possible to render the organism resistant to penicillin.

Similar degrees of increased resistance were found in 4 strains of staphylococci isolated during the course of penicillin therapy for localized infections.

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Prolonged Adrenalin Hypertension and Subsequent Circulatory Failure.*

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Previous reports from this laboratory[1] supported the view that a state of shock which cannot be reversed by substantial infusions of the animal's own blood and which is characterized by pathological changes in the mucosa of the upper intestine can follow hemorrhage; but this only occurs when arterial pressures have been reduced severely for significant periods of time. Diminished blood flow through tissues dominantly due to hypotension seems to be the effective agent. The question remains whether the blood flow through tissues can be throttled to a similar degree of intensive vasoconstriction, while arterial pressures remain essentially normal or even become elevated.

Experimental evidence for this possibility has been sought by two types of investigation, (a) prolonged stimulation of afferent pressor nerves and (b) continued administration of potent vasoconstrictor drugs, notably adrenalin. Results from the use of the former have been consistently negative; those realized by the latter procedure remain contradictory.[2] This is due in part to the fact that prolonged administration of adrenalin causes diverse direct and secondary effects on the heart, circulation and respiration, from which an animal may expire during or following its administration. Among these accidents are pulmonary edema, myocardial insufficiency, ventricular fibrillation and respiratory failure. The possibility also exists that some investigators used doses which were too large and others, doses which were too small.

Methods. In order to compare results with those of hemorrhagic shock, dogs were anesthetized with morphine followed by "just adequate" doses of sodium barbital. Respiration, mean femoral, right atrial and intrathoracic pressures were recorded. Adrenalin chloride (Parke, Davis and Co.) was slowly and continuously infused as a 1:5000 solution into a cannulated femoral vein by means of a Mariotte burette. Table I gives the data from separate experiments. The rate of administration ranged from .0069 to .0398 mg per kilo per minute. The total dose depended partly on the weight of the animal. The duration of the infusions varied from 51 to 120 min.

After cessation of the infusion the animals were observed for 3-5 hr. As a rule, mean arterial pressure declined to, or somewhat below, control levels within 5 to 15 min. Thereafter, three types of sequence were observed: (1) Mean pressure remained above 80 min for 4 to 5 hr. (2) While mean pressure remained reasonably normal, the animal expired suddenly, due to respiratory failure. (3) Mean arterial pressure fell progressively to 40 or 20 mm and the animal expired. Only the latter sequence was regarded as a reasonable criterion of progressive circulatory failure, which was probably irreversible. These are designated by the term, "shock," in Table I. A survey of 10 experiments shows that 2 animals (not included in Table I) died during administration of adrenalin due to causes which had no relation to shock. Two

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2 Wiggers, C. J., *Physiol. Rev.*, 1942, **22**, 74.

TABLE I.

Exp.	Wt, kilos	Dose, mg/K/min	Total dose, mg	Duration of inj. (min)	Mean pressure during inj. (approx.) mm Hg	Dynamic outcome	Autopsy findings
KA 76	12	.0215	13.2	51	186-200	No shock 3 hr	Intestinal mucosa normal. Subendocardial hemorrhagic areas. Lower lung lobes—few hemorrhages. Spleen small.
		and .0398	40	84	156	No shock 7 hr	
78	11	.0198	19.5	92	170-200	No shock 5 hrs	Upper gut mucosa moderately congested. Pleural and sub-endocardial hemorrhagic spots. Some brownish pericardial fluid. Spleen contracted.
79	11.5	.0218	17.4	70	240-210	No shock 4 hr	Upper intestinal mucosa negative. Ileum slightly congested. Stomach mucosa hyperemic. Profuse pericardial effusion. Subepi- and endocardial hemorrhages.
80	16.5	.0239	30	83	240-200	Fall in B.P. to 40 mm in 72 min. Lived 5⅔ hr. Shock	Intense duodenal congestion and swelling—bloody fluid in lumen. Increased pericardial and pleural fluid. Intense subendocardial hemorrhages. Pulmonary congestion—no edema.
81	9	.0228	24.6	120	260	Died failure of resp. 65 min. Shock (?)	Marked engorgement and edema of duodenal mucosa. Small amount clear pericardial fluid. Profuse subendocardial hemorrhage and apical epicardial hemorrhages.
82	9	.0181	20	120	140-180	Died shock 2 hr	Few petechial hemorrhages in duodenum and slight congestion. Large amount of brownish pericardial fluid. Diffuse epi- and pericardial hemorrhages.
84	7	.00694	3.43	70	180+	No shock 3 hr	Duodenal mucosa moderately congested. Small amount pericardial and pleural fluid. Few small subendocardial hemorrhagic spots.
85	6	.018	13	96	220-80	Slight hypotension 70 mm in 2 hr. No shock	Very slight or questionable duodenal congestion. Some pericardial effusion. Few hemorrhagic spots on epi- and endocardium.

animals (80, 82), and questionably a third (81) showed definite circulatory signs of shock. In 5 experiments (76, 78, 79, 84, 85), mean arterial pressure never fell below 80 mm for 3 to 7 hr after discontinuance of the adrenalin infusion.

Necropsies were made on all animals and the most conspicuous changes are recorded in Table I. This serves to indicate that extensive hemorrhagic lesions occurred fairly generally in all animals regardless of the course. Their distribution was far more general than has ever been observed in hemorrhagic shock. Involvement of the endocardium, epicardium, and sometimes the liver was far more common. Small pericardial and pleural effusions were frequently present. However, the duodenal mucosa which showed such characteristic changes in hemorrhagic shock was negative in 3 dogs (76, 79, 85), moderately congested in 3 animals (78, 82, 84) and intensely congested or hemorrhagic in only 2 dogs (80, 81). These observations, correlated with the dynamic course, indicate that prolonged vasoconstriction by adrenalin *can cause* damage to smaller vessels, but its action is by no means as selective as appears to be the case in hemorrhagic shock. Even if we add together the animals which showed *either* a progressive downward trend of blood pressure *and/or* significant intestinal changes (78, 80, 81, 82, 84), prolonged administration of adrenalin gave dynamic or pathological evidence of an impending irreversible state in only half of our animals (total 10 dogs).

Conclusion. In about 50% of our experiments prolonged administration of adrenalin (.00694 to .0398 mg kilo/min.) caused 2-7 hr after cessation of infusion either dynamic evidence of irreversibility or postmortem changes in the upper intestine which resembled those of hemorrhagic hypotension. Adrenalin constriction can lead to shock, but does not unfailingly do so. Our experiments have no bearing on the problems, whether equally intensive generalized constriction occurs in other types of clinical or experimental shock or whether lesser degrees of vasoconstriction can cause similar consequences.

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Reactions of Monkeys to Experimental Respiratory Infections. VI. Spontaneous and Experimental Infections in Nutritional Deficiency States.*

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Clinical observations have indicated that patients affected with certain deficiency diseases are prone to develop infections. Experimental data in support of the apparent relationship of B-avitaminosis to susceptibility to infection in monkeys have been accumulating in recent years.[1-6]

With increased knowledge of the components of the vitamin B complex, experimental diets more accurately known and controlled with respect to vitamin fractions than those previously used, are now available. Our interest has been not only to study spon-

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