from which the milk agent had been eliminated by foster-nursing.

Few mammary tumors develop in mice of strains susceptible to spontaneous tumors if they do not have the mammary tumor milk agent, and the incidence cannot be significantly increased by the injection of estrogenic hormones(11,12). As opposed to these findings, mice of strains both susceptible and relatively resistant to the development of spontaneous mammary cancer have developed tumors following treatment with methylcholanthrene. These observations indicate that there is no positive correlation between the inherited susceptibility to spontaneous and to carcinogen-induced tumors(3,4). In fact, mice of different sublines of the same inbred stock may not show the same response. Breeding females of one subline of the C57 black stock revealed no induced mammary tumors(3) although when animals of the same line obtained the milk agent by nursing the incidence of spontaneous mammary tumors was at least 40% (unpublished data). Mice of another subline of the same strain, with a lower incidence of spontaneous tumors when they possess the milk agent, developed a few carcinogen-induced mammary tumors when females without the agent were maintained as either virgins or breeders and tumors appeared in the males when they were treated with both estrone and methylcholanthrene(4).

In the present study the extracts of 4 mammary tumors induced in the absence of the milk agent in mice susceptible (demonstrable when the agent is present) to the development of spontaneous mammary tumors were found to be free of the agent. Thus, the action of the carcinogen was not dependent upon the presence of a milk agent nor did it induce the genesis of an agent. Squamous metaplasia is characteristic of carcinogen-induced mammary adenocarcinomas and the tumors tested in this study had areas of keratinized stratified squamous epithelium. Dmochowski and Orr(4,8) observed that the degree of squamous metaplasia was greater in induced tumors developing in the low susceptible C57 black stock than in males of the high cancer C3H strain. The microscopic structure of mammary tumors that developed in mice free of the milk agent was similar to that of the carcinogen-induced tumors(13).

Summary. The mammary tumor milk agent was not demonstrable in the aqueous extracts of 4 mammary carcinomata induced by methylcholanthrene in female mice which were susceptible to the development of spontaneous mammary carcinoma but did not possess the milk agent before treatment because of foster-nursing. The action of the carcinogen was thus not dependent upon the presence of a milk agent.

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Received April 14, 1950. P.S.E.B.M., 1950, v74.

Experimental Artificial Left Heart to Permit Surgical Exposure of Mitral Valve in Cats.* (17852)

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The most promising among the methods devised to make practicable intracardiac surgery appear to be those which artificially support the circulation and render the heart bloodless for finite periods of time(1-10). The difficulties encountered in these various

* This work was done under a grant from the Schiff Centennial Fund in Montefiore Hospital, New York City

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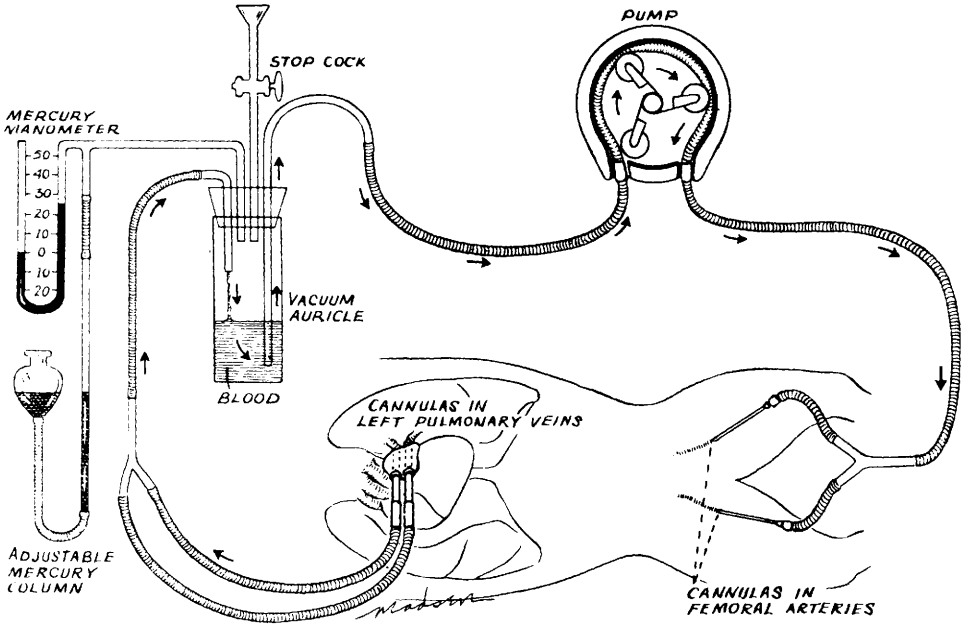

FIG. 1.
Diagram of Extracorporeal Circuit. Arrows indicate direction of blood flow. See text.

bloodpumping and oxygenating systems have generally been in attempting to reproduce the physiology of the lungs. The authors feel that further experimental development of the surgery of the mitral area need not await perfection of oxygenating systems. All that is required for exposure of the mitral valve is that the left side of the heart be bloodless. Our system consists essentially of a method of delivering normally oxygenated blood from the left lung into a glass chamber and thence pumping it into the arterial tree via the femoral arteries; while at the same time, blood from the right lung is prevented from entering the left heart by temporarily occluding the right pulmonary artery with a tourniquet (Fig. 1).

Method. I. *Apparatus.* The apparatus used in this method consists of four main elements (Fig. 2 and 3):

A. *Two stainless steel cannulae* for the left pulmonary veins.

B. *A closed glass chamber* to act as the auricular reservoir. There are 4 openings to this chamber. One opening admits a glass tube which delivers the blood collected from the left lung. A second admits a glass tube to the bottom of the chamber which collects the blood and carries it to the pump. The third admits a glass tube with a stopcock and funnel so that the system may be closed or opened to atmospheric pressure and through which fluids may be added. The fourth admits a glass tube which is connected to an adjustable mercury column and a mercury

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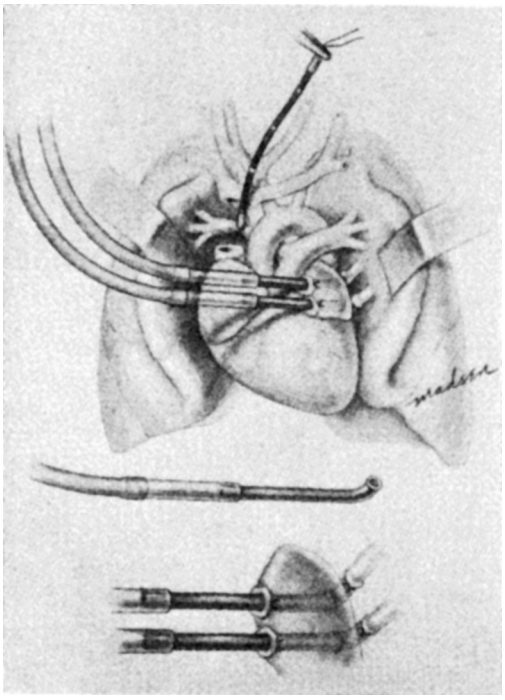

FIG. 2.
(A) Illustration of cannulae in place in left pulmonary veins, and tourniquet occluding right pulmonary artery. (B) Illustration of one pulmonary vein cannula. (C) Cannulae passing through left auricular appendage and auricle and fixed into the left pulmonary veins.

manometer. By controlling the height of the mercury column the pressure in the vacuum auricle can be altered and read on the mercury manometer.

C. *A modified roller-type pump* such as has been used by DeBakey(11) and Gibbon (4). The position of the rollers was controlled by having them ride on completely circular tracks, being held there by phosphor bronze leaf springs. The lumen was controlled by use of shims and thus could be varied precisely by changing the total shim thickness. The creeping of the rubber tube due to the rolling action was prevented by the use of rubber cuffs cemented to the outside of the rubber tube.

D. *Latex rubber tubing* connecting all of the above-described elements. All of the equipment which came in contact with blood was silicone-coated with GE Dri-Film No. 9987.

II. *Technical problems.* Collapse of the pulmonary veins with sealing of the openings of the cannulae by the walls of the veins was encountered. The cannulae, therefore, had to be so designed that they could be aligned with the walls of the vessels; and, the surges of negative pressure, which drew the blood from the veins, and tended to collapse them suddenly, had to be smoothed out. This was done by introducing an air chamber (the artificial auricle) between the cannulae and the pump. It was found that the blood could be removed from the pulmonary veins more rapidly and that the artificial system would be more stable, if the pressure in the artificial auricle was reduced to between −20 and −30 mm of mercury. Other problems arose at the arterial end of the artificial system. In our early attempts the blood was returned to the aorta via a cannula placed in the proximal end of the divided subclavian artery. Seventeen cats survived this procedure for periods varying from 2 to 20 hours, but all

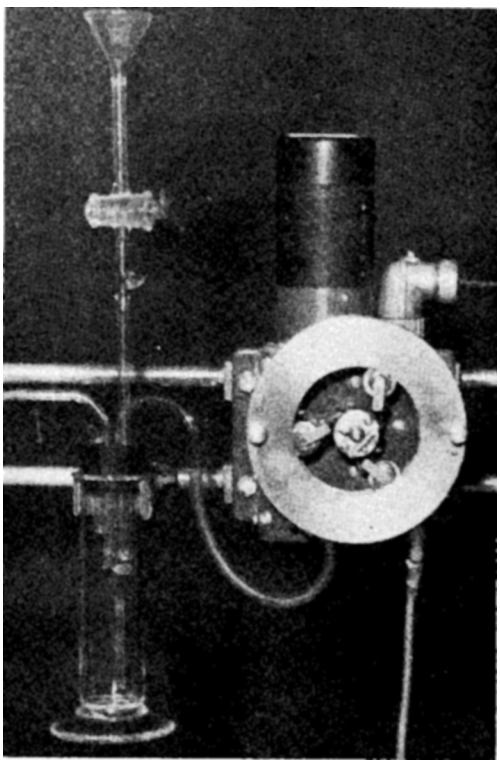

FIG. 3.
Photograph of vacuum auricle and pump.

died without fully regaining consciousness. We believed that this was due to cerebral ischemia rather than insufficient oxygenation of blood because there had been no cyanosis. On reexamining the system, it was realized that large quantities of blood had to be moved into the aorta through the comparatively small orifice of the subclavian artery. A high pressure jet was thus produced which had an aspirating effect on the adjacent opening of the innominate artery and this probably removed significant quantities of blood from the cerebral circulation. This problem was solved by returning the blood to the aorta via cannulae directed cephalad in each femoral artery.

III. *Technic.* The technic used is as follows: The animal is anaesthetized. The right and left femoral arteries are exposed for the insertion of cannulae. The chest is opened by splitting the sternum and both pleural cavities are entered. An artificial respirator attached to an endotracheal tube maintains the respiration with atmospheric air. The right pulmonary artery is dissected free. A silk ligature is passed around it and allowed to lie loosely in place. The left superior and inferior pulmonary veins are dissected free. Elastic threads are passed around them and allowed to lie loosely in place. After heparinization of the animal, cannulae directed cephalad are fixed in both femoral arteries. The pulmonary vein cannulae are then passed through the left auricular appendage and chamber of the left auricle into the openings of the left superior and inferior pulmonary veins. They are fixed in this position with the previously placed elastic threads. The artificial system having been filled with blood from a donor cat is then started. By lowering the mercury column, the pressure in the vacuum auricle is now adjusted to a negative pressure of −25 mm of mercury. The circulation is then maintained for approximately one minute with the animal's left heart and the artificial system in operation simultaneously: the blood coming from the right lung still passes through the left side of the animal's own heart while the blood coming from the left lung is collected by the cannulae and delivered via the artificial system to the aorta. By the end of this time, the previously placed silk ligature tourniquet (Fig. 2A) around the right pulmonary artery is gradually tightened, occluding this vessel. Thus, all of the blood, henceforth, is shunted through the left lung and the artificial system. At this point, either the left auricle or the left ventricle is opened. The steps to discontinue the artificial and restore the normal circulation are now begun. The exploratory incision in the auricle or ventricle is closed. The tourniquet around the right pulmonary artery is gradually released allowing blood to begin passing through the right lung and returning to the animal's left auricle. The elastic ligatures around the cannulae in the pulmonary veins are cut and the cannulae withdrawn from the veins into the animal's left auricular chamber. The pump is stopped and the cannulae removed by withdrawing them until their tips are in the auricular appendage and by ligating the appendage. Protamine sulfate is administered intravenously to counteract the previously administered heparin. The pericardium is loosely reapproximated and the chest wound closed in layers. The cannulae are removed from the femoral arteries and these vessels ligated.

Results. A total of 60 cats were used in this series. The first 53 were lost in the process of developing the final technic. Of the last 7 animals, all recovered from the procedure and survived for periods exceeding 36 hours except for one which was immediately sacrificed to obtain data. Four expired in periods ranging from 36 to 54 hours postoperatively. Two animals which are living to the date of this writing (a period of 3 months) appear to enjoy normal health (Table I). In the last 24 experiments, either the left auricle or the left ventricle was opened while the circulation was maintained by the artificial system and, in every instance, found to be practically bloodless. Direct blood pressure readings from the left subclavian artery revealed that the mean pressure rarely fell below 100 mm of mercury during the entire procedure including the period on the artificial heart.

Discussion. Hemolysis, which might have

TABLE I.
Summary of Results of Experiments Following the Development of the Technic.

Cat No.	Min. on artificial L. heart	Date of exp.	Hr. survived	Autopsy findings
54	28	12/14/49	36	Mucus plug in trachea.
55	15	17	48	Empyema, bilateral, lobar pneumonia.
56	14	19	*	
57	40	20	46	Meningitis.
58	29	24	54	Tracheo-bronchia tree blocked by thick secretions.
59	40	27	0	Sacrificed immediately after procedure. No abnormal findings.
60	32	29	*	

* Alive and well at this writing, a period of 3 mo.

been anticipated due to rapid circulation of blood in large quantities through an artificial system, was not a problem in our technic. By coating the equipment with silicone and designing the pump so that the walls of the rubber tubing never quite collapsed when compressed by the roller, thus minimizing crushing and shearing of red cells, hemolysis became insignificant. Tests for hemolysis in which one unit of citrated human bank blood was circulated through the artificial system at the rapid rate of 500 cc per minute for one hour revealed only faint traces of hemoglobin in the plasma. Although no measurements of the oxygen saturation were made, arterial blood always appeared to be bright red. Experience with pneumonectomies has shown that man and other animals survive indefinitely with one lung removed. It is still to be established whether a human suffering from long-standing mitral stenosis can safely oxygenate all of his blood on one lung for a period long enough to permit intracardiac surgery. It can be seen from Fig. 4 that the blood pressure with the artificial system is essentially a mean pressure, reflecting the surges inherent in the pump whose output is otherwise non-pulsatile. While others(10,12,13) have reported that pulsatile flow is necessary for the normal functioning of organs, it has been our experience that an essentially non-pulsatile flow at approximately normal mean pressures, for periods up to one-half hour, is consistent with the animal's survival.

In this report a method is presented which provides opportunity for further experimental surgery of the mitral valve by rendering the mitral area bloodless for finite periods of time without the use of an artificial oxygenator. Extra-corporeal systems which include oxygenators and also accomplish the above purpose have a broader field of application. Both the right and left hearts, as well as the lungs, are nonfunctioning and bloodless while such an artificial system is in operation. Such surgical problems as the repair of septal defects and operative procedures on the pulmonary arteries are amenable to a direct visual approach with such systems. A further advantage is that the introduction of cannulae to obtain the blood from the superior and inferior vena cavae is technically simpler than the introduction of cannulae into the pulmonary veins. Finally, an artificial heart-lung system might be used as an emergency procedure to tide a patient over a serious cardiopulmonary crisis. On the other hand, it appears that for experimental mitral surgery, systems including oxygenators are more complex than necessary. Moreover, they have not yet reached a stage that allows their ready reproduction and use in laboratories primarily interested in experimental mitral surgery. Our system has only a specialized application in that it would be used for intracardiac surgery of the left heart. For this purpose it seems ade-

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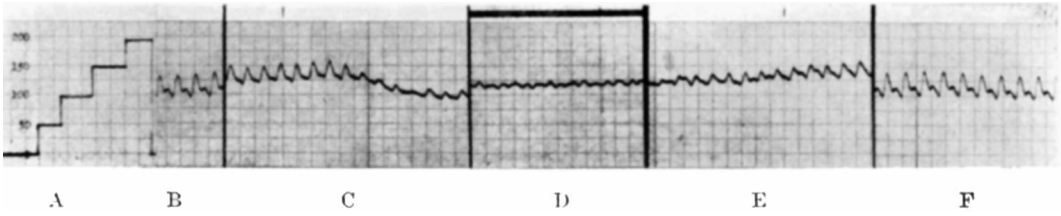

FIG. 4.
Sections of continuous blood pressure tracings in left subclavian artery of Cat No. 59 made with a Sanborn electromanometer and electrocardiograph. (A) Calibration in mm mercury. (B) Before introduction of cannulae. (C) Animal's left heart and artificial system in operation simultaneously. Latter portion: Occlusion of right pulmonary artery with consequent elimination of animal's left heart. (D) Animal completely maintained on artificial system. (E) Change over from artificial system to both animal's left heart and artificial system. (F) Conclusion of experiment.

quate. Its simplicity allows ready reproduction of the equipment in laboratories with modest mechanical facilities. Theoretically, it is conceivable that such a system could be applied to make bloodless the right chambers of the heart§, and even with 2 such systems to make the entire heart bloodless without an oxygenator. The dexterity required to place the cannulae in the pulmonary veins certainly makes less demand upon surgical skill than is generally required in attacking so difficult a problem as intracardiac surgery. The necessity of opening the chest and the heart to introduce the pulmonary vein cannulae is no disadvantage, as this must be done with any system in order to expose the mitral valve. In our system, the blood comes in contact with less artificial equipment and less blood (15 cc in the cat) is required to initially fill the system. Finally, it should be pointed out that the hemodynamics of our system are partly controlled by an intact and functioning right heart which responds to the afferent stimuli from the total animal.

Summary. 1. A system of bypassing the left heart to expose the mitral area for surgery is described.

2. The system consists of delivering normally oxygenated blood from the left lung via cannulae in the pulmonary veins, into a glass chamber and thence, pumping it into the aorta via the femoral arteries, while blood from the right lung is temporarily prevented from entering the left heart. Blood pressures are always maintained at adequate levels, and hemolysis is insignificant.

3. It differs from previously reported extra-corporeal systems in that the right heart and left lung continue to function, eliminating the need for artificially reproducing the physiology of the lungs.

4. In the 7 experiments after the development of the final technic, one cat was immediately sacrificed to obtain data, 4 survived for 36-54 hours and 2 are alive and well at this writing (a period of 3 months).

The authors are grateful for the guidance and help of Dr. H. M. Zimmerman. Dr. Clarence J. Schein assisted at some surgical procedures. Dr. Jacob Halperin aided in recording and interpreting the blood pressure tracings and electrocardiograms. Neuropathological studies were done by Dr. Martin G. Netsky. Mr. Ruthven C. Ferreira rendered valuable technical assistance.

Received February 17, 1950. P.S.E.B.M., 1950, v74.

§ During the progress of this work, Sewell and Glenn reported an experimental method of bypassing the right side of the heart. (Meeting of the American College of Surgeons, Chicago, Oct., 1949.)