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Effect of Intravenous Bacterial Filtrates on Skin Tests and Local Infections.

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In a previous report[1] we have shown that rabbits are often naturally allergic to filtrates of many gram negative bacteria. It was suggested that this allergy is due to the overwhelming predominance of gram negative organisms in the upper respiratory tract of these animals and to the fact that chronic infections are quite common in this region. Positive skin tests are given not only to broth filtrates of *B. lepisepticum* and other bacteria representing the normal nasopharyngeal flora, but to the other organisms such as *B. coli, B. influenzae* and even to such an organism as meningococcus, to which the animal has never been directly exposed. Rabbits lacking this natural allergy develop it about one week after infecting the skin with a virulent strain of *B. lepisepticum.* In fatal infections, skin allergy does not appear. When large necrotic lesions develop, a positive skin test may not be elicited until the 15th day or later, but before healing begins, it becomes quite striking and is of valuable prognostic import. The intensity of reaction usually recedes with the clearing up of the infection and the development of a generalized immunity. During this phase of acquired allergy, the animal reacts non-specifically to the filtrates of many gram negative organisms of widely different groups.

When filtrates of strains of *B. lepisepticum* and other gram negatives are injected intravenously, the reaction is quite different in the allergic and non-allergic rabbit. The highly sensitized animal often develops diarrhea about 20 minutes after the injection. He rapidly goes into shock and dies in convulsions within a few hours, even

[1] Hanger, Franklin M., PROC. SOC. EXP. BIOL. AND MED., 1927, xxv, 230.

when one cc. or less of the filtrate is used; while the non-allergic animal usually will survive 15 cc. or more without marked symptoms. Filtrates from highly virulent strains of *B. lepisepticum* occasionally will kill a non-allergic rabbit. Rabbits completely recovered from a severe *B. lepisepticum* infection and with skin reactions still moderately strong, show no ill effects from very large doses of the filtrate. The striking lesion in animals dying from filtrate injections is marked congestion of the lungs and bronchi with hemorrhage. Occasionally there are hemorrhages in the skin and other organs.

Skin tests made within an hour of intravenous injections of potent filtrates are negative even in animals that usually give strong reactions. Various bacterial suspensions and India ink intravenously produce a similar effect. Skin reactivity is often permanently diminished in an animal receiving one or more intravenous injections. When the skin test precedes the intravenous filtrate by several hours, obliteration does not occur, but an *intensification* of the local reaction is seen, and the site of inoculation often shows bluish discoloration with areas of petechial hemorrhages. In most instances, an extensive local necrosis occurs. Histologically the lesions show marked swelling and disruption of the capillary endothelium. There are minute thrombi in these vessels and many red cells loose in the intercellular spaces. We have never observed this phenomenon except among rabbits naturally allergic (See chart of animals 192 and 198) or rendered allergic by a previous infection. (See chart of animals 208 and 153.) The intensity of the reaction is roughly proportional to the allergy of the animal to the filtrate used. Necrosis is most extensive when the skin test is made 24 hours before intravenous injection and is rare when less than 12 or more than 48 hours have elapsed.

This reaction appears to be non-specific. Skin test sites made with filtrates of R. D. (a virulent strain of *B. lepisepticum*) or of 24/3 and X (non virulent strains of *B. lepisepticum*) or of a colon bacillus, react similarly when a variety of filtrates are given intravenously (See Animals 153 and 150). Occasional rabbits show slight natural allergy to filtrates of streptococcus (See Rabbits 172 and 192). In such animals skin reactions induced by filtrates of *Streptococcus* likewise become hemorrhagic or necrotic when filtrate of one of the above mentioned gram negative organisms is given intravenously. Non-specific irritants such as turpentine, rarely give the reaction (See Rabbits 192, 169, 137 and 172), while plain broth controls have been constantly negative.

We have made but few attempts to study the influence of im-

venous filtrate	R. D.	24/3	X	Haem. Strep.	*B. coli*	Turpentine	R. D. skin infection	travenous	i. v.	R. D.	
+++	V	V					V	R. D.	2 mils.	Severe necrosis	Se ne
++	V	V					V	R. D.	3 mils.	Severe necrosis	Se ne
+++	V	V						*B. coli*	3 mils.	Severe necrosis	Sl ne
+	V	V		V		V		R. D.	3 mils.	Severe necrosis	Sl ne
+++	V		V		V			R. D.	3 mils.	Severe necrosis	
+	V				V			None i. v. 0.2 R. D. filt. in skin test	3 mils.	Very pale	
+	V	V		V		V		R. D.	3 mils.	Slight necrosis	Sl or
++	V		V		V			R. D.	3 mils.	Erythema only	
++	V				V			R. D.	3 mils.	Slight necrosis	
-+++	V	V						R. D.	3 mils.	Moderate necrosis	M ne
++	V	V		V		V		R. D.	3 mils.	Moderate necrosis	Sl ne
++	V				V			R. D.	3 mils.	Erythema No evidence of infection	
+++	V	V		V		V		R. D.	3 mils.	Severe necrosis	Se ne
+++	V				V			R. D.	3 mils.	Severe necrosis	
+++	V	V						R. D.	3 mils.	Very sli't necrosis	Er on
++	V		V		V			*B. coli*	3 mils.	Severe necrosis	
++	V				V			R. D.	3 mils.	Erythema only	
+++	V	V		V		V	V	R. D.	3 mils.	Severe necrosis	M ne
+	V		V		V			R. D.	3 mils.	Erythema only	
+	V				V			R. D.	3 mils.	Slightly hemorrhagic	
+++	V	V						R. D.	3 mils.	Slightly hemorrhagic	Sli he ha
++	V		V		V			R. D.	3 mils.	Few purpuric flecks	
+	V	V		V		V		R. D.	3 mils.	Few purpuric flecks	Er on

mune serum on this phenomenon. Rabbits infected with *B. lepisepticum* form agglutinins and precipitate rather poorly. The serum of such immunized rabbits fails to prevent necrosis as is shown in 198.

We have never succeeded in producing necrosis by injecting filtrate directly into the 24 hour skin test site. It is rather obscure why the filtrate diluted in the blood is more destructive to endothelium than the same filtrate concentrated locally.

Animals suffering from acute or chronic R. D. infections die very readily after receiving a potent filtrate intravenously. Blood cultures which have been proven sterile before the injection subsequently often become positive. An infected skin lesion seldom becomes larger as a result of the filtrate inoculation, but often assumes the purplish hemorrhagic hue shown by the skin tests. Closely related to this phenomenon is the observation that many rabbits after receiving filtrate intravenously develop a clear watery nasal discharge which often becomes purulent within a few days. Typical snuffles follows. It seems probable that these animals are suffering from a latent upper respiratory infection with *B. lepisepticum* and that such small foci react with increased intensity to the injection of antigen. This phenomenon is analogous to focal reactions induced by tuberculin injections in tuberculous individuals.

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Genetic Relations of Chocolate Brown Plumage Color in the Domestic Pigeon.

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All of the numerous color modifications known in the domestic pigeon may be grouped under 3 basic types of pigmentation; black, chocolate, or red. Of these 3 types black and red are by far the best known. Their genetic relationships were fully studied by Cole.[1] Chocolate has long occurred in several varieties of pigeons but the breeder has commonly classed this color with dun (dilute black). It was first recognized as a distinct type of pigmentation by Metzelaar.[2] Three years later Christie and Wriedt[3] reported chocolate

[1] Cole, L. J., *Rh. Is. Agric. Exp. Sta. Bull.*, 1914, 158, 311.

[2] Metzelaar, J., *Am. Pigeon Keeper*, 1924, xxvi, 22.

[3] Christie, W., and Wriedt, C., *Z. f. ind. Abst. u. Vererb.*, 1927, xliii, 391.