Fetal Circulatory Endothelin-1,2 in the Midtrimester

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Abstract
Umbilical-vein blood from eight fetuses who underwent cordocentesis for rapid karyotyping at 19–22 gestational weeks was tested for immunoreactive endothelin-1,2 by means of radioimmunoassay. Endothelin was detected in the serum of all but one of these fetuses. Levels of endothelin-1,2 ranged from 8.5 to 19.2 fmol/ml (mean 13.4 fmol/ml). We speculate that endothelin in the fetoplacental circulation may play a role in the regulation of fetal hemodynamics in utero.

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Introduction
Endothelin-1, a polypeptide produced mainly by endothelial cells, has been shown to be one of the most potent vasoactive substances yet discovered [1]. High circulatory levels of this hormone have been found recently to be associated with essential hypertension, pregnancy-induced hypertension, acute renal failure and acute coronary insufficiency. The fetoplacental circulation is characterized by dynamic and dramatic changes during pregnancy with respect to changing cardiac output, peripheral vascular resistance, blood pressure and blood flow. A recent preliminary study has demonstrated high levels of endothelin-1 in fetuses with growth retardation and umbilical-flow disturbances [2]. We were therefore motivated to investigate whether endothelins are produced and secreted by normal fetuses in the early stages of pregnancy.

Patients and Methods
Eight women underwent ultrasound-guided cordocentesis at 19-22 weeks of gestation for rapid karyotyping due to suspected anomalies. Two milliliters of venous umbilical-cord blood were collected into tubes containing antiproteases (EDTA and aprotinin), centrifuged immediately at 4°C and stored at -20°C until assayed. Informed consent was obtained from each woman undergoing the procedure. The samples were examined for endothelin-1,2 by radioimmunoassay (125I-endothelin-1,2, Amersham International, UK), followed by acidification and passage through Amprep 500 mg C2 columns (Amersham).

Results and Comment
All fetuses were found to have a normal karyotype. No immediate or late adverse effects of cordocentesis were observed in any of the women or their fetuses. Endothelin-1,2 was detected in the serum of all but one fetus. The levels ranged from 8.5 to 19.2 fmol/ml (mean 13.4 fmol/ml). These values are similar to serum levels previously found by us in the plasma of pregnant and nonpregnant women [3]. Endothelin may therefore be produced by fetal endothelium and secreted into the fetoplacental circulation as early as the midtrimester of pregnancy, or possibly earlier. In view of these findings, as well as those of Isozaki-Fukuda et al. [4] showing that asphyxia in labor contributes to significant increases in fetal circulatory endothelin-1 levels, we speculate that endothelin in the fetoplacental circulation may play an important role in the regulation of fetal hemodynamics in utero.

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