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Congenital Hypersensitiveness Transmitted to the Third Generation.*

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In studies on the duration of passive hypersensitiveness we[1] have shown that an animal, passively sensitized *in utero* by passage of antibodies from the mother via the placental route, loses its hypersensitiveness in about 2½ months.

The purpose of the studies undertaken at this time was to determine the duration of active hypersensitiveness which results from sensitization produced in the fetal stage of the guinea pig by passage of antigen via the placental route a few days prior to birth.[2] Thus far we have determined that the animal actively sensitized *in utero* retains its hypersensitiveness for at least 6 months.

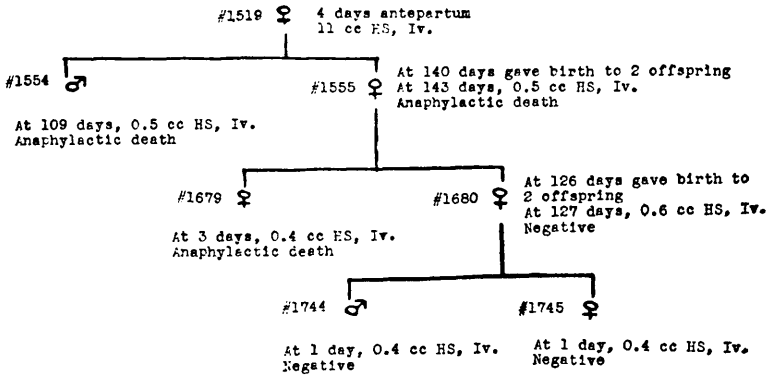
On account of the persistence of this active state in the second generation, it is possible for an animal so sensitized to transmit her antibodies to the fetus and thus passively sensitize the offspring of the third generation. These 2 phases of transmission of hypersensitiveness are illustrated by the following family in which we have a pregnant female injected with 11 cc. horse serum 4 days before parturition. The 2 offspring (second generation) were shown to be actively sensitized by the fact that they exhibited fatal anaphylaxis at 109 and 143 days respectively. The third generation was shown to be passively sensitized, for 1 animal died when 3 days old, requiring no incubation period for the establishment of anaphylaxis. The sensitization had definitely worn off, for the second animal of this generation was shown to be negative at 127 days. These criteria have already been established in the previous studies referred to. The 2 animals of the fourth generation were negative at birth.

To summarize, we have a mother guinea pig who receives a sensitizing dose of horse serum a few days before parturition and thus actively sensitizes her offspring via the placenta. The second generation—in which the active state of hypersensitiveness persists—in turn passively transmits a state of hypersensitiveness to its off-

*This work is being carried on under "The Crane Fund for the Study of Allergic Diseases in Children."

[1] Ratner, B., Jackson, H. C., and Gruehl, H. L., *J. Immunol.*, 1927, xiv, 291.

[2] Ratner, B., Jackson, H. C., and Gruehl, H. L., *J. Immunol.*, 1927, xiv, 303.



spring, the third generation. This passive sensitization wears off in the third generation, before the birth of the fourth generation.

Thus the transmission of hypersensitiveness here is *congenital* and either active or passive in nature. When it is passive it can be transmitted only to the succeeding generation, when it is active it may be transmitted through a second generation to a third generation.

This mechanism, we believe, is intimately associated with the problem of the sensitization of the human fetus.[3]

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Effect of Calcium and Potassium on Action of Ephedrine.

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The action of ephedrine on the isolated heart was studied by several investigators, among them Chen and Meek,[1] Barlow and Sollman,[2] and Da Costa.[3] The latter also made observations on the influence of calcium and potassium upon the paralyzing action of ephedrine on the heart. It seemed, nevertheless, desirable to repeat these experiments especially for the purpose of using them as a basis of comparison with the effects of ions on the action of this substance. We, therefore, carried out experiments with ephedrine and different amounts of calcium and potassium, and also when either one or

[3] Katner, B., *Am. J. Dis. Child.*, 1928, xxxvi, 277.

[1] Chen and Meek, *J. Phar. and Exp. Ther.*, 1926, xxviii, 31.

[2] Barlow and Sollman, *J. Phar. and Exp. Ther.*, 1927, xxx, 21.

[3] Da Costa, S. F. G., *Comp. rend. Soc. de biol.*, 1927, xcvi, 1332.