lose weight more rapidly than unharnessed ones. In one experiment 37 twenty-eight-day-old animals were given the Sherman and Bourquin vitamin G deficient diet until they had reached stationary weight. They were then divided into harnessed and unharnessed groups and each rat was given a vitamin G supplement of 2.0 gm. of skimmed milk powder per week for a period of 8 weeks. The average gain of the unharnessed group for the first 4 weeks was 26.9 gm. with an A.D. of ±2.0 gm., while the average gain of the harnessed rats was 15.4 gm. with an A.D. of ±1.3 gm. The average gain of the unharnessed rats at the end of 8 weeks was 38.8 (A.D. ±4.0) gm., and of the harnessed rats 32.1 (A.D. ±2.1) gm. The prevention of the practice of coprophagy not only decreased the growth rate on limited supplements of vitamin G but also decreased the variation in our experimental results.

6373

Placental Transmission of Alimentary Anaphylaxis.

BRET RATNER.

From the Departments of Pediatrics and Immunology, New York University and Bellevue Medical College, and Children's Medical Division, Bellevue Hospital.

The human and guinea pig placentae are permeable to native proteins and to anaphylactic antibodies, therefore, sensitization may be actively or passively induced in the fetus.[1] It has further been demonstrated that the female guinea pig may sensitize its offspring *in utero* by the inhalation of dry antigenic dusts during pregnancy.[2] Rosenau and Anderson[3] first showed that guinea pigs can be sensitized through feeding. In the experiments detailed below it is shown that a pregnant guinea pig fed an antigenic substance can become sensitized and, in addition, actively sensitize her fetus *in utero*. Pregnant women who are allergic can passively sensitize their offspring to the same substance to which they are sensitive.[4] Normal pregnant women who eat excessively of protein foods may actively sensitize the fetus *in utero,* and when such offspring partake of these particular foods for the first time may manifest allergic reactions.[5]

[1] Ratner, B., Jackson, H. C., and Gruehl, H. L., *J. Immunol.*, 1927, **14**, 249.
[2] Ratner, B., and Gruehl, H. L., *J. Exp. Med.*, 1929, **49**, 833.
[3] Rosenau, M. J., and Anderson, J. F., *Hyg. Lab. Bull.*, 1906, **29**, 67.
[4] Ratner, B., and Greenburgh, J. E., *J. Allergy*, 1932, **3**, 149.
[5] Ratner, B., *Am. J. Dis. Child.*, 1928, **36**, 277.

Large normal female guinea pigs were fed horse serum one to several days before parturition. The animals were placed in an empty metal cage without food or water for 3 to 5 hours before the sensitizing feedings were given, in order to partially empty their stomachs. They were fed by pipette. Any liquid which dripped from their mouths was caught in a dish, taken up in the pipette and refed to the animal, so that the total amount ingested was recorded. If the liquid was given too fast, the animals would choke and cough, so that extreme caution was observed in emptying the pipette very slowly. If an animal did cough, this was carefully noted, in order that false results due to possible passage of the antigen into the respiratory tract would be avoided. The animals took 25 cc. readily at one feeding and where larger amounts were given, 25 cc. feedings at least an hour apart were administered.

Pregnant animals must be handled with extreme care in order not to precipitate a miscarriage. In spite of such precaution, these experiments were difficult to consummate for often the mother animals died during or soon after parturition, or the offspring did not live long enough to be tested. We succeeded in carrying out tests on 23 families. An additional difficulty was the timing, so that the feeding might be given as near parturition as possible, which is necessary to meet the criteria we have laid down[1] for active sensitization of a fetus *in utero.*

At varying intervals after birth, the offspring were given their primary injection of horse serum. In 8 of the families one or more of the offspring, or 25%, were shown to be sensitive as a result of the antepartum feedings of the mother. The mothers in turn were given their primary injection of horse serum, usually on the same day on which the offspring were tested, and 70% of these were shown to have become sensitized, Table I.

In 3 families (Nos. 1, 12, 16) the offspring were sensitized to equal degrees. The 3 offspring of family No. 16 died in anaphylaxis from their first injection of horse serum. In family No. 1 the offspring were born the day following the feeding of the mother, therefore, the sensitization of the offspring demonstrated 48 days after birth must have been active, due to the passage of the antigen via the placenta into the fetal circulation.

Three other litters (Nos. 6, 7, 8) also fall into the category of active sensitization *in utero,* since the interval of time between the mother's feeding and the birth of the offspring was only 4 days in 2 instances, and 5 days in the other. In family No. 8 the one offspring, injected one day postpartum, was negative, showing that

TABLE I.

Placental Transmission of Alimentary Anaphylaxis.

No.	Am't fed pregnant animal cc.	Days Ante-partum	Offspring			Mother	
			Age Days	No.	Reaction after 1st injection	Days post-partum	Reaction after 1st injection
1	100	1	48	1	+	48	+
			,,	2	+		
2	100	1	38	1	0	38	++
			,,	2	0		
3	130	1	43	1	0	43	+
			,,	2	0		
4	200	2	26	1	0	28	++
			,,	2	0		
			,,	3	0		
5	100	2	60	1	0	60	+
			,,	2	0		
			,,	3	0		
			,,	4	0		
6	175	4	50	1	0	50	+
			,,	2	0		
			,,	3	+		
7	200	4	42	1	++	42	+
			,,	2	+		
8	160	5	1	1	0	25	+
			25	2	+		
			,,	3	+		
9	200	8	28	1	0	28	+
			,,	2	+		
			,,	3	++		
10	280	8	6	1	0	41	+
			41	2	0		
11	200	9	21	1	+	46	+
			46	2	0		
			,,	3	0		
			,,	4	0		
12	200	13	22	1	+	22	++++
			,,	2	+		
			,,	3	+		
13	440	14	2	1	0	35	+++
			35	2	0		
14	520	16	13	1	0	33	+
			33	2	0		
15	580	17	13	1	0	13	+
			,,	2	0		
16	460	19	6	1	++++	6	++
			,,	2	++++		
			,,	3	++++		
17*	80	1	4	21	0	28	0
to	to	to	to			to	
23	200	9	60			60	

0, no anaphylactic reaction; +, dyspnea and scratching; ++, marked dyspnea, convulsive movements; +++, severe dyspnea, convulsions, collapse, final recovery; ++++, typical anaphylactic death with completely ballooned lungs, occurring within a few minutes after injection.

* 7 families, with a total of 21 offspring, were entirely negative. 25% of the total offspring were sensitized as compared with 70% of the mothers, and 38% of the offspring of the positive mothers were sensitized.

no antibodies were transmitted, while the other 2 animals of the same litter were positive at 25 days—a long enough period for the transmitted antigen to cause the production of sensitizing antibodies in the young animals.

In family No. 9 the 3 offspring gave varying reactions. These animals, born 8 days after the mother's sensitizing feedings, received a combination of antigen and antibodies which may account for the varying reactions. In family No. 11 one offspring was positive at 21 days while the other 3 were negative at 46 days. These animals may have received a small amount of early formed antibodies which disappeared before the 46-day period.

It is interesting that in some instances the offspring gave greater reactions than the mother, and in others the reverse was true.

When transmission of sensitization was first described by Rosenau and Anderson,[6] it was the result of transmission of antibodies from mothers to offspring and corroborative evidence for this has been given by various investigators. Wells[7] first showed that guinea pigs could be passively sensitized *in utero* to the natural food ingested by the pregnant female. With this in mind, our original work was started to study the mechanism of sensitization *in utero*. We believe that the whole train of evidence presented by us in previous studies shows clearly that not only can fetuses be sensitized passively, but that active sensitization may also occur. Further, this active sensitization *in utero* can be induced by parenteral injection, by inhalation, and finally, as demonstrated by the above data, by alimentation.

We believe that "congenital protein hypersensitiveness" is thus clearly established, both in the human being and lower animal possessing a permeable placenta, and is significant to the experimenter and to the clinician in all studies on hypersensitiveness, infection, or immunity in the young.

---

[6] Rosenau, M. J., and Anderson, J. F., *Hyg. Lab. Bull.*, 1906, **29**, 73.

[7] Wells, H. Gideon, *J. Infect. Dis.*, 1911, **9**, 147.