Proceedings of the British Cardiac Society

THE FORTY-NINTH ANNUAL GENERAL MEETING of the British Cardiac Society was held in the Koninklijk Instituut voor de Tropen, Mauritskade 63, Amsterdam, on Thursday and Friday, 23 and 24 April 1970 as a joint meeting with the Dutch Society. The President, SIR JOHN MCMICHAEL, took the Chair at 9.00 a.m. during Private Business before handing over to the Chairman, R. W. D. TURNER.

Private Business

1 The Minutes of the Annual General Meeting having been published in the Journal (1970, 32, 551) were taken as read and confirmed.

2 The following amendments to the Rules of the Society were agreed:

Rule 4 to be amended to:

There shall be a President of the Society who shall be elected by the members from one of the names put forward by the Council. If, however, any member wishes to submit an additional name his nomination must be signed by ten members and received by the Council at least six weeks before the Annual General Meeting. The President shall be elected for two years and may be eligible for re-election for further periods of one year to a total of five years. He shall be ex officio a member of the Council. He will represent the Society at home and abroad and may preside over meetings of the Council but not at the Scientific Meetings of the Society for which a local Chairman will be elected for each meeting.

Rules 10 and 11 to be omitted.

Rule 14 to be amended to:

The Council shall nominate up to ten names from the Ordinary Members of the Society for each of the Offices (President, Secretary, Assistant Secretary and Treasurer) and for Council Members as holders retire, in accordance with Rules 4 (as amended above), 21 (previously 22) and 24 (as amended below). In the normal course of events the Assistant Secretary shall succeed the Secretary. These names shall be sent out to all Ordinary Members who shall vote by post. The names receiving the most votes shall be elected in each case at the next Annual General Meeting. In the event of a draw for any office, the Council shall decide the member to be elected.

Rule 25 to be amended as follows:

Three Ordinary Members shall be elected in accordance with Rule 14 (as amended above) as Secretary, Assistant Secretary and Treasurer respectively. The Secretary shall hold office for not more than two years and the Assistant Secretary for not more than two years; the Treasurer shall hold office for five years and shall be eligible for re-election. They will all be ex officio Members of the Council.

The remaining Rules will be amended to omit any mention of Associate Members, and this will necessitate arranging them in a slightly different order.

3 The Treasurer reported that there was an excess of income over expenditure in 1969, but that this was smaller than in 1968: £581.17.-, as compared with £673. The decrease was due to increased cost of meetings, secretarial help, and subscriptions to the International Society and European Society of Cardiology.

At the present rate of financial turnover, there would continue to be an excess of income over expenditure as the increase in the number of subscriptions from new members would counterbalance the increasing costs. But in three to four years the income would equal the expenditure unless the size of the Society was enlarged, or the subscription was increased. Council felt that it was essential to form a contingency fund to provide a solid financial backing for the Society, and it was planned to reinvest the capital to obtain better growth of capital, and to invest funds from the deposit account of the Society in similar stock. If there were funds available from the VI World Congress of Cardiology for the Society, these would be used to strengthen the contingency fund. The Congress Fund, which had been used to help with members' expenses at the V World Congress of Cardiology in 1966 would also be available for the VI World Congress. After this, the Congress Fund would be merged with the contingency fund.

4 The following resignations were accepted with regret: Bingham, J. G. M. Hamilton, A. C. Macdonald.

5 Hamer was elected as Secretary of the Society.

6 Sowton was elected as Assistant Secretary of the Society.

7 The following two new Members of Council were elected in place of Tubbs and A. J. Thomas: Donald Ross and Byron Evans.

8 J. H. Wright was elected an Honorary Member of the Society.

9 The following were elected Extra-Ordinary Members of the Society: Cookson, Muir, Bruce Perry, and Sir George Pickering.

10 The following Corresponding Members were elected: Gotthard Schetller, Heidelberg, and Velva Schrire, Cape Town.

11 In accordance with the amendment to the Rules of the Society adopted at this meeting, whereby the category of Associate Member had been abolished, the present Associate Members (with the exception of Rahimtoo and Seymour) were elected Ordinary Members. Shaper was elected an Ordinary Member from Overseas Membership, and the following new Ordinary Members were elected: Peter Fletcher Binnion, Belfast; Peter Carson, North Staffordshire; Douglas Anthony Chamberlain, London; Bernard Melville Groden, Glasgow; John Reynolds Hampton, Nottingham; Alexander Harley, Manchester; Robin Brian Hedworth-Whitty, London; Marian Ion Ionescu (SM), Leeds; Brian Kirby, Edinburgh; John Robert Muir, London; Eckhardt G. J. Olsen, London; Lionel Henry Opie, London; Harry A. Rees, Swansea; Philip Slade (SM), Leicester; Michael Webb-Peploe, London; John Donald Whiteside, Chichester; Magdi H. Yacoub (SM), London.

12 The following Overseas Members were elected from Associate Membership: Rahimtoo and Seymour, and the following were re-elected: David-
son, Hywel Davies, Fulton, Harries, Parry, Resnekov, Somers, and Wilson.

13 Shillingford, Chairman of the Organizing Committee, reported that the arrangements for the VI World Congress of Cardiology to be held in London in September 1970 were moving ahead according to plan. Registrations were coming in satisfactorily, and it looked as though there would be 4,000 delegates including wives.

14 It was confirmed that there would be no Autumn Meeting of the Society in 1970.

15 The Annual General Meeting in 1971 would be a two-day meeting in Sheffield on Wednesday and Thursday, April 14 and 15; this would in part compensate for the lack of an Autumn Meeting in 1970, but was not meant to establish a precedent for a two-day spring meeting.

16 Career Structure in Cardiology
The President reported that a questionnaire had been sent to members of the British Cardiac Society by the Cardiology Committee of the Royal College of Physicians asking for details of the establishment, of the promotion to consultant grade, and of emigration, of Senior Registrars in Cardiology. The results of this questionnaire had come in and had been discussed by the Cardiology Committee. As a result of these discussions, a report on the general situation, including proposals for improvement in staffing, training, and career structure in cardiology, had been prepared and would be discussed by the College Committee next month.

17 The following meetings were announced:
(a) European Association of Paediatric Cardiologists, May 6 to 9, 1970, Warsaw.
(c) The 2nd Czechoslovak Congress of Internal Medicine with International Participation, 15 to 18 September 1970, Bratislava.
(d) International Cardiac Surgery Conference, Melbourne, 27 to 29 May 1971.

18 It had been suggested that abstracts of papers should be circulated in advance of meetings, and though there were a number of difficulties—including the submission of abstracts by members considerably earlier than at present, this proposal would be tried out for the Annual General Meeting in 1971.

The Dutch and British Societies dined together under the Chairmanship of Dr. Erkelens. The President thanked our Dutch hosts for excellent arrangements and emphasized the interconnections of Dutch and British medicine and the continuing influence of Einthoven.

Natural history of Ebstein’s anomaly of the tricuspid valve in childhood and adolescence
Hamish Watson
Interest in Ebstein’s anomaly of the tricuspid valve has been quickened by the successful replacement of severely damaged valves. Patients with Ebstein’s anomaly, however, are notoriously bad operative risks, and the nature of the malformation itself makes its surgical treatment not only difficult but hazardous. Because of this and because the insertion of a prosthesis—itself with a doubtful prognosis—into a growing child seems advisable under only the direst of circumstances, an attempt has been made by the Association of European Paediatric Cardiologists to determine the natural history of Ebstein’s anomaly in childhood and adolescence.

A preliminary survey of some 450 cases collected from 29 countries confirms the impression that though some babies with severe lesions may not survive infancy, most cases do remarkably well after a somewhat slow start. Few develop severe symptoms or die during childhood. Surgical treatment, on the other hand, carries a high mortality and most of those who did not survive it would probably have come to no great harm had they been left alone for a few more years.

The high natural mortality among babies suggests that, as with other severe lesions, this is the area where greater and more intensive effort is required to save lives.

Fate of fixed membranous subaortic stenosis after resection
Jane Somerville, and Julio Montoyo (introduced)
The course of 12 patients, aged 8 to 32 years, was studied 1 to 5 years after open resection of a subaortic membranous stenosis. Preoperative gradients at rest of 50–186 mm Hg were found and angiocardio graphic studies were available. Mild aortic regurgitation was present in 8. Though symptoms noted before operation in 7 disappeared in 6, clinical assessment was difficult as the physical signs were unchanged in 10, and the electrocardiogram improved in only 7.

Postoperative haemodynamic and angiocardio graphic studies were carried out in 8 and showed reduction or abolition of the gradient in the area of the resected membrane. Small subaortic gradients usually below the site of the original obstruction of 5–15 mm Hg were found in 4, and 20–60 mm Hg in 4, rising in 3 with isoprenaline. In 4 patients without electrocardiographic improvement the left ventricle was as thick or thicker than before operation and showed some features seen in obstructive cardiomyopathy, though the membrane had been well removed. Factors present before operation in those with and without this disappointing postoperative course were compared. It was concluded that in a number of patients the disease is not a simple problem of a well-defined obstruction and its removal, but that there may be a congenital abnormality of the whole left ventricular outflow tract.

Beta adrenergic blockade with practolol in hypertrophic obstructive cardiomyopathy
M. Webb-Peploe, R. S. Crosson (introduced), and Celia Oakley
Beta adrenergic blockade with propranolol has been used extensively in the investigation and treatment of patients with hypertrophic obstructive cardiomyopathy, though its mode of action remains unclear. We report here the preliminary results on 5 patients who have been studied at cardiac catheterization using a new cardio-selective beta blocking agent, practolol. Haemodynamic measurements were made at rest, after straight leg-raising exercise, during atrial pacing, and after intravenous isoprenaline injection. The measurements were repeated after 20–40 ml of practolol by intravenous injection.

Changes at rest were slight; however, after exercise practolol reduced heart rate by 10 per cent, left ventricular and diastolic pressures (LVEDP) by 33 per cent, while effective stroke work increased by 12 per cent. The tachycardia induced by isoprenaline was reduced by 11 per cent and LVEDP by 24 per cent.
There was only a slight fall in LVEDP on increasing heart rate by atrial pacing from 60 to 130 beats a minute in 2 patients and the LVEDP was not significantly altered by practolol on repeated pacing at similar heart rates in these patients, showing that the reduction in LVEDP after practolol was not due to a rate effect. Outflow tract gradients were little influenced by practolol.

These results after exercise suggested improved cardiac efficiency after practolol, allowing the same cardiac work to be achieved at a lower LVEDP, and that this action is not primarily rate dependent. Since a rise in LVEDP on effort commonly causes dyspnoea and may induce atrial fibrillation, any therapy that prevents this increase will be beneficial.

**Myocardial and skeletal muscle uptake of $^3$H-digoxin in acute hypokalaemia**

P. F. Binnion, and L. M. Morgan (introduced by Evan Fletcher)

Cardiac glycosides influence sodium and potassium movement in red cells and there is a complex relation between these agents and ion movements, particularly those of potassium. A similar situation occurs with cardiac and skeletal muscle, where digoxin inhibits the transport of potassium across the muscle cell membrane. It has been shown previously that acute hyperkalaemia inhibits the uptake of triitated digoxin by the myocardial muscle cells, and these experiments were carried out to see what influence acute hypokalaemia would have on myocardial digoxin uptake.

Seventeen anaesthetized dogs were divided into two groups. In the first group, 10 dogs were given an injection of $^3$H-digoxin (0.8 $\mu$Ci) intravenously, and one hour later their tissues were removed for analysis. In a second group of 7 anaesthetized dogs glucose and insulin were infused for one hour before the intravenous $^3$H-digoxin was given and this infusion was continued for the next 60 minutes and then the animals’ tissues were removed. Plasma and myocardial potassium was measured using conventional flame photometry, and the tissue $^3$H-digoxin concentration was measured using liquid scintillation counting.

In the control animals the plasma potassium level was 4.0 mEq/l. and the digoxin concentration (in mg. $\times 10^{-6}$ per g. wet weight) was 129 in the left ventricle, 102 in the right ventricle, 83 in the atria, and 22 in skeletal muscle.

The glucose-insulin regimen lowered the plasma potassium in the acute hypokalaemic experiments from a normal resting level of 4.0 mEq/l. to 2.4 mEq/l., and the tissue $^3$H-digoxin concentrations were 206 in the left ventricle, 291 in the right ventricle, 61 in the atria, and 349 in skeletal muscle.

These experiments show that acute reduction of plasma potassium increases the uptake of digoxin by myocardial and skeletal muscle. These results were used to support a hypothesis for the uptake of digoxin by special myocardial receptors and the hypothesis was extended to explain the relation between potassium, digoxin, and myocardial cell metabolism.

**Direct and reflex actions of cardiac glycosides on peripheral circulation of the dog**

M. Webb-Peploe, E. Ambrosioni and J. T. Shepherd (both introduced by J. F. Goodwin)

The direct effects of acetylstrophanthidin and digoxin on the resistance vessels and superficial veins of the hind limb were examined in dogs anaesthetized with thiopentone and chloralose. The reflex responses of these vessels and of the splenic capsule and veins to injection of both drugs into the right atrium in therapeutic doses were also recorded.

In the right iliac artery perfused at a constant flow, changes in perfusion pressure were a measure of changes in hind limb resistance. In the left lateral saphenous vein perfused at constant flow, changes in driving pressure (i.e. the difference between perfusion and femoral vein pressures) reflected changes in superficial venomotor tone. After temporary total arrest of the splenic circulation, changes in splenic venous pressure were an index of reflex changes in smooth muscle tension in splenic capsule and veins.

Acetylstrophanthidin and digoxin injected in graded doses into iliac artery and saphenous vein perfuses after acute bilateral lumbar sympathectomy caused an increase in arterial resistance but no change in venous tone. The cardiac glycosides had therefore a direct constrictor effect on arteriolar but not on venous smooth muscle.

Right atrial injection of acetylstrophanthidin caused reflex dilatation of hind limb resistance vessels and of splenic capacity elements followed by reflex constriction. The initial dilatation and subsequent constriction were shown to be due to stimulation of baroreceptors and chemoreceptors respectively. The superficial veins showed only a constrictor response which, since it persisted after vagotomy and carotid sinus nerve section, was not due to stimulation of baro- or chemoreceptors, nor of receptors in the heart and lungs.

**Effect of cardiopulmonary bypass on plasma digoxin levels**

D. J. Coltart, D. A. Chamberlain, T. W. Smith, and J. L. Mercer (all introduced by John Hamer)

The effect of cardiopulmonary bypass on plasma concentrations of digoxin has been assessed in patients undergoing cardiac surgery. The urinary excretion of digoxin during the operative period and the losses in the oxygenator have also been measured. The measurements were made by radioimmunoassay which provides a specific method with satisfactory accuracy in the therapeutic range.

Relatively small losses occurred during the operative period (mean 0.13 mg.). Plasma concentrations fell initially, largely as a result of dilution of the plasma volume by the pump prime and by transfusion. The concentrations rose again after operation as a new equilibrium was established between plasma and tissue stores. In 8 patients the mean plasma concentrations were 1.9 ng./ml. before operation and 1.7 ng./ml. afterwards. Plasma potassium concentrations may fall over the operative period, and cause increased sensitivity to cardiac glycosides. Digoxin should be administered cautiously after bypass to patients who have been adequately digitalized before operation.

**Assessment of left heart function after myocardial infarction**

P. G. F. Nixon, and D. J. F. Taylor (introduced)

Recordings of left ventricular pulsations and sounds have been shown to give a useful indication of diastolic events in the left ventricle in valvular and primary myocardial disease. This paper presents the findings in 51 cases of acute myocardial infarction where such recordings were taken within three days of the event and thereafter at weekly intervals.

Abnormalities were found in almost all cases and these could be seen to fall...
into four groups which could be ranked in progressive severity as assessed from the clinical state. Serial readings in individual patients during the course of their illness showed that the pattern of abnormality need not be static, and movement from one group to another occurred and was accompanied by appropriate clinical change.

It appeared that as clinical deterioration occurred and left heart pressures rose, the enlarged atrial contraction component, the 'a' wave, diminished in size, and at very high diastolic pressures in the left heart was replaced by a pathological rapid filling wave. This process could be seen to reverse with recurrence of the 'a' wave as the pressures fell and clinical improvement occurred. The presence of an enlarged 'a' wave was not necessarily accompanied by a fourth heart sound; hence phonocardiography alone may give insufficient information.

The technique is repeatable, safe, and painless, and the pattern of change gives a reliable indication of the left heart diastolic pressures.

Expansion of plasma volume in acute cardiac infarction

John Coltart (introduced) and John Hamer

The effect of rapid expansion of the plasma volume on the mixed venous oxygen saturation and central venous pressure has been studied in 14 patients with recent uncomplicated cardiac infarction and 5 patients with cardiogenic shock. The findings are contrasted with the effect of diuretic treatment in 8 patients with recent cardiac infarction and radiological evidence of pulmonary congestion.

Right atrial pressure and oxygen saturation measurements give a useful guide to the haemodynamic state of the patient without undue risk or disturbance. The right atrial oxygen saturation is a good index of changes in the cardiac output. There was a high correlation between the initial right atrial oxygen saturation and the coronary prognostic index.

The uncomplicated patients were given a rapid infusion of 500 ml. of 5 per cent glucose, and showed a significant increase in right atrial oxygen saturation; right atrial pressure did not change and pulmonary congestion was not produced. Three of the five patients with shock showed improvement in right atrial oxygen saturation or pressure, and two of these patients recovered. Frusemide 40 mg. intravenously produced significant improvement in right atrial oxygen saturation and pressure in the patients with pulmonary congestion. Observations without any intervention showed no changes.

The mechanism of these responses and the therapeutic implications were discussed.

Cardiovascular effects of pentazocine in patients with acute myocardial infarction

D. E. Jewitt, B. J. Maurer and P. J. Hubner (both introduced), and J. P. Shillingford

The narcotic antagonist pentazocine has been shown to possess comparable analgesic potency to heroin, methadone, and morphine when given to patients with pain after myocardial infarction. In bedside studies, we have evaluated the haemodynamic effects of intravenous pentazocine 30–60 mg. in 15 patients with acute infarction. A significant rise in mean pulmonary artery pressure (control 20 ± 3 mm. Hg to 33 ± 3 mm. Hg at 10 minutes) and mean aortic pressure (control 98 ± 6 mm. Hg to 117 ± 10 mm. Hg at 10 minutes) occurred in all patients. The rise in systemic pressure resulted from an increase in total peripheral resistance, since cardiac output and heart rate were unchanged. To elucidate the mechanism of these changes pentazocine was given to 5 patients with severe angina undergoing investigation before surgery. After pentazocine in these patients, the rise in peripheral resistance and systemic arterial pressure was associated with a clear increase in left ventricular end-diastolic pressure (mean control 14 mm. Hg rising to 22 mm. Hg at 10 minutes). The raised mean pulmonary artery pressure reflected this change.

An afterload stress of this type is undesirable in patients with acute myocardial infarction.

Computer analysis of ventricular ectopic rhythms in myocardial infarction

C. W. Vellani and J. M. M. Neilson (introduced by K. W. Donald and M. F. Oliver)

The electrocardiograms of 200 patients with myocardial infarction have been recorded continuously on magnetic tape for 24–48 hours after admission to a coronary care unit. An analogue com-
the atrial side of the mitral annulus enclosed in a supporting fabric cylinder. The remaining 8 were mounted on cloth-covered metal or polypropylene supports and placed in the mitral orifice in the same way as a prosthetic valve.

There were 6 hospital deaths, 2 with isolated mitral valve replacement and 4 with multivalve procedures. None was attributable to the fact that a homograft had been used. Of the 5 late deaths, 3 were considered to be due to valve failure and related to the method of valve processing that had been used. All patients have been anticoagulated for three months after operation. There have been two documented cerebral emboli to date, both with full recovery.

Details of postoperative investigations carried out in the longer survivors were given, together with an appraisal of the functional results achieved.

**Haemodynamic findings after homograft replacement of mitral valve**

*George Sutton, Kanu Chatterjee (introduced), and Graham Miller*

Twenty-four patients have been investigated by cardiac catheterization 1 to 15 (median 5) months after homograft replacement of the mitral valve. Simultaneous wedge and left ventricular diastolic pressures and left ventricular cineangiography allowed assessment of homograft gradient and regurgitation, respectively. Left ventricular function was assessed by calculation of left ventricular volumes from single-plane (antero-posterior) cineangiography, applying the area-length method of Dodge.

Wedge pressure and pulmonary vascular resistance fell by comparison with preoperative values, and gradients were insignificant in all patients except those with important homograft regurgitation. Regurgitation was absent in 8 patients (33%), slight in 12 (50%), and important in 4 (17%), of whom 3 have been reoperated. Regurgitation was unvariable and more important in patients with mounted pulmonary valves (2 of whom were found to have perforations) than with aortic valves, mounted or unmounted.

Ejection fraction (EF = left ventricular stroke volume/end-diastolic volume) was not significantly different (0.61 ± 0.09) from studied normals (EF = 0.74 ± 0.10) apart from 2 patients with preoperative ischaemic cardiomyopathy. Higher end-diastolic volumes (with normal ejection fraction) tended to occur in patients with preoperative mitral regurgitation rather than stenosis.

These studies indicate that left ventricular and homograft functions are usually good in patients several months after operation; and that pulmonary homografts may be more likely to develop regurgitation than aortic.

**Replacement of pulmonary valve and pulmonary artery with fascia lata**

*Christopher Lincoln, Marcel Geens (both introduced), Donald Ross, and Marian Ionescu*

The need for pulmonary valve replacement and reconstruction of the pulmonary artery arises (1) in patients with severe pulmonary stenosis or pulmonary atresia suitable for radical correction, and (2) when the aortic valve has been replaced with a pulmonary autograft. Homograft replacement of the right ventricular outflow tract has proved to be satisfactory, but it could be advantageous to use a valve made from autogenous tissue.

In 17 patients with complex congenital heart disease in which pulmonary stenosis or pulmonary atresia was present, and in 18 patients who had undergone aortic valve replacement with a pulmonary autograft, a tricuspid fascia lata valve incorporated within a tube of fascia lata was used to reconstruct the right ventricular outflow tract. No internal frame or metallic strut was used in this valve.

In a follow-up period ranging from 1 week to 4 months no death has occurred. A serious collection at the donor site formed in 4 patients. A short-term unexplained pyrexia occurred in 6 patients. A pulmonary diastolic murmur was present in 3 patients, with no features of right ventricular dysfunction.

The use of living autogenous tissue to replace the right ventricular outflow tract precludes the necessity for long-term anticoagulation and is to be compared with homograft or prosthetic valve replacement at the same site.

**Plasma fibrinogen after valvar replacement**

*Yeos Tessier, Hans Collet, Phornphimol Littleton, John Marshall (all introduced), and Lawson McDonald*

Plasma fibrinogen has been studied in normal subjects and in patients after valvar replacement with either a graft or a prosthetic valve. In the normal subjects and in the patients before operation the levels of plasma fibrinogen were respectively 261 mg./100 ml. (± 8.06) and 300 mg./100 ml. (± 10.80). There was an early postoperative increase in fibrinogen in all patients, which was not significantly different between those with grafts and those with prostheses (grafts: 480 mg./100 ml. (± 15.47); prostheses: 458 mg./100 ml. (± 15.97)). This was followed by a fall with time. However, whereas one year after operation the levels remained high in the patients with prosthetic valves (310 mg./100 ml. (± 8.40)), in those with grafts the levels fell and were not significantly different from the normal subjects (273 mg./100 ml. (± 10.80) and 261 mg./100 ml. (± 8.06)). Analysis showed that the levels of plasma fibrinogen in patients with grafts were significantly lower than in those with prostheses (p < 0.01). This high level of fibrinogen after prosthetic valvar replacement was not due to age, neither was it correlated with the haematocrit (R = + 0.07), nor with the haemoglobin concentration (R = + 0.05). The significance of these results was discussed in relation to observations on the causal mechanism of the raised plasma fibrinogen after prosthetic valvar replacement, and its significance with regard to systemic embolism.

**Proximal tubular sodium reabsorption during water diuresis in patients with heart disease**

*D. G. Gibson, J. C. Marshall and F. E. Lockey (both introduced)*

In order to examine the relation between cardiac state and the capacity to excrete a water load, 10 normal subjects and 61 patients with heart disease were studied during water diuresis. Under these conditions, urine flow approximates to the rate of delivery of filtrate, and therefore of sodium, from the proximal tubule of the kidney to the loop of Henle, while free water clearance is a function of distal sodium reabsorption. In 12 patients with complete heart block, ventricular pacing was associated with increased urine flow and free water clearance. Oral propranolol in 3 normal subjects and in 9 patients with intact atrial septa caused a reduction, while oral aminophylline in 4 normal subjects and 8 patients caused no change. In 6 patients with atrial septal defect, propranolol was without effect. Maximum urine flow correlated with left
ventricular end-diastolic pressure but not mean left atrial pressure in 16 patients with chronic rheumatic heart disease. In 7 patients with ischaemic heart disease, maximum urine flow was higher than in those with chronic rheumatic heart disease and similar increase of left ventricular end-diastolic pressure. These results reflect a close relation between proximal tubular sodium reabsorption and cardiac state and suggest that inappropriate sodium reabsorption at this site may contribute to fluid retention in heart disease.

Insulin secretion in severe heart failure

P. A. Majid, B. Sharma, B. C. Pakrashi, (all introduced), and S. H. Taylor

Insulin secretion has been shown to be severely suppressed in patients with the low cardiac output state associated with cardiogenic shock after myocardial infarction. Insulin secretion tests were therefore carried out in 8 patients with severe congestive heart failure due to valvular or ischaemic heart disease. All were found to have a significant suppression of insulin secretion in response to intravenous tolbutamide. After 4 weeks of intensive medical treatment, the insulin secretion tests were repeated in the 6 patients who survived. In 3 patients who made a good clinical response to treatment the insulin secretion response had returned to normal. In the 3 patients in whom the clinical response to treatment was limited, the insulin secretion response was still severely impaired. It is suggested that the suppression of insulin in severe heart failure is due to a combination of low pancreatic blood flow, possibly preventing an adequate stimulus reaching the pancreas, and a high level of circulating catecholamines which by causing an increase in alpha-receptor activity suppresses insulin production.

Effect of glucagon on myocardial function at controlled heart rates

R. Balcon, C. Smithen (introduced), and G. E. Sowton

Glucagon has been reported to have a beneficial effect on left ventricular function. Its use in patients with myocardial failure after cardiac infarction has therefore been proposed. These effects may be related to the increase in heart rate that usually occurs as a result of this agent. In this study the heart rate has been controlled by atrial pacing. Six patients with aortic Starr-Edwards prosthesis were studied during routine catheterization at least six months after operation. Changes in the time taken for the ball of the prosthesis to cross the cage were used to assess alterations in myocardial contractility. Measurements were made from a phonocardiogram and central aortic pressure tracing. Pulmonary artery pressure and cardiac output were also recorded. Measurements were made before and after the injection of 5 mg. glucagon into the pulmonary artery.

The heart rate increased by approximately 20 per cent in all patients. Systemic arterial pressure rose by 12 per cent. Ball travel time and mean systolic ejection rate, both indicators of myocardial contractility, did not change after glucagon when controlling the heart rate.

We therefore conclude that glucagon has no positive inotropic action independent of heart rate.

Pulmonary arterial compliance in health and disease

S. R. Reuben, J. Butler (both introduced), and G. de J. Lee

Lung capillary blood flow is pulsatile. An increase in precapillary resistance might be expected to attenuate this pulsatility. However, simultaneous measurements of instantaneous pulmonary arterial pressure, flow, and lung capillary blood flow in the dog have shown that the pulmonary arterial compliance (C) falls as arteriolar resistance (R) rises due to hypoxia or serotonin infusion. Consequently the time constant (R x C) remains unaltered and the lung capillary flow pulsatility is preserved over a range of pulmonary arterial pressures.

The autoregulation of lung capillary flow pulsatility has also been studied in patients having routine cardiac catheterization for diseases causing pulmonary hypertension. Pulmonary arterial pressure and flow were measured, using catheter-tip transducers, during lung capillary flow measurement by the N2O-body plethysmograph method. The pulmonary arterial compliance in patients with normal pulmonary arterial pressures was 2·5 ml./mm. Hg. With mild pulmonary hypertension (mean pulmonary arterial pressure 35 mm. Hg), compliance was 1·5 ml./mm. Hg. Thus so far, in patients with mild pulmonary hypertension, pulmonary arterial compliance falls as resistance rises, which tends to preserve the pulsatility of lung capillary blood flow.

Electrical stimulation of heart in study of patients with the Wolff-Parkinson-White syndrome type A

H. J. J. Wellens, R. M. Schuilenburg, and D. Durrer

Using previously described methods, we studied the changes which followed electrically induced right and left atrial and ventricular premature beats in six patients with the Wolff-Parkinson-White syndrome type A (Rosenbaum's classification). We found that: (1) during regular driving at identical rates from right and left atrium, the greatest amount of pre-excitation was seen after left atrial stimulation; (2) a tachycardia could easily be both initiated and terminated by way of a single premature beat from the left side of the heart. In most instances this was impossible using right-sided premature beats; (3) when during a tachycardia with antegrade AV conduction via the His bundle, left and right atrial activation were registered simultaneously, left atrial activation preceded right atrial activation by a considerable time (70–100 msec.).

These results are in agreement with a circus movement or reciprocal mechanism using the AV junction - His pathway in the one, and the anomalous AV connexion in the other, direction as a causal mechanism for tachycardias in Wolff-Parkinson-White syndrome type A. They also suggest that the greater part of the circus movement is localized on the left side of the heart.

The finding that the time relations of the tachycardia could, in only one patient, be influenced by left-sided premature beats suggests that the spatial dimensions of such a circus movement are small and that the anomalous AV connexion is situated not far away from the AV junction.

Exploration of electrical activation in hypertrophic infundibular aortic stenosis (obstructive cardiomyopathy)

R. Th. van Dam, J. P. Roos, and D. Durrer

During surgical correction of left ventricular outflow obstruction, we studied the time course of activation at the epicardial surfaces of both ventricles and in several parts of the left ventricle and the interventricular septum. In the process of this investigation, the design
of the multipolar intramural needle electrodes had to be adapted to the unusual thickness of the hypertrophic left ventricular wall and interventricular septum. The pluriformity of this condition, which causes a diversity in the electrocardiographic signs, also gives rise to a degree of nonuniformity in our findings. These may be broadly summarized as follows. (1) Left ventricular subendocardial excitation is retarded in a varying degree, probably because of a conduction delay in the anterior division of the left bundle-branch. (2) At both surfaces of the interventricular septum, and in the divisions of left and right bundle situated on them, activation starts at normal time intervals. (3) Conduction across the hypertrophic interventricular septum and left ventricular wall occurs at an approximately normal velocity, but takes a relatively long time because of their increased diameter.

Effect of sudden changes in heart rate on refractory periods of ventricular myocardium and specialized conducting system in dog's heart

M. J. van Jansen and R. Th. van Dam

Isolated dogs' hearts with total AV block were perfused according to the Langendorff technique. Electrodes on the right and left bundle-branches and in the ventricular myocardium were used for stimulating and recording. Square wave cathodal current pulses (2 msec. duration) of 1.5 times diastolic threshold strength were used to determine the refractory period (RP) of both tissues. During steady state frequencies the RP of the bundle-branches exceeds that of the myocardium; at faster rates both RPs shorten and the difference diminishes. By way of a special stimulation pattern, the RP after each beat of a new, suddenly accelerated rate could be determined. In the bundle-branches, shortening of the RP after the first beat greatly exceeds that in myocardium; the bundle RP becomes even shorter than the myocardial RP. After the second beat the bundle RP lengths again, exceeding the myocardial RP by 40 msec. The alternation between shorter and longer RP in odd and even beats continues for more than 20 beats, gradually decreasing in size. The myocardial RP is shortened considerably by the first two beats, the influence of the next beats being less; a steady state is reached after several hundred beats. The difference in adaptation of the RPs of both tissues to sudden rate changes is reflected in the conduction of premature impulses. An early premature beat originating in the bundle-branches reaches the myocardium when it has recovered its excitability and is conducted without difficulty. A second early premature beat meets refractory myocardium and is delayed by up to 70 msec.

Effect of lignocaine on excitability cycle of dog and rabbit heart

A. N. E. Zimmerman, E. O. Robles de Medina, P. H. A. Poll, and F. L. Meijler

The antiarrhythmic effect of lignocaine on the heart after myocardial infarction is well established. However, the working mechanism of the lignocaine effect still leaves a great deal of controversy. Until now, the effect of lignocaine on the excitability cycle of the heart has been studied with bipolar stimulation electrodes only; i.e. with both electrodes in direct contact with the heart muscle. In this way the strength-interval curves are a summation of anodal and cathodal stimulation thresholds, which may cause confusion.

We studied the influence of lignocaine on anodal and cathodal thresholds separately of the dog heart in situ, the isolated perfused rabbit heart, and the rabbit heart in situ. Lignocaine was administered at therapeutic levels during perfusion of the isolated heart or at a constant infusion rate in the intact animal.

The anodal threshold was found to be conspicuously raised by lignocaine, while the cathodal threshold was only slightly influenced. With anodal stimulation during lignocaine administration the absolute refractory period was shortened, while the cathodal absolute refractory period remained virtually unchanged. All hearts, whether isolated or in situ, behaved similarly, i.e., anodal thresholds and absolute refractory periods were more influenced by lignocaine than were cathodal thresholds.

We also studied the effect of changing the size of the electrodes (without adding lignocaine) on the anodal and the cathodal excitability curve. Increasing the size of the anodal electrode had the same effect as lignocaine on the anodal excitability cycle, while the effect of the size of cathodal electrode on the excitability curve was negligible.

Microelectrode studies have shown that lignocaine has little or no effect on the electrophysiological properties of single heart cells. We therefore suggest that during lignocaine administration more cells must be stimulated to provoke a propagated premature beat, which may explain the post-infarction antiarrhythmic effect of this drug.

Control of cardiac function by RR intervals in patients with atrial fibrillation

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Control of cardiac function in patients with atrial fibrillation has been attributed to varying end-diastolic filling due to changes in cycle length. In isolated hearts and myocardial strips the direct effect of RR^1 interval on contractile behaviour is well established. This effect also may explain (at least partially) the contractile behaviour of the intact heart in patients with atrial fibrillation. In atrial fibrillation RR^1 intervals are random.

We studied 6 patients with atrial fibrillation and a prosthetic mitral valve. The opening and closing sounds of the valve, and the electrocardiogram, were recorded on magnetic tape. The time between closure and opening of the valve (valve closure time), and the RR^1 interval, were measured on 1000 successive beats. Serial cross-correlation functions between RR^1 interval and valve closure time were computed. The first order cross-correlation coefficient was larger than 0.8, the second order cross-correlation coefficient, though small, was negative in all patients.

These results were compared with the serial cross-correlation functions between RR^1 interval and aortic blood flow in 3 patients with atrial fibrillation during cardiac operations. The first order cross-correlation coefficient between RR^1 interval and either stroke volume or peak flow velocity was close to 0.9. The second and a number of higher order coefficients were slightly negative.

This indicates that valve closure time (approximately equal to the duration of mechanical systole of the left ventricle) and stroke volume are controlled by the duration of preceding RR^1 interval(s). This type of control is similar to that of myocardial contractility by RR^1 intervals in isolated mammalian hearts during random stimulation. It thus seems probable that cardiac function in patients with atrial fibrillation is at least partly controlled by the direct effect of (changing) RR^1 intervals on myocardial contractile behaviour.
An on-line system for the automatic processing of vectorcardiograms

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A highly automated processing system has been developed for analysis and classification of vector-electrocardiograms using a PDP-9 computer. In this project, started some years ago, experience is being obtained with vectorcardiogram processing to reach finally the stage of instantaneous classification with a direct feed-back of the results to the physician.

In our system the emphasis is on extreme patient coding, almost completely automated recording, signal pre-processing, and the elimination of human errors. Part of the system is an automated recording station where the vectorcardiogram together with coding signals are stored on analogue magnetic tape, and patient information is punched on paper tape. The input system further contains specially engineered apparatus such as a decoder, a real time control unit, and an 18 bits input/output buffer. In this way a two-way communication is set up between computer and recording station, which enables the computer to do the processing completely automatically.

The computer program consists of two main parts: (1) input and waveform analysis, and (2) diagnostic classification and output.

The input part is run on a priority base and completes the input of a patient record once started. It decodes the coded signals, checks whether the input identification code is still correct, and digitizes the X, Y, Z, and Z signals. The analysis program localizes the QRS complexes, selects a zero-level, identifies essential landmarks and computes a variety of other desired parameters. Input and analysis are performed simultaneously, reducing computation time by about 40 per cent.

For a vector record of about 30 seconds this part of the program takes 10 seconds.

The diagnostic part implies the classification of vectorcardiograms with the help of computed parameters. Two main approaches are used: one in which various statistical discrimination methods are applied to patient material of well-defined disease categories, the other in which a diagnostic logic is compiled from diagnostic criteria in practical use. Either way, acquiring greater numbers of reliable patient records is a prerequisite for perfecting the diagnostic part. The output part finally gives the results of the waveform analysis and diagnostic classification, together with a summary of the secondary patient information by tele-type and plotter.

Studies on cardiac excitation and clinical implications

D. Durrer

A general description was given of the spatial distribution and temporal sequence of the excitation fronts in the ventricles obtained in 7 isolated normal human hearts.

Excitation is delivered by the anterior fasciculus of the left bundle-branch to the upper part of the anterior paraseptal endocardium and to the middle left septal surface, and by the posterior fasciculus to the middle posterior paraseptal endocardium.

Activation rapidly expands from these three foci of initial depolarization, and involves the left ventricular cavity, probably distributed by the subendocardial conduction system. At the same time, a radial spread of excitation begins in the left ventricular wall, directed towards the epicardial surface, and in a left-to-right direction across the interventricular septum which is mainly activated from the left side.

The right bundle-branch excites the inner surface of the pretrabecular area and adjoining part of the interventricular septum; further right ventricular activation is predominantly tangential.

Epicardial breakthrough in the left ventricle occurs in two areas overlying the terminal portions of the anterior and posterior fasciculi of the left bundle branch. The apex of the left ventricle is activated relatively late. Terminal excitation occurs in the posterobasal left and right ventricles, in the posteroseptal part of the interventricular septum and in the crista terminalis, where the activation wave spreading from the interventricular septum meets excitation progressing in the pulmonary conus.

Some of the clinical implications of disturbances in this activation pattern, caused by bundle-branch block, fasciculus block, intramural block or intraseptal conduction delay are demonstrated by observations made in vivo or in isolated human hearts. The theoretical consequences of these data, regarding cancellation, ‘silent regions’, and the electrical position theory were discussed.

Experiments on long-term preservation of rat heart

F. G. J. Offerijns

It is generally understood that long-term preservation of an organ will be possible only in the frozen state. Experiments were conducted on the influence of low temperatures (below 0°C) on the survival of the isolated rat’s heart. Cryoprotective substances, for example dimethyl sulphoxide, were added to the perfusion fluid. The entry of dimethyl sulphoxide into the extracellular and intracellular space was studied by means of dimethyl sulphoxide labelled with tritium.

We investigated freezing and reanimation of the organ in relation to its weight and age. It was possible to freeze to −30°C and to reanimate hearts from young rats (7–20 days old).

Stereophonic auscultation and stereophonic display

G. E. Freud

The phonocardiogram can be taken synchronously with two microphones attached some distance apart on the chest wall. The sound record gives on auscultation a stereophonic impression. From this stereophonic record the ear can make a reasonable estimation of the origin of a given sound. As the ear is a subjective instrument, we tried to display the information about the localization in such a way that the eye could understand the information. The apparatus used for this splices the information from both signals on the basis of relative loudness and the evidence of distance derived from the absolute loudness. To match eye and ear characteristics a number of non-linear steps is necessary, after which a reasonably interpretable picture is obtained. Examples were shown.

Ischaemic heart disease risk factors in young managers


An investigation of risk factors for ischaemic heart disease was performed in 2 parts.

(1) An inquiry among the members of Netherlands Junior Chambers of Commerce (30 to 40-year-old men in industry, official world, and free professions).
Questions were posed on living, eating, smoking, drinking, and working habits, complaints, diseases, family, weight, physical activity, stress, recreation, and holidays (response 605 = 75%).

(2) A pilot study of 36 northern members, composed of anamnesis, general examination, glucose tolerance test, blood cholesterol, triglycerides, lipids, uric acid, x-ray of thorax, electrocardiogram, vectorcardiogram, telemetry, cardiogram, photoelectric plethysmography, and lung function. Results: 75 per cent physically inactive, 41 per cent overweight, and 46 per cent cigarette smoking. The pilot study revealed among others, 9 abnormal glucose tolerance tests, 19 with more or less disturbed lipid metabolism, 3 abnormal electrocardiograms, and 31 diets containing 41 per cent abundance of fat. Probably the same high percentage of risk factors holds for comparable groups of Dutch people. To stop the increase of mortality from infarction one should strongly stimulate physical activity, stop or lessen cigarette smoking, and eat less calories. Periodic preventive examination of the population should be considered in the near future.

Comparison of coronary angiogram with other parameters (history, electrocardiogram, vectorcardiogram, two-step test, serum lipids) in patients with anginal complaints

A. V. G. Bruschke, A. W. Hanssen and G. van Herpen

From a total of approximately 750 selective coronary arteriographies at St. Antonius Hospital, Utrecht, a continuous series of 750 patients was selected for further analysis. Only patients in whom no other cardiac abnormality than that attributable to ischaemia could be detected, were accepted for this study.

The primary aim of our study was to evaluate the diagnostic importance of the coronary angiogram by studying the statistical association of its results to those obtained by the history, the electrocardiogram, the vectorcardiogram, the two-step exercise test, the serum cholesterol level, and the serum β-lipoprotein level. The investigation also gave us the opportunity to study the reliability of a number of criteria by which the data of the various methods are interpreted. The relation between the coronary angiogram and the angiogram of the left ventricle was also studied. For the statistical evaluation of the results, use was made of the index of merit (I) devised by Kuipers. In this index both the fractions correct-positive and correct-negative predictions are represented. It ranges from 0 (no association) to 1 (perfect association).

The history appeared to have the highest predictive value. The exercise test scored very low, but it should be appreciated that precisely in the most pathological and most easily diagnosable cases the test is not practicable. In 68 cases the statements by the 3 methods with the highest index of merit (the history, the vectorcardiogram, and the serum lipoprotein level) were concordant: in these cases the association with the coronary arteriogram was excellent, I being 0.94. In 101 cases the history and the vectorcardiogram agreed; in this group I was 0.84. In the total material the highest index of merit was obtained if, in the remaining cases in which the history and the vectorcardiogram were contradictory, the decision was made on the basis of the serum β-lipoprotein content. This yielded an index of merit of 0.68 (±0.06). Thus in a considerable proportion of cases coronary arteriography was the only method in which it could be determined whether the patient had coronary artery disease. In addition the coronary arteriogram was the only method which conveyed the correct information concerning the severity and localization of the obstructive lesions. There appeared to be no consistent relation to the angiogram of the left ventricle.

By a careful evaluation of the data obtained by less aggressive methods and more particularly by combining the results of various parameters, it appeared to be possible to delineate the indications for coronary arteriography more clearly.

Myocardial infarction with normal coronary arteriography

A. Bloch, A. V. G. Bruschke, K. J. J. Bruynel, and G. van Herpen

Cases presenting with the signs and symptoms of acute myocardial infarction in which subsequent coronary arteriography did not reveal any obstruction of the coronary arteries have been rarely reported. In this communication, 5 such cases were presented, out of a series of about 800 coronary arteriographies.

All cases were of acute onset (sometimes with a previous history of angina pectoris); in all, the electrocardiogram showed acute changes of repolarization, and in 3, QRS changes indicative of a myocardial lesion were also present. Typical increases in enzyme levels were noted in 4 cases. The coronary arteries were free of obstructive lesions in all cases, but the left ventriculogram was pathological in 3. One case had a recurrence six months later, with the same anterior localization of the electrical disturbance. A second coronary arteriogram now revealed a total obstruction in the anterior descending artery. In another patient, 36 weeks pregnant at the onset of symptoms, a fusiform aneurysm of the anterior descending artery (without narrowing) was demonstrated. The aetiology of these cases remains obscure. The differential diagnosis was discussed.

Congenital coronary artery fistula: report of 17 cases with a note on natural history of lesion

J. J. F. de Nef, P. J. Varghese, and G. Losekoot

A retrospective co-operative study of 17 patients with congenital coronary artery fistula was undertaken, focusing mainly on the natural history of this lesion.

The most common site of this fistula was the right coronary artery, and the right ventricle was the site of drainage in a majority of the patients. There were three ways in which the fistula terminated. In most cases the artery entered straight into the chamber. In a few patients the involved vessel ended in an aneurysm which opened into the chamber, and in others the vessel ended in a convolution of vessels before emptying into the chamber.

Most of the patients were under 20 years of age and were asymptomatic. The symptoms and cardiomegaly on the chest x-ray were well correlated with the size and duration of the shunt. All patients above the age of 35 had symptoms.

A continuous murmur was present in all patients. The site of maximum intensity of the murmur is closely related to the site of drainage and is helpful in the diagnosis of this lesion. Diagnosis was confirmed at cardiac catheterization and angiocardiography. Pulmonary hypertension as a complication occurred in the presence of congestive heart failure, and also when the left atrium was the site of drainage of the fistula.

Eleven patients were operated upon. Indications for operation and the prognosis of the non-surgical group of patients were discussed.
Threshold analysis of implanted pacemakers

H. J. Th. Thalen, Jw. van den Berg, J. N. Homan van der Heide, and J. Nieveen

The follow-up of pacemaker patients has become one of the problems of cardiology today. Special pacemaker clinics have been started, where pacemaker analysis is made by peripheral pulse, electrocardiogram, and x-ray monitoring. New analysis methods have been developed by feeding the pacemaker impulse into an oscilloscope and photographing from the oscilloscope screen. Because of the fast time base of an oscilloscope, a full analysis of the impulse is possible this way. Defects of stimulator and electrodes can be diagnosed, even when the pacemaker is still functioning and exit block has not developed.

However, monitoring of the stimulation threshold of an implanted unit has not been possible so far. To overcome this disadvantage the threshold pacemaker has been developed. In 1968 the first of these stimulators was implanted in patients. Operation and clinical results were discussed.

Quantitation of enzyme release from infarcted heart muscle


A method is given by which the plasma enzyme levels, estimated by a routine technique, can be used to obtain a quantitative estimation of the extent of a myocardial infarction as well as of the time course of enzyme shed-out.

After a myocardial infarction plasma enzyme levels are measured every 4 to 6 hours for a few days. The half-life times of these enzymes in the plasma are calculated from the downslope of the curve obtained, by fitting an exponential decay curve by the least-square method with the aid of a computer. With the half-life times known, a release-curve of the enzymes from the infarcted area can be plotted and the total amount of enzymes released into one litre of plasma can be calculated. As the enzyme activity of one gram of myocardial tissue, which was calculated from samples of heart tissue obtained at cardiac surgery, is known, the area of infarction losing its enzymes into one litre of plasma can be estimated.