

ter trophoblast cultures. We do not agree with this criticism. As cited in our study, our results showing increased invasiveness of first-trimester trophoblasts in vitro corroborate previous in vivo findings. We do, however, agree that we have not fully characterized the different subtype of trophoblasts in our cell population and thus cannot comment on the percentage of the various subtypes. Nevertheless, we do not accept Feinberg's assumption that only undifferentiated villous trophoblasts account for the invasive ability of cytotrophoblasts throughout pregnancy. It can be argued that large numbers of extravillous or differentiated cytotrophoblasts indicate increased invasive capacity. In our study we tried to explain why first-trimester trophoblasts are more invasive than third-trimester trophoblasts in vivo and in vitro. We showed that third-trimester cytotrophoblasts retain invasive abilities that are important for placental physiologic mechanisms throughout pregnancy. The use of cytotrophoblasts in vitro as model for implantation is far from being ideal; it is the only model available for human studies. Thus in this context the applicability of first- and third-trimester trophoblasts for this purpose seems to be appropriate but remain an open issue.

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Pregnancy in an anephric woman

To the Editors: A 42-year-old woman underwent bilateral nephrectomy and cystectomy after 12 years of recidivant urotelial tumors in both kidneys, ureters, and urinary bladder. She was put on periodic hemodialysis treatment and after a period of training was installed at home in April 1993. Since the beginning she was started on recombinant human erythropoietin and reached 10 gm/dl with low doses in spite of anephria (stable schedule 33 U/kg/wk). She had two children, 18 and 16 years old, and very irregular menses, with amenorrhea since January 1994. In October she was seen for abdominal discomfort and severe anemia without ferropenia (hemoglobin 5.9 gm/dl, hematocrit 18%, ferritin 705 ng/ml, saturation 26%); ultrasonography disclosed pregnancy of estimated 17-week duration. At that time the dialysis regimen was 3.5 hours three times weekly. Her medications included calcium carbonate, vitamins, and erythropoietin 2000 U subcutaneously each week. This was increased to 4000 U subcutaneously three times weekly to maintain a hematocrit >28% (sixfold dose increase). Her home hemodialysis schedule was increased to 3 hours four times weekly at 19 weeks' gestation and five times weekly at 23 weeks' gestation, with very good control of her urea and creatinine (mean predialysis urea 100 mg/dl and creatinine 5.5 mg/dl). Initially, blood pressure was controlled with fluid removal, but since the twentieth week predialysis blood pressure was 150 to 160/90 to 95 and extended-release nifedipine (60 mg/day) was added.

Consecutive ultrasonographies showed mild fetal growth retardation and at 26 weeks' gestation she was admitted with premature labor and gave birth to a male infant weighing 550 gm, who died 30 minutes later.

Pregnancy in a woman requiring long-term dialysis is very uncommon, and when it occurs high residual renal function is usually maintained.¹ Fetal loss because of prematurity is frequently the outcome.¹ Our case illustrates a new cause of partial resistance to recombinant human erythropoietin action, only overcome after an important increase in dosage. An unexplained reduction in hemoglobin may be the first sign of pregnancy in women treated with recombinant human erythropoietin in dialysis. Only one pregnancy has been previously reported in an anephric woman, who decided to terminate it electively.² Therefore no cases of successful pregnancy in anephric women have been described. Very few cases of pregnancies in women on dialysis receiving recombinant human erythropoietin have been reported,¹⁻³ and to date there is no consensus for the use of recombinant human erythropoietin in this setting. Although detrimental effects of recombinant human erythropoietin in pregnancy cannot be suggested in our case, its use has not improved outcome of pregnancy¹ and a note of caution must be underlined on its current use, because transfer of erythropoietin from mother to fetus has been demonstrated in mice.⁴

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REFERENCES

1. Hou SH. Frequency and outcome of pregnancy in women on dialysis. *Am J Kidney Dis* 1994;23:60-3.
2. Gladziwa U, Dakshinamurty KV, Mann H, Sieberth HG. Pregnancy in a dialysis patient under recombinant human erythropoietin. *Clin Nephrol* 1991;37:215.
3. Smith KGC, Becker GJ. Pregnancy-related anemia in a hemodialysis patient treated with erythropoietin. *Nephrol Dial Transplant* 1993;8:563-4.
4. Koury MJ, Bonduant MC, Graber SE, Sawyer ST. Erythropoietin messenger RNA levels in developing mice and transfer ¹²⁵I-erythropoietin by the placenta. *J Clin Invest* 1988;82:154-9.

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Effects of maternal inhalation of 40% oxygen on fetal oxygen saturation

To the Editors: In the paper by Dildy et al. (Dildy GA, Clark SL, Loucks CA. Intrapartum fetal pulse oximetry: the effects of maternal hyperoxia on fetal arterial oxygen saturation. *AM J OBSTET GYNECOL*. 1994;171:1120-4) the authors found a significant increase in fetal arterial oxygen saturation (SpO₂) after giving 100% oxygen to the mother during labor but did not find a change in fetal oxygen saturation at a maternal inspired oxygen concentration (FiO₂) of 40%. The authors therefore question the efficacy of maternal oxygen therapy in which inspired oxygen concentrations are primarily <40%.

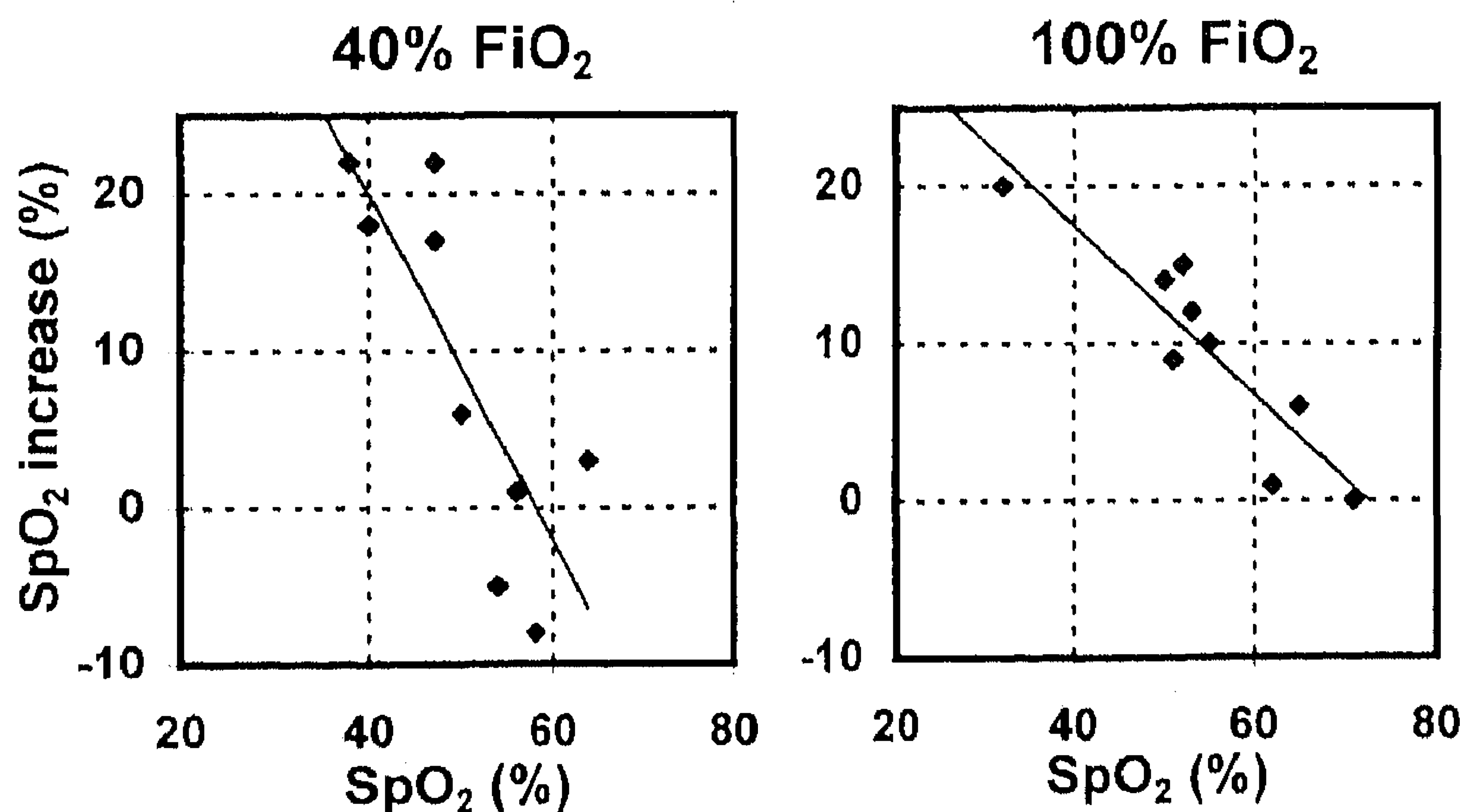


Fig. 1. Fetal SpO₂ increase after 20 minutes of 40% (left) or 100% (right) oxygen administration to mother plotted against initial fetal SpO₂. Data were obtained from Table I of Dildy et al.

With the authors' data concerning the short-term administration of 40% and 100% oxygen, we plotted the fetal SpO₂ increase against the initial fetal SpO₂ (Fig. 1). The Spearman rank correlation coefficient (r_s) is -0.84 at 40% and $r_s = -0.85$ at 100% FiO₂, which is statistically significant at both FiO₂ concentrations (p value 0.005 and 0.004, respectively). From the data points and a linear regression fit (see Fig. 1) it appears that when the initial fetal SpO₂ is around 40%, then the SpO₂ increase is $> 15\%$, at both 40% and 100% FiO₂. At a higher initial fetal SpO₂ level ($> 50\%$) no benefit is seen from 40% FiO₂, but 100% FiO₂ still has some effect on fetal SpO₂. The regression line crosses the x axis at 58% for 40% FiO₂ and at 73% for 100% FiO₂, so that there is a shift to the right with increasing maternal FiO₂.

A similar analysis applied to the authors' data on long-term (45 minutes) maternal oxygen inhalation of 40% oxygen does not show a significant correlation between initial value and increase of fetal SpO₂. This can partly be explained by the somewhat higher mean initial fetal SpO₂ in the long-term administration group compared with the short-term administration group (58% vs 50%). Other clinical characteristics of the two groups studied, for instance, different fetal heart rate patterns, might be other reasons for this observation.

Two animal studies^{1, 2} on the assessment of the accuracy of fetal reflection pulse oximetry report a precision of 5.5% to 6.6% at low saturation values. It is encouraging that the results of the study of Dildy et al. in human fetuses show some fairly good correlations and that fetal reflectance pulse oximetry is apparently a tool suitable for human physiologic studies.

The data of Dildy et al. suggest to us that maternal oxygen administration with both high (100%) and moderate (40%) oxygen concentrations is beneficial to those fetuses who are near a critical oxygen saturation range.³ Further studies using this new technique are warranted. For the analysis of the effects of maternal hyperoxia on fetal arterial oxygen saturation, the initial fetal SpO₂ should be taken into account.

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REFERENCES

1. Jongsma HW, Crevels J, Menssen JJM, et al. Application of transmission and reflection pulse oximetry in fetal lambs. In: Lafeber HN, Aarnoudse JG, Jongsma HW, eds. Fetal and neonatal physiological measurements. Amsterdam: Excerpta Medica, 1991:123-8.
2. Harris AP, Sendak MJ, Chung DC, et al. Validation of arterial oxygen saturation measurements in utero using pulse oximetry. *Am J Perinatol* 1993;10:250-4.
3. Nijland R, Jongsma HW, Nijhuis JG, van den Berg PP, Oeseburg B. Arterial oxygen saturation in relation to metabolic acidosis in fetal lambs. *AM J OBSTET GYNECOL*. 1995; 172:810-9.

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Reply

To the Editors: We appreciate the interest that was shown by van den Berg and Jongsma in our recent publication regarding the effects of maternal FiO₂ on fetal SpO₂ measured by reflectance pulse oximetry.

In our original article, repeated-measures analysis of variance was used to evaluate the short-term effects (group I, 20-minute duration, FiO₂ 21%, 40%, and 100%) and long-term effects (group II, 45-minute duration, FiO₂ 21% and 40%) of supplemental maternal oxygen administration on fetal SpO₂ in normal laboring women. According to van den Berg and Jongsma additional statistical analyses of the data reveal further observations and conclusions.

A matched t test was used to compare means of subgroups, with a two-tailed $p < 0.05$ considered significant. Spearman regression-correlation analysis was used to determine relationships between the initial fetal SpO₂ before oxygen therapy and percent change in fetal SpO₂ $\{[(\text{Initial SpO}_2 - \text{Final SpO}_2) \div \text{Initial SpO}_2] \times 100\}$ after therapy in treatment subgroups, with