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The Heart-Lung Machine was Invented Twice—the First Time by Max von Frey

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In physiology and medicine it is not unusual that discoveries or inventions were made simultaneously or successively, but independent from each other. This is true also for the development of the heart-lung machine. Similar devices were designed and built in Germany and in the United States 50 years apart. The incentive for its development in Leipzig, Germany, originated from a series of systematic and quantitative experiments on isolated perfused organs in the department of physiology of Carl Ludwig (1816–1895).¹ The idea originated that, when an organ was perfused, the O₂ and CO₂ content as well as the metabolic products should be measured in the perfusion fluid by an apparatus that functioned not only as a pump, but that was also a substitute for the lungs. This apparatus was constructed and applied by Max von Frey (1852–1932) (Fig. 1).

Max von Frey was born in Salzburg, Austria, and studied medicine, physics, and mathematics. He joined Carl Ludwig's Leipzig Physiological Institute in 1878.² It was here that he built the respiration apparatus and applied it in experimental studies on dogs. He moved to Zürich, Switzerland, in 1897, and from there to Würzburg, Germany, in 1899. The major emphasis of his research was then on the registration of the pulse and on problems in sensory physiology. He specialized

in mechanoreceptive sensations, perception of pain, and thermal sensations.

The artificial lung that he built together with Max Gruber in 1885³ consisted of the hermetically closed glass cylinder (gg) with a centrally fixed metal core (*Eiserner Füllzylinder*) to reduce the air volume (Fig. 2). The glass cylinder was kept in constant rotation around a slightly oblique horizontal axis so that the venous blood that had entered at the top of the glass cylinder S₁ (*Deckel*) adhered to the inner glass wall. It was collected at the bottom N (*Boden*). While the thin layer of blood moved along the glass surface, it was in contact with O₂ that entered from a bottle (*Sauerstoff-Vorrath*) via the vent V and the manometer M₃ to maintain a constant partial pressure in the glass cylinder. The CO₂-loaded air was sucked from the glass cylinder and was used for analysis (*Luftproben*). CO₂ was absorbed in small bottles containing aqueous barium hydroxide (*Barytflaschen*), and the air was directed into the bottom of the glass cylinder by mercury suction-pressure pumps (*Saug- und Druckpumpen für die Luft*). The amount of oxygenated blood in the glass cylinder could be measured and kept constant. To do this, the tube K, which was filled with 0.5% NaCl, was submerged into the oxygenated blood at N and was divided outside the glass cylinder into the sodium chloride flask (*Kochsalzflasche*) for fluid replacement and into the manometer. The air-containing arm of the latter communicated with the inside of the glass cylinder.

The circulation of blood (the black tubes, top part of Fig. 2) was initiated and maintained by a small 10 ml syringe that was converted into a suction-pressure pump by means of two valves (*Ventile*). The piston of the syringe was connected to an excenter that moved it back and forth and that was mounted on the same driving axle that drove the mercury suction-pressure air pumps. The blood flow was very reproducible due to the accuracy of the gas-powered engine of the Institute. Since the gas measurements in the artificial lung required room temperature, it was necessary to warm up the oxygenated blood (*Vorwärmer*) and to cool down the venous blood (*Kühler*) to room temperature. Both systems were regulated automatically.

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FIG. 1 Max von Frey (1852–1932). Reproduced from Ref. No. 2 with permission of the publisher.

Using this respiration apparatus, the lower half of a dog was perfused and placed in the water container (*Wasserbad für das isolierte Organ*). The animal was bled to death. The abdomen was opened, the intestine was removed from the mesenterium, and the spine was cut above the kidneys. Thus, this preparation included only the kidneys, the pelvic organs, and the hind legs. Glass cannulae were inserted into the caval vein and the aorta below the origin of the renal arteries. To remove the venous blood from the preparation, another dog was exsanguinated, and the blood was pumped from stopcock H₂ to H₄ (Fig. 2), which was connected to the aorta, while stopcocks H₁ and H₅ remained closed.

This respiration apparatus of Max von Frey has striking similarities to the first apparatus specifically designed for cardio-pulmonary bypass, built and used by John H. Gibbon (1903–1973) for animal experiments. Gibbon was motivated in 1931 by the fate of a patient with massive pulmonary embolism who died because pulmonary embolectomy, the Trendelenburg operation, was performed very late as an ultimate, but mostly unsuccessful, procedure.⁴ In 1934, Gibbon started developing the heart-lung machine at the Massachusetts General Hospital in Boston, together with his wife as the only co-worker. The pulmonary artery was occluded in cats to mimic the clinical situation of massive pulmonary embolism.⁵

FIG. 2 The respiration apparatus built by Max von Frey and Max Gruber in 1885 (Fig. 1 in Ref. No. 3).

FIG. 3 The experimental heart-lung machine of John H. Gibbon. Reproduced from Ref. No. 5 (Fig. 2) by copyright permission of the American Medical Association.

The oxygenator consisted of a vertical revolving cylinder that was occupied by a hollow, closed, stationary cylinder (C, Fig. 3). A metal tube (D) passed through the center of the stationary cylinder to the bottom, conveying a mixture of 95% O₂ and 5% CO₂ that then passed up between the stationary and revolving cylinders over the film of blood. Pump (E) moved transferred blood from the venous cannula to the oxygenator, and pump (E') returned the oxygenated blood to the arterial cannula. The pumps were a modification of the perfusion pump of Dale and Shuster in which a rubber finger-cot (F, F') was alternately compressed and expanded by an air piston pump (H) that was driven by an electric motor. Two valves (G) guaranteed the direction of flow. Collapse of the jugular vein was prevented by converting the intermittent flow produced by the pump into a continuous one by inserting into the circuit a closed air chamber (K) in which air was maintained at a negative pressure, and by the use of an automatic magnetic clamp (LQ). Since pulsatile flow of blood into the oxygenator produced foaming, a second air chamber (S) was placed in the blood circuit between the pump (E) and the oxygenator to convert the pulsatile flow into a smooth one. Because of slight dif-

ferences in the output of the two pumps (E, E'), the level of blood collected in the cup (B) of the oxygenator was regulated by a second automatic magnetic clamp (V). The temperature of the blood entering the femoral artery was recorded by a thermometer (W) and was usually between 37 and 38°C. Before the artery and vein of the animal were connected to the apparatus, it was filled with a 6% solution of acacia in a physiologic solution of sodium chloride that was continuously circulated at an even temperature through the oxygenator and the pumps by opening the short circuit (X). The artificial circulation of the animal was started by opening the tubes from the cannula inserted in the right jugular vein (FROM VEIN) and to the centrally directed cannula tied in the right femoral artery (TO ARTERY). The short circuit (X) was closed. Since the saline solution was thereby injected into the animal, there was dilution of the blood as documented by the decrease in the hematocrit. In 1953, Gibbon performed the first successful open-heart operation with an enlarged and more sophisticated heart-lung machine. The patient was an 18-year old girl with a large atrial septal defect.⁶

The comparison between the two designs (Figs. 2 and 3) demonstrates the importance of independent research and the timeliness of physiologic principles for the solution of medical problems. It also shows that an invention can be utilized successfully only when there is an urgent need for clinical application.

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