

5821

Thrombocytopenic Purpura Hemorrhagica Produced Experimentally with Thorium.

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"Thorotrast"* is a fluid which is said to contain thorium dioxide, 25% by weight, in colloidal suspension and which was developed as an injection medium for clinical pyelo-cystography. Kadrnka¹ also administered the drug intravenously in man and animals and found that the thorium was taken up by the liver and spleen in such quantity as to render these organs radiopaque and plainly visible in the roentgen-film. He formulated a routine method for the purpose which required total dosage of 0.8 to 1 cc. per kg. body weight, given in fractions on several consecutive days. He saw no ill effects from this in most cases—in man occasional vomiting, and once in rabbits persistent hemoglobinuria. The only alterations in the blood were slight transient anemia and leukocytosis, although changes in coagulability were apparently not sought. Except for the presence of granules, believed to be metallic thorium, in the reticulo-endothelial cells of the liver and spleen, no gross or minute lesions were discovered. We are studying further the action of this drug in laboratory animals and report production of a purpuric disease.

Eight rabbits were used. Four were given intravenous injections of "Thorotrast", 0.5 cc. per kg., on 2 consecutive days, and 4 were given larger doses. Three of the latter received a single injection of 3 cc. per kg., and the fourth received 3 cc. per kg. each day for 3 consecutive days. Three of the first 4 and 2 of the second had blood tests immediately before the initial injection and again 4 to 6 hours after the last injection, consisting in determination of bleeding time and clotting time, volumetric measurement of the thrombocytic content of the blood, and observations of clot contractility. Bleeding time was measured according to the method of Duke² and the other procedures were those of Van Allen.^{3, 4} Symptoms and radiographic

* The method of preparation has not been published. The drug was obtained from Chemische Fabrik von Heyden, Radebeul-Dresden, Germany.

¹ Kadrnka, S., *Fortschr. a. d. Geb. d. Roentgenstrahlen*, 1931, **44**, 9.

² Duke, W., *Arch. Int. Med.*, 1912, **10**, 445.

³ Van Allen, C., *J. Exp. Med.*, 1927, **45**, 69.

⁴ Van Allen, C., *J. Lab. and Clin. Med.*, 1926, **12**, 282.

effects were also recorded. All but 2 of the rabbits which survived were sacrificed within 24 hours after the last injection. Complete postmortem examinations were made. The histologic and radiographic studies are reserved for another report.

TABLE I.
Data obtained from rabbits before and after treatment with "Thorotrast".

Rabbit No.	Total Dose (cc. per kg.)	Time of Test	Platelets (vol. %)	Bleeding Time (min.)	Clotting Time (min.)	Symptoms	Fate	Gross Findings at Autopsy
1	1	Before	0.85	4.0	7.0	None observed	Living	
2	1	After	0.85	3.0	7.0	"	Killed	Hemorrhages in lungs and kidneys.
3	1	Before	0.77	3.5	5.0	"	"	"
4	1	After	0.35	3.5	5.0	Abortion	"	"
		Before	0.82	5.5	7.0	"	"	"
		After	0.3	3.5	6.5	None observed	Living	"
5	3	Before	No Tests			"	Died	Hemorrhages in heart, liver, kidneys, intestine, and perirenal fat.
		After	0.6	2.0	6.5	"	"	"
6	3	Before	0.0	60—	17.0	Weakness	Killed	Hemorrhages in lungs, mesentery, and retroperitoneal fat.
		After	0.95	2.0	6.7	"	"	"
			0.25	60—	14.0	"	"	"
7	3		No Tests			None observed	Died	Hemorrhages in brain, lungs, liver, kidneys, and subcutaneous fat.
8	9		"	"		Weakness, Hemoptysis	"	Hemorrhages in lungs, heart, subcutaneous tissue. Bloody fluid in pleural, peritoneal, and subarachnoid spaces.

(See accompanying table.) The rabbits with the lowest dose gave no symptoms, except for one, a pregnant female, which aborted after the initial injection. One of the group showed no abnormality of coagulation, but 2 suffered marked reductions in platelets and these had at autopsy petechial hemorrhages in the lungs and renal cortices. None died spontaneously.

Two which received 3 cc. per kg. showed extreme reductions in platelets, marked delays in bleeding time, moderate delays in clotting time, and very slow and incomplete retractions of clot. Weakness

was the only symptom seen, although in the 3 that died the terminal behavior was not witnessed. All rabbits displayed at autopsy extensive extravasations of blood in various internal organs.

The animal with 9 cc. per kg. exhibited marked tendency to bleed from cutaneous abrasions, became weak, and had hemoptysis just before death a few hours after the third injection. Organs and tissues showed extensive hemorrhages.

It is concluded that "Thorotrast", probably due to its content of thorium, given intravenously to rabbits tends to lower the thrombocytic content of the blood and to produce acute purpura hemorrhagica. Amounts 3 or more times the standard dose are usually fatal. The fact that the standard dose was given in 2, rather than in 4 or more fractions as given by Kadrnka, may well account for the difference between our results and his.

5822

Use of Dog Blood Agar for the Differentiation of "S" and "R" Pneumococci.

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In the course of a study on the dissociation of pneumococcus, it became evident that the present method of studying the colony morphology by the use of normal rabbit or horse blood agar plates is not highly satisfactory. This is particularly true in the case of "R" strains derived from Type II pneumococci. When grown on these media the colonies of these "R" strains frequently appear so smooth as to make them almost indistinguishable from their original "S" strains. While many of the "R" pneumococci can be recognized by such a method, yet careful observation and a certain amount of experience and familiarity with the technique, as regarding the degree of light, reflection and magnification are necessary. This report deals with the results obtained by the use of the same medium but slightly modified, the employment of which renders the above qualifications unessential.

It has been found that when making up the blood agar plates (the agar employed has been the ordinary beef infusion agar pH 7.8), if substitution is made of the normal rabbit or horse defibrinated blood, by that of the normal dog, the growth of "S" and "R"