Modern Techniques of Venous Occlusion Plethysmography in the Assessment of Peripheral Vascular Disease

by Dr J Brugmans, Mr A Jageneau, Dr C Harris and Mr M B Emanuel

(Departments of Clinical Research and Applied Pharmacology, Janssen Pharmaceutica, Beerse, Belgium, and Centre for Medical Research, University of Sussex, UK)

When William Harvey in 1628 described his observations on blood circulation in De motu cordis, the importance of his partly experimental and partly speculative results was still unclear. Within a few years Malphighi discovered the capillaries by means of the microscope and described them as tubules. Since these basic discoveries, research on blood circulation has developed in three major directions:

(1) Regulation processes, including homeostasis of the system according to humidity, temperature and nutrition, have been studied. Much of the pioneering work in this field was carried out by Claude Bernard in the mid nineteenth century. During the last 30 years, the understanding of self-regulating control processes has markedly increased. Rosenblueth and Wiener in the 1940s described the blood circulation as a cybernetic system.

(2) Blood vessels also attracted more detailed investigation. Modern microscopic technique gave more information on the terminal vascular bed, demonstrating gradual thinning of wall thickness and decreasing diameters in vessels as small as 5 μm (Wiedemann 1973). This means that blood flows through vessels with diameters equal to or smaller than that of an erythrocyte (7 μm). Microcirculation and metabolic exchange processes, taking place in arterioles, terminal arterioles, capillaries, postcapillary venules and venules have been studied (American Journal of Medicine 1961, Rhodin 1973). For the capillary circulation, precapillary sphincters are thought to be very important, as they are the most distal point at which changes in peripheral resistance occur (Mellander & Johnson 1968). These sphincters are formed by smooth muscle cells which separate arterial and capillary vessels. They afford the ultimate control of blood flow into the capillary circulation. Arterial vessels are smaller in diameter than veins (the ratio of arterioles to venules being approximately 1:3). Larger vessels are neurogenically controlled by the sympathetic or parasympathetic systems, whereas smaller vessels are influenced by myogenic or local metabolic stimuli (Messina 1976).

(3) Blood flow behaviour relative to viscosity and flow has generated particular interest in the last decade.

Historically, the study of blood flow has concentrated on vascular diameters while blood viscosity has been somewhat neglected. Poiseuille in 1840 clearly formulated the connexion between flow rate, pressure, viscosity and the dimensions of the system by the following equation:

\[ i = \frac{\pi \cdot 4Pr^4}{8\eta L} \]

where \( i \) = flow rate,
\( p \) = pressure,
\( r \) = radius of the vessel,
\( \eta \) = viscosity coefficient,
\( L \) = length of the vessel.

It must be mentioned that blood is a heterogeneous suspension which differs markedly from homogeneous suspensions. Blood is described as a non-newtonian fluid, because its viscosity changes with the velocity gradient (shear rate). The viscosity of the plasma alone is higher than that of water, yet it produces only a small fraction of the total blood viscosity.

The flow characteristics of blood are mainly the result of the properties of cellular constituents and cell-cell interactions. Erythrocytes are of profound influence (Dormandy et al. 1972, Murphy 1973). Other important factors are the elasticity of the vascular system (which reacts to increased pressure with a higher permeability) and the inconstant character of blood pressure. These facts mean that the normal application of Poiseuille's law to blood circulation cannot be made without the introduction of correction factors (Weizler & Sinn 1953). The complex interaction between viscosity and vascular diameter may be demonstrated by the fact that not only does pressure promote blood flow, but the combination of high pressure and small sized vessels produces high shear rates in a non-newtonian fluid. This is followed by decreasing viscosity and increasing blood flow.

Paradoxically, blood requires a greater propulsive power when moving slowly. By plotting viscosity changes against the cardiac output, it can be shown that a 10% fall in viscosity produces a 20% rise in cardiac output. This means a linear function of 1:2 without any change in heart rate. Thus, the vascular system is dynamic and reacts quickly to external and internal stimuli, frequently mediated by viscosity changes (Dormandy 1970).

Measuring Techniques
In order to evaluate the blood flow and its changes in both intact and damaged systems, a
measuring technique has been developed which registers the total flow during each time unit, regardless of whether the distribution follows major vessels or collaterals. It is important that results should not be influenced by the origin of the changes of blood flow, which can be occasioned by changes in the blood itself, or in the vessels. These measurements are diagnostically important and may also be included in the evaluation of pharmaco-therapeutic or surgical measures.

Both invasive and non-invasive methods for evaluating peripheral blood flow have been used. Invasive methods include venous drainage, various procedures based upon indicator dilution, electromagnetic flow measurement around the major vessels and the intra-arterial application of microglobules labelled with radioactive tracers. However, invasive methods are not suitable for routine measurement.

Non-invasive methods have been developed on the basis of oscillometric, plethysmographic, calorimetric, ultrasonic and electromagnetic measurements. The most important non-invasive method for measuring the blood flow is venous occlusion plethysmography, which registers the total flow during each time unit regardless of the distribution, origin or change of the flow.

Development of Venous Occlusion Plethysmography
The theoretical basis of venous occlusion plethysmography lies in the fact that an external pressure, usually not more than 50 mmHg, suppresses only the venous flow, while the arterial flow remains unaffected. However, the blood arriving with each pulse wave cannot leave the capillary system of a given limb and therefore produces an increase in the circumference of that limb. This situation occurs for only a few heart beats. Increasing capillary pressure results in a venous pressure greater than 50 mmHg and venous flow then returns. In venous occlusion plethysmography, the increase in circumference of a limb is measured after a well-defined infow time. This increase provides information on the arterial flow.

Brodie & Russell (1905) described the first flow measurements using venous occlusion plethysmography. Today, the principle of the method is still the same. A cuff is placed on the proximal portion of the limb or segment where the blood flow is to be measured. The cuff pressure must be higher than the venous pressure but lower than the diastolic arterial pressure. This must be coupled with a means of measuring the increase in volume of the limb.

Hewlett & Zwaluwenburg (1909) introduced plethysmographic measurement after physical exercise. Lewis & Grant (1926) carried out their measurements in conditions of hyperaemia provoked by exercise or ischaemia. A most important step in the development of plethysmography was the introduction of the mercury-in-silastic strain gauge as a detector (Whitney 1949). Changes in the circumference of the limb are directly transformed into changes in the resistance of a mercury column, resulting in changes in electrical current. The calibration of the strain gauge was simplified by Brakkee & Vendrik (1966) and Barendsen et al. (1971) refined the method, using electrocardiographic triggering of the venous occlusion intervals, allowing semicontinuous measurement of arterial and venous blood flow. This report will describe the Periflow* venous occlusion plethysmograph designed by Janssen Scientific Instruments, which introduces several improvements in plethysmography. These include automatic and rapid inflation of compressed air into the cuff, electronic programming of the measurement parameters, on-line calculation and direct plotting of the measured data.

Pathological Changes of Blood Flow and their Detection
If the organism in general and the blood circulation in particular are understood as cybernetic systems, the numerous feedback processes serve a protective function but are also the source of disturbances and pathological processes. Alterations in feedback mechanisms modify tissue homeostasis and result in changes of peripheral blood flow which help to prevent arteriopathies. A stenosis in one of the major vessels has little effect on blood flow until a critical lumen reduction has been reached. The process of compensation for reduced flow helps to maintain optimal metabolic conditions, but the normal position of the haemodynamic equilibrium is thereby changed. Therefore, early detection of such disturbances is very important if preventive measures are to be taken.

MATERIALS AND METHODS
Instrumentation
The Periflow® consists of two sections, one mechanical and one electronic. The mechanical portion consists of a case containing two 50 litre barrels, 5 electromagnetic valves and a pressure control module. The electronic section consists of a standard 19 inch (53.4 cm) equipment rack, in which are installed two operating XYY1 recorders with electronic two-channel venous and arterial occlusion plethysmographic control units.

Measurements free from artefacts are obtained by a specially shaped, 15 cm wide, non-elastic cuff. This receives the required pressure by coupling over short, wide connexion tubes.

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Fig 1 Influence of venous occlusion in the distal venous system

Tracing 1: ECG; differential lead
Tracing 2: Peripheral venous pressure, directly measured by means of a small catheter in a superficial vein
Tracing 3: Volume changes in the occluded limb (Periflow measurement)
Tracing 4: Moment and intensity of pressure inflation into the occluding cuff (ECG-triggering – 3 heart beats inflation, 2 heart beats deflation)
Tracing 5: Time pulses (seconds)

(1.5 m x 5 cm) with a relatively large pressure reservoir (100 litres). Pressure is regulated by means of magnetic valves. Sensitive measurements are possible because of the very low weight of the mercury strain gauge and its connectors, eliminating pressure effects by the detector unit upon the limb. Reliability of clinical and experimental data is assured by an automatic programme, preventing operating deviation between different measurements. Automatic data processing reduces mathematical effort and calibration is carried out by an electrical calibration circuit. The whole instrument is thus well adapted to practical needs.

To evaluate vascular reactions following ischaemia, the cuff is capable of accepting the suprasystolic pressure values necessary for arterial occlusion. After an optimal time interval of between 1 and 10 min the arterial occlusion is stopped and the flow measurements again start automatically.

The strain gauge has been significantly improved, since the external diameter of 0.6 mm and the internal diameter of 0.3 mm provide low weight with high elasticity. For a 1% elongation, a force of 200 mg is required. For water-bath measurements a special electrically isolated gauge is provided. A linear relationship between resistance and volume deformation of the mercury column is observed up to values at least 50% above the initial value. A mathematically derived relationship between either the circumference or volume of a given limb or segment and the change

Fig 2 Schematic shape of the arterial blood flow curve after arterial occlusion

1 Arterial occlusion
2 Arterial rest flow value
3 50% of the peak flow value
4 Peak flow value (maximum value during the evaluation of reactive hyperaemia, measured in ml/100 ml per min)
5 Time before onset of the peak flow
6 Time until 50% reduction of the peak flow value
7 Period of reactive hyperaemia
8 Period and intensity of reactive hyperaemia (integrated flow-time area during reactive hyperaemia)
in electrical resistance of the mercury column has shown that the limb volume is proportional to the resistance.

The frequency of the mercury strain gauge is determined by the elasticity of the silastic tube and the mass of mercury. It was found to be above 100 Hz. Measurements are carried out at a frequency of 30 Hz. The processes of occlusion and release of the venous flow are triggered by the heart beat, as recorded by an electrocardiograph.

To obtain maximal synchronization between cuff and flow pulse, a delay unit is inserted. Occlusion time is freely adjustable, but intervals are always multiples of the time intervals between two heart beats. After a chosen occlusion interval, the pressure is automatically removed. The same cuff is used to induce ischemia, but in this case the applied pressure is higher. These conditions allow the semi-continuous recording of the peripheral pulse and the measurement of the peripheral flow.

The method has certain disadvantages which are inherent in all venous occlusion plethysmography. For example, it is impossible to take measurements during movement or muscular work of the limb; the limb must be placed at the level of the heart; differentiation between muscular and cutaneous flow is incomplete and the subject must be supine.

*Periflow® Programmes*

Use of the Periflow® allows various measurements to be made. It is important to note that the

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Fig 3 Arterial blood flow in a healthy subject (Above) and in a patient with intermittent claudication (Below):

Upper tracing: volume changes in the limb (cycles of 3 heart beats venous occlusion and 2 heart beats venous return)

Lower tracing: calculated arterial flow during reactive hyperaemia
position of the patient, the position of the limb under investigation and the skin temperature have a great influence upon the reproducibility of the results. The necessary total outflow from the venous system is attained by keeping the limb at heart level.

(1) Venous pressure can be measured from the minimal occlusion pressure of the cuff, at the point where no increase in circumference is detected by the strain gauge. The pressure of the cuff is varied until no further peak in the record is registered.

(2) Peripheral arterial rest flow can be measured by raising the pressure of the cuff to 500 mmHg. Experimental results have shown that a time interval of 5 heart beats (3 for venous occlusion using a pressure of 50 mmHg and 2 for venous drainage) is optimal for one measuring cycle. For this reason, ECG-triggering is an important feature (Fig 1). In optimal conditions the characteristic shape of the recorded curve shows linear ascent within a relatively wide range and allows reliable calculation of flow and/or volume.

(3) Peripheral arterial blood flow associated with hyperaemia can be studied after two different
types of stimulation. Firstly, hyperaemia is produced by an arterial occlusion pressure of 260 mm Hg in the cuff, provided by the Periflow® itself. After a predetermined time interval, the pressure is automatically removed and the measuring procedure starts during the phase of reactive hyperaemia (Fig 2). Secondly, hyperaemia is produced by exercise. The most reliable results are obtained by treadmill walking, but the method is expensive. Consequently, a claudiacometer foot pedal has been developed which allows exercise in the sitting or lying position. The first exercise stage is performed at a rate of 30 depressions/min and the resistance is varied. In the second stage resistance is kept constant and patients carry out the fastest movements possible for 5 min. This kind of exercise yields similar results when compared with the treadmill method, but the equipment is small, simply constructed and easily transportable.

Integration of the diastolic volume changes of a given limb during reactive hyperaemia allows an evaluation of the reserve volume, which is mainly (80%) the result of venous capacity and to a smaller extent (20%) of arterial capacity. Depending upon the duration of the arterial occlusion and the severity of the vascular lesions, differences are observed in the reactive flow and the time until return to the rest flow. In healthy subjects, peak flow is reached very quickly and hyperaemia lasts for only a few min. In patients with arterial insufficiency the curve is flattened (Fig 3). The onset of peak flow begins later and the duration of the reactive hyperaemia is protracted (Dormandy et al. 1972). The possibility of measuring the influence of nicotine upon the arterial flow is clearly demonstrated in Fig 4. The results of flow measurements are expressed as ml/100 ml per heart beat or per min.

(4) Venous distensibility may be derived from the vascular capacity as measured at different cuff pressures and analysed by a separate programme.

(5) Systolic blood pressure can be determined by total suppression of the arterial pulse at a given site in a limb, as detected by the strain gauge. The position of the cuff affects the results, and more distal application yields higher peripheral pressure values.

(6) Time of pulse propagation is detectable with two strain gauges placed at different points.

(7) Relative differentiation of muscular and cutaneous flow requires gauges at different measuring sites and/or two cuffs.

The Periflow® strain gauge venous occlusion plethysmograph may thus be used for the early detection of arterial occlusions, their localization and their continuous evaluation; for the chronological follow up of peripheral lesions; for the evaluation of the results of surgical and medical treatment and in the differentiation of vasospastic and occlusive conditions.

Summary

The connexion between blood viscosity and blood flow is considered from the basis of Poiseuille's law and the fact that blood is a non-newtonian fluid. Among the possible measuring techniques for blood flow, venous occlusion plethysmography has advantages as a non-invasive routine method. The Periflow® is described, a device which provides measurement of venous pressure, peripheral arterial flow before and after stimulation, venous distensibility, systolic blood pressure, and pulse propagation which permits differentiation of muscular and cutaneous flow. Such measurements are considered critical for the early detection of vascular changes and the development of suitable therapeutic measures.

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