abstracts

Human Hepatic Blood Flow and its Relation to Systemic Circulation during Intravenous Infusion of Lidocaine


"Lidocaine has been used as a local anaesthetic agent for well over two decades . . . and has proved to be a potent and safe drug . . . Its effects on the systemic circulation have been studied . . . It has been shown that lidocaine stimulates the systemic circulation in spite of its depressant effect on the isolated myocardium . . . Furthermore, both lidocaine and mepivacaine have dilating as well as constricting effects . . . A connection between low cardiac output, low hepatic blood flow and high steady state levels of lidocaine was reported . . .

"However, the patients . . . do not necessarily have a poor circulation but are often hyperkinetic, due to sympathetic stimulation of the myocardium and subsequent induction of peripheral sympathetic blockade. Moreover, steady states in the blood concentration of lidocaine are seldom reached during the anaesthetic procedure. . . . This study was designed to elucidate the effect of lidocaine on the systemic circulation with special regard to the estimated hepatic blood flow . . .

"Seventeen healthy, young volunteers were investigated . . . They were randomly divided into three groups: two groups who were to receive lidocaine intravenously at a dose rate of 2 or 4 mg/min, respectively, and a third (placebo) group who were to have the same dose of physiological saline. The local anaesthetic was given by means of an infusion pump . . .

"The volunteers were all in a post-absorptive state after fasting overnight. No premedication was given. After infiltrating the skin with a small amount of 0.5% plain mepivacaine (Carbocaine®), the hepatic vein, the pulmonary artery and the femoral artery were catheterized. All investigations were carried out with the subjects in the supine position. Total blood loss from sampling and bleeding was estimated to be 0.37 l. Apart from the lidocaine, nothing but physiological saline was infused throughout the investigation. The total amount of saline given to each individual during the approximately 4 h of the procedure was 1.7 l. In four of the volunteers, a 150-min infusion of lidocaine was given at a dose rate of 4 mg/min. Five volunteers were given placebo over the same length of time, and eight received a 90-min infusion of lidocaine at a dose rate of 2 mg/min . . .

"Cardiac output was determined by the thermodilution technique . . . The heart rate was determined from ECG standard leads. Blood pressures were recorded via an arterial catheter in the femoral artery and the three-
lumen catheter. The tip of the latter was situated in the main part of the pulmonary artery, and its position was checked by fluoroscopy. The pressure in the right atrium (RA) was registered via the opening of a second lumen, which was situated a further 30 cm proximally on the same catheter. The pressure in the right atrium (RA) was registered via the opening of a second lumen, which was situated a further 30 cm proximally on the same catheter. The pressure in the right atrium (RA) was registered via the opening of a second lumen, which was situated a further 30 cm proximally on the same catheter. The pressure in the right atrium (RA) was registered via the opening of a second lumen, which was situated a further 30 cm proximally on the same catheter. Estimated hepatic blood flow (EHBF) was determined according to the modification by Caesar, et al. (1961) of the original constant infusion technique of Bradley, et al. (1945).

"The distributional volumes of five of the volunteers were checked before and after the infusions by the method of Banaszak, et al. (1960). This check revealed only very small alterations in the distributional volume for indocyanine-green (+5%), and hence no corrections for alterations in the distributional volume were made when calculating EHB. Total peripheral resistance (TPR) was calculated. Splanchnic vascular resistance (SVR) was calculated from EHB, mean arterial blood pressure and right atrial blood pressure analogously to TPR. Thus, the mean blood pressure in the hepatic vein was approximated to the mean atrial blood pressure. The systemic vascular resistance excluding the splanchnic (R) was calculated.

"The hepatic fraction of the cardiac output was determined as the ratio EHB/Qt. Left ventricular useful pressure-volume work was determined. The lidocaine concentration in plasma was determined according to a modification of the technique described by Keenaghan (1968), allowing samples of 0.5 ml. All analyses were made in duplicate. The precision of the method, expressed as the coefficient of variation, was 6.5%. The plasma concentrations were converted to blood concentrations, using a conversion factor (A = drug concentration in whole blood/drug concentration in plasma) calculated from the simultaneously determined haematocrit (H) and the partition coefficient of lidocaine between plasma and erythrocytes (K).

"The dose-effect (= time-effect relationships were first evaluated by analysis of variance (ANOVA). The analyses involving both lidocaine groups and the placebo group are not reported separately. The following comparisons were made between the results obtained from the placebo infusion and the respective lidocaine infusions, but statistical evaluation was made only when the above-mentioned ANOVA of the three groups revealed a statistical difference.

"Lidocaine 2 mg/min i.v.

The lidocaine concentration in arterial blood increased throughout the infusion. After 90 min the blood concentration was 0.95 mg/l, corresponding to 1.10 mg/l in plasma. The cardiac output (Qt), heart rate, stroke volume (SV), mean arterial blood pressure (p$a$), total peripheral resistance (TPR) and vascular resistance in the systemic circulation excluding the splanchnic (R), did not change significantly. The useful heart work, expressed as left ventricular stroke work (LVSW), did not alter significantly, but the left ventricular minute work (LVMW) increased significantly.

"Estimated hepatic blood flow (EHB) increased significantly in spite of a non-significant decrease in splanchnic vascular resistance (SVR). The hepatic fraction of the cardiac output (EHB/Qt), however, increased significantly. In the placebo group no significant alterations of the above physiological variables were noted. However, a slight—but statistically non-significant—rise in mean arterial blood pressure and splanchnic vascular resistance was noted.

"Lidocaine 4 mg/min i.v.

The lidocaine concentration in arterial blood increased throughout the infusion. After 150 min the mean blood concentration was 2.02 mg/l, corresponding to 2.40 mg/l in plasma. The heart rate increased significantly and cardiac output (Qt) also increased significantly in parallel. Stroke volume (SV) only increased by 4%.
Mean arterial blood pressure (pa) increased significantly in the group receiving this dose of lidocaine and the left ventricular useful pressure-volume work, expressed as left ventricular minute work (LVMW), and left ventricular stroke work (LVSW) both increased significantly during the infusion.

"Total peripheral resistance (TPR) decreased significantly. Estimated hepatic blood flow (EHBF) increased and splanchnic vascular resistance (SVR) decreased significantly during the infusion, resulting in an increased hepatic fraction of the cardiac output. The systemic vascular resistance excluding the splanchnic (R) did not change during this lidocaine infusion.

"The lidocaine plasma concentration-effect relationships were also evaluated using first order linear regression analysis. The heart rate, stroke volume and left ventricular stroke work were poorly correlated to the lidocaine plasma concentration, but a better correlation was found for cardiac output mean arterial blood pressure and left ventricular minute work. Estimated hepatic blood flow and splanchnic vascular resistance were also better correlated to the plasma concentration of the drug. All the regression coefficients mentioned in the present report differed significantly from zero.

"The physiological methods used in this investigation require a steady state, but an absolute steady state cannot be obtained in this kind of study. It is noteworthy, however, that the changes in the blood concentrations were slow compared with the mean transit times through the splanchnic vascular bed, as well as through the whole systemic circulation. Thus, it is improbable that such changes could interfere with the results to such an extent as to make the conclusions invalid. The present investigation was designed to study the circulatory effects of lidocaine in healthy volunteers, with special regard to the estimated hepatic blood flow.

"The vast clinical experience with lidocaine in the treatment of cardiac arrhythmias has shown that the central systemic circulation is well maintained as long as the blood concentration of lidocaine remains up to 6 mg/1. However, some data have pointed to a depression of the myocardial contractility on administration of lidocaine. Studies revealed that even the myocardial contractility could be influenced in two ways by lidocaine. It is known that lidocaine is mainly broken down in the liver. Patients characterized by a low cardiac index and a low hepatic blood flow, demonstrating that the cardiac output and hepatic blood flow could be the limiting factors for the hepatic uptake and degradation of the drug. In healthy volunteers—as well as in ordinary surgical patients—the estimated hepatic blood flow is considerably greater.

"In the present investigation the stimulating action of lidocaine on the central systemic circulation was confirmed. A positive significant linear correlation was found between blood or plasma concentration of the drug and the heart rate, cardiac output, mean arterial blood pressure and left ventricular minute work. No significant stimulation of the central circulation was observed in the placebo group. However, the limited number of volunteers investigated influences the accuracy of the equation of the regression lines.

"The present results may indicate that the increased blood flow in the hepatic artery is not merely compensatory to a reduced flow in the portal vein, but is a part of a real increase in the hepatic blood flow. Hence, these changes in hepatic blood flow might also influence significantly some of the kinetic predictions made.

"In contrast to the dilating action of low concentrations of lidocaine in the splanchnic area, the reduced vascular
resistance at higher blood or plasma levels, described earlier, must be due to a direct vascular action of the local anaesthetic agent.”

Fluidics and Pneumatics
Principles and Applications in Anaesthesia

“Fluidic and pneumatic technology has matured rapidly in the last ten years and as a result ventilators exploiting this advance are currently being introduced. . . . It seems appropriate, therefore, to introduce the principles and devices used in this new technology in the hope of increasing the anaesthetist’s understanding and hence the usefulness of the machines which employ it. This review offers explanations of the operation and construction of some of the principal fluidic and pneumatic components, and presents designs for an automatic blood pressure cuff inflator, a blood pump and a high performance ventilator. . . .

“The fluid amplifier . . . is based upon the Coanda effect . . . which describes the tendency for a jet of fluid (the fluid can be a liquid or a gas) issuing from a nozzle to adhere to the surface of the wall adjacent to it. . . . The Coanda effect can be seen as a corollary of the venturi effect or the result of Bernoulli’s principle. In the case of the fluid amplifier, the wall to which the fluid jet adheres can be controlled by a lateral jet. . . . Since the lateral control jet need be far less powerful than the main jet, the term fluid amplifier is applied. . . .

“The term fluid device, for example, should rigorously be applied only to devices in which there are no moving parts except the fluid movement itself. All devices with moving parts are pneumatic. The advantage of a fluidic device over a pneumatic device is, of course, its lack of moving parts and hence lack of wear and fatigue. However, the disadvantage is that the fluid stream must be continuous, so that flow is wasted and the energy loss is continuous. Pneumatic devices, on the other hand, can be made to turn on the flow only when necessary and so are less wasteful of energy. It is perhaps for these reasons that current technology tends to use fluidic devices for low pressure, low flow, control logic and then amplifies the output for the control of high pressures and high flows with pneumatic devices. . . .

“About the simplest fluidic device is a flow resistor. There are two types, . . . an orifice, with a nonlinear pressure loss versus flow curve, and the other is a capillary tube, with a linear pressure loss versus flow curve. A variable flow resistor is, of course, the familiar needle valve. . . . Variants of flow resistance devices are also employed as limit switches or detectors for mechanical movement, with the proximity of an object changing the flow paths so as to change a flow resistance. . . . The more interesting fluidic devices, however, are the logic devices. There are several types of fluid logic devices commercially available. . . .

“All of these devices operate using a continuous flow and are therefore designed as low pressure, low flow devices so as to minimize the constant energy loss entailed by their operation. In order to amplify the outputs to useful power levels without large energy losses a pneumatic interface valve is used. . . . Pneumatic devices used to be thought of only in terms of mechanical valves operated by a piston and cylinder arrangement such as the spool valve. . . . Current technology, however, uses a diaphragm poppet design. . . . wherein the only moving parts are flexible rubber diaphragms. . . .

“There are numerous other pneumatic devices of specialized functions including push buttons and on-off switches and at least one other should be noted, and that is the one-way valve. . . . Having described and explained some of the components used in fluidic and pneumatic circuits it remains to illustrate how they may be assembled
into circuits which provide useful and complex functions. The next three sections describe, in order of increasing complexity, a simple automatic blood pressure cuff inflator, a blood pump, and a ventilator.

"Fluidic and pneumatic components and circuits have matured rapidly from their beginnings, and increases in their reliability over the older mechanical-pneumatic devices have made them the rivals of electrically operated components and have led to their use in current ventilator designs. Nevertheless, they do not yet rival the complexity of electronic devices and the next generation of ventilators may be a hybrid of low power digital electronic devices and modern fluidic and pneumatic devices with the resulting benefits of increased versatility and precise control.

"This article describes the construction and operation of fluidic and pneumatic devices in current use, as well as the principles of their use in medical devices. The designs for an automatic blood pressure cuff inflator, a blood pump and a high performance ventilator are presented."

Haemodynamic Changes Due to Clamping of the Abdominal Aorta


"Serious problems arise frequently during anaesthesia for major vascular surgery associated with clamping of the aorta. Haemodynamic changes at the moment of recirculation are readily observed. . . . The hypotension, at times severe, that follows the unclamping of the aorta is not without danger for these arteriosclerotic and hypertensive patients. It is obvious that hypotension, even of short duration, can reduce cerebral, coronary or renal perfusion and jeopardize an otherwise successful operation.

"While the period of unclamping has been thoroughly examined, the events associated with clamping have not received much attention. . . . The proximal occlusion of the aorta during operation for thoracic aneurysm can induce alarming increases in blood pressure and experienced anaesthetists will look for signs of left ventricular failure. . . . The clamping of the distal aorta also induces haemodynamic changes, the most obvious response again being the increase in systolic pressure due to an afterload which could be of clinical significance for these patients. . . . We decided to investigate the haemodynamic changes due to cross-clamping of the abdominal aorta.

"Eighteen patients requiring surgery of the abdominal aorta were included in this study. None presented clinical evidence of cardiac insufficiency or dysrhythmia before operation. . . . After premedication with diazepam 5 mg intramuscularly, induction of anaesthesia was carried out with thiopentone 5 mg/kg, and pancuronium 0.15 mg/kg for tracheal intubation and muscular relaxation. Maintenance was achieved with nitrous-oxide oxygen and fentanyl according to analgesic requirements. Droperidol 0.1 mg/kg was also given before the surgical incision.

"The left radial artery was cannulated under general anaesthesia after testing for adequacy of cubital artery compensatory function. A catheter was placed in the right atrium through the internal jugular vein; its position was ascertained by threading to the right ventricle and withdrawal into the atrium, the characteristic pressure signal being displayed on an oscilloscope.

"All patients were placed on controlled ventilation. . . . Necessary adjustments to maintain \( \text{Paco}2 \) and \( \text{Pao}2 \) within normal limits were rapidly applied. Fluid intake was adjusted to 20 ml/kg/hr before aortic clamping, half the volume consisting of 5 per cent glucose in water and the other half 5 per cent glucose with 0.45 per cent NaCl. A rather liberal fluid intake was administered prior to clamping in order to ensure that hypovolaemia would not
explain the haemodynamic changes. . . . Following occlusion of the aorta, fluid intake was reduced to 6 ml/kg/hr. Blood loss was replaced as accurately as possible.

"Haemodynamic data . . . were inscribed on a polygraph recorder. . . . Pressures were continuously recorded. . . . Cardiac output was determined by injection of indocyanine green dye into the right atrium and detection of the resulting dye dilution curve in the arterial blood. . . .

"It should be emphasized that these patients were free from cardiac diseases, that anaesthesia was conducted without undue myocardial depressant doses that Paco₂ was maintained at normal levels and fluids administered liberally. . . . Under balanced anaesthesia with droperidol-fentanyl-pancuronium, just before aortic cross-clamping, right atrial and arterial pressures as well as heart rate were normal. Nevertheless, the systemic vascular resistance was elevated and the cardiac and stroke indices were at the lower limits of normality. The clamping of the aorta did induce alarming haemodynamic changes.

"The sudden increase in aortic impedance was followed by a 20 per cent reduction in cardiac output at the expense of the stroke volume. . . . It was not possible to document a significant difference in the behaviour of patients with chronic obstruction of blood flow to lower extremities (Leriche) and those with a somewhat more acute disease (aneurysm). Nevertheless, it can be seen that the former have a tendency to show less marked haemodynamic changes. . . .

"It is obvious that an increase in afterload can reduce the cardiac output. Nevertheless, in physiological conditions there are mechanisms which can maintain the stroke volume in spite of this load. . . . A second mechanism can be called upon to maintain the stroke volume against the larger afterload; it is the positive inotropic effect due to systolic pressure increase. . . .

"This Anrep reflex has its importance. It implies that the ventricle can maintain a constant stroke volume against a range of resistances without an increase in end-diastolic pressure. Furthermore, the increase in the rate of rise of ventricular pressure will shorten the systolic time. This Bowditch effect forestalls the reduction in diastolic interval with increasing heart rate. Thus a complete ventricular relaxation is attained before the next systole and the increase in end-diastolic volume is prevented. If we remember that coronary perfusion takes place during diastole, and that subendocardial perfusion is counteracted by the end-diastolic volume, this mechanism is not without clinical significance. . . .

"Absence of homeometric autoregulation is not without interest. If we consider the low values of cardiac output after the first ten minutes of aortic occlusion, before blood loss interferes with the Starling mechanism, the situation can be cause for concern. . . . We are often required to cope with arteriosclerotic hearts or with hypertensive subjects with left ventricular hypertrophy. Their ventricular function curve is already depressed and a further increase in impedance could precipitate failure. . . .

"We have seen that the necessary autoregulation and reflexes are not available and that cardiac performance decreases. It is obvious that anaesthesia must be conducted with great care. Hypertensive crisis and tachycardia must be particularly feared for they increase cardiac work while the time available for coronary perfusion is reduced. This can lead to cardiac failure due to subendocardial ischaemia. On the other hand, anaesthesia must spare sympathetic activity which presides over myocardial contractility and the homeometric autoregulation of the heart. . . .

"Haemodynamic changes due to aortic cross-clamping were examined in 18 patients. It has been shown that the distal occlusion of the abdominal aorta
induces an increased impedance to ejection. Because the mechanisms controlling the autoregulation of cardiac output and the circulatory reflexes are damped by anaesthesia, the augmentation of resistance is not followed by any increase in contractility or vasomotor tone and thus the cardiac output falls. Patients with chronic obstructive disease (Leriche) did not differ significantly from subjects with more acute obstruction (aneurysm), though the latter have a tendency to show more important changes in their haemodynamic response.

The Need for Halothane Supplementation of N₂O-O₂-Relaxant Anaesthesia in Chronic Alcoholics


"Alcohol is the most widely used potentially addictive drug. Problems associated with the anaesthetic management of chronic alcoholics are therefore of major importance to practising anaesthetists. Although clinical experience indicates an increased demand for anaesthetics in chronic alcoholics... the degree and the factors associated with the development of this tolerance in man have hardly been investigated and therefore little is known of them. On the other hand, the development of cross-tolerance between alcohol and different anaesthetics seems to be well-documented in animals..."

"A retrospective study... showed that despite the higher dosages of drugs used in supplementation of N₂O-O₂-relaxant anaesthesia, awareness and signs of inadequate depth of anaesthesia were higher in chronic alcoholics than in control patients..."

"The series comprised 113 patients anaesthetized... for biliary or gastric (mainly proximal selective vagotomy) surgery. An attempt was made to include all patients with heavy alcohol consumption in the study. A careful review of the patients' habits concerning alcohol consumption was made before anaesthesia, and so that the information obtained would be as reliable as possible..."

"The annual consumption of alcohol was estimated on the basis of average weekly or monthly consumption using Bruun's nomograms (1972). For an analysis of the results the patients were divided into the following groups according to their annual alcohol consumption: non-alcoholics (<1 1 pure alcohol), social drinkers (1-15 1) and alcoholics (>15 1). Only patients with good or fair (ASA 1 or 2) general physical condition were included...

"In the present series the demand for halothane supplementation was only slightly increased in alcoholics with an estimated mean annual consumption of 32 ±4 (s.e. mean) litres of absolute alcohol... It appeared that the incidence of alcoholics was higher in the gastric surgery group than in the biliary surgery group... Since gastric surgery itself seemed to increase the demand for supplementation, as compared with biliary surgery, it is difficult to assess whether it was the type of operation or the use of alcohol which was mainly responsible for the increase in the demand for supplementation... This suggests that the overall increase in demand caused by alcohol is clinically fairly insignificant..."

"The various criteria used for halothane supplementation reflect different aspects in the response to pain stimuli and do not ensure a similar depth of anaesthesia in different patients... The interval before verbal contact after N₂O was similar in alcoholics and non-alcoholics... It is not known whether the increased demand for anaesthetics depends upon cross-tolerance between alcohol and anaesthetics or whether it merely reflects a state of anxiety in some alcoholics..."

"It... seems that more detailed information on the development of
cross-tolerance can hardly be obtained in general surgical practice, but must rather be sought in special circumstances (e.g. by studying the responses of alcoholic volunteers to various anaesthetics under experimental conditions). Nonetheless, the clinical significance of cross-tolerance to different anaesthetics should be assessed under clinical circumstances.

"The present results suggest that during N₂O-O₂-relaxant anaesthesia the demand for intermittent halothane supplementation is only slightly increased in chronic alcoholics with an annual consumption of moderate severity. Except for a higher incidence of motor irritability, sweating and lacrimation, anaesthetic management posed no special difficulties in these patients. The possibility of awareness should, however, be considered even during a 'balanced anaesthesia' where halothane is used for supplementation."

A Simple Method for Verifying Endotracheal Tube Placement

"Inadvertent insertion of the endotracheal tube into a main stem bronchus is a common cause of atelectasis and hypoxemia during the course of anesthesia. Several methods have been described for ascertaining the position of the tip of the endotracheal tube in the trachea: auscultation of breath sounds, chest x-ray, and electromagnetic sensing....

"We propose a simple, noninvasive technic for determining endotracheal-tube cuff location.... Following intubation, the cuff is inflated with air in the usual manner. Before the tube is taped in place, 1 ml of sterile saline solution is injected into the pilot cuff. When the endotracheal tube is properly placed and the pilot balloon is compressed and released gently between the fingers..., a gurgling sound is transmitted and can easily be heard with a stethoscope between the cricothyroid cartilage and the jugular notch. This sound indicates that the cuff of the endotracheal tube is located below the vocal cord and several centimeters above the carina.

"If the endotracheal tube is accidentally positioned in one of the main stem bronchi or near the carina, no gurgling sound will be heard.... If this occurs, the tube must be withdrawn until the sound of gurgling is heard between the jugular notch and the cricothyroid cartilage....

"Accidental intubation of a main stem bronchus is a serious complication of endotracheal anesthesia, since intrapulmonary shunting and hypoxemia result. If the right main bronchus is intubated, the right upper lobe bronchus may also be occluded by the tube, due to the short distance between the carina and the orifice of the upper lobe bronchus. Therefore, prompt recognition of bronchial intubation has great practical importance."