of the bacterial dehydrogenases may be altered. Another possibility may be a change in the permeability of the cell or the emergence of a divergent metabolic pathway. This problem can be clarified by isolating and comparing the properties of the same sulfhydryl enzymes from the parent susceptible and resistant strains.

Summary. Furacin inhibits purified jack bean meal urease as well as urease from a susceptible strain of *S. aureus*. Pepsin, trypsin and papain are not inhibited. The malic, succinic, lactic and α-glycerophosphate dehydrogenases of a susceptible strain of *E. coli* are inhibited by Furacin while the formic dehydrogenase is not inhibited. The α-glycerophosphate dehydrogenase of rabbit thigh muscle is not inhibited. Several dehydrogenases from a strain of *E. coli* resistant to Furacin show some cross resistance to p-chloromercuribenzoate and some trivalent arsenicals. A similar phenomenon was observed with the urease from a strain of *S. aureus* resistant to Furacin. It is concluded that Furacin inhibits some enzymes requiring active sulfhydryl groups.

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Right and Left Atrial Pressures in Successive Stages of Oligemic and Normovolemic Shock.* (18421)

HOWARD F. VAN NOATE.† (Introduced by Carl J. Wiggers.)
From the Department of Physiology, Western Reserve University School of Medicine, Cleveland, O.

Using dogs under morphine and barbital anesthesia, with their chests open and under controlled lung inflation, C. J. Wiggers(1) studied the circulatory failure which developed as a result of prolonged hemorrhagic hypotension, and again after reinfusion of the withdrawn blood. It was found that the experiments could be divided into two approximately equal groups: (1) Those in which the circulatory failure developed after reinfusion as right atrial pressure declined, and (2) those in which it supervened despite the fact that right atrial pressure was maintained at or above control levels. The question arises whether the reduction in cardiac output—mainly responsible for the decline of arterial pressure after transfusion(2,3)—is accompanied by changes in left atrial pressure which are in accord or at variance with those in the right atrium. It was the purpose of this investigation to study these pressure relations by simultaneous registration of right and left atrial pressures, for it has never been proved that the beats of the two ventricles are coordinated so perfectly during oligemic and normovolemic shock that changes in filling pressure for the right ventricle are automatically accompanied by similar quantitative or even directional changes on the left side.

Methods. Dogs weighing from 10 to 15 kilos were anesthetized with morphine and sodium barbital at least 3 hours prior to any observations. The chest was opened in the midline, utilizing an electric cautery to minimize blood loss. The trachea was cannulated and respirations were maintained by means of an artificial respirator. Optical tracings of the right and left atrial and the central aortic pressures were taken on a rapidly moving photokymograph by means of calibrated Gregg manometers of adequate frequency and appropriate sensitivity. These were connected by lead tubing to rigid cannulae introduced respectively through the right jugular vein, a left pulmonary vein and the subclavian artery. A segment capsule in the air-

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† Postdoctorate Research Fellow, National Heart Institute, U. S. Public Health Service.

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line from the artificial respirator permitted the optical recording of the respiratory cycle. In addition, mean pressure was recorded continuously on a smoked drum to facilitate standardization of the hypotension levels. A femoral artery and vein were cannulated to withdraw and reinfuse blood. Hemorrhagic shock was produced according to the method developed in this laboratory(4,5) except that a stepwise type of bleeding suggested by Lawson(6) was employed to lower arterial pressure to the 50 mm Hg level within 30-45 minutes. Optical records were taken at frequent intervals and each was calibrated with respect to its individual base line. All records were compared at the same phase of lung inflation. This, in addition to the fact that the respiratory depth and rate were maintained constant, eliminated changes in atrial pressures due to cyclic respiratory changes in venous return, pulmonary resistance or hydrostatic pressure. Of the various ways for determining atrial pressures on optical records(5), measurement of the instantaneous pressure at the end of systole (V pressure) was found to be most expedient and reliable for comparison of records taken at wide intervals of time. It may be recalled that such easily determined pressures represent the pressure initially available for filling of the respective ventricles after the A-V valves open. Whenever clearly indicated, the pressure at the onset of ventricular systole, the Z pressure, was also measured. This theoretically corresponds to the initial intraventricular tension under which ventricular contraction starts.

Results. Shock consistently followed use of the bleeding and transfusion techniques in 16 dogs, but the purpose of this study could only be fulfilled when complete sets of reliable records were realized at spaced intervals throughout the entire 7 to 9 hours required for each experiment. This *sine qua non* proved difficult. Many experiments yielded only partial information or needed to be wholly discarded owing to technical difficulties involved. Among these were experiments in which (a) atrial pressure curves (particularly the left) were obviously distorted, (b) the position of the atrial sounds required readjustment as the volumes of the cardiac chambers changed, (c) the depth and rate of lung inflation could not be kept constant, (d) the animal's temperature could not be maintained at an even control level, or (e) additional anesthesia was required.

As a result of these vicissitudes of experimentation only six experiments were realized in which conditions were wholly satisfactory. Of these, only one experiment the data of which are plotted in Figure 1 displayed a

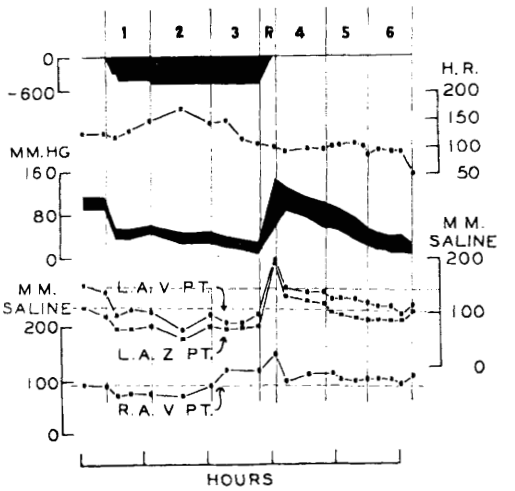

FIG. 1.

Graph of data showing sequence of some cardiodynamic events following bleeding to hypotensive levels and subsequent reinfusion of blood, as indicated in cc by upper black area. Vertical lines indicate (approximately) successive phases of shock adapted to recent nomenclature adopted by Wiggers(5). Order of curves: bleeding and reinfusion volumes; heart rate (H.R.); arterial blood pressure; V and Z points of left atrial pressure (L.A.V. PT. and L.A.Z. PT); V point of right atrial pressure (R.A.V. PT). All atrial pressures are related to level of animal board as zero and show relative changes only; all values are 55 to 60 mm saline higher than actual atrial pressure. Right atrial Z pressures followed V pressures so closely that their plot is omitted to prevent confusion in graphing. *Phases*: 1-3, oligemic shock; 1, bleeding and simple hypotension; 2, impending stage; 3, critical stage; R, reinfusion; 4-6, normovolemic shock; 4, compensatory stage; 5, progressive stage; 6, terminal stage.

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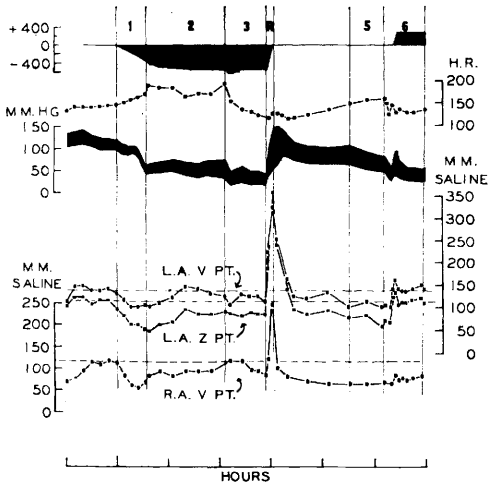

FIG. 2.
Same as Fig. 1.

sustained elevation of right atrial pressure similar to that of a group reported by C. J. Wiggers(1) during the critical period of oligemic shock(3) and during the circulatory failure following transfusion(5,6). A survey of left atrial pressures in this experiment reveals that (a) during the critical phase(3) both Z and V pressures declined in the left atrium, (b) during the period of reinfusion (R) left atrial V and Z pressures rose much more than corresponding right atrial pressures, and (c) during the circulatory failure following transfusion(5,6), V pressure in the left atrium fell below control values, while it remained elevated in the right. The Z pressures in the left atrium also declined but not to levels below control values until the terminal stage(6).

While more experiments are needed, this single experiment supported by casual data from other incomplete experiments, suggests that elevation of right atrial pressure found in a fair proportion of Wiggers' experiments (1) may not be accompanied by a maintenance of left atrial pressure.

In 2 experiments, an example of which is shown in the plot of Figure 2, V pressures fell in both atria during the bleeding(1). Both tended to return to control levels during the impending and critical phases of oligemic shock(2,3). In three experiments, right and left atrial V and Z pressures were reduced during hemorrhage and failed to rise during the subsequent impending and critical periods.

Following reinfusion the elevation of left atrial V and Z pressures greatly exceeded those in the right atrium in all 5 cases. In the right atrium this rise was followed by a prompt drop in pressures to subnormal levels in all 5 experiments. In 3 of these cases, the decline of left atrial pressure stabilized at or above control levels; in the other 2 it fell below them. In the experiment plotted in Fig. 2, an additional 320 cc of crossmatched blood was administered during the terminal stage. This resulted in a slight elevation of right atrial and a marked rise of left atrial pressures to control levels. Despite this rise, systolic, diastolic, and pulse pressures continued to diminish until the end.

Since changes in heart rate have a determining effect on atrial pressures the experimental data were reviewed in an effort to find times in different stages of the experiment when the heart rate remained relatively constant. Two comparisons of left and right atrial Z pressures under such conditions are recorded in Table I.

The data of Exp. 12 were obtained from one of the 2 animals in which both right and left atrial pressures decreased below control values after reinfusion. It will be noted that left atrial Z pressure decreased to a greater extent than the right, both during the stage of impending oligemic and the compensatory and terminal stages of normovolemic shock.

The data of Exp. 10 were obtained from one of the 3 animals in which right atrial Z pressure decreased, while left atrial Z pressure was sustained during postinfusion phases. During the stage of critical oligemic shock both right and left atrial Z pressures decreased very little, but during the progressive stage of normovolemic shock right atrial pressure fell while that of the left atrium remained near a control level.

Such comparisons indicate that the alterations in atrial pressures are not dominated by the changes in heart rate but are due to other causes.

Interpretation of Atrial Pressure Changes. Briefly recapitulated, 3 patterns of change in

TABLE I.

Exp.	Phase	Heart rate per min.	Pulse pressure, mm/Hg	Mean blood pressure, mm Hg	Right atrial Z pressure, mm H_2O	Left atrial Z pressure, mm H_2O	Cardiac index by pulse contour method
12	Control	174	28	113	105	105	3.04
	Impending oligemic stage	175	16	47	80	65	1.59
	Compensatory normovolemic stage	174	43	93	95	70	3.53
	Terminal normovolemic stage	178	23	36	70	60	1.53
10	Control	117	49	116	135	130	1.94
	Critical oligemic stage	132	18	24	130	130	1.08
	Compensatory normovolemic stage	140	55	64	135	130	2.44
	Progressive normovolemic stage	130	19	29	80	125	1.22

the atrial pressures were observed in the post-infusion shock phase: (a) a decrease in both the right and left atrial pressures to low levels, the left decreasing to a greater extent, (b) a decrease in the right atrial pressure to a low level, but a failure of the left to decrease below a control level, and (c) a decrease in the left atrial pressure, the right remaining normal or elevated. If we assume that the post-transfusion circulatory failure in these experiments had been due solely to reduction in venous return(3), right atrial pressure would be expected to decline. With the further probable assumption that the left heart receives a proportional decrement of flow, left atrial pressures should decline even more at the Z and V points‡(7,8). Such a combination of effects was found in 2 experiments only. In the 3 records in which right atrial pressures decreased below control values in the post-infusion phase of circulatory failure, but in which the left did not decrease to the expected amount or actually remained at or above control values, the fall in right atrial pressure would also indicate a decreased venous return. The failure of the left atrial pressure to fall to an even greater extent, as would be expected, however, strongly suggests a depression of the left ventricular muscle in these cases. In the sixth animal, the right atrial pressure remained elevated while the left atrial pressure decreased in the post-infusion phase. Since the initial hemorrhage and the reinfusion indicated a greater distensibility of the right atrium than of the left, some other factor must have operated. The elevation of V and Z pressures in the right atrium allows the conclusion that pressure for filling the right ventricle was adequate. The decline of left atrial V and Z pressure strongly suggests that less blood is returned through pulmonary veins to the left atrium. Excluding a highly improbable increase in pulmonary resistance great enough to impede blood flow to the left atrium, one is forced to the conclusion that depression of the right myocardium must have been concerned. Evi-

‡ This difference is consonant with an elementary proposition emphasized by Little, *et al.*(7,8) that owing to the lesser distensibility of the left atrium the pressure increment required to press a certain additional volume into the left atrium must be greater than that required to force the same additional volume into the right atrium. Obviously, the lesser distensibility of the left atrium *per se* does not create the additional necessary pressure, as wrongly inferred by Nahar *et. al.* (PROC. SOC. EXP. BIOL. AND MED., 1950, v74, 737).

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dence of a dominant left ventricular depression seemed to be present in 3 of these experiments and signs of right ventricular depression in one of them.

Summary and Conclusions. 1. Simultaneous changes in right and left atrial pressures together with aortic pressure pulses were successfully recorded through the experiments in 6 out of 16 dogs which were submitted to standardized procedures of bleeding and reinfusion developed in this laboratory. 2. An analysis of the results supports previous observations from this laboratory that myocardial depression can supervene during the circulatory failure which develops after prolonged hemorrhagic hypotension and subsequent reinfusion of the withdrawn blood. It extends these observations in showing that such myocardial failure may affect either the left or right ventricle dominantly.

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Lysozyme Production in Response to Injury of Gastrointestinal Tract in Dogs. (18422)

HUGO C. MOELLER,* HOMER C. MARSHALL AND JOSEPH B. KIRSNER.
(Introduced by Walter L. Palmer.)
From the Frank Billings Medical Clinic, Department of Medicine, University of Chicago.

The recent investigation of Meyer and his co-workers suggesting a relationship between lysozyme(1) and certain ulcerative diseases of the alimentary tract has aroused widespread interest(2,3). The evidence suggested that lysozyme locally initiated the lesions of chronic ulcerative colitis by removal of the surface mucus, with dissolution of the mucous cells; necrosis of the denuded tissue by proteolytic enzymes, presumably furnished by micro-organisms, subsequently ensued. Wang, Grossman, *et al.*(4) showed that lysozyme produced erosions and hemorrhages in the gastric and colonic mucosa of rats, and increased the digestive effect of hydrochloric acid and pepsin *in vivo*. Lysozyme was considered capable of damaging mucous membranes, but no evidence was adduced that it removes surface mucus from the mucosa.

The hypothesis that the polysaccharolytic activity of lysozyme leads to gastrointestinal ulceration has not been substantiated, as yet, by the demonstration of a lysozyme substrate in the gastrointestinal wall or lumen(5,6). High lysozyme titers have been demonstrated in healing skin incisions, callus of healing rabbit fractures, and in inflammatory exudates(7, 8,9). The possibility exists, therefore, that lysozyme is a result rather than a cause of the inflammatory reaction in chronic ulcerative colitis. To evaluate this possibility, the concentrations of lysozyme were measured before and during experimentally induced injury to the bowel in dogs.

Methods of Study. Lysozyme titers were

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