flashes, as can be shown by varying flash intensity (Table b). (3) Biphasic effects of chlorpromazine. Flash nystagmus like central nystagmus is enhanced by chlorpromazine<sup>6</sup> (Figure 2). Application of the drug makes it possible to evoke flash nystagmus in all animals, even if they had been refractory before. The reinforcement of the eye movements persists for several hours and is followed by a depressory phase. The period of enhancement of flash nystagmus is much longer (4–6 h) than that observed for central nystagmus.

Flash nystagmus differs from central nystagmus in the limited frequency range of stimulation (Figure 2) and in the position of the optimum, which is 40-60 c/s for excitation of the optic nerve<sup>2</sup>. This divergence is under closer study.

Quantitative differences are also apparent between optokinetic and flash nystagmus. The optokinetic stimulus is much more effective: all animals give a positive response and in the same animal the optokinetic reaction is much more intense than flash nystagmus.

Zusammenfassung. Monokuläre Reizung des Kaninchens durch Lichtblitze ruft einen Nystagmus hervor, dessen Richtung identisch ist mit der Richtung der Augenbewegungen, die durch elektrische Stimulierung des ipsilateralen Nervus opticus verursacht werden. Die anhaltende Beleuchtung des kontralateralen Auges hemmt die Nystagmusreaktion.

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- <sup>6</sup> F. Bergmann, J. Gutman, and M. Chaimovitz, Exp. Neurol. 5, 210 (1962).
- <sup>7</sup> The authors wish to thank the Joseph Porton Trust for their generous support of this work. They are indebted to Mr. R. Knafo for preparation of the drawings.

## PRO EXPERIMENTIS

## A Technique for Repetitive Long-Term Measurement of Aortic Pressure and Cardiac Output in the Unanaesthetized Dog Using an Implanted Catheter

Techniques for studying circulatory dynamics in unanaesthetized animals are gaining increasing interest due to the realization that anaesthetics cause considerable changes in cardiovascular function and may greatly influence reactions to drugs. In the course of cardiovascular studies in unanaesthetized dogs we have developed a new method, allowing continuous or repeated recording of aortic pressure pulses and cardiac output over periods of many months. Because visitors to our laboratories have shown considerable interest in this method we present its details in this report.

Principle of the method. A Teflon® catheter is inserted into the abdominal aorta from the femoral artery. The catheter is connected to a syringe needle with a stopcocktype valve embedded in a polyamide plate which is held in place by subfascial implantation.

Assembly of catheter and materials used. The Teflon® catheter (internal diameter 1.0 mm, external diameter 1.5 mm) is connected to a syringe needle with a valve of the stopcock type. The needle, which is made of stainless steel, is embedded and fixed by Araldite® in a polyamide plate consisting of a flat ring and a crossbar; it passes through the crossbar at an angle of approximately 25° to the plane of the ring itself. In order to prevent kinking the first 4 cm of the catheter beyond the ring are reinforced by a second Teflon® catheter (internal diameter 1.6 mm) with a spiralled surface contour. Details are given in Figures 1 and 2.

Operating procedure. Mongrel dogs weighing 12-20 kg are anaesthetized with pentobarbital (30 mg/kg i.v.). Under strictly aseptic conditions an incision of about 3 cm is made over and parallel to the distal part of the femoral artery. After splitting the fascia the artery is dissected free from surrounding tissue and ligated. The Teflon®

catheter is then introduced into the femoral artery and threaded up to the point at which the ring itself prevents further progress. Thus the part of the needle extending beyond the crossbar and protruding into the Teflon® catheter lies within the artery. This proximal part of the catheter is anchored to the artery by ligatures which themselves are fixed to the polyamide plate. The plate is

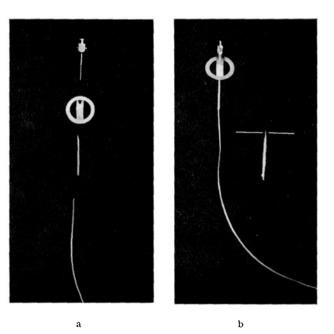


Fig. 1. (a) Single parts of the catheter (before assembly). From top to bottom: syringe needle with valve of the stopcock-type, polyamide ring with crossbar, Teflon® catheter with spiraled surface (reinforcing catheter), aortic Teflon® catheter. (b) Catheter assembled and ready for implantation. At the right, key to close and open the valve.

then placed on the muscle and covered by the fascia, which is closed loosely by catgut ligatures. The skin is sutured with nylon thread leaving only the metallic needle head above the skin surface (Fig. 3). The catheter is filled with sterile saline and the valve opening covered with a polyethylene cap.

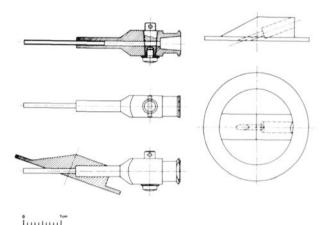


Fig. 2. Working draft of the syringe needle with stopcock valve and of the polyamide ring with crossbar.

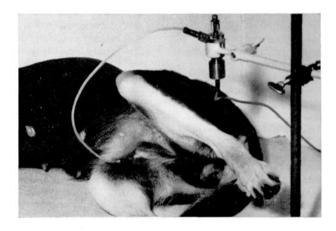


Fig. 3. Unanaesthetized dog with implanted aortic catheter during recording of aortic pressure pulses. This photograph was taken 10 months after implantation of the catheter.

The length of the catheter may be chosen at will. For our hemodynamic studies we found it most suitable that the tip of the catheter should lie between the origin of the renal arteries and the aortic bifurcation. During the first few days penicillin and streptomycin are given routinely. As a rule the wound heals within two weeks and thereafter the animal is ready for experimental study.

Postoperative procedures. Blood clotting presents no problem. The catheter is flushed with saline at the beginning and end of each experimental period. To open and close the valve we use a special key (Figure 1).

Apart from a protective bandage no special care is necessary. Infection, either local or general, has not occurred although connecting the catheter to the recording apparatus is not done under strictly aseptic conditions. As of now we have prepared over 20 dogs with the described procedure and used them in circulatory studies for many months. One of the dogs in current use has had a functioning catheter for more than one year. Death, when it occurs, is usually caused by perforation of the aorta due to chronic traumatization of the aortic wall by the tip of the catheter. Autopsy shows obliteration of the lumen of the cannulated femoral artery. The aortic part of the catheter is often found to be incorporated into the vessel wall, only the last few inches lying free in the lumen. Embolic episodes during life were not recognized in contrast to earlier experiments in which catheters were implanted in the carotid artery.

Applicability. We have used this method of aortic catheter implantation for repeated measurements of aortic pressure pulses as well as for the determination of cardiac output with the dye-dilution method. For the latter purpose aspiration and reinfusion of the arterial blood was performed under strict aseptic conditions. The dye was injected by a second catheter of the same type implanted into the right jugular vein, the tip lying in the right atrium.

Zusammenjassung. Es wird die Herstellung und Implantation von Aortenkathetern beim Hund beschrieben. Die Methode erlaubt wiederholte, kontinuierliche blutige Messung des Aortendrucks sowie die Bestimmung des Herzminutenvolumens am wachen Tier.

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Abteilung für experimentelle Medizin, F. Hoffmann-La Roche & Co., AG, Basel (Switzerland), December 14, 1964.

## Quantitative Measurements of Microscopic Changes in the Vascular Bed

A method for measuring microscopic changes in vascularity could find many research applications, as standard methods are not accurate enough. Quantitative X-ray fluorescence microanalysis has made it possible to measure vascularity changes in vivo within areas 50–750  $\mu$  across. The method is applicable to surface areas or membranes

A focused X-ray beam from an X-ray microscope is passed through an aperture system consisting of two molybdenum electron microscope apertures. The aperture close to the X-ray source has the smallest diameter. The other aperture serves as a scatter trap and defines the size of the area analysed. The specimen is placed on top of this aperture. X-ray fluorescence is generated in the specimen and radiates in all directions. A sector of this radiation is then analysed by a proportional counter and a multichannel pulse height analyser. This system can discriminate between the different wavelengths of the fluorescent radiation. On an oscilloscope, a curve is seen in which each peak is due to one element and its height is proportional to the quantity in the specimen. The