Profiles in Cardiology

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Ivan Petrovitch Pavlov

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Ivan Petrovitch Pavlov (1849–1936) (Fig. 1) was born September 14, 1849, as the son of a priest, in the region of Rjäsan, about 200 km from Moscow.¹ As a student in St. Petersburg, he attended the lectures and demonstrations of Elias Cyon² whom he admired because of his surgical skills in animal experiments. Pavlov became the active collaborator of Cyon's and took physiology as his major subject.³ After Pavlov obtained his M.D. degree in 1883, he was sent by the Military-Medical Academy in St. Petersburg to Germany where he worked for two years in the laboratories of Rudolf Heidenhain in Breslau and of Carl Ludwig in Leipzig. In 1890, Pavlov was appointed extraordinary professor of pharmacology in Tomsk and moved to St. Petersburg, where he was appointed professor of physiology at the Military-Medical Academy in 1897. In 1904, he was the first physiologist to be awarded the Nobel Prize in Physiology or Medicine for his work on the physiology of digestion.⁴ Both under the czars' and the Soviet regime, he had well equipped laboratory space and resources. He was highly respected in the scientific community and attended many international conferences throughout his life, including the International Physiological Congress 1929. He died on February 27, 1936.

In his monograph on the physiology of digestion⁵ and in his Nobel lecture,⁶ Pavlov described the surgical procedure that enabled him to study the influence of the central nervous system on the secretion of gastric juice in dogs. First, he created a chronic fistula of the stomach and inserted a tube to collect and quantitate gastric secretion. He then mobilized the esophagus in the middle of the neck, cut it transversely, and sutured the proximal and distal end into the skin so that the food that was chewed and swallowed by the dog fell out at the proximal

end of the esophagotomy. He called this procedure "sham feeding." Before, during and after this sham feeding, gastric juice was collected. About five minutes after the feeding began, the quantity of gastric juice increased, especially if meat or bread was fed. When the vagus nerves were cut (which was done in a two-step approach), secretion of gastric juice stopped. When the peripheral end of the cut vagal nerve was stimulated electrically, secretion of gastric juice occurred again. Based on these findings, Pavlov concluded that the brain has an influence on secretion via the secretory centrifugal vagal nerve fibers. A similar experimental approach with a chronic salivary gland fistula was used routinely to study the conditioned reflex.

In the field of circulatory physiology, Pavlov studied the innervation of blood vessels and the effect of vagus nerve stimulation on the heart while he was in Leipzig working at the Physiological Institute with Carl Ludwig.^{7,8} Pavlov used a state-of-the-art flowmeter that was an improved version of the "Stromuhr."⁹ With this instrument (Fig. 2) he measured the stroke volume in dogs. The animals were anesthetized with morphine and muscle relaxation was achieved with curare. To prevent the negative chronotropic effect of vagus stimulation, atropine was used. Experiments were performed with artificial ventilation in both closed-chest and open-chest animals. The vagus nerve was prepared in the neck and above the diaphragm, cut, and the peripheral end was stimulated electrically.

The instrument was inserted between the left and right ventricle, that is, between the carotid artery and the jugular vein. The glass reservoir A (Fig. 2) was filled from the left ventricle (Lv), the reservoir B emptied into the vein (Rv). They were connected by a thin glass tube, thus resembling the original "Stromuhr."⁹ At the beginning of an experiment, reservoir B was filled with defibrinated blood, the same amount as arterial blood flowed into reservoir A. The blood flow was directed by the double wedge (k) which pressed the rubber tubes (ab') and (a'b), respectively, against the immobile iron plates (p). Two electrical batteries served to ensure the alternate occlusion of the two rubber tubes until reservoir A was filled from the left ventricle and reservoir B was emptied. Battery I (on top of Fig. 2) regulated the magnets at (III) and (III') that attracted the lever on which the double wedge was mounted so that one pair of the rubber tubes, (ab') or (a'b), was closed. The other battery (1) regulated the switch of current generated by battery I. This was triggered by a floating rod which, when blood was flowing into reservoir

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FIG. 1 Ivan Petrovitch Pavlov. Reprinted from Ref. No. 6 with permission of © The Nobel Foundation.

FIG. 2 The flowmeter that Pavlov used in his experiments. Reprinted from Ref. No. 7.

A, pressed a small plate at (4) against a pin at (5) so that lever arm (V) was attracted by the magnet and the double wedge (k) was forced to close the arterial inflow to reservoir A.

With this highly sophisticated instrument, Pavlov demonstrated that stroke volume increased when the vagus nerve was stimulated. This effect was more pronounced in animals in which heart function was already depressed. He had difficulty interpreting this result and hypothesized that the heart could receive more blood in diastole or eject more blood in systole. However, he had no direct information on the relaxation of the heart and on the inotropic mechanisms. In addition, the results he had obtained were variable. It is interesting to speculate that Pavlov, on the basis of this experimental experience, decided to do chronic experiments in animals as far as gastric function and the conditioned reflexes were concerned. In these later studies, the acute surgical procedure was done well in advance of the careful and repeated observations which were extended over weeks.³ On the other hand, in his early cardiovascular experiments, Pavlov acquired his surgical experience and manual dexterity for which he was well known.³

Pavlov became very famous for his studies on the gastrointestinal tract and on the central nervous system, but his first experimental experience was in cardiovascular research. His experiments on cardiac output were done at a time when the principle for measuring it¹⁰ had already been developed in 1870 by Adolf Fick (1829–1901). At that time, however, it was not yet possible to get mixed venous blood from the pulmonary artery. It was only much later, in 1929, that Werner Forssmann (1904–1979) introduced cardiac catheterization by experimentation on himself.¹¹ The first data on cardiac output in humans were published shortly thereafter.¹²

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