Short Communication

IMMUNOGLOBULINS AND MEASLES ANTIBODY IN SERA OF NEWBORN Cynomolgus Monkeys AND IN MILK OF THEIR MOTHERS

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(Received May 23, 1983. Accepted June 17, 1983)

SUMMARY: The changes in the serum immunoglobulin (Ig) level and in the measles antibody titer were examined with colony-born infant cynomolgus monkeys from 0 day to 26 weeks in age. In addition, their mother-monkey’s milk was analyzed for Ig.

The decrease in the IgG level after birth was more remarkable in the infants born with high IgG levels than those born with low IgG levels. The IgM level prominently increased for the first 3 weeks after birth in the infants born with low IgG levels, while the increase was not so prominent in those born with high IgG levels. Anti-measles antibody titers decreased linearly with a half-life of 3.4±0.4 weeks after birth regardless of the titer at birth. A significant amount of IgA, a very small amount of IgM and little IgG were detected in the milk collected just after parturition. Ig of any class was no longer found in the milk collected one to 6 weeks after parturition.

These results suggest that the initial level of transplacentally transferred IgG must be one of the important factors influencing the subsequent development of infant monkey’s own immunoglobulin synthesis.

Maternal immunoglobulins (Ig) transferred through the placenta is said to protect the infant from various infections during the early postnatal period. Our previous study (Fujimoto et al., 1982) showed that IgG of infant cynomolgus monkeys decreased during the first 3 months after birth and thereafter started to increase, reaching an adult level at 5 years of age. The IgM level in infant monkeys increased with age from a very low level at birth, showing a characteristically rapid increase for the first month after birth. Recently, we reported that in the cynomolgus monkey fetuses the placental transfer of maternal IgG had started by 84 days of fetal age increasing with the fetal age, and nearly the same level as the maternal one was attained by the time of birth (Fujimoto et al., 1983). Such immunological development observed in the cynomolgus monkey from fetal through adult life is very similar to that in man as reported by Stiehm and Fundenberg (1966) and Buckley et al. (1968).

Allansmith et al. (1968, 1969) reported that the human infant born with...
a low IgG level showed little decrease in its IgG level after birth. According to Vlahović et al. (1973), the increase of IgG following its initial decrease after birth occurs earlier in the infants born with relatively low IgG levels than those born with normal adult IgG levels. Regarding the changes in the IgM level in human infants, however, no difference was observed between those born with low IgG levels and those with normal adult IgG levels (Vlahović et al., 1973). These results suggest negative effect of transplacentally acquired Ig on Ig synthesis in infants.

This paper deals with the changes in the serum immunoglobulin level and in the measles antibody titers in colony-born infant cynomolgus monkeys to find the relationship between the IgG level at birth and the development of infant’s immune response. The immunoglobulin levels in cynomolgus mother’s milk are also dealt with in this paper.

The infant cynomolgus monkeys examined were born from mothers who became pregnant by the usual 3-day mating system (Honjo et al., 1975). The gestation periods of these mother monkeys were 160–167 days, being within the average gestation length (163±5 days) of the cynomolgus monkey at Tsukuba Primate Center (Cho, 1981). Twelve infants were bled once a week until the 6th week after birth and the other 11 once every 3 weeks until 26 weeks of age. Milk of the mother monkeys of the 12 infants of the former group was collected once a week from 0 day to 6 weeks after parturition.

![Fig. 1. Sequential changes in the serum IgG level in infant cynomolgus monkeys from birth to 6 weeks of age.](image)
Blood was withdrawn from the femoral vein without anesthesia of the animals. Milk was collected by the same procedure as previously described (Nishikawa et al., 1976). Blood and milk sera were separated by centrifugation at 4°C and stored at −80°C until use.

IgG concentrations were determined by the single radial immunodiffusion (SRID) method using the rabbit anti-cynomolgus monkey IgG serum described previously by Fujimoto et al. (1983). For SRID of IgA and IgM, goat antihuman IgA and IgM sera were used, respectively (Fujimoto et al., 1982).

Hemagglutination inhibition (HI) titers of anti-measles antibody were measured by the procedure described by Suzuki et al. (1981).

Sequential changes in serum IgG levels in infant monkeys are presented in Fig. 1. The IgG levels in the newborn infants ranged from 11.0 mg/ml to 24.7 mg/ml at birth. In spite of wide variation at birth, the IgG levels converged at a point of around 10 mg/ml at the 4th to 5th week of age. In three infants born with IgG levels lower than 15 mg/ml, their initial levels remained unchanged throughout the first 3 weeks after birth. When the IgG level (y in mg/ml) in the infant was expressed as a function of age (x in weeks): y=a+bx

\[ y = a + bx \]

a statistically significant correlation (r=0.93, p<0.01) was observed between the IgG level at birth and the decreasing rate (b) of IgG until the 4th week of age (Fig. 2).

The two types of the change in the IgM level in infant monkeys seen in

Fig. 2. Correlation between the IgG level at birth and its decreasing rates until 4 weeks of age in cynomolgus monkey infants.

Foot note: Symbol b indicates the rate of decrease in the IgG level in the infant monkey when the IgG level (y in mg/ml) from birth to 4 weeks of age was expressed as function of age (x in weeks), as y=a+bx.
Fig. 3. Two types of the change in the IgM level in the first 6 weeks of life.
Foot note:  

a: Three infants born with IgG levels below 15 mg/ml.
b: Seven infants born with IgG levels not lower than 15 mg/ml.

Fig. 4. Sequential changes in the hemagglutination inhibition (HI) titer of anti-measles antibody in infant cynomolgus monkeys.

half-life = 3.4 ± 0.4 weeks
n: 11
the first 6 weeks of life are shown in Fig. 3. A rapid increase in IgM was observed at the age of 2 to 3 weeks with three infants who had IgG levels lower than 15 mg/ml at birth. Such increased IgM decreased again until the 6th week of life when a higher level than that at birth was still retained (Fig. 3-a). The IgM levels of seven infants born with IgG levels not lower than 15 mg/ml showed mild increases. Also in these seven cases, IgM decreased again to about 10% of the adult level at 6th week of age (Fig. 3-b).

The decrease in the HI titers of anti-measles antibody in infants is illustrated in Fig. 4. The HI titers just after birth varied greatly, ranging from $2^8$ to $2^{10}$. Subsequently, the titers lowered linearly with the increase of age regardless of the titers and the IgG level at birth. The half-life period of the anti-measles antibody calculated from the HI titer was estimated at $3.4 \pm 0.4$ weeks.

With regard to Ig in milk, the levels of IgA, IgM and IgG in the milk collected immediately after parturition were $44.0 \pm 24.5\%$, $7.2 \pm 4.0\%$ and $0.9 \pm 0.2\%$ of respective adult serum levels. No Ig of any class was detected in milk collected one to 6 weeks after parturition.

It was reported that the level of circulating IgG affects the rate of its catabolism in man (Fahey and Robinson, 1963; Waldman and Strober, 1969). The present study revealed that the infant monkeys born with high IgG levels had a trend of more pronounced decrease in IgG than those born with low IgG levels. At the same time, anti-measles antibody, an example of transplacentally transferred IgG of maternal origin, decreased linearly after birth irrespective of its titer at birth. These findings suggest that the infant monkeys born with low IgG levels synthesized more IgG than those born with high IgG levels. Such a difference in quantity of self-synthesized IgG between those born with high and low IgG levels may indicate that the humoral immune response must occur earlier or more actively in the latter than in the former.

Takenaka and Takenaka (1982) reported that the IgM level of infant Japanese monkeys rose abruptly during the first 20–30 days after birth, and thereafter decreased until 50–60 days of age. Similar changes in the IgM level were observed also in our infant cynomolgus monkeys. Furthermore, we have demonstrated that the increase in the IgM level after birth was more prominent in the infant born with a low IgG level than that born with a high IgG level. This also supports the above-mentioned assumption that the IgM response must have been well retained longer to compensate their low IgG available at birth.

With the infant monkey nursed by its mother, transfer of Ig in milk, if present, to the infant via the gastrointestinal tract has to be considered. However, only the milk collected immediately after the parturition contained IgA of about one-half the level in adult serum, a trace of IgM and little IgG. Therefore, the mother's milk contributes very little, if any, to the increase in the serum Ig level in the infant monkey.

In conclusion, the development of immune competence in infant cyno-
molgus monkeys is influenced partly by the level of serum IgG of maternal origin transferred via placenta.

REFERENCES


