Nitric oxide (NO) is important to maintain a low resistance in the placental circulation, hence an adequate exchange of gases and nutrients between mother and fetus. Disturbances of placental perfusion, such as those occurring during uterine contractions before or during delivery are frequently responsible for transient, disruption of fetal gas exchanges. The aim of this study was to investigate the functional role of the NO system in umbilical vessels and in HUVEC during physiologic labor or during labor associated with fetal stress. We combined HUVEC molecular analysis with the laboratory analysis of NO, nitroso-hemoglobin (NOHb) and eNOS activity in umbilical arteries and vein in pregnancies concluded with spontaneous or operative labor and/or by programmed caesarean section. These were coupled with the post-natal evaluation of the NO system. The results we found are that in umbilical vein NO and NOHb levels were lower in pregnancies with elective cesarean section and that newborns delivered after labor presented an increase of circulating NO, as compared to controls delivered by programmed caesarean section. Particularly, a marked increase in NO levels was noted in blood drawn 24 hours after birth. Circulating levels of NO proportionally decreased 72 hours after delivery, more quickly for newborns delivered without labor. On the other hand the HUVEC extracted from umbilical vein from pregnancies terminated without labor presented higher NO formation, eNOS expression and enzymatic activity compared to those terminated with labor. These findings agree with NO plays a strategic role in the fetal-placental circulation in the stress of labor and particularly when fetal distress is present and the presence of labor influences the setting of nitric oxide system in newborns.