

Literature Briefs

C. Philip Larson, Jr., M.D., Editor

Briefs were submitted by Drs. J. Adriani, C. M. Ballinger, N. Bergman, R. B. Boettner, P. P. Bosomworth, D. R. Buechel, M. T. Clarke, J. E. Eckenhoff, M. Helrich, J. J. Jacoby, R. L. Klein, W. H. Mannheimer, F. C. McPartland, A. Patterson, J. W. Pender, R. E. Ponath, A. D. Randall, H. S. Roe, N. Rosenbaum, and L. J. Saidman. Briefs appearing elsewhere in this issue are a part of this column. Abstracts of Russian and Japanese literature were obtained from *Excerpta Medica Foundation*.

ARRHYTHMIA Studies were carried out in the isolated rabbit heart to determine the effect of various substances upon the ventricular fibrillation threshold by direct effect on the cardiac musculature. Low potassium in the perfused fluid lowered the threshold 3.5 times; high potassium raised it 4 times. Epinephrine, when infused into the aortic cannula at rates below that causing marked arrhythmias, failed to produce marked changes in the fibrillation threshold. Carbachol or chloroform alone had no effect on the threshold; however, if epinephrine was infused when either one was included in the perfusion fluid, the fibrillation threshold was significantly lowered. Procaine in the perfusion fluid raised the threshold. Raising the perfusion pressure from the normal 40 mm. of mercury to 56–80 mm. of mercury also raised the threshold whether the heart was tested immediately or some time after the pressure had been raised. (MacConaill, M., and Murnaghan, M. F.: *Influence of Various Agents on the Ventricular Fibrillation Threshold in the Isolated Perfused Rabbit's Heart*, *J. Physiol.* 179: 55 (July) 1965.)

ARRHYTHMIA Hemodynamic consequences of atrial and ventricular arrhythmias were studied in 32 patients, 27 of whom had clinical or laboratory evidence of heart disease. No significant change in cardiac output was

found with paroxysmal atrial tachycardia; however, artificially induced atrial tachycardia caused a significant rise in cardiac output, mean systemic pressure, tension time index and stroke power reaching a maximum increase at about 100 beats per minute. Conversion of atrial fibrillation to a sinus rhythm was not associated with significant improvement in cardiac output; the reason for this is not clear. Perhaps the waves of atrial contraction are so weak in patients with long standing heart disease and atrial fibrillation that they are unable to significantly improve ventricular filling after conversion is accomplished. Multiple ventricular premature contractions caused a fall of about 20 per cent in cardiac output and stroke volume. Bigeminal rhythm produced an even greater reduction in cardiac output. Peak systolic pressure from the regular pacemaker was about 20 mm. of mercury higher than that from the ectopic pacemaker. Spontaneous ventricular tachycardia caused a marked decrease in stroke volume, injection time and stroke power, although the cardiac output was essentially unchanged due to the tachycardia. In patients with complete heart block, the cardiac output was improved by increasing the rate to a range of 62–93 beats. A further increase in rate was associated with a fall in cardiac output and evidence of failure indicating that these patients were operating near the peak of their cardiac reserve. (Ben-Chimol, A., and others: *Hemodynamic Consequences of Atrial and Ventricular Arrhythmias in Man*, *Amer. Heart J.* 70: 775 (Dec.) 1965.)

ARRHYTHMIA Potassium loss from the myocardial fibril plays a role in the pathophysiology of ventricular arrhythmias. Taurine, a nontoxic, naturally occurring substance in the myocardium, is an antiarrhythmic agent due to its ability to retard myocardial potassium loss. Taurine is also helpful in digitalis

toxicity. (Read, W. O.: *Ventricular Arrhythmias*, Minnesota Med. 48: 124 (Oct.) 1965.)

ARRHYTHMIA Some battery-operated implanted cardiac pacemakers may have their rate so increased by radio frequency waves from diathermy apparatus and other machines that ventricular fibrillation may result. Radar waves *per se* do not cause fibrillation, but by heating the unit or the electrodes, they may destroy the pacemaker or burn the heart. (Lichter, I., and others: *Radio-frequency Hazards with Cardiac Pacemakers*, Brit. Med. J. 1: 1513 (June 12) 1965.)

CARDIOVERSION Conversion of chronic atrial fibrillation to sinus rhythm by direct current countershock was successful in 37 of 40 patients. The remaining 3 were eventually converted to sinus rhythm only after cessation of digitalis therapy. As full digitalization may hinder chances for successful cardioversion, routine cessation of digitalis therapy 7-12 days prior to planned cardioversion is employed. Possible mechanisms by which digitalis might interfere with cardioversion are diminished conductivity of the A-V node and bundle of His, increased refractory period, and myocardial electrolyte changes. (Stern, S.: *Effect of Maintenance Doses of Digitalis on the Rate of Success of Cardioversion*, Amer. J. Med. Sci. 250: 509 (Nov.) 1965.)

BLOOD VOLUME Preoperative and postoperative blood volume determinations (RISA method) were performed on 37 patients with congenital and acquired cardiac lesions who underwent total cardiopulmonary bypass. The blood volume reached its lowest value in the immediate postoperative period in spite of apparently adequate blood replacement, while hemoglobin and hematocrit values lagged behind and reached their lowest values not before the third postoperative day. The longer the perfusion time, the lower the postoperative blood volume. This may be the result of changes in blood distribution and composition due to plasma loss into wound cavities and tissues, mechanical damage by the pump, disturbances of acid-base balance and/or of the coagulation mechanism, hyperthermia, as well as circulatory failure. (Staudacher, M. and

Helmert, F.: *Blood Volume in Open Heart Surgery*, Thoraxchirurgie 13: 374 (Oct.) 1965.)

POSTPERFUSION SYNDROME Open heart surgery under total cardiopulmonary bypass is frequently complicated by postoperative hypoxia. Clinical studies have shown that this desaturation is the result of a venous admixture effect caused by ventilation-perfusion inequalities and true right-to-left intrapulmonary shunts. The etiology of the condition is obscure. Experiments were conducted to show whether the histologic lesions and the functional deterioration were due to deprivation of pulmonary blood supply during the bypass or were associated with perfusion of the lungs. By means of a modified heart-lung bypass, one of the dog's lungs was excluded from the normal pulmonary arterial input while the other received a normal flow of mixed venous blood. The role of homologous blood in the production of the postperfusion pulmonary syndrome was studied. Using a hemodilution technique, the postperfusion lung syndrome was reduced in severity. Nevertheless, the occurrence of similar basic patterns of histologic changes, with both homologous blood and with the hemodilution technique, suggested the homologous blood was only one factor involved in the production of the syndrome. (Nahas, R. A., and others: *Post-Perfusion Lung Syndrome, Role of Circulatory Exclusion*, Lancet 2: 251 (Aug. 7) 1965; Nahas, R. A., and others: *Post-Perfusion Lung Syndrome, Effect of Homologous Blood*, Lancet 2: 254 (Aug. 7) 1965.)

PUMP PRIME Homologous blood frequently results in problems of compatibility, clotting, as well as cerebral, pulmonary, and renal changes, in addition to the administrative and economic disadvantages associated with the use of large quantities of whole blood. Low molecular weight dextran, glucose in water, glucose in saline, balanced electrolyte solutions, and others have been used as partial or total priming fluids for perfusion. At present no single perfusate has been shown to be definitely superior to all others in enough respects to warrant its universal acceptance. Generally a compromise is achieved between the use of dextrose in water and balanced elec-

trolyte solutions with some evidence available that the addition of low molecular weight dextran may be beneficial. Fewer electrolyte and hemolysis changes are observed with a combination of 0.2 per cent saline in dextrose than with 5 per cent dextrose in water used alone. The use of mannitol should be reserved for the postoperative phase rather than placed routinely in the perfusate. (Paton, B. C., and Rosenkrantz, J.: *Non-Hemic Priming Fluids for Extracorporeal Circulation*, Dis. Chest 48: 311 (Sep.) 1965.)

HEART CATECHOLAMINES Significant decreases in catecholamine concentrations were found in tissue from the right atrium, both ventricles and the interventricular septum in dogs that had undergone bilateral cervical vagosympathectomy. The cause of this depletion is not certain, but it may be due to destruction of intracardiac adrenergic nerves or a relatively increased utilization of catecholamines which exceeds the capacity of cardiac tissues to synthesize or bind these substances. (Jellinek, M., and others: *Effect of Cervical Vagosympathectomy on Myocardial Catecholamine Concentration*, Amer. J. Physiol. 209: 951 (Nov.) 1965.)

HEART DEPRESSION Methoxyflurane, even in a weak concentration of 18.8 mg./100 ml., consistently decreased the contractile force of the heart preparation. Halothane also consistently depressed heart action. Comparison of the two agents showed no definite difference, but halothane perfused after methoxyflurane had a transient restorative effect on the heart after causing a short period of A-V dissociation or bigeminy. This transient restoration of the heart was not observed when methoxyflurane was perfused after halothane. Methoxyflurane perfused after adrenaline sensitization of the heart consistently caused A-V block and sudden ventricular arrest. (Wakai, I., and others: *A Study of the Direct Effects of Fluothane and Penthrane on the Isolated Heart Preparation* (Japanese), Jap. J. Anaesth. 14: 472, 1965.)

CIRCULATORY DEPRESSION A significant depression of circulatory conditions occurred with an increase of halothane concentration in the blood. Circulatory depression

was relatively mild when the concentration was below 5 mg./100 ml., was more marked at 10 mg./ml., and was approximately 30 per cent below the control value when the concentration was 15 mg./100 ml. When the blood concentration was above 20 mg./100 ml., cardiac output was reduced 40 per cent and left ventricular work 60 per cent with no significant change in total peripheral resistance. It appears that the cardiocirculatory system is significantly depressed when the concentration of halothane is in excess of approximately 13-17 mg./100 ml. blood. (Yoshida, T., and others: *Study on Hemodynamics during Fluothane Anesthesia* (Japanese), Jap. J. Anaesth. 14: 575, 1965.)

HEART PACING A bipolar catheter pacemaker has been employed, usually as a temporary measure prior to insertion of a totally implantable battery-operated device, in 58 patients with heart block. The catheter pacemaker is also indicated for temporary pacing when complete heart block leads to congestive heart failure, uremia, or organic mental syndrome. It may be used to tide patients over operative or rigorous diagnostic procedures or an acute myocardial infarction. Catheterization is performed through the (right) external jugular vein, passage being controlled by fluoroscopic image intensifier. The heart is continuously monitored electrocardiographically. The ideal site for the catheter tip is the outflow tract of the right ventricle; pacing is maximally effective when good contact with the endocardium is established. Complications of the procedure were frequent, including four fatalities, two of which occurred during catheterization. Failure to pace was usually caused by malposition or breakage of the catheter, poor electrical connections, or run-down batteries. (Gordon, A. J.: *Catheter Pacing in Complete Heart Block*, J.A.M.A. 193: 1091 (Sept. 27) 1965.)

CORONARY BLOOD FLOW Coronary blood flow to various parts of dog myocardium is correlated with the rates of Rb⁸⁶ clearance from that part. A very significant correlation exists between the pressure loads of each ventricle and the fraction of coronary flow each receives, flow being relatively greater in the

ventricle with the greater load. (Love, W. D., and others: *Comparison of the Effects of Nor-epinephrine, Angiotension, Depyridamole, Dig-
toxin, and Reserpine on the Regional Distribu-
tion of Coronary Blood Flow*, *J. Lab. Clin.
Med.* 66: 423 (Sept.) 1965.)

CEREBRAL BLOOD FLOW Employing an electromagnetic flowmeter and pressure transducers, internal carotid arterial blood flow and pressure were measured continuously in awake patients during incremental increases in cerebrospinal fluid pressure to a level slightly below each patient's diastolic blood pressure. The control value of mean carotid flow for the group was 201 ml. per second obtained at a cerebrospinal fluid pressure of 190 mm. of water. Flow decreased as cerebrospinal fluid pressures increased so that at a cerebrospinal fluid pressure of 920 mm. of water, mean flow averaged 25 per cent less than the control value. There were no observed changes in blood pressure, heart rate, electrocardiogram, or electroencephalogram. Slight autoregulation of flow was found at the highest level of cerebrospinal fluid pressure in 4 patients. In 3 additional patients, angiographic studies indicated that the cerebral veins lying with the subarachnoid space are not collapsed at cerebrospinal fluid pressures of 1,000 mm. of water. (Greenfield, Jr., J. C., and Tindall, G. T.: *Effect of Acute Increase in Intracranial Pressure on Blood Flow in the Internal Carotid Artery of Man*, *J. Clin. Invest.* 44: 1343 (Aug.) 1965.)

CRITICAL OPENING PRESSURE Critical opening pressure (COP) or critical closing pressure (CCP) of blood vessels is considered to be an index of the constricting force exerted by vascular smooth muscle. A spectroscopic technique for estimating these pressures is as accurate as the auscultatory and microscopic methods and simpler to perform. The COP in 26 subjects ranged from 1 to 22 mm. of mercury with a mean of 11 ± 5.0 (S.D.). The COP of small vessels in the fingers was decreased by digital nerve block, general body heating and preparation for measurement of basal metabolic rate. This technique should be useful in the study of factors contributing to alteration in peripheral resistance to blood

flow under various circumstances. (Gaskell, P.: *Measurement of Blood Pressure, Critical Opening Pressure and Critical Closing Pressure of Digital Vessels under Various Circumstances*, *Canad. J. Physiol.* 43: 979 (Nov.) 1965.)

MICROCIRCULATION The microcirculation in the ear chamber was studied during hypothermia and rewarming of 50 rabbits. The main causes of poor tissue perfusions during hypothermia were found to be increased blood viscosity, arterial hypotension, and pooling of blood in the true capillaries and small venules. Intravascular erythrocyte aggregations played a relatively unimportant role. (Suzuki, M., and Penn, I.: *A Reappraisal of the Microcirculation During General Hypo-
thermia*, *Surgery* 58: 1049 (Dec.) 1965.)

HYPERTENSION In a retrospective study of 434 patients with mitral valve disease, systemic hypertension was much commoner than in the population at large. Renal infarction was present in 72 per cent of the 133 necropsies performed. There was a close association between atrial fibrillation, renal infarction and systemic hypertension with incidence increasing with age. Conversion of rhythm with decrease in renal embolization may be indicated, especially as most renal infarcts pass unnoticed. (Obeyesekere, H. I., and others: *Systemic Hypertension and Mitral Valve Disease*, *Brit. Med. J.* 2: 441 (Aug. 21) 1965.)

FAT EMBOLISM Fat embolism occurs most commonly in the second and third decades of life, when long-bone fractures are frequent, and in the sixth and seventh decades, when fractures of the hip are frequent. The time of onset is variable from a few hours to four days after trauma. Symptoms result from reduced blood flow to the affected organs, e.g., lungs (dyspnea and cyanosis) and cerebral cortex (disorientation and delirium). Clinical signs include temperature elevation, tachycardia, and tachypnea. An evanescent petechial rash may be seen across the root of the neck, in the axilla or conjunctiva. Laboratory studies demonstrate lipuria and increased serum lipase values in about 50 per cent of patients. General supportive measures include resuscitation from shock, administration of oxygen, and

avoidance of unnecessary transportation. Specific treatment is directed at lowering the plasma lipid value and improving the microcirculatory flow patterns. Small intravenous doses of sodium heparin will achieve a chylolytic effect without the risk of hemorrhage. Dextran-40 improves microcirculatory flow by reducing intravascular aggregation of erythrocytes and by exerting a siliconizing effect on injured blood vessel walls. (Evarts, C. M.: *Diagnosis and Treatment of Fat Embolism*, J.A.M.A. 194: 899 (Nov. 22) 1965.)

PULMONARY EMBOLISM Following experimental pulmonary embolism due to autogenous thrombi, there is a redistribution of ventilation away from the nonperfused to perfused lung segments. The air shift is not sufficient to prevent an increase in alveolar dead space and arterial-alveolar carbon dioxide tension difference. The shift cannot be explained on the basis of measured mechanical changes that follow autogenous embolism. Arterial hypoxemia was observed only in the presence of massive thromboembolism. One important mechanism is right-to-left shunting. The small decrease in diffusing capacity observed after embolism did not account for the degree of hypoxemia observed. Not all pulmonary emboli result in complete cessation of blood flow to the involved lung segment. Acute embolism as produced in these studies does not lead to any ultrastructural change in the lung for periods up to 3 hours. (Levy, S. E., and others: *Ventilation-Perfusion Abnormalities in Experimental Pulmonary Embolism*, J. Clin. Invest. 44: 1699 (Oct.) 1965.)

PULMONARY EMBOLISM Of 12 pulmonary embolectomies, there were 3 survivors, none of whom was over 65 years of age. The single common denominator among the non-survivors was cardiovascular collapse nonresponsive to vasopressor drugs. The indication for embolectomy is sustained peripheral hypotension; a patient who sustains an acute, massive pulmonary thromboembolism but who is not hypotensive requires, rather, inferior venal caval ligation and careful observation. Pulmonary arteriography should confirm the diagnosis prior to embolectomy. Cardiac arrest, which occurred in more than half the patients

in this series, can be prevented or adequately managed by peripheral cannulization and partial cardiopulmonary bypass prior to thoracotomy. The cardiac arrest which occurs just after opening the pericardium is probably related to acute distention of the right ventricle. Total cardiopulmonary bypass, because it provides adequate time for deliberate attack, is the modality of choice for the removal of emboli. The inferior vena cava should be ligated at the time of embolectomy to prevent further embolization. Embolectomy in other than life-threatening situations is probably unwarranted. (Sautter, R. D.: *Massive Pulmonary Thromboembolism*, J.A.M.A. 194: 336 (Oct. 25) 1965.)

PHLEBOTOMY Patients with a combination of erythrocytosis and ischemic heart disease may experience a decrease in the frequency of anginal attacks and an increase in effort tolerance following reduction of the hematocrit by phlebotomy. This improvement is attributed to a change in the viscosity of the blood subsequent to the phlebotomy. Clinical improvement of the patients with the combination of ischemic heart disease and erythrocytosis is usually achieved with the reduction of the hematocrit to between 45 and 47 per cent. (Burch, G. E., and DePasquale, N. P.: *Hematocrit, Viscosity and Coronary Blood Flow*, Dis. Chest 48: 225 (Sept.) 1965.)

SHOCK To study the effects of body position in shock recovery, a standardized form of hemorrhagic shock was induced in rats by maintaining arterial pressure at a level of 35 mm. of mercury for 210 minutes. After reinfusion of blood, animals were placed in special cages in a head-down, head-up and horizontal position. In the head-down position, 2 of 13 animals survived; in the head-up position, 6 of 12 animals lived; all animals maintained in the horizontal position survived. Duration of survival and responsiveness score, a measure of cerebral status, were much better in the horizontal than in either the head-down or the head-up positions. The possibility that the head-down position increases survival after shock due to blood loss was excluded with a high statistical confidence in this study and raises additional doubt of the value of the Trendelenburg position for routine treatment

of protracted shock due to hemorrhage. (Weil, M., and Whigham, H.: *Head-Down (Trendelenburg) Position for Treatment of Irreversible Hemorrhagic Shock*, *Ann. Surg.* 162: 905 (Nov.) 1965.)

DEXTRAN Aggregation of erythrocytes is increased by dextran and the sedimentation rate is increased. These effects are influenced by the molecular weight of the dextran used. Dextran with a molecular weight of 51,000 or less has no effect. The higher the molecular weight, the greater the effect. (Richter, W.: *Lowest Molecular Weight of Dextran Fractions with Aggregating Effect of Human Erythrocytes*, *Acta Chir. Scand.* 129: 457 (May) 1965.)

LOW MOLECULAR WEIGHT DEXTRAN Low molecular weight dextran was administered postoperatively to 23 patients, 8 of whom were in a state of moderately severe shock, 10 in compensated shock, and 5 were healthy young male patients admitted for elective surgical procedures. Cardiac output, central venous and arterial pressure, mean transit times, total peripheral resistance and blood volumes were measured. After the dextran was administered, there were marked elevations in central venous pressure and significant increases in cardiac index. These were accompanied by decreased peripheral resistances and mean transit times. These effects were most pronounced in the shock patients, less pronounced in the compensated shock patients, and minimal in the controls. The hemodynamic responses were generally maintained for about four hours. (Carey, J. S., and others: *Circulatory Response to Low Viscosity Dextran in Clinical Shock*, *Surg. Gynec. Obstet.* 121: 563 (Sept.) 1965.)

FLUIDS IN SHOCK The hemodynamic responses to whole blood, low molecular dextran, clinical dextran, plasma, albumin and saline were evaluated in a series of 20 postoperative patients. Nine patients were in a state of shock at the time of the study; the remainder were partially resuscitated with transfusion therapy but were considered to be in compensated shock. Serial measurements were made of cardiac output, mean transit

time, arterial and central venous pressures, total peripheral resistance, central blood volume and stroke volume before, during and after the administration of each of the various types of plasma volume expanders. A marked and significant improvement in hemodynamics followed the administration of low molecular dextran in both groups of patients. These effects were minimal or absent after blood transfusions. Normal saline produced transient hemodynamic effects which were often ended at the termination of the infusion. Clinical dextran produced a lesser but more lasting hemodynamic improvement. The responses to albumin and plasma were of similar time course but were only about 50 per cent of the response to low molecular dextran. All plasma volume expanders lowered the hematocrit value and decreased peripheral resistance and transit time. Low molecular dextran reduced blood and plasma viscosity and improved flow properties of blood in small vessels. The net effect was increased venous return and shift of blood volume to the central circulation. By contrast, blood transfusion increased erythrocyte concentration, viscosity, and, except in hypovolemia, failed to improve significantly the cardiovascular responses. (Carey, J. S., and others: *Comparison of Hemodynamic Responses to Whole Blood and Plasma Expanders in Clinical Traumatic Shock*, *Surg. Gynec. Obstet.* 121: 1059 (Nov.) 1965.)

DIBENZYLINE IN SHOCK Phenoxybenzamine, 1 mg. per kg. of body weight, was administered intravenously to 25 patients with a variety of disease entities and to one normal anesthetized volunteer. The drug led to prompt vasodilation. Blood or plasma expander was required in most patients to prevent an unacceptable degree of hypotension. Seven patients were in a state of severe shock, 6 of whom died. It was doubtful that vasodilation caused death, but it may have been a contributing factor in 5 of them. Ten patients received the drug as pretreatment prior to a major surgical procedure. One of these patients died but the death was unrelated to vasodilation. Phenoxybenzamine effectively blocked vasospasm caused by sympathomimetic amines, and the sympathomimetic amines are therefore ineffective antagonists. The data

suggest a use of the drug in prevention of renal vasoconstriction from trauma, blood transfusion and the like. (Eckenhoff, J. E., and Cooperman, L. H.: *The Clinical Application of Phenoxybenzamine in Shock and Vasoconstrictive States*, *Surg. Gynec. Obstet.* 121: 483 (Sept.) 1965.)

VASOPRESSORS Hemodynamic effects of norepinephrine and angiotensin were compared in 31 patients with nonhemorrhagic shock or hypotension. Norepinephrine produced a slightly higher cardiac output than angiotensin. Norepinephrine was considerably more effective than angiotensin in patients with heart failure but not in those with reduced blood volumes. These pressor drugs usually increase cardiac output in hypotensive patients. The need for correction of occult blood volume depletion before administering norepinephrine and for caution in the use of angiotensin in patients with left ventricular failure is emphasized. Since cardiac output was increased to normal in only 6 patients, it is suggested that these drugs seldom correct the hemodynamic abnormality and should be viewed primarily as emergency supportive therapy. (Cohn, J. N., and Luria, M. H.: *Studies in Clinical Shock and Hypotension. II. Hemodynamic Effects of Norepinephrine and Angiotensin*, *J. Clin. Invest.* 44: 1494 (Sept.) 1965.)

CATECHOLAMINES Most of the norepinephrine in the blood originates in the sympathetic nerve endings, while most of the epinephrine is secreted by the adrenal medulla. Circulating levels of both compounds vary markedly although the primary stimulus is sympathoadrenal activation. Although most of the norepinephrine in tissue is synthesized from its amino acid precursor *in situ*, as much as 20 per cent of the norepinephrine in certain organs such as the heart is taken up from the circulation. Vanillyl-mandelic acid is the major end product of catecholamine metabolism. Alterations in the physiologic disposition of norepinephrine and epinephrine occur in such clinical states as cardiomegaly, thyrotoxicosis, congestive heart failure, pheochromocytoma, and monoamine-oxidase inhibition. (Wurtman, R. J.: *Catecholamines*, *New Eng. J. Med.* 273: 637, 746 (Sept.) 1965.)

ACID-BASE BALANCE Occasionally in acid-base balance studies only small quantities of blood are available, so these authors determined whether the Van Slyke-Sendroy nomogram is applicable to pregnant women and newborn infants for calculation of plasma CO_2 content and CO_2 tension when only the pH, whole blood CO_2 content and oxygen capacity are known. The calculated values caused errors of less than 0.5 mm./liter in plasma CO_2 content and less than 1 mm. of mercury in CO_2 tension. Thus, a considerable saving of blood is possible when the Van Slyke-Sendroy nomogram is used, and it is valid for men, pregnant women and newborn infants. (Erdmann, W., and Hellegers, A. E.: *The Applicability of the Van Slyke-Sendroy Nomogram to Maternal Blood and Blood of Newborn Infants*, *Amer. J. Obstet. Gynec.* 93: 723 (Nov.) 1965.)

ACID-BASE BALANCE Infraarenal occlusion in the course of aortic surgery causes anaerobic production of lactate in the legs; but hydrogen ion changes are small, transient and not significant at normothermia and hence not implicated in the hypotension that follows release of the aortic clamps. (Johnstone, J. H., and others: *Metabolic Changes after Aorto-iliac Occlusion*, *Brit. Med. J.* 2: 974 (Oct. 23) 1965.)

ACIDOSIS AND CARDIAC OUTPUT Effects of metabolic and respiratory acidosis on cardiac output was investigated in anesthetized, paralyzed, and artificially ventilated dogs. Cardiac output decreased as severity of metabolic acidosis increased. Elevation of arterial carbon dioxide tension increased cardiac output in the presence of a mild metabolic acidosis but diminished cardiac output in the presence of a severe metabolic acidosis. These changes could be quantitatively expressed in terms of pH and arterial carbon dioxide tension and a nomogram is presented, permitting prediction of variations in cardiac output in dogs for any given acid-base status. (Carson, S. A., and others: *Variation in Cardiac Output with Acid-Base Changes in the Anesthetized Dog*, *J. Appl. Physiol.* 20: 948 (Sept.) 1965.)

TRANSFUSION ACIDOSIS The major factors responsible for metabolic acidosis dur-

ing massive blood replacement are excess lactate production due to inadequate tissue perfusion, hypothermia from the cold bank blood and the high lactate, pyruvate and citrate content of bank blood. In patients who received less than 20 units of acid-citrate-dextrose preserved bank blood a significant reduction in mortality was achieved by the elimination of exogenous calcium salt administration and the use of a device for warming the blood. Since the measures had no appreciable effect upon mortality after 20 units of blood replacement, exogenous sodium bicarbonate was employed to counteract a high theoretic acid load. The use of sodium bicarbonate in a ratio of 44.6 mEq. for every 5 units of bank blood resulted in a reduction in mortality rate from 38 to 8 per cent in patients transfused with 20 or more units of blood. (Howland, W. S., Schweizer, O., and Boyan, C. P.: *The Effect of Buffering on the Mortality of Massive Blood Replacement*, *Surg. Gynec. Obstet.* 121: 777 (Oct.) 1965.)

BRONCHOSPASM In response to a questionnaire study to gather clinical experiences of acute bronchospasm during anesthesia, 62 cases were contributed from various hospitals in Japan. Among these cases, 23 were associated with bronchial asthma, 11 cases with other bronchopulmonary diseases such as pulmonary emphysema, chronic bronchitis or pulmonary tuberculosis, and one was of allergic etiology other than bronchial asthma. However, many acute attacks of so-called bronchospasm occurred during anesthesia with no apparent relationship to these diseases. The incidence of bronchospasm was approximately 1 per 3,000 anesthetics. Bronchospasm occurred most frequently following the administration of thiobarbiturates. Seven cases were encountered with halothane anesthesia which would suggest that there is a certain limit to the protective effect of halothane against bronchospasm. Mechanical stimulation or irritation of the tracheobronchial tree was often considered to be a trigger mechanism of bronchospasm, e.g., during endotracheal intubation, suctioning of trachea and operative trauma to the tracheobronchial tree. Curare, Mylaxen, succinylcholine and neostigmine were causative agents in some cases, though in other cases, succinylcho-

line alleviated the bronchospasm. Theophylline derivatives, bronchodilator agents and corticosteroids were usually effective in counteracting the spasm. In conclusion, for treatment of bronchospasm it is important to rule out mechanical obstruction among possible causes, and then to apply oxygen with positive pressure and to administer bronchodilator or adrenocortical hormones. (Shinohara, S., and Inamoto, A.: *A Statistical Study on Bronchospasm* (Japanese), *Jap. J. Anaesthesiol.* 14: 612, 1965.)

CARBON MONOXIDE POISONING

The efficacy of 5 per cent carbon dioxide in resuscitation of dogs poisoned with carbon monoxide with and without pretreatment with sodium pentobarbital was studied. The animals were exposed to approximately 0.24 per cent carbon monoxide in air until respiratory failure was reached. They were then resuscitated by spontaneous breathing of 100 per cent oxygen or 5 per cent carbon dioxide in 95 per cent oxygen for 60 minutes. More rapid elimination of carbon monoxide from the blood occurred when 95 per cent oxygen with 5 per cent carbon dioxide was breathed than with the oxygen alone. This was related to the increased pulmonary ventilation resulting from the stimulating effect of 5 per cent carbon dioxide. Pretreatment with sodium pentobarbital diminished but did not prevent the hyperpnea. (Killick, E. M., and Marchant, J. V.: *The Effect of Barbiturates on the Resuscitation of Dogs from Severe Acute CO Poisoning*, *J. Physiol.* 180: 80 (Sept.) 1965.)

CARBON DIOXIDE RESPONSE

Hypnosis is accompanied by respiratory depression as measured by the respiratory response curve displacement. In a study of 9 healthy volunteers during hypnosis, the CO₂ response curve was displaced to the right an average of 6.9 mm. of mercury at an alveolar ventilation of 15 liters/minute. In typical drug studies, morphine sulfate in 10 mg. doses gave an average CO₂ displacement to the right of 4.4 mm. of mercury at an alveolar ventilation of 20 liters/minute. Hypnosis can produce as much and possibly more respiratory depression than 10 mg. of morphine sulfate. (Katz, J.: *Respiratory Response to Carbon Dioxide in the Awake*

and *Hypnotic States*, J.A.M.A. 193: 767 (Sept. 6) 1965.)

HYPERBARIC RESPIRATION Emphysema, a disease of the lung with areas of air trapping mixed with normal areas communicating with the exterior, might be treated by hyperbaric gases. On applying pressure rather rapidly, a greater mass of gas would more quickly enter more normal areas of the lung and less normal areas would become smaller. On depressurization, however, if done very slowly and with every effort to maintain airways patent, gases would leave all areas of the lung at the same rate. That this hypothesis is partly correct is seen in improvement in 10 of 16 disabled emphysematous patients after such therapy in ways that might be expected, e.g., in residual volume, vital capacity and expiratory reserve volume. Such improvement gradually waned but could be renewed by subsequent treatment. There was no change in timed expiratory air flows. The gas or gases used are immaterial. Subjectively and clinically patients are more improved than can be demonstrated objectively. (Yanda, R. L.: *Hyperbaric Research in Chronic Pulmonary Disease*, Amer. Rev. Resp. Dis. 92: 564 (Oct.) 1965.)

PULMONARY EMPHYSEMA Undue collapsibility of the central airways (trachea and mainstem bronchi) may be a significant cause of obstruction to expiratory airflow in pulmonary emphysema. As this is largely a mechanical problem, it should be amenable to surgical correction. Support of the posterior tracheal wall with a Marlex polyethylene graft prevents collapse and invagination of the posterior tracheal wall. Support of the lateral and anterior walls may also occasionally be necessary. Surgical candidates must meet the following criteria: (1) evidence of serious obstruction of expiratory airflow, (2) definite evidence of major airway collapse via bronchoscopy and cinebronchography, (3) preservation of adequate pulmonary parenchyma, (4) absence of permanent changes in the right sided circulation. Patients who respond adequately to medical therapy are not considered for surgery. Significant improvement occurred postoperatively in 7 of 12 patients as measured

clinically and by repeated pulmonary function studies and cinebronchography. (Rainer, W. G., Feiler, E. M., and Kelble, D. L.: *Surgical Technique of Major Airway Support for Pulmonary Emphysema*, Amer. J. Surg. 110: 786 (Nov.) 1965.)

HYPOVENTILATION Thin people as well as fat people may chronically underventilate, with resultant hypoxemia, hypercarbia and acidosis. The clinical picture is similar to that characterizing the Pickwickian; somnolence, headache and stupor. If untreated, the eventual outcome is polycythemia, congestive heart failure and cor pulmonale, all refractory to digitalis or diuretic therapy. The absence of dyspnea, normal pulmonary function studies and restoration of normal blood-gas values by spontaneous hyperventilation exclude primary pulmonary disease as the cause of hypoventilation. The abnormally depressed ventilatory response to inhaled carbon dioxide in these people suggests that the idiopathic hypoventilation results from dysfunction of respiratory regulating mechanisms in the brain. Adequate ventilation must be re-established by prolonged respirator therapy before drugs will be effective in treating the sequelae of right and left ventricular failure. (Grant, J. L., and Arnold, W.: *Idiopathic Hypoventilation*, J.A.M.A. 194: 99 (Oct.) 1965.)

HYPOXEMIA Following general anesthesia, almost every healthy surgical patient shows a low arterial Po_2 . Oxygen by nasal catheter at a 5 liter per minute flow is sufficient to relieve this diminished arterial oxygenation. Patients with pulmonary disease show more marked depression of the arterial Po_2 and are not adequately helped by nasal oxygen. These patients should receive oxygen therapy by face mask. (Heller, M. L., and others: *Postoperative Hypoxemia and its Treatment with Nasal Oxygen: Polarographic Study*, Surgery 58: 819 (Nov.) 1965.)

HYPOXIA AND ALCOHOL To determine the effects of alcohol upon the time of useful consciousness of a person suddenly subjected to hypoxic conditions, 10 normal men were subjected to an atmosphere simulating 25,000 feet in an altitude chamber. After their

oxygen masks were removed, they performed various tasks requiring mental and physical coordination until definite hypoxic symptoms were manifested. Later, these same subjects repeated the experiment after the ingestion of whiskey in only slightly greater amount than that of a martini. This drug produced an overall drop of 38 per cent in the time of useful consciousness at 25,000 feet. Today's airplanes, both military and civilian, routinely fly at 30,000 to 40,000 feet and pressurized aircraft with emergency oxygen systems provide the apparent answer to man's breathing requirements in an atmosphere incapable of supporting human life. However, in the event of rapid decompression, the seconds required for man to adjust to an emergency oxygen system may be critical. Factors affecting hypoxia are the suddenness, severity, and duration of decompression and the physical condition of the subject. Decompression rate is inversely proportional to the size of the aircraft, provided the size of the defect allowing decompression remains constant. The time limitation for the onset of hypoxic symptoms is directly proportional to the atmospheric pressure, being 30 seconds at 40,000 feet. This study demonstrates that alcohol significantly reduces man's resistance to the effects of hypoxia. Because this resistance is vital in so many aspects of upper atmospheric travel, this factor alone would decry the use of alcohol prior to or during flight. (Nettles, J. L., and Olson, R. N.: *Effects of Alcohol on Hypoxia*, J.A.M.A. 194: 1193 (Dec. 13) 1965.)

AIRFLOW RATES A comparative study of the inspiratory and expiratory flow rates was performed on patients with asthma, bronchitis, emphysema and heart disease. In all patients, reduction of expiratory flow rate was associated with increase of the ratio of inspiratory to expiratory flow rates. The results support previous findings that there is no significant difference between the resting inspiratory resistance to air flow in patients with asthma, bronchitis, emphysema, or heart disease and that the ratio of inspiratory to expiratory flow rates is of no value in distinguishing between the four conditions. (Williams, M. H., and Kane, C.: *Expiratory and Inspiratory Flow Rates in Chronic*

Obstructive Pulmonary Disease, Dis. Chest 48: 262 (Sept.) 1965.)

LUNG FUNCTION Pulmonary diffusing capacity (DL_{CO}) and pulmonary capillary blood flow (Q_c) were determined in 5 normal subjects in a hyperbaric chamber at pressures of 3.5 to 4.8 atmospheres absolute. DL_{CO} was found to decrease progressively with increasing oxygen tension. The reciprocal $1/DL_{CO}$ increased linearly with rising mean intracapillary oxygen tension from 110 to 3,200 mm. of mercury. DL_{CO} was not changed significantly by independent variation of nitrogen partial pressure from 30 to 2,400 mm. of mercury at constant alveolar oxygen tension. The pulmonary diffusing surface did not measurably alter with exposure to an alveolar oxygen tension of 2,400 mm. of mercury for 10 minutes before the measurement of diffusing capacity. An average 14 per cent decrease in DL_{CO} was accompanied by a drop in Q_c . These changes were thought to result from the subjects' prolonged inactivity in the chamber during decompression rather than to be due to oxygen inhalation or to increased barometric pressure per se. (Nairn, J. R., and others: *Diffusing Capacity and Pulmonary Capillary Blood Flow at Hyperbaric Pressures*, J. Clin. Invest. 44: 1591 (Oct.) 1965.)

LUNG FUNCTION Cardiac output imposes the principal limit to maximal oxygen uptake in the normal exercising subject. Following pulmonary resection, reduction in ventilatory capacity, diffusing capacity or maximal cardiac output might impose a lower limit to maximal oxygen uptake. The factors limiting oxygen uptake were studied in 8 patients after recovery from resection of 45 to 67 per cent of their lungs. Maximal oxygen uptake was reduced in all patients, although not in proportion to the amount of lung resected. Although some degree of partial airway obstruction was noted in all patients, in no instance could the reduction in maximal oxygen uptake be ascribed to impaired ventilation. Reduced diffusing capacity appeared to contribute significantly to the reduction in maximal oxygen uptake only in the 2 patients with least lung remaining. Since maximal oxygen uptake in 5 of 7 patients was not limited either

by reduced ventilation or diffusing capacity, it must have been limited by reduced cardiac output. (Degraff, A. C., Jr., and others: *Exercise Limitation Following Extensive Pulmonary Resection*, *J. Clin. Invest.* 44: 1514 (Sept.) 1965.)

LUNG FUNCTION In 73 patients with acute myocardial infarction, 78 per cent showed objective evidence of pulmonary congestion associated with arterial hypoxemia and increased alveolar-arterial oxygen gradients. The mean oxygen tension of those who died was 52 mm. of mercury and in survivors, 63 mm. of mercury. While the more severe hypoxemia may reflect more severe disease, it may also more importantly affect the outcome. Oxygen therapy rapidly relieved most cases of hypoxemia, while more severe cases responded to the addition of rapidly acting intravenous diuretics. Unless shock was present, these cases did not show hypercarbia, metabolic acidosis or bicarbonate depletion. (McNicol, M. W., and others: *Pulmonary Function in Acute Myocardial Infarction*, *Brit. Med. J.* 2: 1270 (Nov. 27) 1965.)

LUNG FUNCTION Function of each lung was studied before and at intervals up to 207 days after irradiation of the right hemithorax with 4,500 r in five dogs. Significant reductions in minute ventilation, oxygen uptake, carbon dioxide output, diffusing capacity, compliance and inspiratory capacity occurred in the irradiated lung as compared with the nonirradiated side. There was no improvement in function as the study progressed as well as no compensatory increase in function of the nonirradiated lung. Radiographic and anatomical changes in these animals varied considerably among animals. (Teates, C. D.: *Effects of Unilateral Thoracic Irradiation on Lung Function*, *J. Appl. Physiol.* 20: 628 (July) 1965.)

LUNG FUNCTION Contradictory results in previous studies on effects of elevated transpulmonary pressure on dead space ventilation and pulmonary shunting are due to multiple and complex changes caused by alterations in transpulmonary pressure. In the present study using dogs, pulmonary perfusion was controlled by right heart bypass and

constant volume ventilation was provided by a pump respirator. Methods for calculation of fraction of lung volume perfused but not ventilated and also that ventilated but not perfused are presented. Alveolar shunt compartment decreased as transpulmonary pressure increased over the lower range of transpulmonary pressures studied. No significant change in alveolar dead space compartment was detected as transpulmonary pressure varied. (Workman, J. M., and others: *Alveolar Dead Space, Alveolar Shunt, and Transpulmonary Pressure*, *J. Appl. Physiol.* 20: 816 (Sept.) 1965.)

LUNG BLOOD FLOW Previous work has shown that in a vertically positioned isolated dog's lung, distribution of perfused blood in the lung varies with pulmonary artery pressure. By varying pulmonary artery pressure, it was possible to perfuse all the lung or to have increasing proportions of the upper and middle lobes unperfused. In the present study, difference in carbon dioxide tension between end-tidal gas and pulmonary venous blood and also ratio of alveolar dead space to alveolar tidal volume increased as the proportion of unperfused lung increased. In contrast, venous admixture component varied little as increasing amounts of lung became unperfused. It is concluded that uneven distribution of blood flow caused by hydrostatic pressure differences down the lung may seriously interfere with CO₂ exchange when pulmonary artery pressure is low but that this type of uneven distribution affects oxygen exchange much less. (West, J. B., and Jones, N. L.: *Effects of Changes in Topographical Distribution of Lung Blood Flow on Gas Exchange*, *J. Appl. Physiol.* 20: 825 (Sept.) 1965.)

LUNG MECHANICS A significant decrease in compliance of the lung occurred in 5 healthy, young subjects breathing against artificial expiratory resistance both at rest and during exercise. This is due to changes in pulmonary blood volume and decreased uniformity of intrapulmonary gas mixing which might contribute to changes in ventilation-perfusion ratios under these conditions. (Hanson, J. S., and others: *Alterations in Pulmonary Mechanics with Airway Obstruction During*

Rest and Exercise, J. Appl. Physiol. 20: 664 (July) 1965.)

LUNG SURFACTANT Lung extracts prepared by foam fractionation and mincing from rabbits and cats which had been kept in oxygen until death occurred showed increased surface tension when compared with control animals. When rats were kept in oxygen till death occurred, extracts from their lungs prepared by mincing of lung tissue showed greater surface tension than controls, but extracts prepared by foam fractionation showed no change. In addition, there were species differences among animals in survival time in oxygen at atmospheric pressure. These various species differences may represent differences in pathogenesis of oxygen intoxication. No change in blood which could account for the observed alterations in pulmonary surface tension could be demonstrated. (*Giammona, S. T., and others: Effect of Oxygen Breathing at Atmospheric Pressure on Pulmonary Surfactant, J. Appl. Physiol.* 20: 855 (Sept.) 1965.)

LUNG SURFACTANT Unilateral atelectasis was maintained for varying periods of time in rabbits by means of pneumothorax. On reinflation of the subsequently excised atelectatic lung, decreased inflatability, progressing with duration of collapse, occurred during pressure-volume measurements with both air and saline but deflation characteristics of atelectatic lungs were normal. Surface active material could be extracted from atelectatic lung but in quantities less than that from control lungs. Altered tissue characteristics rather than absence of surface active material provides the best explanation for the decreased inflatability of the lung following atelectasis in these experiments. (*Levine, B. E., and Johnson, R. P.: Effects of Atelectasis on Pulmonary Surfactant and Quasi-static Lung Mechanics, J. Appl. Physiol.* 20: 859 (Sept.) 1965.)

LUNG MECHANICS The excised lungs from fresh and macerated stillbirths, from babies with intrauterine pneumonia or with hyaline-membrane disease and from anencephalics were artificially expanded by inflating the lungs with small-volume increments of

air and recording the resulting pressure until rupture took place. Pressure-volume curves of the excised lungs show that the pressure needed to expand the lungs is less than 50 cm. of water, whereas the pressure at which rupture occurred is greater. (*Rosen, M., and Laurence, K. M.: Expansion Pressures and Rupture Pressure in the Newborn Lung, Lancet* 2: 721 (Oct. 9) 1965.)

OXYGEN TOXICITY Rabbits exposed to 100 per cent oxygen in a closed chamber at one atmosphere of pressure exhibited progressive difficulty in breathing after the first 24 hours, with the average time of death at 72-hours exposure. At necropsy, the lungs were large, dark, heavy and liver-like, weighing an average of one-third more than the controls. A definite loss of surface activity of the lungs was noted and attributed to a loss of surfactant and/or to the presence of inhibitors of surface activity. Although oxygen therapy may be absolutely essential to overcome hypoxia to maintain life, serious consideration should be given to keeping the alveolar oxygen tension as low as possible to avoid the hazards of oxygen toxicity. (*Collier, C. R., Hackney, J. P., and Rounds, D. E.: Alterations of Surfactant in Oxygen Poisoning, Dis. Chest* 48: 233 (Sept.) 1965.)

NEOMYCIN Experiments were conducted in 116 dogs to reappraise the effect of intraperitoneal neomycin during anesthesia. Serious respiratory depression occurred following large doses of intraperitoneal neomycin when ether anesthesia or muscle relaxants such as succinylcholine and curare were used. There was very mild respiratory depression with large doses and no depression with usual neomycin doses when cyclopropane, Fluether and halothane were used. Blood levels of neomycin were measured after installation of the drug intraperitoneally. The age of the animal or the presence of hypothermia did not effect the rate of absorption. There was a slight increase in rate of absorption in dogs with peritonitis. Calcium chloride proved to be much more effective than edrophonium, neostigmine or calcium gluconate in reversing the respiratory depression obtained. (*Walker, J., and*

others: *Evaluation of Intraperitoneal Neomycin*, *Ann. Surg.* 162: 634 (Oct.) 1965.)

PRESSURE BREATHING Negative pressure breathing increases pulmonary capillary blood volume (V_c) and diffusing capacity for carbon monoxide (D_L) to a degree comparable to that occurring with moderate exercise. Oxygen consumption is not similarly increased, indicating that the increase is not related to the metabolic effects of muscular activity. The increase in D_L with negative pressure breathing is attributable to an increase in the size of the effectively ventilated pulmonary capillary bed. The increase in V_c during negative pressure breathing must be due, at least in part, to better distribution of perfusion but it seems certain that previously open capillaries are also being distended, probably as a mechanical consequence of the applied negative pressure. (Steiner, S. H., Frayser, R., and Ross, J. C.: *Alterations in Pulmonary Diffusing Capacity and Pulmonary Capillary Blood Volume with Negative Pressure Breathing*, *J. Clin. Invest.* 44: 1623 (Oct.) 1965.)

PRESSURE BREATHING During continuous positive pressure breathing (CPPB) in anesthetized hypothermic dogs, minute and alveolar ventilation decreased, alveolar and arterial carbon dioxide increased, anatomical deadspace increased but alveolar dead space did not change. During continuous negative pressure breathing (CNPB), minute and alveolar ventilation increased with accompanying decreases in alveolar and arterial carbon dioxide tension. Cardiac output fell significantly during CPPB due to decreases in heart rate and stroke volume but during CNPB little change in cardiac output occurred. Hypothermic dogs were able to tolerate an imposed stress such as continuous pressure breathing and can increase oxygen consumption during continuous negative pressure breathing as do normothermic dogs. (Salzano, J., and Hall, F. G.: *Cardiopulmonary Effects of Continuous*

Pressure Breathing in Hypothermic Dogs, *J. Appl. Physiol.* 20: 669 (July) 1965.)

RESPIRATOR THERAPY Respirators are of value in some cardiac patients to reduce the work of breathing. Thirteen patients who had undergone cardiac surgery were studied during the first ten hours postoperatively. A volume-controlled respirator which delivered 50 per cent oxygen in air and a pressure-controlled respirator which delivered 40 per cent oxygen in air were used. Results were similar with both units. End-expiratory pressures were set at +4, 0 and -4 cm. of water. Central venous pressure, left atrial pressure and arterial pressure were not significantly altered. There was no evidence that cardiac output was altered. Positive end-expiratory pressure resulted in a rise of arterial P_{O_2} averaging 46 mm. of mercury. Negative end-expiratory pressure caused a reduction of similar magnitude. (Hill, J., and others: *Correct Use of Respirator on Cardiac Patient After Operation*, *Arch. Surg.* 91: 775 (Nov.) 1965.)

RESUSCITATION DEVICE Success in performing cardiopulmonary resuscitation on an emergency basis depends on the presence of two people. A device is described which enables one person to perform cardiac compression and mouth-to-mouth breathing simultaneously. The device consists of (1) an anesthesia face mask which is attached snugly to the patient's face by an elastic head band; (2) a B.M.R.-type mouth piece to fit in the resuscitator's mouth; (3) a flexible corrugated kinkless tube for connection of the mask to the mouth piece; and (4) a set of two valves of Saad and Ruben types. In cadavers, tidal volumes of 800 to 1,400 ml. could be maintained during external cardiac compression. (Bailey, W. C.: *Discussion of a Portable Device that Allows Emergency Cardiopulmonary Resuscitation to be Performed by One Person*, *Bull. Tulane University Medical Faculty* 24: 291 (Aug.) 1965.)