PHYSIOLOGY

FURTHER EXPERIMENTS WITH OUR MECHANICAL HEART-LUNG-DEVICE

BY

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Using our mechanical heart-lung-system and our method of artificial circulation we performed a series of experiments in dogs to study the possibilities of intra-cardial operations.

The apparatus (2) (3) (fig. 1), which is designed and has sufficient capacity for use in man, consists of two units of six pumps, representing the artificial right and left heart respectively, an oxygenator and an automatic device preventing air to enter the arterial system. The oxygenator was, untill now, the most difficult part and the weakest point in an apparatus for artificial circulation. Our oxygenator or artificial lung, the spiral oxygenator, is of a quite new type, which has the great advantages that the oxygenation of 4 to 5 liters blood per minute is very good and that neither hemolysis nor foaming occurs, even if the blood circulates for hours through the apparatus. Our results with this new principle of artificial oxygenation are very satisfying.

Our method of extra-corporeal circulation (1) (2) (3) is very simple and can be applied with only very little damage to the subject. We introduce a catheter through the right external jugular vein into the vena cava superior close to the heart, and a second catheter high up in the vena cava inferior through the right femoral vein. Both catheters are connected with the artificial right heart, which sucks the blood from the venae cavae just before it would enter the heart. Then this venous blood passes the artificial lung and is oxygenated. The artificial left heart forces the blood into the femoral arteries in which T-canulas are inserted. A small part of the blood proceeds in the normal direction to the hind limbs, the greater part in abnormal direction in the aorta, and from here normally into the various arterial branches. In this way the whole circulation in the subject is maintained, the coronary and the bronchial circulation included.

As is formerly described (2) we tested the capacity of the apparatus in dogs with a bodyweight of about 32 kilograms, using only one half of the apparatus. As these experiments proved that half of the apparatus was sufficient to maintain life in dogs of 32 kilograms, we may readily assume that when the whole apparatus is used, the circulation and

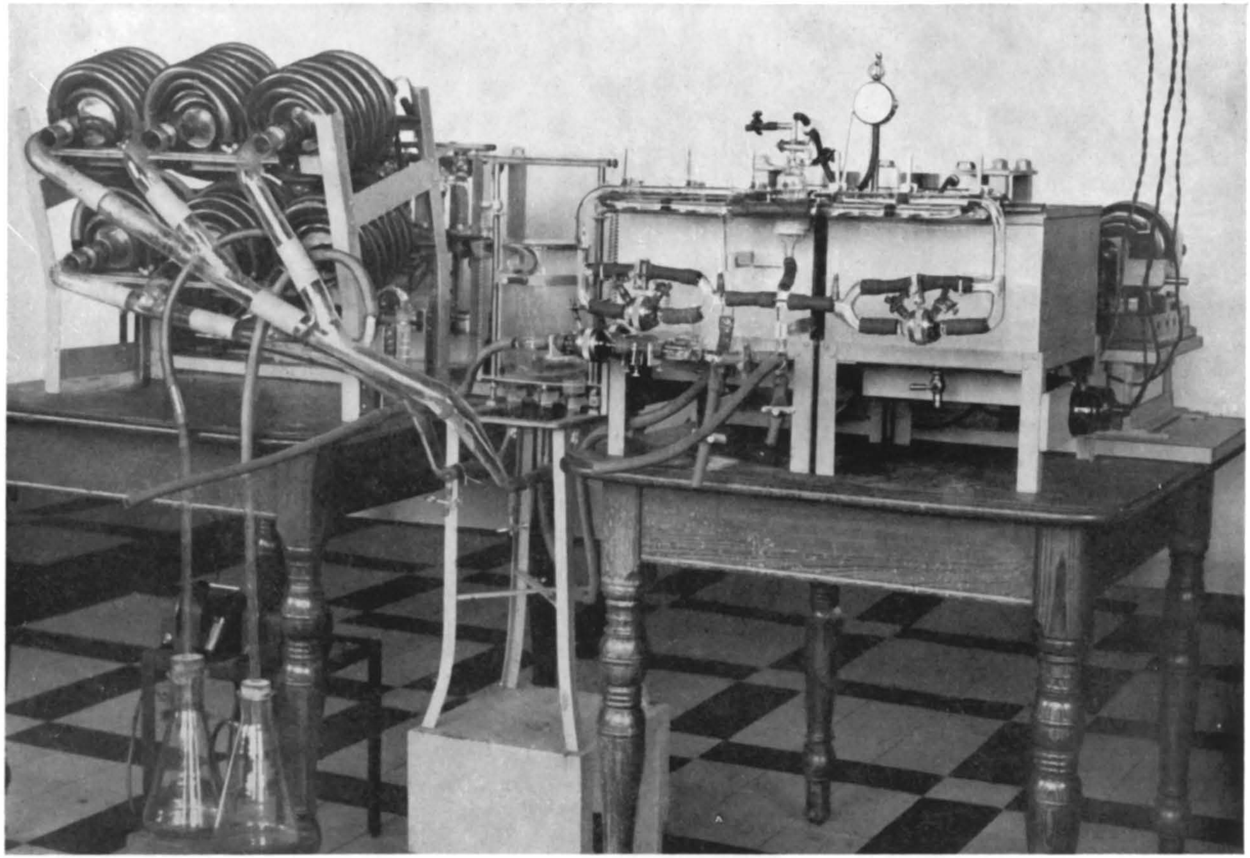

Fig. 1. Overall view of the apparatus.

oxygenation will be sufficient for a normal man of about 64 kilograms bodyweight.

Blood-pressure experiments.

From our experiments with artificial circulation in dogs (see below) it appears that the animals support this circulation for hours without a sign of early or later distress. This means that the circulation in the whole organism, especially in the heart and the nervous system is sufficient. Nevertheless we measured the bloodpressure in a carotid artery during artificial circulation in dogs. As the oxygenated blood is forced with a certain pressure by the artificial left heart into the femoral arteries, the pressure in the carotid artery will be less, and might possibly be too low for an adequate circulation of the brain. Our experiments, however, showed that the carotic pressure is very good. In one experiment we recorded e.g. during an artificial circulation of 1½ hours, in a dog of 25 kilograms, a mean carotic pressure varying between 100 and 80 mm Hg, which is a normal pressure for a dog. During this experiment we stopped the mechanical device from time to time to see how the blood-pressure would react. It is clear that the organic heart immediately resumes its function if the blood is not sucked away from the caval veins; but we were anxious to see whether the blood-pressure is restored quickly. These experiments showed that an (artificial) carotic pressure of e.g. 100 mm fell to 30 or 40 mm the moment the artificial heart was stopped, but that this (now organic) pressure rose again to about 100 mm within about ½ minute. This means that the organic heart remained in good condition.

We did not measure the pressure in the coronary arteries, but in our later experiments in which the heart was opened, it occurred now and then that a very small branch of a coronary artery was severed. In such cases we saw the blood spout from the vessel, which indicates that there was a real good pressure even in the small branches of the coronary system.

Re-animation experiments.

These experiments have little or nothing to do with artificial circulation, but as they were easily to perform with our apparatus, we did some in dogs.

The procedure runs as follows: a catheter is brought in the inferior caval vein and a canula in a femoral artery. Setting to work only the mechanical right-heart-pumps, practically all the animal's blood is aspirated, driven through the oxygenator and assembled in the reservoir. In this way the animal is practically totally bleeded. In most cases the respiration of the animal stops after some minutes; in some cases the heart also ceased to function (continuous check by electro-cardiographic recording). After the respiration has been absent for some 6 to 10 minutes (or in the case the heart stops, immediately hereafter) the left mechanical heart-pumps are put to function and the (oxygenated) blood is pumped back into the animal through the femoral artery. If the stillstand of the respiration (resp. the heart) has not been too long, the animal revives and survives in quite normal condition. Thus the animal has been clinicaly dead for some time and is reanimated.

One of our experiments of this kind ran as follows.

Dog, greyhound, 25 kilograms.

Narcosis: morphine-kemithal; 140 mg heparine Vitrum.

2^{53}	:	Respiration: 14 per min.; mean blood pressure (art. fem.) 120 mm Hg.
3^{00}—3^{08}	:	In 8 minutes time nearly 2 liters blood are aspirated from the animal.
3^{09}	:	Respiration has practically ceased; now and then a gasp. Arterial blood pressure 20 mm or less.
3^{17}	:	Eyelid reflexes nearly imperceptible.
3^{18}	:	Stretching of the hindlegs; no more gasps.
3^{19}	:	Electro-cardiogram much deformed, very small and very slow; almost absent.
3^{20}—3^{25}	:	The blood is pumped back into the animal.
3^{23}	:	Respiration 14 per min.; deep.
3^{25}	:	Electro-cardiogram better; fast.
3^{30}	:	Eyelid reflexes very feeble.
3^{31}	:	Blood pressure 130 mm.
3^{40}	:	Respiration 20 per minute.
4^{33}	:	Eyelid reflexes normal; animal moves hig legs and opens his eyes.
6^{00}	:	The animal tries to stand and to walk.
7^{30}	:	The animal walks and drinks.

Next and following days: The animal (which has been ,,dead'' for about 10 minutes) behaves normal.

The heartless dog.

This is more a curiosity than an experiment. In one of our experiments, whilst the artificial circulation was in function, the heart of the animal stopped rather suddenly, after the thorax had been opened. As this dog was lost for the experiment, we clamped the big vessels very close to the heart and removed the heart from the animal. Thanks to the artificial circulation the animal still ,,lived'' and showed (in very deep narcosis and with curare) undiminished eyelid reflexes and active retraction of the tongue during a period of about one hour; after which period we finished the experiment.

Experiments on artificial circulation.

The experiments described above are more or less adventitious; we actually aimed to study the possibilities of intracardial operations. For these operations an artificial circulation of about 40 minutes may be long enough, but we also performed circulation experiments of much longer duration.

The dogs supported artificial circulation lasting from 45 minutes to 4 hours very good; they recovered soon, and behave, months after the experiments, still normal. With one exception we did not observe any early or later distress. One of our dogs was killed 5 weeks after the experiment and examined thoroughly by the pathologist. (Prof. VAN NIEUWENHUYSE). He could not detect any abnormality which might have resulted from the artificial circulation. It is of special importance that the microscopic examination of the heartmuscle showed no alterations whatsoever.

The exception referred to above concerns a dog, who, after a 4 hours' artificial circulation, showed troubles of vision. At this moment, more than 6 months after the experiment, his sight is still diminished, but otherwise he is in a very good condition.

After these circulation experiments it seemed permitted to proceed with the aid of a thoracic surgeon to the complete operation, i.e. to open a heart cavity in dogs.

One has to realise, though, that the opening of the heart is a very serious procedure, during which the animal has to stand several interventions. First the catheters and canulas must be inserted, the blood sufficiently heparinised, and the artificial circulation with a mixture of the animal's own blood and that of a donor established. Then the animal has to be in deep narcosis and gets curare to facilitate work in the thorax. Further the thorax must be opened wide, and at last, after clamping eventually big vessels temporarily, the heart must be opened. The animal may endure each of these measures separately very well, but the accumulation of them may bring him in great danger.

The large thoracic wound can easily give rise to intra-thoracic afterbleeding in the heparinised animal, which may become fatal especially in dogs, as they have badly develloped mediastinal pleurae, compared with men.

Moreover, the nursing of dogs is rather difficult, much more difficult e.g. than of human patients. Thus altogether, the operative opening of a heartcavity is undoubtedly a serious procedure.

In the beginning of our experiments we did not realise this sufficiently and made the mistake to start at once with the complete operation. With the result that our first animals, although they had stood the opening of the heart very well and had all come in apparently good condition from the operation table, died 2 to 6 hours later.

Taught by this experience we proceeded step by step from now.

Artificial circulation in curarised dogs.

The animal is curarised so that he makes no respiratory movements.

Like the normal dog, the curarised animal stands the extra-corporeal circulation without harm and survives promptly.

Opening of the thorax in curarised dogs with artificial circulation.

In these experiments we payed special attention to the intrathoracic secondary hemorrhage.

As I pointed out already formerly (2, 3) the necessity to make use of an anti-coagulant is a weak point in artificial circulation procedures, during which big operations are performed. As soon as it is possible to construct the apparatus in such a way (e.g. by coating its surfaces or by using a special material as perhaps some plastics) that one is absolutely sure that no bloodclotting can occur, even after hours, we may leave out the anti-coagulant. But as long as such measures are not yet absolutely reliable, I think we had better make use of an anti-coagulant, as the smallest clot can cause unrestorable damage to the subject.

We used protamine-sulphate intra-venously as anti-heparine, but we have the impression that injection of protamine-sulphate is not quite harmless under the given circumstances. So in other experiments, we applied the protamine-sulphate locally on the innerside of the thorax-wound by means of spongostan soaked with protamine-sulphate. Moreover we gave transfusions with citrateblood. With both methods we had good results; the animals survive and recover in 1 of 2 days; we prefer, however, the local application of the protamine-sulphate.

One could also think of exsanguination after the operation, to eliminate the heparine, but we did not use this method.

Opening of a heart-cavity.

With this final operation we were also successfull now. The following is an abridged protocol of such an experiment.

Dog, male, 20 kg.

anaesthetic: morphine, kemithal.

heparine 110 mg.

After insertion of catheters and canulas curare (intercostrin): 10 mg.

16^{25}	:	*Artificial circulation started.*
16^{32}	:	Thorax is opened.
16^{35}	:	Incision of the pericard.
16^{36}	:	Pulmonary artery clamped.
16^{37}	:	Broad incision of the left auricle. The auricle is dry, the mitral valve is visible and accessible.
$16^{48}—17^{11}$	:	Closing of heart and thorax (drain).
17^{00}	:	2 mg prostigmine; 1 mg atropine.
17^{17}	:	*Artificial circulation stopped;* Catheters and canulas removed.
17^{30}	:	5 cc protamine-sulphate.
17^{40}	:	850 mg coramine; penicillin 100.000 U.

18^{00}—20^{00}: Transfusion of 400 cc citrate blood.
21^{00} : The animal has woken up from narcosis.
Second day: walks and drinks.
Third day: is very active, walks, drinks and eats.
Eighth day: sutures removed; dog behaves entirely normal.

Every time again it is amazing to see how, after clamping the pulmonary artery, the left auricle can be opened very widely without any blood flowing, so that one can see and has access to the mitral valves. If we open the right auricle both venae cavae are clamped, and in this case the venous blood of the coronary system has to be aspirated. This is easily done; the aspirated blood is collected in a sterile vessel and put in the reservoir of the system, so that it is not lost for the animal.

By the coronary vessels one can see very clear that the oxygen supply to the heartmuscle is good: one immediately sees the difference in colour between the veins and the arteries of the coronary system.

Although we reached our aim in so far that we have shown now that a dog can survive the whole procedure of the opening of an auricle and that it is thus possible with our method of artificial circulation to make the heart accessible to intracardial operations, we are continuing our experiments.

I am much indebted to my coworkers, especially to Dr van Goor, who mostly directed the pre-operations, to Dr Punt, who a.o. filmed our apparatus and experiments, and to the thorax-surgeon Dr Brom, who performed, with his assistents, the cardiac operations.

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