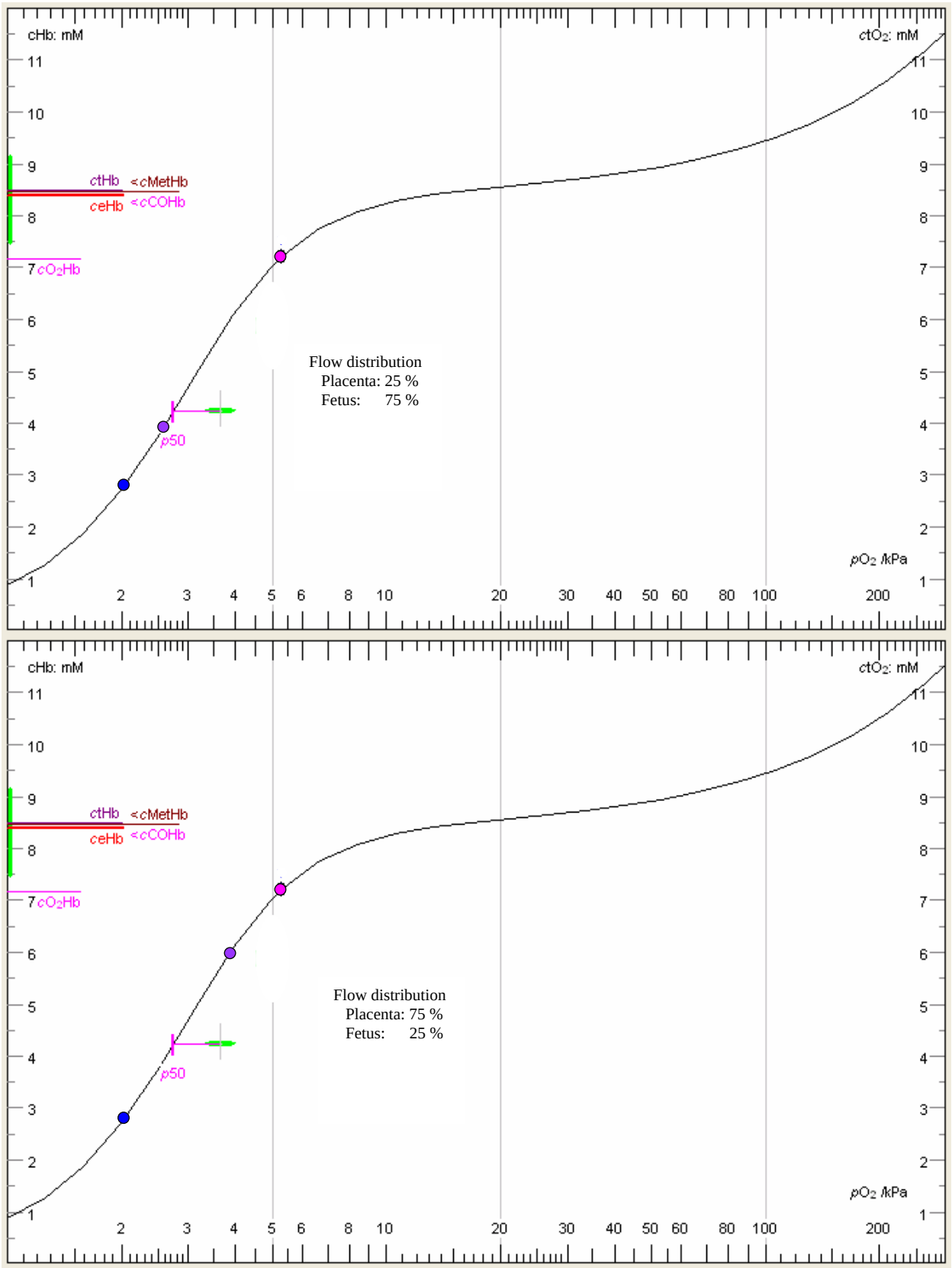

Fig. 4. The oxygen status of umbilical vein (pink), umbilical artery (lilac), and fetal mixed venous blood (blue) with flow distributions between fetus and placenta of 75/25 (top) and 25/75 (bottom). In both cases the fetal mixed venous pO_2 falls from 2.6 to 2.0 kPa as compared to the optimal flow distribution of 50/50 shown in Fig. 3.

Increasing the placental flow to 75% would pull the values of the umbilical artery up but the gap between the umbilical artery and mixed venous blood would increase, and the pO_2 of the mixed venous blood would again drop to 2.0 kPa. A flow distribution of 50/50 between the fetus and the placenta is the optimal flow distribution, which ensures the highest fetal mixed venous pO_2. The fetus may, however, benefit from a change in flow distribution among its own tissues and, for example, increase the blood flow to the head at the expense of the flow to the lower body.

The adult has another mechanism of improving the oxygen delivery to the tissues; that of *shifting the oxygen binding curve to the right*, and thereby facilitating the oxygen release in the tissues. This is a convenient mechanism, for example during muscular exercise where lactic acid causes a fall in pH and a rise in p_{50} due to the Bohr effect. But it is only effective when we operate at the top part of the oxygen binding curve. The fetus benefits from a displacement of the curve to the left which is accomplished by the fetal haemoglobin. A hypoxic fetus would actually benefit from a further displacement to the left, but it would never benefit from a displacement to the right, and hence an acidosis is never an advantage for the fetus.

The fetal mixed venous pO_2 is strongly dependent on two maternal variables: the blood flow through the placenta and the maternal arterial oxygen extraction tension. The latter may be increased by increasing the arterial pO_2, the haemoglobin concentration, and the half-saturation tension (p_{50}).

A fetal mixed venous pO_2 of 2.2 kPa, as estimated at the 40th week, is less than half of the normal mixed venous pO_2 of the adult of 5 kPa, where 3.5 kPa is a *"critical"* value below which the mean end-capillary oxygen diffusion gradient becomes too low to support a normal oxygen supply to the cells. One explanation of the relatively high adult mixed venous pO_2 is that the blood is a mixture of quite varying pO_2. Blood from the coronary sinus may have a pO_2 as low as 2.2 kPa, whereas venous blood from kidney and skin have much higher values, because the blood flow to these organs is not purely nutritive but serves to provide glomerular filtration and temperature regulation as well. Nevertheless, it is surprising that the normal mixed venous pO_2 of the fetus at term can be as low as 2.2 kPa and even lower if we take the biological variation into account. Apparently the fetus tolerates a lower end-capillary oxygen tension difference between erythrocytes and mitochondria and the only explanation is that the average diffusion distance is shorter and/or the total endothelial diffusion area larger; in other words the average capillary density must be higher in the fetal tissues than in the adult.

We have only provided estimates of normal mean values in Tables and Figures. The experimental data indicates an *individual variation* in the pH and pCO_2 of the umbilical vein and artery which is only slightly higher than the variation in the arterial pH and pCO_2 in the adult. For the pO_2, however, the data indicates a biological standard deviation as high as 1 kPa or a coefficient of variation of about 20 %. This means that we get very wide 95 % reference intervals with a great overlap between umbilical artery and vein. This variation is much larger than the variation of the arterial and mixed venous blood of the adult and we must suspect that part of the variation is analytical rather than biological. The reference interval for the mixed venous pO_2 of the adult is narrower than that of the arterial pO_2 even on a logarithmic scale, as if the regulation of the mixed venous pO_2 is more important than regulation of the arterial pO_2. It is tempting to speculate that the variation in the fetal mixed venous pO_2 is also less than the variation in the $pO_2$of the umbilical vein and artery.

THE OXYGEN EXTRACTION TENSION

In the adult, the oxygen extraction tension of the arterial blood, defined as the pO_2 obtained by extracting 2.3 mmol of oxygen per litre of blood, is a valuable parameter of the "oxygen extractivity", i.e. the ability of the arterial blood to give off a given amount of oxygen to the tissues without an undue fall in pO_2. The oxygen extraction tension reveals whether a fall in arterial oxygen tension or haemoglobin oxygen capacity or a rise in haemoglobin oxygen affinity is compensated or not (7).

A similar measure of the oxygen extractivity of the umbilical vein blood is equally useful because the triad: oxygen tension, haemoglobin oxygen capacity, and haemoglobin oxygen affinity, interact and compensate for each other in the same way as in the adult. A normal pO_2 in the umbilical vein is no guarantee that the fetal mixed venous pO_2 is normal, it might in fact be low if the haemoglobin concentration is decreased. The mean value for the oxygen extraction tension of the umbilical vein (Table 1) falls slightly, from 3.1 to 2.9 kPa, from the 30th to the 40th week. This indicates that the much greater fall in pO_2 of the umbilical vein (5.3 to 4.2 kPa) is partly compensated by the rise in haemoglobin concentration (8.4 to 9.2 mmol/L), as previously pointed out by Soothill and co-workers (8). In spite of the modest fall in oxygen extraction tension, the estimated fetal mixed venous pO_2 falls considerably (2.6 to 2.2 kPa), and the reason is the simultaneous increase in a-v total oxygen concentration difference (1.8 to 2.0 mmol/L).

CONCLUSION

Our calculations indicate that at the 30th gestational week there may be diffusion equilibrium across the placenta for hydrogen ion, carbon dioxide, and oxygen, while a progressive placental insufficiency with an apparent umbilical arterio-venous shunting of up to 30 % or more develops towards end of term. This causes falling umbilical pO_2 values with gestational age. We have estimated that the fetal mixed venous pO_2 falls from about 2.6 kPa at the 30th week to about 2.2 kPa at the 40th week. More accurate measurements are needed to substantiate these findings. Future measurements on umbilical vein and artery blood obtained by cordocentesis should be performed using a pH-blood gas analyzer supplemented by a haemoximeter to allow calculation of the complete oxygen status of the blood. Preferably maternal arterial blood should be sampled simultaneously. This would allow better estimates of the composition of the placental venous blood, estimates of the placental function, and estimates of the fetal mixed venous pO_2.

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