Different types of fetal nucleated cells are found in venous blood of pregnant women providing a source for non-invasive prenatal diagnosis. Of these cells short-lived fetal nucleated erythrocytes have emerged as the most promising type of fetal cell for this purpose. In this study we first evaluated if fetal sex could be determined in maternal venous blood by in situ hybridisation with a Y chromosome specific probe, without prior enrichment of fetal cells. Blood samples from 39 women, 6 to 39 weeks pregnant were studied. Secondly we studied the presence of nucleated erythrocytes in blood from pregnant women. For this purpose 51 women between 6 and 17 weeks of gestation were selected. Nucleated erythrocytes were enriched by both positive and negative magnetic activated cell sorting with use of antibodies to the cellsurface antigens glycophorin A and human leukocyte common antigen, CD45 respectively. Identification of nucleated erythrocytes was performed by alkaline phosphatase anti-alkaline phosphatase immunostaining by means of anti-GPA. In 40 of these women who carried a male fetus the origin of the identified nucleated erythrocytes was studied by in situ hybridisation with X and Y specific probes. Fetal sex was correctly identified in 77% of the studied pregnancies without prior enrichment of fetal cells. Nucleated erythrocytes were detected in 94% of the studied women at the range of 1 to 230. None of the nucleated erythrocytes detected in the blood from the women carrying a male fetus were fetal. Our results show that reliable prenatal diagnosis on fetal cells in maternal blood is not possible without enrichment of fetal cells and that enrichment of fetal nucleated erythrocytes requires more efficient and specific enrichment techniques as a majority of them seems to be of maternal origin.