ABSTRACTS OF CARDIOLOGY

Edited in collaboration with Abstracts of World Medicine

Use of "Dibenzylamine" as a Vasodilator in Patients with Severe Digital Ischaemia. D. G. FRIEND and E. A. EDWARDS. *Arch. intern. Med.*, 93, 928-937, June, 1954.

"Dibenzylamine" (N-phenoxyisopropyl-N-benzyl-β-chloroethylamine hydrochloride) is one of a series of compounds related to "dibenamine" (N:N-dibenzyl-β-chloroethylamine) whose chief characteristic is their ability to block adrenergic impulses. It is active on both intravenous and oral administration and exerts a striking effect on the peripheral vessels. In normotensive and hypertensive subjects the peripheral blood flow has been found to increase by as much as 500% after intravenous injection of the drug, but in patients with peripheral arterial disease there was much less increase in blood flow. Central effects are less marked than those at the periphery. The vasodilatation results in hypotension, the blood pressure falling by 15 to 20 mm. Hg.

The present authors have given dibenzylamine to 23 patients with digital ischaemia, 14 of them having true Raynaud's disease and 9 ischaemic changes due to other diseases. The drug was given in capsules by mouth four times daily, the total daily dosage varying from 20 to 80 mg.

Marked benefit resulted in patients whose symptoms were chiefly due to vasospasm. All the patients with true Raynaud's disease experienced a warmth of the hands and feet, with loss of the paroxysms of vasospasm and relief from pain due to ulceration of the finger-tips. Similar relief was obtained in a case of scleroderma in which there were changes in the fine peripheral vessels. Inconsistent results were observed in cases where organic vascular occlusion was predominant.

The authors consider that dibenzylamine is the most effective vasodilator drug currently available. They are of the opinion that it will give better results than sympathectomy in most cases of ischaemia of the fingers, but that it may not prove so effective for ischaemia of the toes. This is partly because organic occlusion occurs more frequently in the vessels of the legs and partly because lumbar sympathectomy is technically a satisfactory procedure.

J. Lister

The Relation between Tuberculosis and Congenital Heart Disease, with Special Reference to Pulmonary Stenosis. G. FEGIZ and M. MANCUSO. *Arch. Chir: Torace*, 11, 401-425, July-Sept., 1954.

It was for long thought that pulmonary tuberculosis and congenital heart disease, especially in its cyanotic forms, were incompatible. This was probably because

many seriously affected patients died of the heart disease and mild cases went unrecognized. In fact the association has been reported for almost all types of congenital cardiac lesion, and the incidence is particularly high in pulmonary stenosis.

The authors here present, from the Institute of Surgical Pathology, University of Rome, 3 cases of tuberculosis among 28 patients with pulmonary stenosis, representing an incidence of over 10%, as compared with only one case of tuberculosis among 110 patients with Fallot's tetralogy. The poor pulmonary blood circulation, resulting in an inadequate supply of antibodies and lymph, is thought to predispose to infection, just as the opposite state of affairs which exists in mitral stenosis is thought to protect the lungs. In the 3 cases described pulmonary valvotomy was performed, with subsequent improvement in the tuberculous condition. The first patient had no other treatment, and follow-up examination for over 3 years showed rapid and complete healing; the other 2 patients received streptomycin. Single examples of the association of tuberculosis with tricuspid atresia, the Eisenmenger complex, and transposition of the heart are recorded. No case could be found of associated tuberculosis in patients with atrial septal defect or patent ductus arteriosus.

A. Paton

Atrial Septal Defect. Clinical and Physiologic Response to Complete Closure in Five Patients. S. G. BLOUNT, H. SWAN, G. GENSINI, and M. C. MCCORD. *Circulation (N.Y.)*, 9, 801-812, June, 1954.

Direct closure of an uncomplicated atrial septal defect was performed under hypothermia on 5 patients aged 4 to 26 years, with good results in all cases. Cooling to 25° to 30° C. was effected by immersion in ice water under anaesthesia. Operation was by the method of Lewis and Taufic (*Surgery*, 1953, 3, 52; *Abstracts of World Medicine*, 1953, 14, 124) in which an anterior, transverse, bilateral thoracotomy with splitting of the sternum gives access to the right atrium, which is opened under direct vision with occlusion of cardiac inflow for a period not exceeding 10 minutes. The defect was closed with silk sutures, strict measures being taken to prevent coronary arterial air embolism.

The physiological investigations carried out and the selection of suitable cases are discussed in detail. Patients with a large shunt but without gross pulmonary hypertension are the most suitable, and 4 out of the 5 cases operated upon were of this type.

Postoperative investigation of the patients showed that the defect had been completely closed in all cases, but

the pulmonary arterial pressure was slightly raised in 2 patients, probably owing to structural changes in the pulmonary capillary bed.

S. F. Stephenson

Results of Pulmonary Valvotomy and Infundibular Resection in 100 Cases of Fallot's Tetralogy. M. CAMPBELL, D. C. DEUCHAR, and R. BROCK. *Brit. med. J.*, 2, 111-122, July 17, 1954.

In a previous paper (Campbell and Deuchar, *Brit. med. J.*, 1953, 1, 349; *Abstracts of World Medicine*, 1953, 14, 215) the results of treatment by the anastomotic or indirect type of operation introduced by Blalock in 200 cases of congenital pulmonary stenosis were reported, including 165 cases of Fallot's tetralogy. The authors now report the results in a parallel series of 100 cases of Fallot's tetralogy in which a direct attack was made on the stenosis, and pulmonary valvotomy or infundibular resection, or both, was carried out at Guy's and the Brompton Hospitals, London, and discuss in some detail the 61 cases operated on before the end of 1952. Of these 61 patients, 23 underwent valvotomy, 25 infundibular resection, and 13 the combined operation, and a "very good" or "good" result was obtained in 39 (64%), compared with 77% of the series treated by the Blalock type of operation. The operative mortality in these early cases was 18% compared with 8.5% for the anastomotic procedure, but for the whole series of 100 the mortality fell to 15%.

The technical details are not discussed, but it is emphasized that the direct operation is not a "blind" one, since the exact position and degree of the stenosis can be accurately assessed by external examination and the diagnosis verified by means of direct pressure readings and, if necessary, by introduction of a finger into the right ventricle. It is also stressed that the operation on the stenosis itself should be persisted with until satisfactory pressure records are obtained, which may involve 10 or 12 instrumental entries into the heart.

After operation a reduction in cyanosis was noted which was proportionate to the increase in exercise tolerance, but the maximum clinical improvement was sometimes delayed for a period of months. The average haemoglobin level fell from 130 to 103%, and the cardio-thoracic ratio increased by 4 to 5 points, these being similar to the findings after anastomotic operations. The electrocardiographic changes following the direct operation are discussed in detail. Postoperative cardiac catheterization showed widely varying pressure changes; in general, however, the removal of stenosis led to an increase in pulmonary flow from preoperative values ranging from 40 to 55% of the systemic flow to values ranging from 75 to 150%. Arterial oxygen saturation rose from 75 or 80% to 90 or 95% in some cases.

The danger of over-correction of the right-to-left shunt and production of a condition like Eisenmenger's complex by opening up the pulmonary stenosis too freely is a theoretical criticism of the direct operation, but there is no evidence that this ever occurs in practice, since the stenosis cannot be so completely removed so as to allow the pulmonary circulation to bear the full brunt of the right ventricular thrust.

[This article, taken in conjunction with its predecessor,

affords a most valuable and important contribution to the study of the results of surgical treatment of pulmonary stenosis. In Fallot's tetralogy there would appear to be little difference between the results of the indirect and direct operations. But if in the future hypothermia and other developments will permit opening of the heart to relieve the stenosis and at the same time to close the inter-ventricular septum the advantages will all be on the side of the direct operation.]

T. Holmes Sellors

The Long-term Prognosis of Cardiac Infarction. G. I. SHMAL'TS. *Klin. Med. (Mosk.)*, 32, 58-67, May, 1954.

The end-results of cardiac infarction have become much better in recent years than formerly.

The author has studied 180 patients in various stages of cardiac infarction; these he defines as: (1) the stage of shock, lasting 2 or 3 days; (2) the stage of consolidation, lasting from the 4th to the 15th day; and (3) the stage of myocardial sclerosis. Of these 180 patients, 2 died in the first stage, and 23 in the second and third stages (but 2 of these from causes other than the results of infarction); 12 of the 23 died from cardiovascular failure (7 after a second infarction), 8 in an anginal attack, and one from spread of thrombosis along the branches of the coronary arteries. Of the 7 patients suffering a second infarction, 4 died in less than one year, one lived a year after the second attack, one survived for 2 years, and one for 4 years.

Age is an important factor, for whereas 4 out of 43 patients aged between 41 and 50 died (9.3%), 17 of 101 aged between 51 and 70 died. Sex appears to have little effect, the reported higher mortality in women being due to the later average age of onset. The prognosis is worse with infarcts of the anterior wall than those of the posterior wall, and still worse if both are involved. The presence of hypertension before infarction is of bad prognostic significance, since although there was no marked difference in the percentage of deaths during the 3 years of this investigation between those with and those without hypertension, yet amongst those surviving infarction 3 years or more the proportion with a history of hypertension was notably lower than in a group with a shorter interval between their infarction and the date of review, suggesting that patients with hypertension tend to die earlier than those with a normal blood pressure before infarction.

The most important factor in prognosis, in the author's opinion, is the willingness of the patient to submit to a strict regime of absolute rest in the early stages of the disease. Of the 155 surviving patients in the present series, 109 resumed their former work and 26 undertook lighter work; about half (71) of these 135, however, had to give up work at intervals owing to anginal attacks. Resumption of work should not be permitted or attempted until at least 3½ to 4 months after the attack.

L. Firman-Edwards

The Patient's Capacity for Work after Myocardial Infarction. A. T. NOVIKOV. *Klin. Med. (Mosk.)*, 32, 67-74, May, 1954.

The outlook for patients with myocardial infarction has much improved in recent years. In the present communi-

cation the author reviews 171 cases treated between 1945 and 1952 (including 12 patients treated before 1945 who were re-admitted with a second infarct or for symptoms of chronic coronary insufficiency). The patients, who were all men engaged in intellectual work and subjected to frequent mental strain, were divided into three groups: (1) 107 whose illness had been followed over a number of years; (2) 29 whose capacity for work was assessed only on discharge from hospital and who had since left for other districts; and (3) 35 who died during the period under review.

Of those in Group 1, 87 were found capable of work for varying periods, this figure representing 51 per cent of the total number of patients, and 81 per cent of the group. As to age, 9 of them were between 36 and 40, 48 between 41 and 50, 29 between 51 and 60, and one was over 60. Full office hours of work were resumed by 69 of them, while only 18 had to have their working hours curtailed; but 32 of the full-time workers had eventually to give up work, as had 3 of the short-time workers.

Of the patients in Group 2, 15 were found to be capable of work, and 14 incapable. The latter included 8 with septal infarcts which involved also the anterior or antero-lateral wall, while the remaining 6 had infarction of the anterior, posterior, or antero-lateral walls without septal involvement; 11 of these patients had had anginal attacks before their infarction for periods varying from 2 to 9 years. Among the 15 found capable of work there were none with infarcts involving the septum.

Of the 35 patients in Group 3, 13 died after the first infarct, 21 after a second infarct, and one after a third. In 13 cases death occurred in the first 3 days of the illness, in 7 between the 8th and 13th days, in 11 after 4 to 12 months, and in 4 cases after 2 to 3 years.

The author concludes that the prospect of returning to work is poor (1) in cases with a history of frequent anginal attacks before the infarction; (2) in those with frequent anginal attacks after the infarct or with evidence of cardiovascular insufficiency; and (3) in those with septal involvement. Strangely enough, ventricular aneurysm is, in his experience, not necessarily a contra-indication to resumption of work. In those with limited capacity, the working time should not exceed 6 hours per day.

L. Firman-Edwards

Circulatory Changes in Acute Myocardial Infarction.

R. P. GILBERT, M. GOLDBERG, and J. GRIFFIN. *Circulation* (N.Y.) 9, 847-852, June, 1954.

At Cook County Hospital, Chicago, the cardiac output was determined with Evans blue by the method of Hamilton in 20 subjects soon after acute myocardial infarction. The arterial and venous blood pressure, arm-to-tongue circulation time, plasma volume, and hæmatocrit were also determined. Of the 20 patients, 13 showed signs of congestive heart failure and severe shock. The average cardiac output in the whole series was 3.3 litres per minute (S.D. 1.6) and the circulation time 32 seconds (S.D. 16). In individual patients the degrees of reduction of cardiac output and prolongation of the circulation time compared with normal values were roughly proportional to the clinical severity of the attack. Vasoconstriction, tending to sustain the blood pressure,

was evidenced by an increased peripheral resistance. No major changes in plasma volume were found even when shock was sustained. The authors suggest that the aim in treating patients with heart failure and sustained shock following acute myocardial infarction should be to increase the cardiac output. In this connexion the recent work on pressor amines and intra-arterial infusions is of considerable interest and it is hoped that more experimental work will be done in this field.

A. I. Suchett-Kaye

Acute Myocardial Infarction Treated by the Chair Rest Regimen. Thirty Consecutive Cases Managed by the Levine Armchair Method. J. L. WILSON and J. H. WARD. *J. Amer. med. Ass.*, 155, 226-230, May 15, 1954. 18 refs.

The authors report the results obtained with a chair-rest regimen in the management of 30 consecutive proved cases of myocardial infarction at the United States Naval Hospital, Bremerton, Washington. The patient was lifted into a large, comfortable, upholstered chair by the bedside as soon as shock had passed and the presence of complications had been excluded. The majority of the patients tolerated 3 to 6 hours in the chair on the first day and at least 10 hours on the third or fourth day. Other treatment included administration of anticoagulants, support for the lower limbs by application of an elastic bandage or, preferably, elastic stockings, and administration of oxygen, liberally in the first 48 hours and then as a routine for one hour after each meal during the first week. At night the head of the bed was raised to avoid hypostatic congestion of the lungs. The patient was assisted to a bedside commode, thus avoiding the exertion necessary in using a bed-pan. After 21 days walking was allowed, activity being gradually increased during the next 14 days. On the average the patient was up in a chair on the 5th day, seated all day by the 8th day, ambulant by the 24th, and discharged on the 33rd day.

Of the 30 patients, 3 died—one from massive infarction involving the posterior and lateral aspects of the heart, one from rupture of the left ventricle, and one from perforated peptic ulcer and peritonitis in addition to acute myocardial infarction.

H. G. Farquhar

Long term Anticoagulant Therapy. Further Experiences.

J. TULLOCH and I. S. WRIGHT. *Circulation* (N.Y.) 9, 823-834, June, 1954.

As a contribution to the study of the problems of the long-term prophylactic and therapeutic use of anticoagulant therapy in thrombo-embolic conditions, a detailed analysis of 227 cases treated in out-patients at the New York Hospital and in private practice with dicoumarol or tromexan (ethyl biscoumacetate) for 4 weeks or longer is presented. Some of the patients had been taking anticoagulants for as long as 8 years. The conditions treated were mainly rheumatic heart disease with peripheral and pulmonary embolism, thrombophlebitis, myocardial infarction, and myocardial ischæmia. A total of 546 thrombo-embolic episodes had occurred before treatment with anticoagulant drugs, recurrent thrombophlebitis with pulmonary embolism

alone accounting for nearly two-thirds of these, and in all cases the aim of long-term anticoagulant treatment was to prevent the occurrence of further episodes.

At the start of treatment the prothrombin time was estimated 2 or 3 times weekly, later only once weekly, and after a few months once every 10 to 14 days or at longer intervals. A prothrombin time of 25 to 30 seconds (normal control times 14 to 16 seconds) was aimed at, hæmorrhagic complications being liable to occur with a prothrombin time of 40 seconds or over: 43 patients (18.9%) suffered such complications on 70 occasions. Treatment was not stopped when the bleeding was not severe—for example, subcutaneous ecchymosis or slight bleeding from the gums or from hæmorrhoids—and the prothrombin time relatively low, but 11 patients had to be given vitamin K or K₁ and two of these also received fresh blood; one patient died from cerebral hæmorrhage. On the other hand, in 33 subjects (14.5%) the prothrombin time was well over 40 seconds on 51 occasions without the occurrence of bleeding.

The authors realize that continued treatment with anticoagulants does not give complete protection from thrombo-embolic incidents, even when the prothrombin time is markedly prolonged—indeed, 26 patients (11.4%) experienced a total of 40 definite or possible thrombo-embolic episodes during treatment. They conclude, however, that “properly controlled out-patient anticoagulant therapy is relatively safe and will lessen the incidence of thrombo-embolic episodes in patients previously suffering from such complications”.

A. I. Suchett-Kaye

Treatment of Venous Thrombosis with Anticoagulants.

Review of 1135 Cases. J. MARKS, B. M. TRUSCOTT, and J. F. R. WITCOMBE. *Lancet*, 2, 787–791, Oct. 16, 1954.

In the Cambridge area during the past 5 years 1,135 patients with superficial and deep peripheral venous thrombosis have been treated with anticoagulant drugs. The regimen used was the administration, as soon as the diagnosis was made, of ethyl biscoumacetate, 1.2 g., or phenylindanedione, 250 mg. by mouth, and the intramuscular injection of heparin, 150 mg., with hyaluronidase, 0.1 mg. This was followed by heparin in a dose of 50 mg. combined with 0.1 mg. hyaluronidase 4-hourly for four doses only. Subsequent dosage with phenylindanedione or ethyl biscoumacetate was regulated by the trend in the level of the prothrombin time as estimated by a modified Quick one-stage technique. Bed rest and splinting were advised for patients with pain, but active exercises in bed were encouraged as soon as pain subsided. On the average, patients attained freedom from pain in 18 hours in cases of superficial venous thrombosis and in 3 to 4 days in those of deep thrombosis, while the average stay in bed was 3 to 5 days in the former and 5 to 7 days in the latter. Hæmorrhagic incidents were rare, and it was possible to treat 307 of the patients in their own homes without the occurrence of untoward side-reactions. Three patients died while undergoing anticoagulant therapy, all from pulmonary embolism. In the 5-year period of the study, despite vigilance in the early diagnosis and treatment of venous thrombosis in

the leg, 54 cases of sudden, unheralded, fatal pulmonary embolism occurred among patients who were not receiving anticoagulants.

The authors conclude that the morbidity and mortality of peripheral venous thrombosis can be materially reduced by anticoagulant therapy, but the incidence of fatal, unheralded pulmonary embolism remains uninfluenced.

Bernard Isaacs

Renal Hæmodynamics in Valvular Heart Disease. J. HIMBERT, A. THÉARD, P. GELÉ, L. SCÉBAT, and J. LENÉGRE. *Arch. Mal. Cœur*, 47, 747–766, Sept., 1954.

Measurements of the renal plasma flow (R.P.F.) by determining PAH clearance, and of the glomerular filtration rate (G.F.R.) by determining mannitol clearance, were made on 60 patients with varying degrees of disability caused by valvular heart disease. None had evidence of renal disease, and few were over 50 years of age. They were classified in five groups: (I) with normal heart or with lesions causing no disability; (II) with pulmonary congestion due to mitral stenosis, but without heart failure; (III) recovering from congestive heart failure; (IV) in congestive heart failure without œdema; and (V) in congestive failure with œdema.

There was a progressive diminution in the average R.P.F. from Group I to Group V, with some overlapping of the individual values between groups: in all cases in Group V, however, the values were well below the lowest limit of normal. A similar diminution in the average G.F.R. was noted, but this fell to a smaller degree than the R.P.F., so that the filtration fraction rose progressively from Group I to Group V. In Group V, the only group with œdema, the G.F.R. was not significantly lower than in Group IV. No clear relationship between the G.F.R. and the presence of œdema was found, for in 2 out of the 9 patients with œdema the G.F.R. was virtually normal, whereas in some patients in Group III who had recovered from failure with œdema the G.F.R. was still significantly reduced.

J. A. Cosh

Calcification of the Mitral Valve Annulus and Its Relation to Functional Valvular Disturbance. M. A. SIMON and S. F. LIU. *Amer. Heart J.*, 48, 497–505, Oct., 1954.

Calcification of the mitral valve annulus is not infrequent. Its incidence was 10 per cent in 590 unselected, consecutive autopsies on subjects of all ages. The incidence was higher in individuals over 50 years of age.

While calcification of the annulus of the mitral valve may occur in rheumatic heart disease, it is primarily a degenerative process similar, in many respects, to arteriosclerosis. In the majority of cases the process does not affect the mitral valve leaflets. Variable degrees of calcification of the aortic valve, presumably on a non-rheumatic basis, were associated in approximately 25 per cent of the subjects whose hearts showed calcification of the mitral valve annulus.

In a selected series of 24 cases of mitral annulus calcification, apical systolic murmurs presumably referable to the mitral valve, were heard in 15 cases. In 9 of

these 15 cases the quality of the murmurs was such (loud, rough, or musical) as may be associated with functional derangement at the mitral orifice, and in 5 instances a clinical diagnosis of mitral regurgitation was made.

Extensive calcification of the mitral valve annulus which may produce variable degrees of mitral regurgitation can be strongly suspected in individuals over 50 years of age having loud, rough, or musical systolic apical murmurs who give no history of previous rheumatic heart disease.—[From the authors' summary.]

Biopsies of the Lung and Atrial Appendages in Mitral Stenosis: Correlation of Data from Cardiac Catheterization with Pulmonary Vascular Lesions. J. DENST, A. EDWARDS, K. T. NEUBUERGER, and S. G. BLOUNT. *Amer. Heart J.*, 48, 506–520, Oct., 1954.

Lung biopsies from 23 patients with mitral stenosis who were studied by cardiac catheterization prior to mitral commissurotomy were examined histologically. In the majority of cases the muscular arteries and arterioles exhibited prominent fibroelastic intimal thickening, and in 32 per cent the media appeared hypertrophic. In general, a positive correlation existed between the degree of vascular alteration and the pulmonary arteriolar resistance and mean pulmonary arterial pressure in the more severe cases of pulmonary hypertension. The hemodynamic pattern varied considerably in patients who exhibited less severe vascular lesions. A functional component was believed to be of as great importance in the development and maintenance of pulmonary hypertension as the organic vascular changes. It was considered that surgery should not be denied the patient either on the basis of data obtained by cardiac catheterization or because of the pulmonary vascular lesions, which are not usually severely obstructive although almost always present.

The histologic findings in 75 resected atrial appendages were reviewed; the results were in general agreement with those of other recent investigations.—[Authors' summary.]

Experiences in the Surgical Treatment of Aortic Stenosis. W. H. MULLER, A. A. KATTUS, J. F. DAMMANN, and R. T. SMITH. *J. thorac. Surg.*, 28, 516–535, Nov., 1954.

The authors give a brief history of the surgical treatment of aortic stenosis, and present the results in 25 of their cases subjected to aortic valvotomy by the trans-ventricular route.

Of their 25 patients, one group of 16 had "pure" aortic disease; calcification of the valve was present in 13 of these cases and also in 8 out of the 9 in the second group, in which associated mitral disease was present. The patients' ages ranged from 14 to 63 years. There were 4 operative deaths, 2 in each group. The authors stress the difficulty of objective postoperative assessment, but from the patients' statements conclude that the results in the cases of isolated aortic disease were better than in those with associated mitral valve lesion. The authors conclude that the early results are encouraging.

J. R. Belcher

Antibiotic Therapy of Bacterial Endocarditis. VI. Subacute Enterococcal Endocarditis: Clinical, Pathologic and Therapeutic Consideration of 33 Cases. J. E. GERACI and W. J. MARTIN. *Circulation (N.Y.)*, 10, 173–194, Aug., 1954.

During the first decade of treatment of bacterial endocarditis with antibiotics, 33 (approximately 10%) of the cases encountered at the Mayo Clinic were caused by enterococci (Lancefield's Group-D streptococci), which are highly resistant to penicillin. Endocarditis followed a urological procedure in 16 of the 33 cases, transurethral resection of the prostate accounting for 12 of these. In 15 cases there was no history of antecedent heart disease, while 2 patients had congenital, and the rest probably rheumatic, cardiac lesions. The usual clinical features were present, and major embolism occurred in 23 cases.

The organism isolated from the 31 treated patients were tested *in vitro* for sensitivity to various antibiotics, alone and in combination, by a bacteriostatic plate-dilution method, and in 5 cases the bactericidal effect of antibiotics added to active cultures was studied by means of survival counts. In each case the most effective combination was that of penicillin with dihydrostreptomycin. Of 18 patients treated with penicillin alone, only 7 were cured, whereas of 12 patients given adequate doses of penicillin and dihydrostreptomycin, the infection was controlled in 10.

[For full practical details of the recommended therapy and its bacteriological control the original paper should be consulted.]

D. Emslie-Smith

Myocardial Toxoplasmosis. J. W. PAULLEY, R. JONES, W. P. D. GREEN, and E. P. KANE. *Lancet*, 2, 624–626 Sept. 25, 1954.

Three cases in which myocarditis was believed to be due to toxoplasmosis were seen at the East Suffolk and Ipswich Hospital in the 12 months ending June, 1954. It is suggested that toxoplasmosis should be considered as a possible aetiological factor in any case of myocarditis of unknown aetiology. The first patient, a mentally dull man, had a pleural effusion, recurrent hemiplegia, and an enlarged heart. The patient's serum was positive for toxoplasmosis by the dye test at 1 in 64 and by the complement-fixation test at 1 in 16. There was a strong family history of mental retardation and unexplained "myocarditis". The other 2 patients had idiopathic cardiomegaly; the serum in one of these was positive for toxoplasmosis by the dye test at 1 in 32 and by the complement-fixation test at 1 in 16, and in the other at 1 in 512 and 1 in 32 respectively. A necropsy report on a sister of the first patient revealed "a non-specific myocarditis in the healing phase following severe focal necrosis". Blood culture for *Toxoplasma* was negative.

The authors believe that these were cases of chronic toxoplasmosis, probably acquired rather than congenital.

E. G. Rees

Splitting of the First and Second Heart Sounds. A. LEATHAM. *Lancet*, 2, 607–613, Sept. 25, 1954.

An auscultatory and phonocardiographic study of the heart sounds in health and disease is presented in this

paper, which is based on experience at the London Hospital and the National Heart Hospital, London. Only those sounds which can be clearly heard are considered in detail.

Splitting of the first heart sound is found in most healthy people and is usually more easily heard during expiration. The second component of the split first sound is usually louder at the tricuspid area and occurs after the initial rise in pressure in the carotid artery. It is thought, therefore, that the first element is due to closure of the mitral valve and the second to closure of the tricuspid valve. The interval between the sounds is usually 0.02 to 0.03 second. Splitting of the first heart sound must be distinguished from the addition of an auricular sound, a presystolic murmur, and the early systolic click of a dilated pulmonary artery or ascending aorta. An added auricular sound preceding the first sound is of lower pitch, and is separated by a wider interval than is common with a split first sound. A presystolic murmur is loudest at the apex after exertion and is commonly accompanied by a loud first sound, an opening snap, and a mid-diastolic murmur. The early systolic click which sometimes accompanies dilatation of the pulmonary artery or the proximal aorta is sharp in quality and loudest at the base of the heart; it is heard at the apex only if very loud.

The second heart sound is normally split because of the slightly asynchronous contraction of the ventricles and earlier closure of the aortic valve. The interval between the two components is wider in inspiration (0.05 second) and may not be detectable in expiration. The gap between the aortic and pulmonary components of the second heart sound is unduly wide in the presence of pulmonary stenosis and of conduction delay due to right bundle-branch block. This wide splitting is best appreciated in expiration, during which the interval is normally very small or undetectable. A combination of an early pulmonary systolic sound and a widely split second sound suggests the presence of pulmonary stenosis; but wide splitting may also be due to early closure of the aortic valve in mitral incompetence. Conduction delay in left bundle-branch block may cause wide splitting due to very late closure of the aortic valve. This state of affairs can be recognized by the fact that the gap diminishes in inspiration when pulmonary valve closure is delayed. In pulmonary hypertension the second heart sound at the pulmonary area is loud, but splitting may be absent or the gap extremely small.

The third heart sound can usually be distinguished from the pulmonary component of a split second sound by its quality, site of maximum intensity, and behaviour during respiration. Its differentiation from an opening snap is important, because of its completely different significance; in mitral valvular disease it indicates incompetence rather than stenosis.

[This paper is very concise and well illustrated and should be consulted in the original.] *D. W. Barritt*

Cardiac Involvement in Hemochromatosis. H. P. LEWIS. *Amer. J. med. Sci.*, 227, 544-558, May, 1954.

Hemochromatosis is a rare disease and its presence is often only recognized at necropsy. Its manifestations

are varied: it may occur without causing pigmentation or diabetes, and it may present primarily as a cardiac disease; it is this aspect of the condition which is discussed in this paper from the University of Oregon Medical School.

The excessive storage of iron which occurs in hemochromatosis may come about in three ways: it may be (1) endogenous, from increased absorption of iron; (2) exogenous, excess iron entering the body by way of multiple blood transfusions; or (3) due to nutritional disturbances, such as pellagra, which cause increased accumulation of iron in the tissues. The author describes 2 cases which illustrate the endogenous and exogenous mechanisms respectively.

Discussing the effect on the heart the author suggests that biochemical changes in enzyme systems and the destruction of phosphate-containing protein substances in the nuclei and sarcoplasm of cardiac muscle by the excess iron may be the cause of myocardial failure rather than any actual injury caused to the cardiac muscle cells by deposits of hemosiderin. Cases of myocardial hemosiderosis are extremely refractory to the ordinary treatment usually employed for congestive heart failure. It is suggested that repeated bleeding may remove some of the excess of iron and so prevent cardiac damage.

James W. Brown

Atrial Septal Defects. A New Surgical Approach and Diagnostical Aspects. [In English]. V. O. BJÖRK, C. CRAFOORD, B. JONSSON, S. R. KJELLBERG, and U. RUDHE. *Acta chir. scand.*, 107, 499-515, July 6, 1954.

Before surgical treatment of an atrial septal defect can be undertaken, catheterization of the heart is always necessary in order to verify the diagnosis, to calculate the size of the shunt, and to measure the pulmonary arterial pressure. It is noted, however, that where the defect is close to the valvular plane the main stream of blood is directed towards the tricuspid orifice and is expelled directly into the right ventricle with negligible mixing in the right atrium, so that a ventricular septal defect may be wrongly suggested by the results of blood gas analysis. The authors, working at the Karolinska Institute and Hospital, Stockholm, have found the usual methods of angiocardiology unsatisfactory for the adequate radiological diagnosis of atrial septal defects and have therefore devised a new technique whereby the contrast medium is injected into the left atrium by means of a catheter passed through the defect via the saphenous vein. In addition, an inflatable balloon fixed to the catheter and filled with contrast medium is used to outline the defect and indicate its size. With this technique it is possible to demonstrate or exclude a complicating mitral stenosis, but a co-existing abnormal venous return cannot be excluded.

A new method is described for the closure of an atrial septal defect which is a modification of the operation devised by Sondergaard and Husfeldt. A groove is then dissected between the atria from a point between the superior vena cava and the right superior pulmonary vein down to the inferior vena cava, continuing until the muscle bundles are seen crossing from one atrium to the other. Guided by a finger introduced through the right

auricular appendage, a curved needle is then introduced at the root of the aorta 1 to 2 cm. behind the origin of the right coronary artery, passed subendocardially behind the defect until the valvular plane is reached, rotated forwards to avoid the coronary sinus, and brought out behind the inferior vena cava. The needle is brought out through the left atrial wall as close to the atrio-ventricular border as possible. The heavy (No. 4 or 5) silk thread which has been passed with the needle is then tied over a piece of fascia or muscle in the dissected groove between the cavæ and the right pulmonary veins and drawn tight until the palpating finger finds the defect completely closed.

Of the 12 patients so treated, 10 have survived the operation and the immediate results seem satisfactory, although it is too soon yet to assess the end results, the longest follow-up being 7 months. The article is fully illustrated, and detailed descriptions are given of 4 of the cases treated.

F. J. Sambrook-Gowar

Repair of Atrial Septal Defects in Man under Direct Vision with the Aid of Hypothermia. F. J. LEWIS, R. L. VARCO, and M. TAUFIC. *Surgery*, 36, 538-556, Sept., 1954.

The authors discuss some of the advantages and disadvantages of hypothermia in performing intracardiac operations, and stress the simplicity of the procedure in comparison with the setting up of an artificial circulation. They remark that when possible it is obviously better to repair atrial septal defects by direct vision, and report, from the University of Minnesota Medical School, 11 cases in which they were able to do this with the aid of hypothermia. They describe their technique in detail, and stress the importance of exploring the defect completely by palpation through the auricular appendage before the auricle is opened. Cooling was achieved by means of refrigerating blankets (illustrated) containing tubes through which a solution of alcohol at 25° F. (-4° C.) was run. The defects were, when possible, repaired with interrupted sutures.

Of the 11 patients, one died during the operation and one 3 days later of complete heart block, in another case the operation had to be abandoned because of fibrillation, but in 8 cases the septal defect was successfully sutured; in 5 of these cases postoperative cardiac catheterization showed no evidence of a shunt. Ventricular fibrillation occurred in 4 of the patients, but was easily controlled on each occasion. The authors state that the greatest hazard of the operation is erroneous preoperative diagnosis. In their opinion all adults who are suffering from atrial septal defect and who have symptoms should undergo this operation, and that when the operative risk has diminished still further probably all cases should be treated surgically.

J. R. Belcher

Mitral Valvular Disease Associated with an Inter-atrial Communication. Y. BOUVRAIN and A. SIBILLE. *Sem. Hôp. Paris*, 30, 3414-3424, Oct. 6, 1954.

Reviewing 91 cases of mitral valvular disease associated with an interatrial communication collected from the literature, together with 5 of their own previously reported with Soulié (*Arch. Mal. Cœur*, 1954, 47, 97), the authors stress the need for accurate diagnosis of the condition in view of the recently acquired possibility of

surgical treatment. It is shown that a persistent ostium secundum (ovale) is three times as common as a persistent ostium primum, and that the mitral valve is affected by endocarditis twice as frequently as by a congenital abnormality. The clinical features were found to vary widely; signs of the septal defect may be clear or absent, while those of mitral disease are often diminished by the presence of the first lesion. Fluoroscopy is of paramount importance, and shows almost invariable enlargement of the heart, especially of the right side, pulsatile expansion of the median arc with dilatation of the pulmonary arteries, a small aorta, and backward compression of the œsophagus, the heart being sometimes pyriform and median as in pericarditis; yet the influence of mitral stenosis on this picture is negligible.

Cardiographic findings were available in one-third of the cases described. All except three revealed right-sided preponderance, but the incidence of right bundle-branch block could not be determined. Cardiac catheterization, in the few cases in which it was employed, gave conclusive evidence of the presence of septal defect, whereas angiocardigraphy was of little help. The authors point out that if auscultation yields unequivocal evidence of mitral stenosis the septal defect can readily be diagnosed; serious difficulty arises, however, when the septal defect is undoubted but the signs of mitral disease are inconclusive. In the 96 cases reviewed death, at an average age of 40 years, was usually due to congestive heart failure, but infants may die from pulmonary œdema. One of the patients described survived to the age of 82.

R. S. Stevens

Pulmonic Valvular Stenosis. Results and Technique of Open Valvuloplasty. H. SWAN, H. C. CLEVELAND, H. MUELLER, and S. G. BLOUNT. *J. thorac. Surg.*, 28, 504-515, Nov., 1954.

Pulmonary stenosis, whether in combination with a patent interatrial septum or as an isolated lesion, is not a benign condition, and the present authors recommend surgical treatment in all cases in which the systolic blood pressure in the right ventricle exceeds 75 mm. Hg. They note that the results obtained with the "blind" approach are unpredictable, the pressure gradient across the stenosed area often remaining high despite an apparently adequate operation. They have also been dissatisfied with the results of operation by the trans-ventricular route, and have therefore developed a method whereby the pulmonary valve can be divided under direct vision through the pulmonary artery. They describe the technique in detail; in essence it consists in opening the pulmonary artery under hypothermia after the aorta has been clamped and the venæ cavæ occluded with tapes. The valve can be clearly seen and two incisions are made at 180 degrees to each other from the valve opening right out to the ring, this forming a sort of bicuspid valve. A finger should always be passed through the valve into the ventricle to confirm the absence of infundibular stenosis.

Of 7 patients operated on at the University of Colorado School of Medicine, Denver, by this technique, all have survived, and the postoperative catheterization studies have shown that the results, as judged by determination

of pressure gradients, are better than those in cases in which the blind technique was used. *J. R. Belcher*

Absence of the Left Pulmonary Artery. A Report of Six Cases with Autopsy Findings in Three. J. S. MCKIM and F. W. WIGLESWORTH. *Amer. Heart J.*, 47, 845-859, June, 1954.

The authors report, from the Children's Memorial Hospital (McGill University), Montreal, 3 cases of absence of the left pulmonary artery confirmed at necropsy and 3 presumptive cases in patients still living (all aged 5 years), and on the basis of these and 11 cases reported in the literature in which the absence of one or other pulmonary artery was found they discuss the anatomical, clinical, angiocardigraphic, and radiographic features of this condition.

In practically all the reported cases the anomaly has been associated with some other form of congenital heart disease, particularly Fallot's tetralogy. As a rule the pulmonary artery has been absent on the side opposite to that of the aortic arch, so that when the left pulmonary artery is absent the aortic arch is usually right-sided.

Paul Wood

Additional Observations Concerning the Physiology of the Hypertension Associated with Experimental Coarctation of the Aorta. H. W. SCOTT, H. A. COLLINS, A. M. LANGA, and N. S. OLSEN. *Surgery*, 36, 445-459, Sept., 1954.

In experiments carried out on 97 dogs at Vanderbilt University School of Medicine, Nashville, Tennessee, the carotid and femoral blood pressure was first measured periodically during 7 to 30 days by direct puncture of these arteries, after which aortic coarctation was produced either by bridging the gap in a divided aorta by anastomizing the cut end of the left subclavian artery to the distal portion of the aorta, or by excising part of the wall of the aorta and suturing the cut edges together to produce aortic narrowing. It was found that to produce hypertension the coarctation must reduce the diameter of the aorta by 60 to 80 per cent.

Observation showed that a coarctation above the origin of the renal arteries was followed, after a latent interval of 4 to 5 days, by a gradual increase in carotid arterial pressure, the mean femoral arterial pressure, after an initial depression, also being increased. Constriction of the aortic isthmus was followed by an immediate rise in blood pressure, but this disappeared within 4 to 5 hours to give way to the gradual development of hypertension. The acute hypertension was therefore considered to be mechanical in origin. The chronic hypertension following coarctation of the aorta, however, is considered to be intimately concerned with the blood supply to the kidneys, since it occurred only if the aortic constriction was above the origin of the renal arteries and was great enough severely to restrict renal blood supply, and did not arise if the aortic constriction was below the origin of the renal arteries. Further experiments showed that the hypertension regressed when one kidney was transplanted so that its blood supply was derived from the aorta above the site of constriction, although this occurred only if the remaining kidney was

removed; moreover, regression of the hypertension did not occur if the transplanted kidney derived its blood supply from vessels below the constriction. There was also no demonstrable change in the level of brachiocephalic blood pressure when the aorta was compressed or even completely severed below the origin of the renal arteries. Bio-assay of renal venous blood of some of the animals rendered hypertensive in this manner seemed to suggest that a pressor substance, "phirentasin", was circulating in the blood and that this disappeared when the hypertension regressed. It is concluded that these experiments confirm that the kidneys are intimately concerned in the production and maintenance of the hypertension associated with coarctation of the aorta.

H. E. Holling

Oral Administration of a Potent Carbonic Anhydrase Inhibitor ("Diamox"). I. Changes in Electrolyte and Acid-Base Balance. A. LEAF, W. B. SCHWARTZ, and A. S. RELMAN. *New Engl. J. Med.*, 250, 759-764, May 6, 1954.

"Diamox" (2-acetylamine-1 : 3 : 4-thiadiazole-5-sulphonamide), a highly potent, relatively non-toxic inhibitor of carbonic anhydrase, was given by mouth to 5 patients with congestive heart failure and one normal subject in doses ranging from 0.25 to 3 g. a day. In all 6 subjects there was an immediate rise in urinary pH, a fall in excretion of titratable acid and ammonium, and an increased excretion of water and potassium. Only in 3 subjects was there a sodium diuresis and in none a significant chloride diuresis. A slight or moderate loss of weight occurred in 5 patients. None developed hypokalaemia, but hyperchloremic acidosis occurred in all 6 subjects and persisted throughout the period of treatment despite the fact that the composition of the urine became restored to control values within a few days of starting treatment. This restoration was attributed to the reduction in filtered bicarbonate resulting from the initial bicarbonate diuresis, which "would obligate less hydrogen ions in the reabsorption of bicarbonate and might therefore permit restoration of titratable acid and ammonium excretion with the same reduced over-all exchange of hydrogen".

K. G. Lowe

The Interplay of Coronary Vascular Resistance and Myocardial Compression in Regulating Coronary Flow.

C. J. WIGGERS. *Circulat. Res.*, 2, 271-279, May, 1954.

A study of the phasic flow curves derived from the coronary sinus in dogs indicates that venous blood from the areas of the heart supplied by both right and left coronary arteries drains into the coronary sinus. By comparing the coronary sinus flow during systole plus the period of isometric contraction with that during the rest of diastole it was found possible to assess the extent to which coronary flow is influenced by variations in the force of ventricular contraction and in coronary vascular resistance. The author's findings suggest that the main effect of ventricular compression is not to reduce coronary flow but to improve it, possibly by a massaging action.

[This paper is difficult to compress and should be read in full.]

C. Bruce Perry