Proceedings of The British Cardiac Society

The Autumn Meeting of the British Cardiac Society was held at the Royal College of Physicians, London, on Thursday and Friday, November 2 and 3, 1967. The President, Shirley Smith, took the Chair at 9.00 a.m. during Private Business. He then welcomed Professor Erkelens and upwards of forty members of the Dutch Cardiac Society who were attending the first joint meeting of this kind. At the Scientific Session which followed, the Chair was taken by Sir Thomas Holmes Sellors.

PRIVATE BUSINESS

1. The President reported with deep regret the deaths of Terence East and F. van Dooren.
2. The Minutes of the Annual General Meeting having been published in the Journal (1967, 29, 937) were taken as read and confirmed.
3. The Treasurer reported that the financial position was still satisfactory and that secretarial expenses were £4 less than last year. The cost of the booklet had increased owing to the addition of a page for Cardiovascular Research and extra pages for the Thomas Lewis Lectureship and new members. £50 had been given to the Society of Cardiological Technicians as agreed at the last meeting. The Congress Fund investments remained the same at £732.18.4, and the Deposit Account held £300. The current account held £211.7.2.
4. The Secretary reported that the Annual General Meeting will be held on April 18, 1968, in Liverpool under the Chairmanship of Wyn Jones. Epstein will be the Local Secretary.
5. The Autumn Meeting will be held on December 5 and 6, 1968, at the Royal College of Physicians.
6. The Secretary reported that he had not yet received the full particulars of the Asian-Pacific Congress of Cardiology to be held in Tel-Aviv from September 1 to 7, 1968.
7. The Secretary reported that information and registration forms for the V European Congress of Cardiology, to be held in Athens from September 8 to 14, 1968, had been received and would be circulated to members.
8. The President spoke of the progress of plans for the VI World Congress of Cardiology to be held in London in 1970. Preparations by the Organizing Committee were well advanced, but it was reported with regret that Mounsey had felt obliged to resign as Chairman. Shillingford was appointed Chairman and Goodwin Vice-Chairman of the Organizing Committee.
9. Goodwin reported that the document on the Career Structure in Cardiology which he had circulated recently had been discussed with the President of the Royal College of Physicians who had expressed sympathy with the views contained therein. The Cardiology Committee of the College would discuss the matter before the end of the year, and it was intended to approach the Ministry for discussions. With the support of the Society and the Royal College of Physicians, it should be possible to improve the existing unsatisfactory situation, but the problem was not easy and a full solution would take some time.

After the Scientific Meeting the Society dined together at the Royal College of Physicians, with Shirley Smith in the Chair. The guests included Dr. Erkelens, Sir Max Rosenheim, Professor Snellen, Professor and Madame Durrer, and Professor Henry Neufeld. Shirley Smith proposed the health of the President and Members of the Dutch Cardiac Society, and Dr. Erkelens replied.

MANAGEMENT OF GUANETHIDINE-RESISTANT HYPERTENSION

By Gerald Sandler (introduced by D. Verel)

In a recent personal 5-year survey of 224 guanethidine-treated hypertensives, 38 patients (17%) had unsatisfactory blood pressure control. The approach to the management of these guanethidine-resistant patients has been based on the hypersensitivity of the peripheral arterioles to noradrenaline which is induced by administration of guanethidine.

In the first instance the demonstration of adequate adrenergic blockade by guanethidine in resistant patients has been shown by using the Valsalva manoeuvre (abolition of the reflex bradycardia normally following release of expiratory airway pressure, and results showed that similar adrenergic blockade was present in guanethidine-treated patients with and without satisfactory blood pressure control. In the next stage of the study phenoxycobenzamine was used to assess the influence of endogenous circulating noradrenaline in maintaining the high blood pressure in the guanethidine-resistant patients. The drug was given intravenously both before and after guanethidine treatment in 21 hypertensive patients who were subsequently divided into 2 groups according to
blood pressure response to treatment with oral guanethidine. The pre-guanethidine response to phenoxybenzamine was similar in the 2 groups, but after guanethidine treatment the fall in blood pressure with phenoxybenzamine was greater in those patients not responding to guanethidine than in those who responded well.

A more direct approach was then adopted by determining the blood pressure response to infusion of noradrenaline in patients on guanethidine with and without satisfactory blood pressure control. It was found that a greater and more sustained rise of blood pressure occurred in those patients with inadequate blood pressure control, indicating increased sensitivity to noradrenaline in these patients.

Finally, oral phenoxybenzamine was used in the outpatient treatment of 18 guanethidine-resistant patients. The drug was given in combination with guanethidine and considerably improved blood pressure control was obtained.

**MITRAL VALVE REPLACEMENT WITH AORTIC HETEROGRAPHS**

(Clinical Results)

By Geoffrey H. Wooler, and Marian I. Ionescu (introduced)

Because of the disadvantages connected with the use of prosthetic valves and as the experimental methods of grafting the mitral valve did not prove satisfactory for clinical use the authors developed a technique for mitral valve replacement using reconstructed heterologous aortic valves—reinforced by a semi-rigid teflon ring—sutured above the mitral annulus, inside the atrial cavity.

The technique of preparing and inserting these grafts is briefly described. Using this method 30 patients with mitral and tricuspid disease were operated upon since February 1967. The immediate post-operative results are discussed on haemodynamic and clinical grounds. Data concerning follow-up studies up to 9 months since the operation are presented to evaluate the results obtained—(clinical condition, phono, and apexcardiography, catheterization findings, and angiocardiology).

Technical and biological reasons for using this method are given. Clinical and experimental data are discussed concerning the long-term fate of aortic heterografts in the mitral position especially in relation to the manner of reconstructing, sterilizing, and preserving the heterologous grafts.

**PACEMAKER TREATMENT OF PATIENTS WITHOUT HEART BLOCK: A NEW APPROACH TO THE MANAGEMENT OF INTRACTABLE ARRHYTHMIAS**

By Edgar Sowton

A frequent clinical problem is the choice of antiarrhythmic drugs for the patient with multiple arrhythmias which may be complicated by periods of sinus rhythm. The use of cardio-depressant drugs in sufficient doses to prevent rapid supraventricular arrhythmias may lead to severe depression of ventricular function and may cause dangerous bradycardia or even asystole if the patient returns to sinus rhythm.

This problem can be dealt with by the use of an implanted long-term pacemaker with a fixed minimum rate which is programmed to avoid competition with any spontaneous rhythm. The ventricular rate cannot fall below the pacemaker minimum but can increase freely with no risk of pacing stimuli falling in the vulnerable period. Under these circumstances anti-arrhythmic drugs such as propranolol can be given in large doses without dangerous depression of cardiac function.

This dual approach has been used clinically in six patients for periods of over a year. Treatment has been successful in patients with atrial flutter, varying supraventricular tachycardias, atrial fibrillation inadequately controlled by digitalis, and Wolff-Parkinson-White syndrome.

**ELECTROPHYSIOLOGICAL ASPECTS OF PAIRED STIMULATION**

By R. T. van Dam

When the ventricles are stimulated electrically, activation mainly occurs by myocardial propagation and the specialized conduction system contributes little to ventricular excitation. During paired stimulation, the propagation of activation caused by an early second stimulus occurs during the functional refractory period of the myocardium and is slower than that following the first stimulus. This causes a difference in form and duration of the electrocardiograms evoked by both stimuli.

Institution of paired stimulation also results in a progressive shortening of myocardial refractoriness which disappears gradually when paired stimulation is discontinued. The "on"-effect is faster than the "off"-effect: both depend on the interval between first and second stimulus. In old myocardial infarction, paired stimulation results mainly in a retardation of excitation; in fresh myocardial infarction it almost invariably causes ventricular fibrillation.

**ULTRASONICS IN CARDIAC DIAGNOSIS**

By R. B. Pridie (introduced), J. F. Robinson, and J. J. Key (introduced)

The application of ultrasonics to cardiology has provided a further aid to diagnosis in a limited, but important, aspect of the specialty. It can be applied at the bedside, gives rise to no discomfort to the patient, and provides a quick and reliable result. This method has two principal applications at present: (1) the assessment of mitral valve function, (2) the detection of a pericardial effusion.

**Mitral valve disease.** Echocardiography records the note and amplitude of movement of the anterior cusp of the mitral valve. We have studied 60 cases of rheumatic

* Papers marked with an asterisk were given by members of the Dutch Cardiac Society.
mitral valve disease; the results show a close correlation with the subsequent angiographic and surgical appraisal. From this experience we believe that in the future this method may be of considerable help in the diagnosis of cryptic mitral stenosis, e.g. in Lutembacher's syndrome, or conditions mimicking mitral stenosis, e.g. cor triatriatum.

Pericardial effusion. Clinically the differentiation between pericardial effusion and cardiomegaly can be difficult: echocardiography can, in most cases, assist in the differentiation. In pericardial effusions, the echo received from the anterior wall of the chest and the echo received from the anterior surface of the heart diverge in systole. In patients with cardiomegaly (without effusion) the two tracings are always parallel.

Ultrasonic patterns in Mitral Valve Disease

By C. F. P. Wharton (introduced by Charles Baker)

It is possible to measure the speed of closure and amplitude of movement of the anterior leaflet of the mitral valve from reflected ultrasonic waves.

In a series of 60 cases of mitral valve disease, 3 distinct patterns were found from the ultrasonic readings. These 3 patterns were found to correlate closely with pure mitral stenosis, mixed stenosis and regurgitation, and pure mitral regurgitation. The assessment of the mitral valve lesion was made from operative findings, haemodynamic studies, and left ventricular angiography.

Of the series 25 patients had pure stenosis, 20 a mixed mitral lesion, and 15 pure mitral regurgitation.

Ten patients with mitral stenosis who had apical systolic murmurs were found to have no evidence of mitral regurgitation either at operation or on left ventricular angiography. These 10 patients all gave purely stenotic patterns on ultrasound cardiography.

Those patients with mitral stenosis who underwent valvotomy were restudied after operation. A characteristic change in the ultrasound pattern was seen.

Importance of Accurate Cardiac Diagnosis in Pregnancy

By R. M. Marquis

It has long been recognized that exercise tolerance is the best general guide to the fitness of a woman with heart disease for the burden of pregnancy and labour.

An analysis of 1477 pregnancies in women with heart disease, supervised in the Simpson Maternity Pavilion of the Royal Infirmary of Edinburgh during the last 19 years, has demonstrated that the cardiac diagnosis is sometimes of greater significance than the exercise tolerance. The incidence and severity of rheumatic heart disease in pregnancy have decreased progressively. The rheumatic lesion was severe in only 705 pregnancies, but this group included 9 deaths. In contrast, the incidence of congenital heart disease has increased. In most of the 240 pregnancies the malformation was mild or had previously been treated surgically, but 4 deaths occurred in the 45 with severe malformations. Accurate cardiac diagnosis has been shown to be of particular importance in rheumatic mitral stenosis and in congenital malformations with severe outflow obstruction or high pulmonary vascular resistance.

The Simpson experience is correlated with that of others in an attempt to clarify the management of heart disease as a complication of pregnancy.

Frank Vectorcardiogram Related to Right Ventricular Pressure

By E. Fletcher, S. Lal, and P. Binnion

The Frank vectorcardiogram QRS loop was recorded in three planes in 25 patients in whom right ventricular pressures were obtained by cardiac catheterization. The QRS loops were analysed by planimetry and selective instantaneous, maximum, and half-area angles were determined, together with right-to-left ratio and quadrantic areas. The anatomical diagnosis included mitral stenosis, cor pulmonale, congenital heart disease, and miscellaneous cases including cardiomyopathy and pulmonary lupus erythematosus. In most cases of right ventricular hypertrophy, the QRS loop in the horizontal plane showed more consistent rightward and anterior displacement, except in cor pulmonale when the QRS loop displacement was more posterior, and the figure-of-eight vector loop was more common in this plane. The angle of the half-area vector gave more consistent indication in any plane of changes in the right ventricle rather than any other instantaneous vector angles. There does not appear to be any consistency in the shape of the QRS vector loop and dynamic changes in the right ventricle. When intraventricular conduction is normal, the shape of the QRS loop appears to be determined more by the anatomical diagnosis than by haemodynamic changes.

Physiological Basis for Recognizing Ventricular Hypertrophy in the Vectorcardiogram

By A. C. Arrittenius

A study of a mathematical model, based on section of a normal human heart, showed that a simplified theory, i.e. of uniform propagation of excitation fronts from the end points of the main branches of the bundle of His, was consistent with the findings of the epicardial excitation obtained by direct leads from the exposed human heart. It was also found that the breakthrough of excitation at the epicardial surface correlated with specific inflection points of the QRS loop in the vectorcardiogram. The intervals between these points can be used to differentiate normal vectorcardiograms from those with either right or left ventricular hypertrophy.
Electromagnetic Flowmeter as a Monitor of Blood Flow in First 24 Hours After Reconstructive Surgery of Arteries of Lower Limb

By Stuart B. Renwick (introduced), Ivor Gabe, and Peter G. Martin (introduced)

Blood flow in 11 patients, after reconstructive surgery of the arteries of the lower limb, was monitored by the implantation of a miniaturized flow transducer and the use of a square wave electromagnetic flowmeter. This was subsequently removed under local anaesthesia after periods ranging from 18 to 27.5 hours. No complications due to this implantation were seen and the wounds healed primarily.

After femoro-popliteal reconstruction (7 cases), flow increased rapidly till at 10-12 hours it was three times the initial flow recorded in the theatre, and then gradually declined. This increase in flow corresponded to the appearance of hyperaemia of the foot. In one patient occlusion of a vein bypass was diagnosed which would have been missed clinically for some hours.

After profunda femoris reconstruction (2 cases) the increase in flow is more rapid, being maximal after 2 hours.

To simulate distal occlusion, and to determine the distribution of blood flow in the limb, cuffs were transiently inflated at various levels.

Implantation of flow transducers after vascular surgery in our hands has been without complication and has enabled early detection of vein graft occlusion in one patient. It should lend itself to the evaluation of various agents to increase blood flow in limbs in the post-operative phase.

Results of Surgical Treatment of Hypertrophic Obstructive Cardiomyopathy of the Left Ventricle*

By E. L. H. Verbiest, H. A. Snellen, H. Hartman, and J. P. Roos

The results of the surgical treatment in 12 patients with hypertrophic cardiomyopathy—with (3) and without (9) subvalvular aortic stenosis—are presented. Ages at operation ranged from 11 to 43 years. The post-operative follow-up period extended from 8 to 52 months. Except for one case, one single surgical technique was employed, using an original punch instrument for relieving the muscular obstruction. Appreciation of the results is based on the comparison of pre- and post-operative symptomatology, carotid pulse tracing analysis, and haemodynamic data (pressure gradient over left ventricular outflow tract and end-diastolic left ventricular pressure).

Phonocardiography appears to be important in the preoperative assessment of the different types of the hypertrophic cardiomyopathy (with and without obstruction), as in the recognition of the combination of the obstructive form with subvalvular aortic stenosis. In a previous study the excellent correlation of the haemodynamic and simultaneously recorded phonocardiographic data was demonstrated. Symptomatology, carotid pulse analysis, and left heart catheterization showed striking and concordant improvement in most patients. Bad results were seen in one case with left ventricular insufficiency and atrial fibrillation at the operation, and in another case with the non-obstructive type of hypertrophic cardiomyopathy. After resecting only the subvalvular membrane in the combined type (hypertrophic obstructive cardiomyopathy plus subvalvular aortic stenosis), the typical haemodynamic picture of pure hypertrophic obstructive cardiomyopathy appeared. In two patients a small gradient at rest remained but increased conspicuously after drug administration (isoprenaline and amyl nitrite), though both patients regained normal left ventricular end-diastolic pressures.

Surgical Correction of Ostium Primum Defects Using Profound Hypothermia

By I. Anderson, P. A. Cullum (introduced), C. E. Drew, A. Harris, and Aubrey Leatham

The major surgical problem in the repair of ostium defects is the correction of mitral regurgitation. During the past 8 years 17 patients with ostium primum defects have been treated using profound hypothermia. Two patients died in the immediate post-operative period. Two patients developed complete heart block, one of whom died 5 years later. Fourteen patients are well and asymptomatic. A patch for closing the atrial septal defect was used on only four occasions.

All the survivors have been followed-up, and nine have been re-investigated by cardiac catheterization and angiocardiography. The characteristic deformity of the left ventricular outflow tract remains unaltered, and mitral regurgitation is absent or trivial except in one case.

The satisfactory post-operative results, judged by re-investigation, are in great part due to the clear operative field afforded by complete circulatory arrest using profound hypothermia, permitting accurate approximation of the mitral cleft.

Left Axis Deviation With Right Bundle-Branch Block in Ventricular Septal Defect Before and After Surgical Closure

By H. Kulbertus, J. Coyne (both introduced), and Katherine A. Hallidie-Smith

A trivectorial analysis of the scalar electrocardiogram has been applied to 276 tracings from 140 patients with ventricular septal defect and 136 patients with the tetralogy of Fallot. The typical pattern of atrioventricular canal (counterclockwise rotation of the frontal loop, left axis deviation of the mid sector, and a right bundle-branch block) was found in 15 patients (5-5%). In all but one of these 15 patients the operation revealed an unusual type of ventricular septal defect: an endocardial cushion type of ventricular septal defect in 6 patients, virtual absence of the interventricular septum or incomplete common ventricle in 5 patients, multiple defects in
the muscular septum in 3 patients, ventricular septal defect with aortic incompetence in one patient.

Twenty-four patients (9.2%) with an uncomplicated infracristal ventricular septal defect of moderate size, who did not have an atrioventricular canal cardiographic pattern before operation, acquired it after operation.

The atrioventricular canal pattern is thought to be due to direct trauma to the fibres of the right bundle-branch and to the superior division of the left bundle-branch. The same pattern when present before operation is thought to be related to abnormalities of the conduction system, producing premature excitation of the posterobasal area of the left ventricle and/or left superior intraventricular block.

The association of right bundle-branch block with left superior intraventricular block is frequently complicated by complete heart block, which occurred in the post-operative period in 11 out of the 39 patients (28%) who showed the atrioventricular canal type of cardiogram either before or after operation.

The prognostic implications of these conduction abnormalities are discussed and their possible role in cases of unexplained sudden death after surgical repair of ventricular septal defect are discussed.

AORTOGRAPHY IN FALLOT'S TETRALOGY AND ALLIED LESIONS

By Simon Rees and Jane Somerville

Routine aortography was performed in 40 patients. Fallot's tetralogy was present in 26, pulmonary atresia in 11, and transposition with pulmonary stenosis in 3. At the same investigation, right ventricular angiocardiography was carried out, and this frequently failed to demonstrate the complete anatomy of the systemic contribution to the pulmonary blood flow.

Aortography clearly delineated the site and size of surgical anastomoses, collaterals from the aorta and its branches, unsuspected persistent ductus arteriosus, and the anatomy of the coronary arteries. The findings were correlated with the presence or absence of a continuous murmur. In patients with a continuous murmur, the aortogram always demonstrated systemic vessels supplying the lungs. With a patent surgical anastomosis a continuous murmur was always present, which in some patients persisted when the anastomosis became blocked owing to enlargement of the bronchial arteries. In 6 patients without a continuous murmur, the aortogram revealed a ductus in 2 and unexpectedly large collateral arteries in 4.

Routine pre-operative aortography has been found to be a simple procedure and has not added morbidity to the investigation, particularly as the catheter entered the aorta from the right ventricle in 85 per cent. Success of radical correction of Fallot and pulmonary atresia has in part depended on removal of systemic to pulmonary communications and aortography has provided useful information which was not always apparent from a right ventricular angiocardiogram. It has been found to be particularly indicated in patients with continuous murmurs or in those with deep cyanosis and inconspicuous murmurs.

WATERSTON'S OPERATION (AORTA TO RIGHT PULMONARY ARTERY ANASTOMOSIS) FOR CYANOTIC HEART DISEASE

By M. Yacoub (introduced), Jane Somerville, and D. N. Ross

Waterston's operation was performed in 20 patients with cyanotic heart disease aged 8 months to 14 years. Fallot's tetralogy was present in 15, pulmonary valve atresia in 2, tricuspid atresia in 2, and underdeveloped right ventricle in one. Immediate relief of cyanotic attacks and dyspnoea occurred in all. The improvement was maintained throughout the period of follow-up, and all except 2 patients were acyanotic at rest.

Heart failure occurred in the post-operative period in 40 per cent, but this was only troublesome, persisting for three months, in one patient. Preferential flow of blood into the right lung occurred in 75 per cent, and in 50 per cent was associated with unilateral pulmonary oedema in the first week after surgery. Post-operative investigation with catheterization and aortography confirmed the larger flow into the right pulmonary artery. No patient was found to have pulmonary hypertension, even when the shunt had produced heart failure.

This anastomosis, performed through a right thoracotomy, has been found to be easy to make and constantly successful, irrespective of the size of the patient. Techniques to avoid making too large a stoma and for directing the flow into both pulmonary arteries by making the anastomosis behind the superior vena cava were demonstrated. This operation has particular advantages in the infant, and we use it in preference to other anastomoses in all forms of cyanotic heart disease.

FREQUENCY ANALYSIS OF HEART MURMURS APPLIED TO DETECTION OF AORTIC INSUFFICIENCY*

By F. G. Schlesinger, E. van Vollenhoven, A van Rotterdam, and T. Dorenhos

The detection of aortic insufficiency is of considerable practical importance in patients with rheumatic heart disease in whom mitral surgery is considered.

With conventional phonocardiography by means of a set of four filters, time relationships are clearly defined and some information as to frequency is available. However, for the detection of aortic insufficiency a more detailed kind of frequency analysis appears helpful. The heart sounds were recorded on magnetic tape and a highpass filter was included in the recording equipment to minimize extraneous noise. The analysing equipment consists mainly of a tape recorder, a wave analyser, a gate circuit, a rectifier, a squarer, an integrator, a scope, and a camera.

The results of this analysis were correlated with the results of other diagnostic methods (haemodynamic studies, angiocardiography) and findings at operation in 30 patients.
NATURAL HISTORY OF PERSISTENT DUCTUS ARTERIOSUS

By Maurice Campbell [Published in full, vol. 30, 4.]

DAY-TO-DAY CIRCULATORY CHANGES IN PATIENTS WITH CONGESTIVE FAILURE DUE TO CHRONIC BRONCHITIS

By A. S. Abraham, I. D. Green, R. B. Cole, R. B. Hedworth-Whitty (all introduced), and J. M. Bishop

The pulmonary arterial pressure, cardiac output, arterial blood gas tensions, and plasma volume were measured daily in 7 patients with congestive failure secondary to chronic bronchitis with airway obstruction. A fine nylon catheter introduced via an antecubital vein, was floated into the pulmonary artery, and a polythene catheter inserted into a brachial artery. Both these catheters were left in situ for the five days of the study, the main aim of which was to relate changes in pulmonary arterial pressure to blood gas tensions, blood volumes, and the onset of diuresis. The patients were studied again some three weeks later. A fall in pulmonary arterial pressure preceded any change in body weight or plasma volume in the 3 patients who had a diuresis, and continued throughout the period of study, without any significant change in blood gas tensions or cardiac output. The pulmonary arterial pressure showed no significant change in the remaining patients during the first five days, though it dropped considerably before the patients were discharged home. At this stage the Pao2 had risen and the Paco2 had fallen in all patients.

Oxygen and infusions of acetylcholine into the pulmonary artery produced a substantial fall in pulmonary arterial pressures, occasionally to levels seen after recovery.

The significance of these observations with regard to the exacerbation of pulmonary hypertension during such acute episodes was discussed.

MYOCARDIAL BLOOD FLOW AT DIFFERENT HEART RATES IN PATIENTS WITH COMPLETE HEART BLOCK

By R. B. Hedworth-Whitty, E. Housley, and A. S. Abraham (all introduced by Ian R. Gray)

The relation between myocardial blood flow and heart rate was studied in five patients with complete heart block. Myocardial blood flow, determined by the nitrous oxide method, was measured at the patient's idioventricular rate and at a paced rate of 80 and 100 a minute. Within this range myocardial blood flow and myocardial oxygen consumption were found to be directly related to the heart rate and left ventricular work. Between the patient's idioventricular rate and a paced rate of 80 a minute the duration of diastole was directly related to the myocardial blood flow per beat, but a further shortening of diastole between heart rates of 80 to 100 a minute was associated with a rise in flow per beat. The possible mechanisms accounting for these findings are discussed.

EFFECTS OF BETA-ADRENERGIC BLOCKADE DURING EXERCISE IN HYPERTENSION AND ISCHEMIC HEART DISEASE

By E. Shinebourne, J. Fleming (both introduced), and J. Hamer

Propranolol has been used in the treatment of systemic hypertension, but its mode of action and efficacy in this condition have not been fully established. In this study 10 patients with hypertension and 8 with ischaemic heart disease were exercised on a treadmill at different work loads before and after intravenous propranolol. Consecutive exercise studies were also carried out without pharmacological intervention; these showed no significant haemodynamic changes.

Arterial blood pressure was measured directly and cardiac output was determined by the indicator dilution technique. Heart rate, peripheral resistance, ejection rate, and pressure-time per minute were estimated.

In both groups of patients beta-adrenergic blockade caused a moderate fall in blood pressure by decreasing cardiac output; there was no change in total peripheral resistance. These effects were greater on exercise. Pressure-time per minute decreased, but this does not necessarily mean a reduction in myocardial work, as heart size is known to increase after propranolol. Ejection rate decreased, indicating a reduction in the velocity of contraction of the ventricular muscle. The therapeutic benefits of propranolol may well depend chiefly on the latter mechanism.

OBSERVATIONS ON HEART CELL CULTURE*

By G. E. Freud

The hearts of 3-day-old rats are used to obtain single heart cells by trypsinizing. These cells are cultured in plastic discs. The contractions of the cells or even a part from one cell can be measured by the changes in luminoscence. This preparation is useful to study the properties of the muscle cell without disturbing effects of haemodynamics or innervation. Spontaneously, regularly beating heart cells show equal contractions, beat for beat. When digitalis is added in an overdosage, the beating becomes irregular. These contractions are much like those registered in a complete irregularly beating heart, showing that the relations between interval and contraction are largely dependent on pure muscle cell properties. A strong contraction develops after a long interval, and a weak contraction after a short interval. To study these effects without drug intoxication the observed cells were electrically stimulated. Thresholds were measured and strength-interval relations studied; these appeared to be comparable to those obtained in hearts in situ. At threshold the excited area of the cell is minimal. The spread of excitation is dependent on the number of synchronously excited sarcomeres. This explains the latent period, dependent on stimulus strength. Electrically induced aberrant intervals show the same properties as hearts in situ. The restitution curve depends on pure muscle properties.
Intracellular Electrolyte Concentrations in Heart Disease

By John Hamer, Joan McAlister, Irene Stielow, and Douglas Chamberlain (the last three introduced)

Although there is evidence of loss of cellular potassium in patients with severe heart disease who have had diuretic treatment, it is not known whether this loss leads to a reduction in the fluid content of the cells or whether the potassium is replaced by sodium.

We have examined this problem in 20 patients who were being prepared for valve replacement operations, and who were free of oedema at the time of study. Total exchangeable sodium (Na) and potassium (K) were measured with Na and K, and total body water by the titrim method. The volume of cellular water was obtained indirectly by measuring extracellular fluid volume from the dilution of sulphate labelled with 35S. We have devised a new method of counting radioactive sulphate based on the use of a scintillating anionic exchange resin.

There was good agreement between the total body water and the total cation space (Na + K), indicating that there was no osmotic gradient between the cells and the extracellular fluid, and that all the exchangeable sodium and potassium was osmotically active.

The reduction in total exchangeable potassium (K) was confirmed, but there was little increase in total exchangeable sodium (Na). The loss of potassium from the cells appears to be associated with a reduction in total cell mass, and there is no evidence that potassium has been replaced by sodium.

The effect of these changes on the management of the patients is discussed.

Some Hydrodynamic Factors Affecting Lung Capillary Blood Flow in Man

By N. Karatzas (introduced) and G. de J. Lee

Lung capillary blood flow has a characteristic pulsatile velocity profile in man imposed by the pressure events taking place simultaneously at the arteriolar and venular ends of the capillary system. These, in turn, are dependent upon simultaneous events taking place in the right ventricle and left artium, modified by the physical characteristics of the arteries, alveolar-capillary system, and veins connecting them.

The nitrous oxide body plethysmograph method, combined with simultaneous pulmonary vascular pressure measurements during cardiac catheterization provide opportunity for studying the effects that changes in the pulmonary arteries, alveolar capillary system, and veins each individually may have upon lung capillary blood flow. (1) The pulmonary arterial system accommodates up to 66 per cent of the right ventricular stroke volume during systole for subsequent discharge through the lung capillaries during diastole. Tachycardia reduces this distensibility. (2) Pulmonary arterial hypertension, by increasing resistance in precapillary vessels, reduces the pulsatility of capillary blood flow so that pulmonary arterial resistance can be assessed indirectly from the N2O uptake measurements. (3) The physical relationships regulating opening and closure of the alveolar capillaries have been demonstrated in man. (4) The effects of changes in the impedance to capillary outflow into the veins imposed as a result of left atrial pressure events has been examined. Evidence is presented that reversal of blood flow through the lung capillaries may take place in mitral incompetence.

Computer Analysis of the Interval-Contractility Relationship during Random Stimulation of the Isolated Rat Heart

By F. L. Meijler, J. Strackee, F. J. L. van Capelle, and J. C. du Perron-Maas

The variations in haemodynamics in patients with atrial fibrillation have mainly been attributed to changes in left end-diastolic pressure (Frank-Starling mechanism) due to the differences in R-R intervals. At the same time it has been demonstrated that when changes in diastolic filling are absent, as in isolated hearts, the contractile force is still dependent on the duration of preceding R-R interval(s). The question arises as to whether or not the direct relation between interval and myocardial contractility also plays a role in the variability of haemodynamic parameters in patients with atrial fibrillation. In a first attempt to answer this question isolated perfused rat hearts were stimulated with a rhythm of the same mathematical properties as the ventricular rhythm of those patients.

Isotonic contractions and electrocardiograms of these hearts were recorded on magnetic tape. After suitable conversion by means of an analogue to digital converter (IBM 9X12), the data were processed by a digital computer (IBM 7094). Contractility was expressed by the height, area, and the maximum of the first derivative of the contraction. Serial cross-correlation coefficients were computed between R-R interval and each contraction parameter. The first coefficient (the correlation) turned out to be highly positive, the second order coefficient though small was found to be negative. From these findings it can be concluded that during this irregularity the contractile behaviour of isolated hearts is strongly related to the preceding R-R interval(s). Thus this relationship may indeed play a role in the variability of haemodynamics in patients with atrial fibrillation.

Pacemaking in Complete Heart Block Complicating Acute Myocardial Infarction

By B. W. Lassers, J. L. Anderton (both introduced), and D. G. Julian

In 17 months, 50 patients with complete heart block complicating acute myocardial infarction were managed in the Coronary Care Unit of the Royal Infirmary, Edinburgh. Bipolar pacing catheters were introduced percutaneously via the subclavian vein in most patients...
with greater than first degree heart block, and recently
in all patients with bundle-branch block. On the basis
of clinical, haemodynamic, and ventilation/perfusion
studies, pacing was instituted only if there was clinical
evidence of inadequate cerebral or peripheral perfusion.
Hypotension and bradycardia were found to be unreliable
indications for pacing. Pacing increased cardiac output
and systemic blood pressure but had little effect on right
atrial or pulmonary arterial pressures. Patients were
paced at the slowest rate consistent with an adequate
clinical response, and this was usually found to be be-
tween 80 and 90 a minute. Catheters were removed 72
hours after the last episode of advanced heart block.
The most serious complication encountered was ventri-
cular fibrillation (7 patients). Ventricular demand
pacing units were found to reduce this risk. Although
pacing is a potentially dangerous procedure it was re-
sponsible for a small reduction in mortality.

INCIDENCE AND SIGNIFICANCE OF RELATIVE
HYPOVOLEAEMIA AS A CAUSE OF SHOCK ASSOCIATED
WITH ACUTE MYOCARDIAL INFARCTION

By Howard N. Allen, Ronald Danzig, and H. J. C. Swan
(all introduced by Aubrey Leatham)

Patients in the coronary care unit treated for shock
associated with acute myocardial infarction were divided
into two groups based on their central venous pressure
and response to venous loading. Those patients who did
not present with signs of congestive heart failure and
whose central venous pressure did not rise significantly
after infusion of a test load of 5 per cent dextrose in water
were treated with large volumes of intravenous fluids and
were classified as "treated relative hypovolaemia". All
the patients who did not meet the above criteria were
treated with drugs, including digitalis preparations and
alpha- and beta-adrenergic agents and were classified as
"other therapy". Of 30 patients treated during a 10-
month period, 24 were managed with other therapy and
only 7 of these patients survived, while all 6 patients
managed for relative hypovolaemia survived. The
response to treatment in the latter group included (1) an
average increase in systolic blood pressure of 37 mm. Hg,
(2) an increase in urine flow from less than 20 ml./hr.
in each patient to greater than 30 ml./hr. in every patient,
and (3) only a slight change in central venous pressure.
The significant incidence and favourable prognosis
associated with relative hypovolaemia illustrate the need
for evaluation of all patients with cardiogenic shock for
the presence of this condition.

RIGHT ATRIAL ELECTROCARDIOGRAM
IN THE ANALYSIS OF ARRHYTHMIAS FOLLOWING
ACUTE MYOCARDIAL INFARCTION

By D. E. Jewitt, Y. Kishon (both introduced),
M. Thomas, and J. P. Shillingford
[Published in full, vol. 30, 97.]

ARCUS SENILIS AND CORONARY HEART DISEASE

By Noel J. Hickey (introduced), Risteard Mulcahy,
and Brian J. Maurer (introduced)

The frequency and intensity of arcus senilis was noted
in 484 male patients with classical coronary heart disease.
These data are compared to the findings in 465 apparently
healthy male control subjects matched for age. The
incidence of arcus senilis in the patients is correlated with
the following 13 parameters: age, family history,
cigarette smoking habits, weight, resting diastolic blood
pressure, alcohol intake, fat folds, total calories from fat,
per cent calories from fat, total calories from carbohydrate,
glucose tolerance test, total lipids and cholesterol,
and calories derived from sucrose.

The following conclusions were reached: (1) There is
a significantly higher incidence of arcus in the patients.
(2) Heavy arcus, absent in the younger subjects in the
control group, was present in the patient group at all ages.
In the younger age-groups heavy arcus is probably pre-
crictive of coronary heart disease. (3) In the patient
group there is a significant association between arcus and
the following attributes: age, obesity and sucrose intake.

PHYSICAL TRAINING OF PATIENTS AFTER
MYOCARDIAL INFARCTION*

By J. Pool, H. W. H. Weeda, and L. L. M. Thomas

Patients who have had a myocardial infarction have a
diminished physical working capacity. This appeared
from reported studies and also from studies made in our
department. For this reason it seems worthwhile to try
and recondition this group of patients.

The patients were trained on a bicycle ergometer, five
days a week in the out-patients' department. A maxi-
mum exercise test was done before and after training.
The maximum oxygen uptake increased considerably
in nearly all patients. In addition the myocardial
ischaemia diminished, as apparent from the vector-
cardiogram.

ABNORMAL PLATELET BEHAVIOUR IN PATIENTS
WITH CARDIAC INFARCTION

By C. H. Bolton, J. R. Hampton (both introduced),
and J. R. A. Mitchell

The formation of a mass of adherent platelets is an
important step in arterial thrombosis, but we do not
know how this cell-to-cell adherence is brought about,
nor, as yet, has a consistent difference between the plate-
let behaviour of subjects with and without thrombosis
been demonstrated.
Platelets are negatively charged, and this charge must
in some way be overcome before adherence can occur.
Their charge can be measured by micro-electrophoresis,
and aggregating agents such as ADP, noradrenaline,
thrombin, and collagen have been shown to produce a
biphasic change in mobility. In normal subjects and
patients with chronic diseases other than vascular disease,
peak mobility is induced by the same concentration of both ADP and noradrenaline. However, in patients with cardiac infarction we have observed a differential effect of ADP and noradrenaline, and have shown that this differential pattern can be conferred on normal platelets by incubation with the cell-free plasma from abnormal subjects.

We have now characterized this "transferable factor" and have shown that it has two components: one is a labile protein of low molecular weight, while the other is a stable protein of very high molecular weight. The former is a low density lipoprotein and the constituent which influences platelet electrophoretic behaviour is its phospholipid moiety.

This observation provides a possible link between abnormal lipid patterns in patients with cardiac infarction and abnormal platelet behaviour.

**IMPORTANCE OF SELECTIVE CORONARY ARTERIOGRAPHY IN THE DIFFERENTIAL DIAGNOSIS OF ANGINAL COMPLAINTS**

By A. Bruschke

Anginal, or pseudo anginal, complaints may occur (A) "primarily" or (B) accompanying aortic or mitral valve disease. Sometimes it may be extremely difficult, if not impossible, to establish the cause of these complaints, especially in group B.

In our hospital selective coronary arteriograms have been made in about 200 cases. From this series, a number of cases will be selected in which this investigation yielded information not obtainable by "conventional methods". The correlation with clinical, chemical, electrocardiographic, and vectorcardiographic findings was demonstrated. The consequences of the angiographic findings were discussed.

The purpose of the communication is to demonstrate the importance of coronary angiography in these cases.

**LIGNOCaine IN MANAGEMENT OF ARRHYTHMIAS FOLLOWING ACUTE MYOCARDIAL INFARCTION**

By D. E. Jewitt, Y. Kishon (both introduced), M. Thomas, and J. P. Shillingford

Continuous electrocardiographic monitoring of patients with acute myocardial infarction has established that the development of ventricular tachycardia and ventricular fibrillation may be preceded by frequent ventricular extrasystoles.

Earlier work has shown that lignocaine is of value in the management of ventricular arrhythmias occurring during or after cardiac surgery. We have assessed the haemodynamic effects of intravenous lignocaine when used to abolish and suppress ventricular arrhythmias after myocardial infarction. Our studies have established that lignocaine in a dose of 1–2 mg./kg. intravenously is safe and effective as an antiarrhythmic agent, and is without deleterious effects on the circulatory state. This assessment involved serial measurements of cardiac output, mean arterial pressure, right atrial pressure, systemic vascular resistance, and continuous electrocardiographic monitoring.

The range of arrhythmias which may be effectively controlled by lignocaine has been defined. Preliminary comparisons have been made between lignocaine and procaine amide used in the same clinical situation. Particular attention has been paid to toxic side-effects following single intravenous injections and continuous 24-hour infusions of lignocaine. Effective blood levels of lignocaine have been defined.

**HAEMODYNAMIC EFFECTS OF ACUTE DIGITALIZATION FOLLOWING MYOCARDIAL INFARCTION**

By Raphael Balcon, Henrik Frick (both introduced) and Edgar Sowton

Eleven patients in sinus rhythm who had myocardial infarction during the preceding 48 hours were studied; all had clinical evidence of cardiac failure but were not hypotensive. Pulmonary artery and aortic pressures and samples were obtained via small percutaneous catheters and cardiac output was measured by dye dilution.

Control measurements were made for at least 30 minutes before rapid digitalization with the intravenous injection of 0.25 mg. acetyl beta strophanthidin (7 cases) or 0.5 mg. digoxin (4 cases). One patient experienced anginal pain 8 minutes after intravenous digoxin.

Digitalization produced a mean fall of 5 beats a minute in heart rate, with no change in aortic or pulmonary artery pressures. Cardiac output fell in all cases, the mean drop being 15 per cent between 30 and 60 minutes after the injection. Subsequently, the output rose again. It is concluded that rapid intravenous digitalization is not indicated in patients of this type.

**TREATMENT OF AV CONDUCTION DISTURBANCE IN ACUTE MYOCARDIAL INFARCTION BY ARTIFICIAL PACEMAKING**

By Richard Sutton (introduced by Aubrey Leatham)

Experience in treatment of 46 cases of acute myocardial infarction with AV conduction disturbance by artificial pacemaking between August 1961 and August 1967 is presented. Twenty-six patients have been treated with ventricular-inhibited pacemaker units used externally. This technique was introduced in November 1965. Twenty patients have had fixed rate external pacemaker units. Endocardial electrode catheters have been inserted in all patients.

The over-all mortality was 46 per cent. The mortality of fixed rate pacing was 55 per cent; 6 out of 11 of these were from ventricular fibrillation. The mortality of
ventricular-inhibited pacing was 38 per cent; 3 out of 10 of these were from ventricular fibrillation.

Of the 25 survivors, 24 patients have been followed-up for an average of 7 months. Two patients have died 2 and 3 months, respectively, after their acute infarctions. Two patients required long-term pacing for persistent complete heart block (4% of whole group). The remaining 20 patients are in sinus rhythm (41% of whole group).

Indications for institution of pacemaking in this situation, and the length of time for which pacing should continue, are discussed. The natural history of the condition has been studied and inferences regarding prognosis have been drawn.