centration of the alloxan solution, fasting prior to alloxan injections, and the composition of the diet.[18-21]

The development of alloxan diabetes apparently depends upon the difference in the susceptibility of the islet tissue as compared to other body tissues. If the range is sufficiently great so that marked islet destruction with only minor damage to other tissues can be obtained, diabetes can be produced. This differential is apparently found in most mammalian species. In the guinea pig, however, the islet tissue appears no more susceptible than other tissues and the resistance of both to alloxan is much greater than is found in the rat.

Summary. The parenteral administration of various dosages of alloxan, up to those which were fatal, failed to produce diabetes in guinea pigs. Neither glycosuria nor hyperglycemia was observed. Animals deficient in ascorbic acid, partially pancreatectomised or starved prior to alloxan administration, also failed to develop diabetes, although starvation apparently increased the toxicity of alloxan.

The guinea pig is much more resistant to the diabetogenic and the toxic action of alloxan than is the rat, and the pancreatic islet cells appear no more susceptible to alloxan than the cells of several other tissues.

We are indebted to Merck and Co., Inc., Rahway, N. J., Corn Industries Research Foundation, New York City, Sheffield Farms Co., Inc., New York City, and the Wilson Laboratories, Chicago, Ill., for generous supplies of materials used in these studies.

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Anaphylactoid Shock Produced by Anti-Platelet Serum.*

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Decrease or even absence of platelets is well known during anaphylactic, peptonic and tryptic shocks. The rate of platelet disappearance is very rapid[1] and a relationship between the severity of anaphylactic shock and the amount of blood platelets removed from circulation has been emphasized.[2] The role of the platelet in the mechanism of these types of shock is not yet clear, but its interference has been verified.[3-5] Our purpose was to produce an anaphylactoid shock using a substance known as capable of inducing an experimental thrombocytopenic purpura. Substances known as producing experimental thrombocytopenia and purpura are estradiol benzoate[6] or urethane in the dog.[7] These substances act only after at least a week of daily administration and seem to be specific to dogs. These substances are not indicated to removing the platelets abruptly from the circulation with its sudden destruction and

* Aided by a grant from dr. Guilherme Guinle.

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TABLE I.

Animals	No.	Wt (g)	Dose of normal serum* (ml/100 g body wt)	Reactions
Guinea pigs	6	270-660	1.0	None
Rats	9	170-260	0.5	"
Rabbits	5	1100-1600	0.2	"
Dogs†	4	1600-2000	1.0	‡

* Normal rabbit serum was injected into dogs, guinea pigs and rats. Normal guinea pig serum was injected into rabbits.

† Arterial pressure was taken in another dog (6.2 kg) after injection of normal rabbit serum (0.4 ml per 100 g body weight). The blood pressure after drop (4 cm Hg) came back to normal level after a few minutes and remained normal for more than ½ hour.

‡ Soon after the injections some discomfort was observed, sometimes followed by evacuation. One dog presented more acute symptoms such as vomiting and fainting. All these abnormalities disappeared within 10 minutes and the animals remained normal for hours thereafter. A typical picture of shock was not observed.

TABLE II.

Animals	No.	Wt (g)	Dose of serum (ml/100 g body wt)	Death from shock		Animals recovered showing purpura 48 hr
				No. of animals	Time, min.	
Guinea pigs	30	128-684	.30-1.0	22	2-60	8
Dogs	7	450-7200	.10-1.0	—	—	6*
Rabbits	12	1700-3200	.11- .18	3	3-15	9
Rats	7	110-240	.10- .50	5	3- 6	2

* One puppy was sacrificed 3 hours after the injection and purpuric lesions in the intestine were very conspicuous.

purpura, but anti-platelet serum is a powerful tool for this purpose and could be applied to several species. Anti-platelet serum produces a classical picture of thrombocytopenic purpura: absence or reduction of platelets in circulation, petechiae in the intestine, skin, lungs and heart; bleeding time very prolonged, normal coagulation time, clotting retraction delayed or absent and in non-fulminating cases severe anemia through intestinal hemorrhages. According to the amount administered the animal may be killed in 24 hours or, after decrease of blood platelet volume to zero, a regeneration is processed and the number of platelets becomes normal again.

We have administered intravenously a large amount of very active anti-platelet serum trying to obtain anaphylactoid phenomena in dogs, rabbits, guinea pigs and rats. The positive results of these experiments are presented in this paper.

We used 1:16 antidog-platelet, 1:16 anti-guinea pig-platelet and 1:16 antirat-platelet sera prepared in rabbits by repeated intravenous injections of platelets. The antirabbit-platelet serum was of 1:8 titre and has been prepared in guinea pigs by repeated injections in peritoneum. The platelets were obtained by fractioned centrifugation and washed several times with saline. The titration of the sera was made by the purpurigenic method.[8] 29 animals were used as control for the administration of normal serum intravenously injected in the same amounts as the higher doses in the experiments with the anti-platelet serum. The control results are shown in Table I.

Adult dogs (weight between 6.5 and 9.0 kg) have been injected with smaller doses of normal rabbit serum (one dog with 0.2 ml and 3 others with 0.4 ml per 100 g body weight). Reactions consisted in general malaise and evacuation with prompt recovery within 2 minutes after injection.

Fifty-nine animals (33 guinea pigs, 1 adult dog, 1 young dog, 5 puppies, 12 rabbits and 7 rats) have been studied. The results are summarized in Table II.

Guinea pigs. Guinea pigs were injected thru the heart. Twenty-two animals died

[8] Tocantins, L. M., *Arch. Path.*, 1936, **21**, 69.

within 1 hour (70%), 9 showed the typical signs of shock with recovery and died 24 to 48 hours later with signs of purpura. Two animals died after severe thoracic hemorrhage. Only one animal presented no symptoms of shock and died 24 hours later with signs of purpura. The picture of shock obtained was identical to those classically described: respiratory discomfort followed by violent dyspnea, urination, evacuation, convulsions and death usually within 10 minutes after the injection. At autopsy very conspicuous emphysema of the lungs was always observed. This find was confirmed by microscopic examination in several animals: edema and hemorrhage were also always present.

Dogs. The dogs were injected in the jugular or saphenous vein. With the doses employed we were not able to obtain fatal outcome. A puppy sacrificed 3 hours after the onset of shock showed a dark enlarged liver and very conspicuous purpuric lesions in the intestine. The signs of shock were agitation, urination, evacuation, vomiting, tenesmus followed by elimination of mucus with small amounts of blood, prostration and pronounced drop of body temperature.

Rabbits. The rabbits were injected in the marginal vein of the ear. Fatal shock was obtained after dyspnea and convulsions. At autopsy the characteristic extreme dilation of the right side of the heart was found.

Rats. Rats were injected in the dorsal vein of the tail. Dyspnea and convulsions were the most conspicuous signs observed. At autopsy a very typical emphysema of the lungs was found.

To observe another sign usually found in anaphylactic peptonic and tryptic shocks, *i.e.*, decrease of pressure, the carotidean pressure of some animals (2 dogs, 5 rabbits and 3 guinea pigs) was registered. One adult dog (7.2 kg) was anesthetized with liquid Dial (Ciba) the pressure drops to 50% of its normal value one minute after injection and falls as low as 5% of its initial level after 8 minutes; then the pressure rises but remains at 25% of its initial value after one hour. One young dog (3 kg) showed a strikingly similar picture. Pressure changes showed a very different picture in rabbits and guinea pigs. One rabbit anesthetized with Dial and 4 rabbits and 3 guinea pigs anesthetized with urethane showed a very uniform picture: in the first 30 to 45 seconds the pressure drops 50 to 75% from the initial level and then increases very rapidly attaining hypertensive figures from 125 to 200% of normal value, about one minute after the beginning of the injection. Those high values remain for about one minute, then drop to normal or below normal levels within a few minutes.

Numerous indications of interrelationship between signs observed in purpura and some described in anaphylactic phenomena can be pointed out. Shwartzman and Arthus phenomena have been considered allergic local hemorrhage, the mechanism of which has been long ago related to a purpuric manifestation.[9,10] Petechiae in the intestine, blood in the intestinal lumen and bloody evacuation are typical of anaphylactic shock in the dog. Thrombocytopenic experimental purpura in dogs is characterized by intestinal petechiae, blood in the intestinal lumen and severe anemia through intestinal hemorrhage, all these signs being secondary to the fall of the blood platelets.[11] Numerous cases have been described of purpura in man of an allergic nature interpreted as an anaphylactoid purpura.[12] Therapeutical substances have been imputed as causing sensitization in man producing purpuric phenomena as well as allergic reactions.[13,14]

The abrupt removal of circulating platelet by a specific serum, causing sudden destruction of this blood element accompanied by anaphylaxis-like reactions, seems also to indicate a common basic mechanism of thrombocyto-

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[14] Watson, C. J., *et al.*, *J. Lab. and Clin. Med.*, 1947, **32**, 606.

penic purpura and anaphylactic, tryptic or peptonic shocks.

The results presented in this paper show another possible means for producing anaphylactoid shock, *i.e.*, by injecting intravenously a large amount of an active anti-platelet serum. The similarity of various signs described in purpura with some verified in allergic or anaphylactic phenomena is emphasized.

Summary. Intravenous injection of large amounts of active anti-platelet serum produces in dogs, rabbits, guinea pigs and rats a picture of severe shock quite similar to anaphylactic shock. Relationship between purpura and anaphylactic phenomena is emphasized.

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Thermolability of the Bacterium-Phage Complex.

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The infection of susceptible host cells by bacterial viruses may lead to several interesting events affecting primarily the host. A number of investigators have reported an interfering effect on the growth of unrelated viruses[1-3] while others have shown that infected cells no longer divide[2,4] or were incapable of adaptative enzyme production.[5] In the course of our investigations on the effect of sodium chloride on phage formation by staphylococci at elevated temperatures,[6] it was observed that the bacterium-phage complex was much more thermolabile than either the bacterium or phage alone. The present paper is a brief account of these observations.

The K race of phage active upon *Staphylococcus aureus* (K strain) was employed throughout these experiments. Quantitative determinations of [phage] were performed by Gratia's[7] method and viable cell counts were made by plating appropriate dilutions in tryptose agar and counting the colonies developing after 24 hours incubation at 36°C. Stock bacterial cultures were prepared by harvesting the growth from tryptose agar cultures in Roux flasks after incubation at 36°C for 18-24 hours. The suspensions were chilled for one hour in an ice-water bath and were used to make mixtures in tryptose phosphate broth containing 1 x 10^8 organisms/ml. To aliquots of these preparations phage was added in concentrations varying from 5 $\times$ 10^7 to 2 $\times$ 10^8 plaque units/ml; aliquots without added phage were maintained as controls. Samples were removed at once from the experimental mixtures and controls for determination of the viable cell counts.

As soon as samples had been taken, the tubes were immersed in the ice-water bath for an additional hour. At this time aliquots were removed for plaque determinations and viable cell counts. The latter were assumed to be a measure of the uninfected bacteria since infected cells cannot reproduce and form colonies. The plaque counts were considered to indicate the number of infected cells for it is known that phage uptake by bacteria is rapid even at 5°C and that little phage remains unattached to cells after sorption has proceeded for one hour.[8]

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