Short Communication

THE PLACENTAL TRANSFER OF IgG IN THE CYNOMOLGUS MONKEY

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SUMMARY: The placental transfer of IgG from the mother to her fetus was investigated with colony-bred cynomolgus monkeys. Very low levels of IgG were detected in sera of 84 days old fetus, indicating that transplacental transfer of IgG had started by this fetal age. Afterwards, gradual increase in the IgG level continued till 140 days of fetal age. A marked increase in the level was noted after 140 days of fetal age, during the last 4 weeks of full gestation term. Fetal anti-measles antibody increased in a pattern similar to that in the IgG level. The IgG level and anti-measles and anti-streptolysin O antibody titers of newborns never exceeded those of their mothers.

In all mammalian and avian species, newborn animals receive antibodies from the mothers and the mechanism of transfer and the type of antibody transferred vary among animal species (Burnet, 1969).

Human immunoglobulins are transferred across the heamo-chorial placenta from the mother to her fetus and this transfer is restricted to IgG class alone (Jones, 1976). In case of non-human primates, the IgG level of the newborn rhesus monkey at the time of birth was somewhat lower than the maternal level, decreasing gradually to the lowest level at 35 to 45 days of age; after that the level began to rise and attained to an adult level by one and half years of age (Eitzman, 1970). Recently, we reported that the serum IgG level of newborn cynomolgus monkeys on the day of birth was nearly equal to the adult level and that it decreased during the first 3 months after birth, while IgA and IgM levels of the newborns were very low at birth (Fujimoto et al., 1982). Similar findings were reported also with the Japanese monkey (Takenaka and Takenaka, 1982). Thus, IgG may be considered to be the only immunoglobulin class that is transferable through the placenta from the mother to the fetus in non-human primates like in man.

This paper, a part of our immuno-physiological studies on maternofetal relationship, deals with the changing pattern of the IgG level in fetal blood with increasing fetal age in the cynomolgus monkey. Additionally, IgG and
TABLE I
Fetal and newborn IgG concentrations at different gestation ages

<table>
<thead>
<tr>
<th>Group</th>
<th>Gestation age (days)</th>
<th>Number of fetuses and newborns tested</th>
<th>IgG level (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetus</td>
<td>84</td>
<td>3</td>
<td>94, 170, 174</td>
</tr>
<tr>
<td></td>
<td>112</td>
<td>3</td>
<td>380, 600, 750</td>
</tr>
<tr>
<td></td>
<td>130</td>
<td>3</td>
<td>915, 1125, 1226</td>
</tr>
<tr>
<td></td>
<td>140</td>
<td>3</td>
<td>734, 1020, 1335</td>
</tr>
<tr>
<td></td>
<td>142–146</td>
<td>6</td>
<td>1466±208*</td>
</tr>
<tr>
<td>Newborn</td>
<td>150–157</td>
<td>9</td>
<td>1789±438*</td>
</tr>
<tr>
<td></td>
<td>158–168</td>
<td>19</td>
<td>2029±366*</td>
</tr>
<tr>
<td></td>
<td>169–170</td>
<td>5</td>
<td>2267±326*</td>
</tr>
</tbody>
</table>

* mean±S.D.

anti-measles and anti-streptolysin O antibodies in the newborns were compared with those in their mothers.

For this study, 51 pregnant cases were produced by the usual 3-days mating system described elsewhere (Honjo et al., 1975). The numbers of the fetuses and the newborns used are tabulated in Table I by the age class. In our system, the gestation age means the duration from the 1st day of mating to the day of cesarean section or natural delivery.

Blood specimens of fetuses were collected by heart puncture. In the newborn, blood was taken from the femoral vein within 24 hr after birth. Corresponding maternal sera were taken at the same time as the newborns' samples were taken. Sera were separated at 4°C and stored at −80°C until use.

IgG was purified from pooled adult cynomolgus monkey sera by ammonium sulfate precipitation and column chromatography on DEAE-cellulose and Sephadex G-200. Antisera against the cynomolgus monkey IgG were prepared by immunizing rabbits with purified IgG suspended in Freund's complete adjuvant. Purity of IgG and the monospecificity of the antisera were confirmed by immunoelectrophoresis.

IgG concentration in the serum was measured by the single radial immunodiffusion method. Concentration of purified IgG in a standard solution was determined by the Biuret method.

Anti-streptolysin O activity was determined with the streptolysin O reagent (Wako Co., Osaka).

The hemagglutination inhibition (HI) antibody titer to measles virus was determined by the procedure described previously by Suzuki et al. (1981).

The differences in the antibody level between newborns and their mothers were statistically examined for significance by the F-test.

Table I shows the IgG concentrations in cynomolgus fetuses and newborns of different ages. The IgG concentrations in three 84-day-old fetuses ranged between 94 and 174 mg/ml and increased with the increase of fetal
A marked increase in the fetal and newborn IgG levels was observed after more than 140 days of gestation age. As illustrated in Fig. 1, the IgG concentration in the fetus or the newborn (y in mg/ml) was statistically expressed as an exponential function of gestation age (x in days); that is

\[ y = 9.2 \times 10^{-0.8} x^{3.8} \]  
\( r = 0.94, \ p < 0.01 \)

Figure 2 shows HI antibody titers in cynomolgus fetuses and newborns of different ages. In two of the three 84-day-old fetuses, HI antibody was detected at low levels and increased with the increase of gestation age.

Antibody determinations in full-term newborns and their mothers are presented in Fig. 3 (a)-(c). Newborn cynomolgus monkey sera were significantly lower by about 10–15% than their mothers in regard to the IgG level (p<0.01) and the HI antibody titer (p<0.01). No significant difference was observed in the anti-streptolysin O antibody titer between newborns and mothers (p<0.05).

In summary, IgG and anti-measles antibodies were detected in sera of 84-day-old fetuses. Thereafter, anti-measles antibody titer increased in parallel with the increase in the IgG level. These findings suggest that the transplacental transfer of IgG starts by 84 days of fetal age. The subsequent in-
Fig. 2. HI antibody titers in fetuses and newborns of different gestation ages. Footnote: The open circle represents the fetus obtained by cesarean section; the closed circle the newborn.
crease in the fetal IgG level may also be due to the increase in transplacentally transferred IgG.
According to Hyvarinen et al. (1973), the IgG level of human fetus increased linearly in response to the fetal age from 24 to 42 weeks. In the cynomolgus monkey, however, the increase in the fetal and newborn IgG levels was expressed as an exponential function of gestation age. The results indicate that the transplacental transfer of IgG in the cynomolgus monkey occurs more efficiently in the last term of gestation than in man. Therefore, the last gestation period seems to be particularly important for transfer of IgG in the cynomolgus monkey.

The levels of IgG and anti-measles and anti-streptolysin O antibodies in human neonatal cord blood were significantly higher than in the maternal blood (Kohler and Farr, 1966; Allansmith et al., 1968; Toivanen et al., 1968). Contrary to these human data, Eitzman (1970) found that both the IgG level and the specific antibody level against the flagellar antigen of Salmonella in newborn rhesus monkey were lower than those in their mother monkeys. The present study also demonstrated that the IgG level and the anti-measles and anti-streptolysin O antibody titers in newborn cynomolgus monkeys were somewhat lower than those in their mother monkeys. These results seem to suggest that the transferability of IgG via placenta is rather lower in the monkey than in man, although the cynomolgus monkey placenta will regulate the transfer of immunoglobulin from the mother to the fetus in a manner similar to human placenta. Immunological characterization of the cynomolgus monkey will be helpful in the use of this animal species as a model for the study of perinatal immunology.

REFERENCES