FACTORS OF ANIMAL IMMUNE REACTIVITY

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The question of the factors determing immune reactivity of an animal has formed the object of study by a number of investigators. They noted [1, 3] that repeated immunization contributed to formation of antibodies. However M. I. Raisky was the first to make a proper assessment of the significance of this phenomenon for the process of immunogenesis. He established that as a result of initial immunization the animal organism undergoes a significant transformation, and thanks to this, acquires the capacity to respond, with a more intense precipitin-formation reaction, to repeated introduction of the same type of antigen.

The correctness of the law-governed process established by M. I. Raisky was then confirmed by his works and other teachings [1, 5, 6].

In order to study the immuno-biological law-governed principles underlying the process of formation of antibodies and also to clarify the causes and conditions influencing this process, we made an analysis of extensive experimental, material gathered during 15 years on sera containing precipitin obtained for forensic medicine purposes.

EXPERIMENTAL METHODS

We used in our study different varieties of rabbits (chinchilla, blues, albinos) — which were immunized with the blood serum of various species of animals — horse, ox, sheep, pig, cat, hen and also with human blood serum.

EXPERIMENTAL RESULTS

All the animals were by no means able to respond to immunization with a sharply marked antibody-formation reaction. 506 rabbits out of 2171, i.e., 23.3 per cent did not produce precipitins at a titer of 1: 1000 either as a result of initial or as a result of repeated immunization. This was a so-called relatively refractory or weakly immunogenic group of rabbits. 925 rabbits i.e., 42.6 per cent, produced precipitins at a sufficiently high titer (1:10,000 and over). Finally there was a fairly large group of experimental animals - 740 - i.e., 34.1 per cent, which responded with a precipitin formation reaction, which however, was at a comparatively low (1:1000 and 1:5000) titer. The cause of the variability in the immune reactivity of the various animals in response to introduction of the same antigen has so far not been established with certainty. Our knowledge on this question does not go beyond indisputably correct, but too general, concepts asserting the existence of individual immuno-biological peculiarities of the animal organism.

However, as our investigations showed, besides individual peculiarities of the organism, of great importance for the immuno-reactivity of the animal is the species specificity of the antigens, used in immunization. This is demonstrated by Table 1.

TABLE 1

Formation of Precipitins in Rabbits in Relation to the Species Specificity of the Antigen.

Species of albumin used for immunization	Total number of animals	Results of immunization						
		Not producing precipitatins		Producing precipitins at a titer				
				1:10,000 and more		1:1000-1:5000		
		Number of animals	% of total number	Number of animals	% of total number	Number of animals	% of total number	
Serum of hen	93	10	10.7	63	67.8	20	21.5	
Serum of horse	243	35	14.4	117	48.1	91	37.5	
Serum of sheep	177	27	15.3	100	56.5	50	28.2	
Serum of pig	271	46	16.9	140	51.7	85	31.4	
Serum of ox	245	43	17.9	125	51.0	77	31.1	
Serum of human	863	231	26.8	299	34.6	333	38.6	
Serum of dog	172	65	37.8	56	32.5	51	29.7	
Serum of cat	107	49	45.8	25	23.4	33	30.8	

It is clear from Table 1 that in the largest number of experimental rabbits (89.3%) precipitins formed in response to immunization with serum albumins of hens. In this experiment only 10.7% did not produce an antibody.

Formation of precipitins proceeded actively in the rabbits in response to introduction of horse serum. Of 243 rabbits, only 35, i.e. 14.4%,proved incapable of producing precipitins while the remaining group of experimental animals (85.6%) produced antibodies at a sufficiently high titer. Less often the rabbits formed precipitins upon immunization with sheep serum albumins (84.7%), pig (83.1%), ox (82.1%), human (73.2%) and in particular cases upon immunization with the serum of a dog (62.2%) and a cat (54.2%). Of 172 rabbits immunized with dog serum 65, i.e., 37.8%, did not produce precipitins, and of 107 experimental animals, immunized with cat serum, 49, i.e., 45.8% showed themselves to be incapable of producing antibodies in the same experimental conditions as in immunization of the rabbits with other serum albumins.

It is clear from Table 1 that the largest number (67.8%) of rabbits producing precipitin in the sera at the highest titer (1:10,000 and over) is achieved with immunization by the serum albumins of hens, somewhat less with immunization by the sheep serum albumins (56.5%), pig (51.7%), ox (51%), horse (48.1%).

As a result of immunization of the rabbits with the human blood serum,precipitins at a high titer (1:10, 000) were obtained only in 34.6% of the animals,and an even smaller number of rabbits produced such sera upon immunization with dog serum albumins (32.5%) and in particular cases with cat serum albumins (23.4%).

The facts outlined give grounds for assuming that the capacity of the organism to respond with production of antibodies depends not only on the individual characteristics of the animal but on the species specificity of the antigen taken for immunization.

The serum albumins of a cat, dog and man were less effective antigenic stimuli for the rabbits than the serum albumins of a horse, ox, pig, sheep and in particular cases of a hen. The albumins of birds (hen), the farthest removed physiologically and hence antigenically from rabbits, proved to be the most effective antigenic stimulus. On the other hand, the serum albumins of a cat proved to be a less effective antigenic stimulus for the rabbits. Upon immunization of the rabbits with the cat albumins the number of animals giving precipitin sera at a high titer was almost three times less than with immunization by the hen serum albumins.

Our investigations also showed (Table 2) that the capacity of the organism to produce precipitins stands in a definite relationship to the weight of the immunized animal.

It will be seen from Table 2 that rabbits of the largest weight produced precipitin sera of high titer in relation to all the eight species of serum proteins without exception, with which the rabbits were immunized, which indicates the law-governed pattern of this phenomenon.

TABLE 2

Formation of Precipitins in Relation to Weight of Animal.

Species of albumin used for immunization	Total number of animals (weight from 1500 to 2000 g)	Giving serum titer of 1:10,000		Total number of animals (weight 2000 g and over)	Giving serum at a titer of 1:10,000 and over	
		number of animals	% of total number		number of animals	% of total number
Serum of human	294	77	26.2	473	163	34.4
Serum of horse	83	28	33.7	145	85	58.6
Serum of ox	83	26	31.3	159	97	61.0
Serum of sheep	67	36	53.7	99	60	60.6
Serum of pig	92	35	38.0	169	103	60.9
Serum of dog	48	17	35.4	106	43	40.6
Serum of cat	35	7	20.0	81	30	37.0
Serum of hen	17	11	64.7	52	42	80.8
Total	719	237	32.9	1284	623	48.5

The rabbits weighing between 1500 and 2000 g corresponded usually to 5-6 month old animals, consequently, one may speak of a less marked capacity to form antibodies in younger rabbits. The results of our observations on the dependence of precipitin formation on weight or age of the rabbits is in complete accord with the known facts in immunology [1] regarding the less marked immunoreactive properties in young animals than in old ones.

We set out in Table 3 the results of our investigation of the process of antibody formation in relation to the sex of animals.

TABLE 3

Formation of Antibodies in Relation to Sex of Animal.

Species of albumin used for immunization	Sex of animals	Total number of animals	Not producing precipitins		Producing precipitins, at a titer			
					1:10,000 and more		1:1,000 and 1:5000	
			number of animals	% of total number	number of animals	% of total number	number of animals	% of total number
Serum Human	Male	392	95	24.3	166	42.3	131	33.4
	Female	368	121	32.9	117	31.8	130	35.3
Serum Horse	Male	107	12	10.2	66	61.7	29	27.1
	Female	109	23	21.1	51	46.8	35	32.1
Serum Ox	Male	115	15	13.0	69	60.1	31	26.9
	Female	112	29	25.9	55	49.1	28	25.0
Serum Sheep	Male	65	7	10.8	46	70.7	12	18.5
	Female	94	20	21.3	53	56.4	21	22.3
Serum Pig	Male	123	16	13.0	72	58.6	35	28.4
	Female	142	30	21.1	76	53.6	36	25.3
Serum Dog	Male	74	29	39.2	28	37.8	17	23.0
	Female	88	32	36.4	31	35.2	25	28.4
Serum Cat	Male	55	22	40.3	19	34.5	14	25.5
	Female	52	23	44.2	13	25.0	16	30.8
Serum Hen	Male	51	3	5.9	36	70.6	12	23.4
	Female	39	7	17.9	28	71.8	4	10.3
Total	Male	982	199	20.3	502	51.1	281	28.6
	Female	1004	285	28.4	424	42.2	295	29.4

It is clear from Table 3 that upon immunization with the proteins of hens both males and females just as frequently produced precipitins at a high titer. Upon immunization with dog proteins the percentage of less active rabbits was slightly higher in the males (39.2%) than in the females (36.4%).

As our material demonstrates there is no essential difference between male and female rabbits in their capacity to form precipitins with serum albumins. The slight difference existing between them may be attributed to such causes as pregnancy, birth, feeding of young, factors with an indisputable influence on the function of antibody formation. However, we did not succeed in following up the significance of these factors.

Our investigations showed that the organism's capacity to respond with production of precipitins depends also on the repetitiveness of the immunizing stimulus produced by the same type of antigen.

TABLE 4

Formation of Precipitins as a Result of Initial Immunization and of Re-immunization.

Species of albumin used for immunization	Total number of animals	Serum obtained at titer 1:10,000			
		after 1st course of immunization		after re-immunization	
		number of animals	% of total number	number of animals	% of total number
Serum of ox	245	36	14.7	125	51.0
Serum of sheep	177	29	16.4	100	56.5
Serum of pig	271	60	22.1	140	51.7
Serum of horse	243	26	10.7	117	48.1
Serum of human	863	155	17.9	299	34.6
Serum of dog	172	4	2.3	56	32.5
Serum of cat	107	6	5.6	25	23.4
Serum of hen	93	17	18.3	63	67.8
Total	2171	333	15.3	925	42.6

A 2, 3, or 4-fold or larger increase in the immuno-reactivity of the animals as a result of staggered (in 3 weeks, 2-4 months) re-immunization, as is clear from Table 4, was seen in all groups of rabbits, independent of the species specificity of the antigen applied for immunization. These findings testify to the constancy of the phenomenon and completely concur with the lawful sequence observed by M. I. Raisky in 1915 - increase in immuno-reactivity of the organism as a result of initial immunizing stimulation.

Thus, our investigations showed that the capacity of the organism to produce precipitins depends not only on the individual features of the animal but is to a considerable degree also determined by the species specificity of the antigen, used in immunization, weight (age) of the immunized animal, repetitive nature of the immunizing stimulation by one and the same type of antigen and also to a certain extent by the sex of the animal.

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