

MICROBIOLOGY AND IMMUNITY

ON THE FACTORS AFFECTING THE SPECIFICITY OF IMMUNE SERUM FORMATION

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As is known, animals respond fairly frequently to the administration of one type of antigen by the formation of antibodies to other types of antigens also, which had not been used in the immunization. For example, rabbits immunized with human serum not infrequently develop antibodies not only to human protein, but also to the serum proteins of other kinds of animals. Some rabbits develop additional (nonspecific) antibodies to the serum protein of dogs and cats, others to the proteins of horses and sheep, still others to hog protein, still others to all the above antigens, etc. The reason for the formation of such precipitins has not been studied until the present. No satisfactory explanation has yet been given, why, when rabbits are immunized with the same antigen, some animals form specific sera, others, on the contrary, develop sera containing additional (nonspecific) antibodies and of the most varied composition at that. It has not yet been possible to establish any regularity of this complex process.

The present investigation is devoted to the study of the factors affecting the specificity of the formation of immune precipitating sera.

EXPERIMENTAL METHODS

Sera were obtained from rabbits immunized with the serum proteins of horse, bull, ram, hog, cat, dog, hen and man.

Each serum, if its titre was high enough, i.e., gave a precipitation reaction with the homologous antigen taken in a dilution of 1:10,000 after not more than 10 minutes, was tested for specificity by us against 7 different antigens taken in a dilution of 1:1000. For example, serum specific against human protein was tested for specificity against the proteins of a bull, ram, hog, horse, dog, cat and hen. Serum specific against horse protein, in addition to these antigens, was tested against human protein, etc. Sera were considered specific which did not give a precipitation reaction with heterologous proteins in the course of 30 minutes, and within an hour with human serum.

EXPERIMENTAL RESULTS

Much experimental material, a single method of immunizing and testing the sera, exceptional case in studying them in accord with the requirements of forensic medicine for which the sera were prepared, allowed us to find some regularities which lie at the basis of the process of forming specific and additional (nonspecific) antibodies. The data regarding the specificity of the precipitating sera are presented in Table 1.

The experiments showed that the ability of the system to respond with the reaction of additional (nonspecific) antibody formation is inversely proportional to the duration of the immunization: specific sera are obtained several times more often in response to the initial immunization than in response to prolonged, multiple immunization.

TABLE 1

Specificity of Sera After an Initial Course of Immunization and Re-immunization

In response to what type of protein the sera were obtained	Course of immunization	Number of sera studied	Number of these found to be specific	
			absolute number	%
Man, horse, hog	First	219	66	30.1
The same	Re-immunization	458	34	7.4

TABLE 2

Specificity of the Sera Depending on the Generic Origin of the Antigen Used for Immunization

Types of protein used in immunization	Number of sera studied	Number of them proving to be nonspecific against the proteins of						
		Ram	Hog	Horse	Man	Cat	Dog	Hen
Bull	143	143	115	94	92	78	62	0
Ram	118	Bull	Hog	Horse	Man	Cat	Dog	Hen
		118	77	65	48	40	40	0
Hog	161	Bull	Ram	Horse	Man	Cat	Dog	Hen
		99	85	84	81	81	72	0
Horse	129	Hog	Man	Bull	Ram	Cat	Dog	Hen
		97	91	89	87	85	74	0
Man	346	Cat	Dog	Hog	Horse	Bull	Sheep	Hen
		304	287	258	253	228	215	0
Cat	27	Dog	Man	Hog	Ram	Horse	Bull	Hen
		27	24	19	17	17	15	0
Dog	60	Cat	Man	Hog	Ram	bull	Horse	Hen
		58	50	47	39	34	17	0
Hen	71	Bull	Ram	Hog	Horse	Man	Cat	Dog
		0	0	0	0	0	0	0

The ability of the system to develop additional antibodies, as seen from Table 1, depends also on the individual peculiarities of the animals. Thus, in spite of completely identical conditions of immunizing and maintaining the experimental animals, 7.4% of the rabbits responded by developing only specific antibodies. However, what these individual peculiarities of the animals are remains unknown.

The specific or nonspecific nature of the immunological reaction of the rabbits depends also, as our experiments showed, on the generic origin of the antigens used for immunization (Table 2).

It is apparent from Table 2 that all the precipitating sera obtained against hen proteins were specific and did not react with the serum proteins of mammals—bull, ram, hog, horse, man, cat and dog. In their turn, all the precipitating sera against mammalian protein (bull, ram, hog, horse, man, cat and dog) did not give a nonspecific precipitation reaction with the proteins of hens. These facts indicate that the immunization of rabbits with the serum proteins of birds (hens) is not accompanied by the formation of additional antibodies against the proteins of distant genera of animals and, on the contrary, immunization of rabbits with the serum proteins of mammals (bull, ram, hog, horse, man, dog, cat) does not lead to the formation of additional precipitins against the serum proteins of a different class—birds (hens).

The ability of this or that individual to respond with the reaction of additional (nonspecific) antibody formation appeared accidental at first, entirely dependent on the individual peculiarities of the immunized animal only. However, analysis of a large number of experimental material permitted us to establish that the nature of the nonspecific reaction with which rabbits respond to parenteral administration of serum proteins is not chance and is determined by the nature of the antigens used in the immunization.

As is seen in Table 2, the precipitating sera obtained against bull protein contained antibodies against ram proteins in all cases, precipitins against hog proteins in 115 sera of 143, against horse proteins in 94, against human protein in 92, against cat protein in 78, and against dog protein in 62. A similar reaction was observed in rabbits during immunization with ram protein also.

A similar type of reaction of additional antibody formation was observed in the rabbits when immunized with hog proteins. The sera of these rabbits contained additional antibodies to bull proteins, less often to ram, horse, human, cat and especially dog proteins.

Another type of immunological reaction of additional antibody formation was observed in rabbits when immunized with the serum proteins of cat and dog. The precipitating sera against dog proteins contained antibodies to cat proteins in almost all cases (58 out of 60); the majority of sera contained additional antibodies against human and hog proteins; somewhat less often additional antibodies against ram, bull and, especially, horse proteins were found.

The sera of rabbits immunized with cat proteins gave a similar reaction. A similar immunological reaction of additional antibody formation was observed in rabbits immunized with human serum proteins.

The third type of immunological reaction of additional antibody formation was observed in rabbits immunized with horse proteins. Sera against horse proteins contained additional antibodies most often against hog proteins, second in order of frequency were found antibodies to human proteins, then with constantly lessening frequency were found additional antibodies to bull, ram, cat and least often to dog proteins.

Thus, our investigations showed that rabbits most often respond by forming additional antibodies against the serum proteins which have the greatest antigenic similarity to the proteins used for immunization. When immunizing rabbits with the serum proteins of a bull, antibodies are always formed against sheep proteins and vice versa. Immunization of rabbits with the serum proteins of a cat always, or almost always, lead to the formation of antibodies against dog proteins and vice versa. The serum proteins of bulls, rams or hogs always produce a similar reaction of additional antibody formation when one of these types of proteins is used to immunize rabbits. In response to administration of one of these proteins (bull, ram or hog) rabbits most often develop additional antibodies in response to the two other types of serum proteins. Rabbits immunized with bull, ram or hog proteins also react similarly in forming other additional antibodies. Most often they form additional antibodies to horse and human serum proteins and somewhat less frequently to cat and dog proteins.

Another type of reaction of additional antibody formation is observed in rabbits when immunized with cat, dog or human serum proteins.

In response to the administration of one of these types of proteins, rabbits most often develop additional antibodies against the two other types of serum proteins. The rabbits react analogously with respect to other additional antibodies. Most often they form additional antibodies against hog serum proteins and somewhat less often to horse, bull and ram proteins.

Horse proteins cause a reaction of additional antibody formation different from the first two types of reactions.

Apparently at the basis of the similarity or difference in the rabbits' reaction of additional antibody formation is the greater or lesser similarity between the serum proteins of mammals. The serum proteins of the bull, ram, and hog cause similar immunobiological reactions of additional antibody formation and, consequently, have the greatest antigenic similarity among themselves. The serum proteins of man, with respect to the ability to cause the formation of additional antibodies have the greatest antigenic similarity to the serum proteins of cat and dog and the least similarity to the serum proteins of bulls and rams.

The serum proteins of the horse, with respect to the nature of the reaction of additional antibody formation they cause in rabbits, should be separated into a special intermediate group which is similar antigenically to the serum proteins of the bull-ram-hog group as well as to the serum protein group of man-cat-dog.