tious particles making contact with susceptible cells in the CNS. The failure of these experiments would seem to indicate that either the physiological stresses were inadequate, or at the time at which they were applied the virus was absorbed by other tissues and was no longer available to the CNS. It is of interest, in this connection, that no virus was recovered in the prodromal period from blood or lungs; very little virus was recovered from brains. From the finding that very little virus is required to initiate infection in animals by intracerebral inoculation, it may be concluded that there is an abundance of susceptible cells in the CNS; but their capability to produce virus is of a relatively low order as compared to chick cells in ovo or tissue culture. The amounts of NDV recovered from brains of infected hamsters were of the same order of magnitude as those amounts recovered from brains of other mammals(4).

From the observation that several hamsters inoculated with sterile diluents developed pneumonitis, it is possible, although evidence is lacking, that the inoculum may have provoked the multiplication of a latent infectious agent other than NDV. The pneumonitis in the inoculated animals, therefore, may be due to either: a) NDV infection despite poor recovery of virus from the lung tissues. b) accumulation of cytotoxic products of cells infected with NDV as suggested by others(7), or c) multiplication in the lung of a latent agent which interfered with multiplication of NDV.

Summary. Hamsters injected intracerebrally or by peripheral routes with NDV developed encephalomyelitis and pneumonitis. The amount of virus required to produce infection varied for each route, being least by the intracerebral route and highest by the subcutaneous route. Virus was recovered from the brain but not from the lungs or blood in the prodromal stages. The manifestations and pathology of the resultant encephalomyelitis were similar irrespective of route of inoculation.

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Postsystolic Myocardial Augmentation: 1. Effect Upon an Induced Shock State.* (26719)

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Different types of mechanical assistance have been considered in management of central circulatory insufficiency. Four major maneuvers have been considered: (1) total or partial cardiopulmonary bypass; (2) postsystolic myocardial augmentation; (3) veno-arterial shunt; and (4) selective right or left ventricular bypass. In postsystolic myocardial augmentation the augmenting ventricle (Fig. 1) is a blind-ended diverticulum which aspirates blood during the true ventricular systole and returns the blood to the arterial tree during true ventricular diastole, when the aortic valve is closed. Thus, the ventricle contracts against reduced resistance. Such counter-cycling can reduce and

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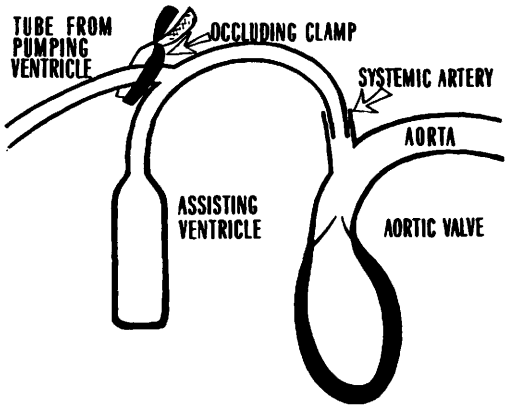

FIG. 1.

perhaps eliminate the intraventricular pressure curve. The real problem lies in phasing and synchronization of the augmenting ventricle. We have developed such equipment and an electronic circuit which, utilizing the QRS complex of the electrocardiogram, enables the phasing of the augmenting systole to be accurately placed.

Methods. In the initial phase of this investigation it was necessary to ascertain the most suitable arteries for cannulation according to the effect which such cannulation would produce upon the central pulse. Fifty-two dogs, weighing from 15 to 30 kg, anesthetized with 30 mg per kilo of pentobarbital, and heparinized with 1 mg per kilo, were used. Experiments were so designed that cardiac output and blood volume changes could be recorded directly in conjunction with phasic changes in blood pressure.

The arteries used for connection with the augmenting ventricle were cannulated with graded, tapered plastic catheters. The connection between the animal and the augmenting ventricle was achieved with rigid Tygon tubing, and the system was primed with 50 to 100 ml Ringer's solution. To obtain information as to the pulse form in different phases of postsystolic augmentation, since many such pulse tracings may be complex to interpret, the largest vessel available should be used. The abdominal aorta was cannulated with a large, stiff cannula just rostral to its bifurcation.

The effect of cannulating the aorta was closely approximated by cannulating both femoral arteries simultaneously. In the human, the femoral vessels are large enough to give adequate effect on the pulse when cannulated through the profunda femoris vessels of one or both sides, and there is no need to seek other vessels. After the preliminary attempts upon dogs, the abdominal aorta was selected, to establish the necessary parameters. The aortic cannula was connected to the augmenting ventricle by a short Tygon tube one-half inch in diameter, and the ventricle was seated in its actuator. The actuator was electrically triggered in the usual fashion; the subsequent aortic pulse recorded and studied through a recording cannula attached to a Statham P23B strain gauge, recorded upon the oscilloscope, then photographed with a modified Polaroid Land camera so that immediate permanent records were obtained. This pulse tracing was recorded simultaneously with the ECG tracing which also recorded the phase of the triggering of the assisting ventricle through an electronic circuit designed to show this point as an upright line following the QRS wave and named by us the "A" wave (Fig. 2).

Intravascular pressures measured with Statham P23B gauges were recorded through plastic catheters introduced into the left ventricle through puncture of the wall of the left atrium in the open-chest dog, or into the aortic arch through a carotid artery. Vena caval pressures were measured utilizing a catheter passed through the external jugular vein. Esophageal temperature was maintained at a normal level. In those experiments in which left ventricular pressure was determined or in which the subclavian artery was used for connection with the augmenting ventricle, the open-chest preparations were used, and ventilation was accomplished using a modified Vivian Thomas positive pressure respirator.

The augmenting ventricle was that of the Davol pump, which is a ventricle-type pump with a passive valve. This pump incorporates means for synchronizing the action of the pumps with any EKG signal or pacemaker, a feature of particular interest for augmented circulation. Mere synchronization of the pump with the EKG signal would not make

possible the desired end results since the R wave merely indicates onset of systole. Because the mechanical action of the heart and the subsequent hydraulic end results in the aorta are not simultaneous with onset of systole, it was necessary to devise means not only for synchronizing the pump with the EKG but also a circuit so as to provide the proper phasing of the action of the pump with the hydraulic events of the aorta. By controlling the synchronization and, at the some time, controlling air pressure in the exhaust to determine the rate at which systole and diastole are made, it is possible to provide a synchronized pulse pattern of any desired form. Although at this time there is apparently no evidence which demonstrates the superiority of pulsatile flow over non-pulsatile flow or *vice versa*, there can be no argument that if the systolic pulse pressure is reduced, the work load of the heart is also reduced.

Twenty control dogs were prepared as follows. An infusion of norephinephrine was administered to dogs from which one-third of total calculated blood volume was removed before beginning infusion. Norepinephrine was administered in such dosage and at such speed over a 40 minute period that the systemic arterial blood pressure was elevated to a level from 220 to 240 mm/Hg during the period. All of these control animals died within 2 hours. Examination disclosed a diffuse hemorrhagic myocarditis. Details of this preparation will be reported elsewhere. An experimental series was designed in which the animals were placed upon postsystolic myocardial augmentation following production of the lethal shock state.

Results. The results obtained in a representative group of dogs subjected to postsystolic myocardial augmentation are shown in Table I.

In the 5 examples cited there is no essential difference in cardiac output of an individual animal before or after being placed upon postsystolic myocardial augmentation (last column, Table I). The decrease in left intraventricular pressure in all cases in which the animal was undergoing augmented circulation is significant. The elevation of arterial blood pressure measured in the aorta is appreciably higher during augmentation than during the control period. The column headed VC, or ventricular component, demonstrates that portion of the pressure curve which is contributed by true ventricular contraction. It is apparent that in the physical system in which cardiac output remains constant but in which intraventricular pressure is reduced, the work of the heart must also be reduced.

TABLE I.

	O_2, cc/min.	A/V O_2 diff., cc/100	LVP mm Hg	AP mm Hg	VC	CO/ min.
A	110	3.5	164/0	158/120		3.124
	112 (PSA)	3.5	50/6	250/120	38	3.200
B	146	8.8	160/0	164/132		1.859
	144 (PSA)	7.9	90/2	240/128	36	1.714
C	84	3.1	148/2	144/119		3.709
	80 (PSA)	2.8	100/0	214/130	21	2.857
D	154	4.2	160/0	158/130		3.666
	142 (PSA)	4.0	95/5	250/130	34	3.550
E	106	5.2	168/0	164/129		2.038
	104 (PSA)	5.1	83/2	220/110	38	2.132

O_2, cc/min. = oxygen consumption, ml O_2 STPD /min.
A/V O_2 = difference in cc/min. ml O_2 STPD/100 ml blood.
LVP = left intraventricular pressure.
AP = systemic arterial pressure.
VC = ventricular component—that portion of resultant pressure curve contributed by contraction of true ventricle.
CO/min. = cardiac output (calculated by direct Fick principle), l/min.

Table II shows representative results in 5 animals which were subjected to hemorrhage and administration of an infusion of norepinephrine as described under *Methods*. The marked hypotension following this

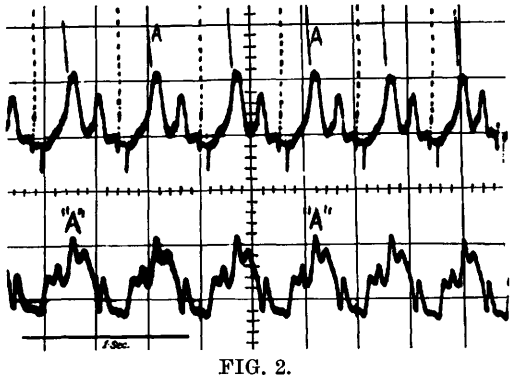

FIG. 2.

TABLE II.

Initial AP, mm/Hg	AP ff cessation, norepinephrine and hemorrhage	Pressure after 2 hr PSA	Survival time, hr
155/130	40/30	145/ 60	3
188/130	45/40	140/ 60	4
178/149	55/45	134/ 64	5
160/138	50/45	190/ 88	48
166/140	43/40	163/100	5

AP = systemic arterial pressure.
PSA = postsystolic myocardial augmentation.

maneuver is illustrated; elevation of blood pressure is seen following postmyocardial systolic augmentation; and whereas survival period in all of these control animals thus prepared has been 2 hours, survival time here has been significantly increased by augmented circulation (Fig. 3).

Discussion and applications. While previous attempts have been made to accomplish augmentation of the circulation by withdrawal of blood during systole and reinjection during diastole, difficulties have been encountered in 2 ways: (1) size of the pump must be adequate effectively to change blood pressure; (2) timing of reinjection must be such as effectively to accomplish reinjection during the short period of ventricular diastole.

What are the untoward effects of incoordinated phasing? Obviously, if the reinjection phase of the augmenting ventricle occurs synchronously with systole of the true ventricle, the resultant force will oppose the rate of ejection of the true ventricle, and thus increase its work load. The work performed by the left ventricle is directly proportional to the stroke volume times the resistance against which the stroke volume is ejected; thus, if the resistance is decreased, the work of the left ventricular myocardium is proportionately decreased.

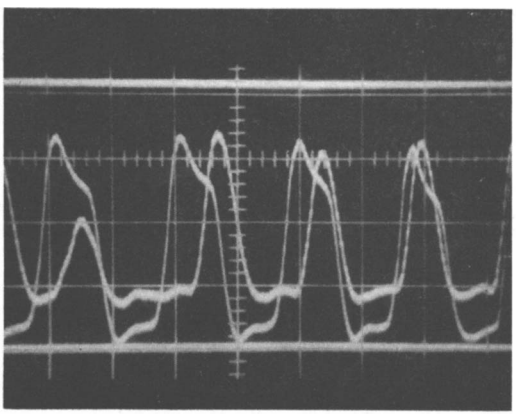

FIG. 3.

The method which we have developed allows the work of the myocardium to be reduced to a minimum so that blood pressure and flow may be maintained at a high level in the greater circulation. A device has been designed which functions in 2 stages. The first stage maintains adequate diastolic pressure in the systemic circulation; the second stage removes a great percentage of the work load of the left ventricle.

Summary. 1. Equipment has been developed which removes blood from the circulation during cardiac systole, thereby reducing intraventricular systolic blood pressure and reducing the work of systolic ejection of the heart. This equipment reinjects the blood during ventricular diastole, thereby increasing diastolic blood pressure and providing coronary blood flow. 2. An electronic circuit has been developed which enables the phasing of the augmenting systole to be accurately placed in relationship to the QRS complex of the EKG. Thus, timing of reinjection may be placed at any desired interval after the "R" wave of the EKG. 3. An animal preparation (dog) has been developed which combines a cardiac lesion produced by administration of norepinephrine combined with removal of one-third of the circulating blood volume and which is uniformly fatal. This procedure uniformly results in death of the control animal within an average period of 2 hours. Such animals uniformly develop dilated hearts and marked hypotension. 4. Survival time of animals thus prepared has been uniformly increased by application of the procedure of postsystolic myocardial augmentation. 5. The dilated heart and hypotensive state of the standardized animal in the preparation described above is reversed, and normal circulatory dynamics are approximated by application of this technic.

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