BAKER INSTITUTE

RESEARCH

1953

ALFRED HOSPITAL

The Baker Medical Research Institute derives its main financial support from the Thomas Baker (Kodak), Alice Baker and Eleanor Shaw Benefactions. It is also dependent upon donations from private sources. The latter may be allocated to an Endowment Fund.

The Clinical Research Unit is a department of Alfred Hospital, and is recognised by the University of Melbourne for the purpose of providing facilities for candidates proceeding to the degrees of M.Sc. and Ph.D.

The scientific activities of both organisations are co-ordinated, and both are accepted as "approved research institutions" by the National Health and Medical Research Council, from whom grants are received for specific research work.

Research Fellowships are awarded by the Appointors for Research Scholarship Funds of the Hospital in consultation with the Research Advisory Committee of the Board of Management.

Twenty-Seventh Annual Report

of

THE THOMAS BAKER, ALICE BAKER, AND ELEANOR SHAW MEDICAL RESEARCH INSTITUTE

and

Fifth Annual Report

of

ALFRED HOSPITAL CLINICAL RESEARCH UNIT

and

RESEARCH FELLOWS

1953

ALFRED HOSPITAL, PRAHRAN,
VICTORIA, AUSTRALIA

BAKER MEDICAL RESEARCH INSTITUTE

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Alfred Hospital Clinical Research Fund	R. J. SAWERS, M.B., B.S., M.R.A.C.P.

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R. R. ANDREW, M.D., M.R.C.P.	"Sol. Green"
D. G. DUFFY, M.D.,M.R.C.P., M.R.A.C.P. . . .	"J. F. MacKeddie"
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ANNUAL REPORT OF THE DIRECTOR

This report gives an account of the work carried out in 1953 by the various research groups working within the Alfred Hospital, and it emphasises the integration of effort of the staff of the Baker Institute and the Clinical Research Unit, and of the various Research Fellows. Together these organisations form a compact research centre, the work of which is directed to clinical research in its various phases.

Clinical research may be defined as the planned study of the phenomena of disease in man, and must therefore cover fields of science as diverse as the basic medical sciences, bed-side medicine and field studies in the social aspects of medicine. It must also cover the problems of the design and use of investigational equipment and tests for these purposes. The details of the work carried out which are reported in the scientific section of this report show that all these aspects of clinical research are being explored in so far as they apply to the problems studied.

The basic organisation for research now available within the Hospital is provided by the Institute and Clinical Research Unit, and is based on a number of sections headed by full-time workers of diverse scientific backgrounds. These comprise biochemistry, physiology, biophysics, pharmacology and clinical medicine. Into this framework can be fitted part-time workers and Fellows who may stay for a shorter or longer period. In this way it is possible to preserve the initiative of the individual worker, and yet make available to any project the maximum co-ordination and assistance from workers of widely differing scientific disciplines. The arrangements also make it possible to give recent graduates in medicine or medical sciences the opportunity to try their hand at research under the guidance of skilled research workers. To these ends the fellowships available greatly enhance the value of the two established research organisations.

At the present time, when developments in the University are leading to the establishment of Chairs of Medicine and Surgery, it is pertinent to consider what should be the relationship between a research centre in a teaching hospital and the University departments. That the research groups at Alfred Hospital are carrying out a University function cannot be doubted, and the University recognises the Clinical Research Unit as an appropriate place for work to be done by candidates for certain post-graduate degrees. On the other hand, the expense in time, money and personnel of research projects in desirable fields is often beyond the resources of a University department, or would lead to a diversion of effort such as to produce a general unbalance in its activities. Research groups, such as ours, with their own sources of income therefore provide in their own fields a supplement to University research activities. However, because of the wide range of knowledge necessary for clinical research, it is highly desirable that the closest links should exist between the University and the research groups, and isolation of their activities is to be avoided.

Of the people attracted to clinical research there will be those trained in basic medical sciences such as biochemistry, biophysics, pharmacology and others, but the greatest number will come from the ranks of medical graduates. Some of these will make research their career, others will be essentially clinicians who have an interest in some particular problem which they wish to investigate, still others will be clinicians who wish to acquire something of the research disciplines to aid them in their practice of medicine. It has now become possible to help all these types by means of fellowships, and it has been possible to arrange a two-way traffic between the clinical and research fields so that each, according to their ability, may work in the research groups or obtain experience in clinical medicine. This applies at all levels, from the recent graduate to the honorary medical staff.

The general plan of scientific investigation remains unchanged, but the scope of all the projects has been enlarged. The studies of the mechanism of blood coagulation have led to a new technique for the quantitative assay of prothrombin and the recognition that haemophilia is a symptom complex produced by at least two different blood deficiencies. A study of the clinical and heredity problems in haemophilia is in progress. The mechanism of the control of body water volume in man continues to provide a major research project which is being conducted by clinical, physical and animal studies. The investigations into hypertensive diseases now embrace physiological, pharmacological and clinical aspects and out of this study has emerged a project to study the pharmacology of adrenaline and noradrenaline. Largely clinical studies are being made of peripheral vascular diseases and diseases of the heart valves. Investigations of the heart's electrical activity continue both on clinical and experimental levels, and some new concepts are becoming apparent. Towards the end of the year a new project was commenced in order to study energy production in the heart muscle. Apart from these investigations, which are directed to the cardiovascular system, studies are being made of the biological action of some of the anterior pituitary and adrenal hormones, and the physiology of the intestinal tract. These investigations are reported in detail in the scientific section of this report.

During the year construction of two new laboratories has enabled better distribution of space for the increased number of workers in the centre. Even this increased space, however, is fully occupied as the activities of the Institute and Clinical Research Unit continue to expand.

The Trustees of the Institute and the Board of Management of the Hospital have continued to make available facilities for members of the staff to visit other centres. For several months during the year a member of the pharmacology department of the University was a guest worker in the Institute, and during the coming year a Fellow from the Post-graduate School of Medicine, London, will join the research group of the Hospital. This interchange of ideas between workers in different centres is proving most valuable.

The National Health and Medical Research Council continues to support several of our projects, and a grant has been received from the recently established Life Insurance Medical Research Fund of Australia and New Zealand for another project. The help of these bodies is gratefully acknowledged.

The following organisations have made gifts to the Institute library during the year, and our thanks are expressed to them, and to various libraries that have loaned us journals, and particularly to the librarians, whose assistance is greatly valued:

Alfred Hospital Library.
Commonwealth Department of Health.
Hallstrom Institute of Cardiology.
L'Institut Bunge.
Institute of Dental Research, Sydney.
Institute of Medical and Veterinary Science, Adelaide.
International Anesthesia Research Society.
Imperial Chemical Industries of Australia and New Zealand.
Kanematsu Institute.
Mayo Clinic.
Medical Research Council, London.
Middlesex Hospital Medical School.
National Health and Medical Research Council, Canberra.
Organisation for Scientific Research, Indonesia.
Queensland Institute of Medical Research.
Rockefeller Institute of Medical Research.
Staten Seruminstitut, Copenhagen.
South African Institute of Medical Research.
U.S. Army Medical Library.
Walter and Eliza Hall Institute.

As in previous years, much assistance has been given to us by members of the Honorary Medical Staff, by all Hospital departments, by various members of the University staff, by Dr. F. G. Morgan (C.S.L.), Dr. A. W. Turner (C.S.I.R.O.), and by Dr. Lewis and other members of the staff of Kodak A/sia Pty. Ltd. The members of the Institute Advisory Panel have always been very ready to help, and I wish to thank all these persons for their assistance.

It is a pleasure for me to thank the Trustees of the Institute and the Board of Management of the Hospital for their continued generous support, and to thank members of the staff for their co-operation during the past year.

T. E. LOWE, Director.

31st December, 1953.

REPORT OF SCIENTIFIC INVESTIGATIONS

BLOOD COAGULATION

THE COUNTERACTION OF BLOOD ANTITHROMBIN**

P. Fantl, S. O'Brien and A. G. Marr.

Thrombin, the enzyme which clots fibrinogen, is formed from certain components of blood plasma, and in normal shed blood is liberated in amounts far greater than required for the production of a normal clot. This excess of thrombin is inactivated by factors, present in plasma and serum, known as antithrombins. Because it was thought that the clotting properties of blood in certain deficiencies might be enhanced by diminishing the antithrombin activity, investigations were carried out to find means to counteract the antithrombic activity of plasma and serum. It was found that a number of phenols inhibit antithrombin, and that there are quantitative differences among the phenols with regard to this ability. For instance, the cresols are more effective than quinol, but m-cresol was found to interfere with clotting reactions. Pyrocatechol was considered the most satisfactory inhibitor of antithrombic activity to use for further work, which has been directed to the assay of prothrombin and the measurement of the rate of thrombin formation in shed blood.

The Assay of Prothrombin

Two methods are applied for the assay of this clotting component. One is used for clinical work, and gives an indication of the haemostatic condition of a patient, whilst the other method aims at determining the absolute prothrombin concentration. It is essential to apply both methods of examination in certain blood deficiencies connected with the prothrombin complex. However, the absolute assay of prothrombin is difficult, and existing techniques are unsatisfactory. It was therefore decided to utilise the observations made on the antithrombic activity of phenols to develop a new technique for the quantitative estimation of prothrombin. A study of the conversion of prothrombin into thrombin under a variety of experimental conditions indicated that the addition of pyrocatechol to clotting mixtures containing diluted blood, plasma or serum gave the maximum yield of thrombin. This fact was utilised, and a procedure for the assay of prothrombin was developed with reagents commonly available to laboratories connected with hospitals.

The Rate of Thrombin Formation in Shed Blood.

One problem which offers occasional difficulties is to decide whether a person is a "bleeder" or whether his haemorrhage is due to trauma. It is, of course, realised that bleeding may be due to a blood deficiency, or to a deficiency in the vascular system. Only in a few instances are quantitative procedures for the determination of clotting factors available, and therefore is it possible to make a definite statement. In the case of persons suspect of suffering from a mild deficiency belonging to the group of haemophilias, the available tests have not always been satisfactory. It was thought that the determination of the rate of thrombin formation in blood may supply the answer to this problem. This study is being carried out in normal persons, and their rate of thrombin formation is compared with that of the blood of suspected bleeders.

**In this report of Scientific Investigations, those projects marked (**) were supported wholly or in part by grants from the National Health and Medical Research Council, and that marked (*) was supported by a grant from the Life Insurance Medical Research Fund.

BETA-PROTHROMBOPLASTIN DEFICIENCY RESEMBLING HAEMOPHILIA**

P. Fantl and R. J. Sawers.

Until a few years ago haemophilia was the only congenital haemorrhagic condition recognised as being caused by a derangement of the plasma thromboplastin complex although an acquired haemorrhagic tendency due to an inhibitor of the thromboplastin complex has been recognised for some time. Recently it became apparent that the term "haemophilia" covers several unrelated diseases. The first indication that more than one type of deficiency could produce a "haemophilic" syndrome came from the occasional observation that blood specimens taken from two apparent haemophiliacs, each of which had a prolonged whole blood clotting time, when mixed had a coagulant action nearly as effective as normal blood. As a result of examinations of 36 male bleeders, who previously on clinical grounds and laboratory evidence were considered to be haemophiliacs, it was found that six patients were suffering from a deficiency different to that in haemophilia. The evidence for this deficiency has to be established by laboratory tests, since the clinical symptoms of this new condition are identical with those of classical haemophilia. The detection of this bleeding tendency depends on the stability of the new factor in stored plasma in contrast to the antihaemophilic factor, which is lost during storage. According to previous work carried out in this Institute, and the recent concepts of the thromboplastin complex, the following sequence of events leading to thromboplastin formation in shed blood is suggested. Two precursors of thromboplastin called alpha- and beta- prothromboplastin occur in the circulation. They become activated to alpha or beta thromboplastin. The amount of thromboplastin so formed, however, is only sufficient to initiate clotting, and cannot convert all the prothrombin into thrombin. In the presence of an adequate number of thrombocytes and calcium ions additional formation of thromboplastin occurs, so that there is now conversion of all prothrombin into thrombin.

HAEMOPHILIA

R. J. Sawers.

The study of haemophilia commenced last year has been continued along three lines: case finding in the State of Victoria, study of clinical and hereditary aspects, and an investigation of the coagulation abnormalities.

With the continued assistance of the staffs of the public hospitals in Melbourne, the names of 120 cases have been collected. Of these, 92 are believed to be living, and in all instances patients and their relatives are being interviewed. This information about other cases of haemophilia in the families interviewed indicates a total number of cases in the State in excess of 120 living patients.

The clinical study includes a detailed investigation of symptomatology, of medical and surgical management and of social problems. It is evident that the clinical severity of the disease varies from time to time in an individual, and also there is evidence of a different clinical course in members of the same family. By a special technique developed for the purpose, the skin bleeding time in haemophiliacs has often been found to be prolonged. It is hoped that the changing clinical state may be related to this phenomenon.

The study of the hereditary aspects of the disease has revealed no unexpected findings.

The coagulation studies have shown haemophilia to be a syndrome (see page 9) due to deficiency of at least one of two or more factors which are intimately connected with the thromboplastin complex. This observation, however, as yet cannot be correlated with the clinical aspects, for it has not been possible to determine from the clinical study the factor which is deficient.

Patients with haemorrhagic diseases originally thought to be haemophilia are being studied for comparison of the clinical aspects, and to obtain a better understanding of the haemostatic mechanisms.

CONTROL OF BODY WATER VOLUME IN MAN**

The study of the control of body water volume in man so far has been directed mainly to the overall behaviour of the total water content of the body and an elucidation of the physical principles involved in its control. This year the study has been extended to consideration of partition of the water in the various compartments of the body and to some animal studies which it is hoped will throw light on the mechanism operating in man.

CLINICAL STUDIES

T. E. Lowe, R. E. Fraser and J. Upfill.

Quantitative observations of the way in which the water content of the body changes during diuresis from oedema, and during the formation of oedema have been discussed in previous reports. It was found that the daily water balance of these patients undergoes cyclic variations, and that these changes can be represented by a family of curves. Under certain conditions this rhythmical change may be suddenly altered. Detailed examination of this phenomenon led to the conclusion that early changes in water balance in these patients were under the control of an unknown number of opposing forces, which were normally in a dynamic balance. These forces tend to disturb or return to normal the body volume. As body water volume is normally stable over long periods, and usually returns to that volume after disturbances, it must be assumed that the point of dynamic balance of the forces is determined by a receptor mechanism sensitive to the volume of the whole or some specific part of the body. These studies indicated that the water content of the body may be likened to a water storage reservoir, which has a continuous inflow and outflow of water, and is subject to the physical laws of an "open" system. Further, as reported last year, this basically simple concept was incorporated in a mechanical model in an endeavour to simulate the phenomena observed in clinical cases.

The first model, which consisted of a tank in which the level of water controlled both inflow and outflow of water, represented only one pair of controlling forces. The changes in volume of this system under various experimental conditions imitated in many ways the changes seen in man, both during the loss and the gain of oedema. However, it became apparent from the behaviour of the model that a detailed study of the changes of intake and output of fluid in these patients, as distinct from the change in total volume, was of importance.

When these changes were studied it was found that the correlation between the response of the model and that of the patient were in agreement in only approximately half of the cases. In this first model the changes in inflow and outflow of fluid in response to changes in volume of the system were always in opposite directions, i.e., if the volume change impressed on the system produced

an increase of outflow there was a concomitant reduction of inflow and vice versa. However, if either the inflow or outflow was increased without interference with the volume of the system, then the other changed in the same direction. Examination of the records of patients recovering from oedema, and becoming oedematous, showed that changes in intake and output of fluid might be in the same direction or in opposite directions, i.e., in the recovery phase from oedema the patient might show a diminished intake of fluid associated with an increased output of fluid, or he might show an increasing intake of fluid with a very much greater increase of output. This phenomenon could not be imitated in the model, and it was thought that the discrepancy indicated the presence of more than one set of opposing forces in the body.

A second model in which two pairs of opposing forces were incorporated was therefore made. In this model there were two water containing tanks in parallel with two inflow valves. Both the height of fluid in the tanks and the difference in height of fluid in the two tanks controlled inflow. With such a system after suitable adjustments in the volume of fluid in the two tanks, and the release of restraint to return to its normal balance point, the changes in inflow and outflow might move either in the same direction or in opposite directions. This behaviour corresponded to that observed in the patients, and it appeared likely therefore that there were at least two sets of opposing forces actuated by different mechanisms present in man.

Further study of clinical material revealed cases in which changes in cardiac action definitely and rapidly influenced the water content of the body. In illustration two cases may be mentioned. The first, a patient with traumatic haemopericardium, developed congestive cardiac failure over a period of some days. After the removal of fluid from the pericardial sac, there was a very rapid and extensive diuresis. The second was a patient who had gross congestive cardiac failure, and was given ouabaine intravenously. This produced a rapid and sudden fall of central venous pressure, associated with a marked diuresis which continued until the patient was oedema free. The mechanical model as constituted could not mimic this behaviour, as it had no pump-driven circulation. Another model was therefore made which contained two sets of opposing controls, and a pump-driven circulation.

This third model consisted of two units each containing a reservoir in which the height of fluid controlled the inflow, and also the outflow of fluid. This reservoir formed part of a circuit through which fluid was driven by a pump. The outflow valves of the two systems were interlocked in such a way that an increase of fluid volume in one tank increased the outflow from its own outflow valve, and diminished that from the outflow valve of the other system.

In this model the volume in one reservoir and hence the inflow and outflow of that side are influenced by the state of the second system. Taking one side to represent the fluid volume of the body and the other to represent a second set of forces controlling body fluid volume, it has been possible to mimic the changes in inflow and outflow of fluid in response to changes of volume in the system, and in response to increased inflows or outflows, as they are seen in the patient. Further, by interfering with the pumping power in the circuit, it has been possible to show that disturbances in the pumping mechanism by producing changes in the pressure pattern and fluid flow in the system can influence the inflow and outflow of fluid and also the volume of fluid within the system.

It seems therefore that, by an integration of three controlling factors—two of opposing forces and a third representing a circulating mechanism—that it is possible to imitate in this model the changes seen in the water content of the human body in the diseased conditions so far studied. If one of these pairs of factors be considered to be concerned with volume regulation, as has previously been discussed and thought very probable, then it is very likely that the second pair of forces represent the osmotic pressure control, which has been demonstrated by Verney to exist in animals.

PHYSICAL STUDIES

B. McA. Sayers.

The studies initiated last year on the formal equation which represents physiological factors and mechanisms operating in maintaining the body water equilibrium have been continued. A search is being made for modifications of factors in the equation which can be shown to fit clinical observations. In particular the interconnection of electrolytes and water in various combinations is being investigated. Certain overall combinations of electrolytes have been found to be conserved as an overall system whilst conservation or balance of the electrolytes separately is not necessary. The excretion of water in relation to sodium concentration, other things being equal, can be predicted by this method.

ANIMAL STUDIES

R. Fowler.

The Volume of Body Fluid Compartments

There are as yet no tracer dilution methods generally applicable to the clinical measurement of these volumes, and a search was begun for methods that might be both reliable and expedient enough for routine clinical use.

In rabbits, thiosulphate was found to give a quick and reproducible estimate of extracellular fluid volume. It seems the most favourable substance yet for clinical work.

The use of urea to estimate total body water is being investigated.

Experimental Heart Failure.

It is notoriously difficult to induce congestive heart failure in animals, but such animals could be most useful for fluid balance and compartment volume studies. Accordingly attempts have been made to induce heart failure in rabbits by producing hypertension or by mechanically interfering with the heart's action.

Intrapericardial injection of iodine was found to be a simpler and more consistent method than creation of a carotid-jugular fistula, constriction of the renal arteries, or constriction of the thoracic or abdominal aorta. Iodine causes a constricting pericarditis in about 10-14 days, followed by generalised oedema and visceral congestion.

Fluid Balance in Normal Rabbits.

So far it has only been possible to study patients in normal fluid balance for short periods, so that little is known of the normal patterns of variation in intake, output and fluid balance curves.

Such observations have now been made over several months on normal rabbits, and will be continued. Already they suggest that the patterns seen in patients with oedema are also features of the normally acting mechanism.

HYPERTENSIVE STATES

MECHANISM OF HYPERTENSION

A. J. Barnett and R. E. Fraser.

The study of the mechanism of human arterial hypertension by comparing the effects of the injection of hexamethonium bromide in hypertensive and normotensive persons has been continued. The proportionally larger fall in both systolic and diastolic blood pressure in hypertensive compared with normotensive persons has been substantiated by an increased number of observations. This indicates an increased sympathetic effect in the hypertensive persons. Analysis of the findings shows a significant difference between the responses of the pulse rate in the two groups. Whereas in the hypertensive subjects there was usually little change in the pulse rate following methonium, in the normotensive persons it rose significantly. It is believed that this difference is due to a diminished response of the heart rate to vagal blockade in the hypertensive subjects which could be due to decreased vagal tone on the heart rate. Both the relatively increased sympathetic effect (on the blood pressure) and decreased vagal effect (on the heart rate) in hypertensive subjects could be explained on the basis of insensitiveness of the carotid sinus.

CLINICAL TRIAL OF HYPOTENSIVE DRUGS

A. J. Barnett and R. E. Fraser.

The trial of treatment of patients with severe and malignant hypertension with methonium compounds has been continued, and the series of patients treated has been enlarged to fifty. The results in 22 patients who have completed at least six months' treatment and fifteen patients who have died during treatment, have been analysed, and the value of treatment—at least over a period of a few months to three years—has been asssessed. The treatment has proved of great value in relieving symptoms, particularly headache, cardiac dyspnoea, congestive cardiac failure and visual impairment.

The cardiac, ocular, renal and cerebral status of patients has been followed at intervals up to two years. The cardiac, ocular and cerebral status has usually improved or remained unchanged, but in a few it has become worse. Fifteen patients have died within six months of commencing treatment: Cerebral vascular accidents were the most common cause of death, and only one of the fifteen patients had good blood pressure control.

Treatment by oral therapy and by injection has been compared. It has been found that better blood pressure control and more symptomatic benefit was obtained with the injection treatment.

We consider that the first stage of the study—determination of the value or otherwise of the treatment over a relatively short period of months or a few years—is completed and shows that the treatment is of definite value. A second stage of the study, determination of the value of the treatment over the long period of the course of the disease, has now been entered.

A new methonium compound, "Ansolysen,"† is now available, and the effectiveness of treatment by this is being compared with treatment by hexamethonium bromide.

†"Ansolysen" is being supplied by May and Baker Ltd.

SECONAL SEDATION TEST

A. J. Barnett and R. E. Fraser.

Sedation tests using barbiturates have been widely employed to assess the part played by sympathetic nervous activity in the maintenance of hypertension. The results of such tests have accordingly been held to predict the effect of interrupting sympathetic nervous activity in individual hypertensive patients. We have investigated this claim by comparing the effects of a seconal sedation test and a standard test injection of hexamethonium bromide in hypertensive patients. No correlation was observed between the hypotensive responses induced by the two tests, and it was concluded that seconal sedation is valueless in assessing the "neurogenic" component of hypertension.

SYMPTOMATOLOGY

D. G. Duffy and H. B. Kay.

Over the past two years a series of cases of established hypertension have been assessed to determine whether the hypertensive state or other associated conditions have caused the symptoms.

The series comprised 121 cases, of whom 86 were females and 35 were males. The incidence of various symptoms amongst the group was as follows:— Headache, 63; breathlessness, 66; fatigue, 27; dizziness, 25; palpitation, 8.

The diastolic blood pressure readings ranged in the males from 100-150 mms. Hg with a mean of 120, and in the females from 100-180 mms. Hg with a mean of 127.

Headache.

In only seven of the 63 patients who complained of headache could it be attributed solely to the hypertensive state. In the others the headache was considered to arise from anxiety states and "nervous tension" in 23, nuchal fibrositis in nine, sinus infection in six, uraemia in four, and migraine in two. There were twelve patients in whom headache was infrequent and of undetermined cause.

Dyspnoea.

An attempt was made to estimate pulmonary efficiency and to relate results to the patient's symptom of breathlessness.

A standard exercise test was used to produce respiratory discomfort. The patient's tidal air and vital capacity readings were taken on a Benedict-Roth spirometer before the exercise test and again afterwards, the test being repeated on a number of occasions at subsequent visits.

The results revealed a number of difficulties in devising a suitable test to demonstrate altered respiratory function. Vital capacity measurements were of little significance, and variations of tidal air volumes appeared to be related more to "nervous tension" than to objective or subjective change in respiratory function. Variations in the ventilation per minute also bore no relationship to the clinical state of the patient as regards dyspnoea.

From the study of these patients it is thought that the complaint of breathlessness may relate to discomfort arising in the thoracic musculature rather than to any change in pulmonary ventilation.

Fatigue.

In most cases there was cardio-vascular disease of sufficient moment to account for this complaint. There were, however, a few cases with diastolic pressures over 130 mm. mercury in whom the hypertensive state alone appeared to be responsible despite apparently normal cardiac function.

No satisfactory means of measuring fatigue has been devised.

No hypotensive measures were adopted except in severe cases of headache due to hypertension, and no lowering of blood pressure levels was observed in the other cases despite relief from symptoms.

In conclusion, it is considered that the symptomatic improvement shown in many cases could be attributed merely to the interest of the observers and the non-specific measures of treatment employed.

PHARMACOLOGY OF ADRENALINE AND NORADRENALINE**

G. A. Bentley.

Assay of Adrenaline and Noradrenaline in Urine.

In the previous report the importance of determining the urinary excretion of noradrenaline and adrenaline in patients with hypertension was discussed, and the difficulties in the methods of assay pointed out.

During the year the fluorimetric assay technique of Weil-Malherbe and Bone was investigated, and found to give satisfactory results when pure adrenaline or noradrenaline was used. However, when extracts of urine from normal patients were used, unexpectedly high results were obtained. This interference was traced to the presence of hydroxytyramine, which occurs in normal urine in fairly high concentration.

Therefore another assay method was sought. Lund's method, using oxidation with manganese dioxide, was modified to give a considerably increased sensitivity, and to give a simultaneous assay for both adrenaline and noradrenaline. Hydroxytyramine does not interfere in this method.

It is hoped to apply these methods to a study of the output of pressor amines in urine of both normal and hypertensive patients.

Mode of Action of Adrenaline.

As the mechanism of the dual action of adrenaline (excitatory on heart, inhibitory on gut) is not understood, experiments were undertaken in an attempt to discover whether the action is primarily on the cell membrane, or on the contractile mechanism of the cell.

(a) Investigation of the Cell Membrane.

Isolated rabbit gut, and toad heart preparations were suspended in perfusing fluids of varying ionic composition, and the response of the tissue to adrenaline was noted. In solutions containing low potassium concentration, the response of the gut is first reduced, then sometimes reversed. This aspect of the problem is still being investigated, and no conclusions are yet possible.

(b) Investigations on the Contractile Mechanism: Action of Adrenaline on Adenosine Triphosphatase Activity.

Experiments were designed to test whether adrenaline had a differential action on the A.T.P.-ases from intestine and heart. Conflicting results have been obtained up to the present time, due to non-specific pH effects, and interference by other phosphatases.

DISEASES OF THE PERIPHERAL BLOOD VESSELS

LIMB VESSELS

A. J. Barnett and R. E. Fraser.

Clinical Features.

Data on a large number of patients with vascular disease in the limbs are being accumulated, and it has been found that the condition is best considered in terms of clinical syndromes rather than as pathological states.

Circulatory disturbances of the upper limbs have been more closely studied than previously. Although attacks of ischaemia in the hands are frequently diagnosed as due to Raynaud's disease, the syndrome is not common in this country, and many patients with these attacks have some underlying structural abnormality, which may be constriction of the subclavian artery at the thoracic outlet, occlusive arterial disease of the vessels of the hand, or scleroderma. Occlusion of the long arteries of the upper limb—brachial, radial and ulnar—is uncommon. This is in contrast to the lower limb.

The study of arterial disease of the upper limb has been made by clinical tests, aided by calorimetry and arteriography.

Diagnostic Methods.

The investigational methods for occlusive arterial disease have been extended by the use of a calf plethysmograph in the study of patients with intermittent claudication.

Arteriography is now more widely performed with the help of members of the X-ray department. Previously this was restricted to femoral and brachial arteriography. Aortagraphy is now being used as well, and is proving useful in demonstrating lesions of the lower end of the aorta and the iliac arteries.

Therapeutic Measures.

The studies on the use of intra-arterial infusions of histamine in patients with intermittent claudication are being continued. Intra-arterial injections of papaverine are also being used. Also heparin is being given by intramuscular injection to some patients with this condition. There is some indication that all these methods may be of value, but the number of patients treated so far is too small for firm conclusions to be drawn.

Vascular grafting promises to be a very valuable method in certain patients, and members of the Thoracic-surgical Unit have made arterial grafts in two of our patients with marked benefit. Further patients are being selected for this procedure, but from our assessment of their general condition and arteriographic studies we believe that less than 10 per cent of patients with occlusive arterial disease will be suitable.

The use of a local vasodilator ointment is being tried for ischaemia of the fingers. Glyceryl trinitrate ointment, which had been used by others, was not readily available to us because of difficulty in its preparation. A trial was made of various dilator agents, and finally ethyl nicotinate ointment was considered most suitable. It is too early to report on the value of this method.

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CEREBRAL VASCULAR DISEASE

R. McD. Anderson.

An investigation into the aetiology of spontaneous intracranial haemorrhage has been commenced, and a personal series of fifty autopsies has been performed. These, in addition to another 100 cases culled from the hospital records, are to form the basis of a statistical approach to the subject.

If these cases are grouped according to the site of haemorrhages, some interesting facts at once appear, which may be of clinical and pathological significance.

In subdural haemorrhage there is frequently no history of trauma.

Most subjects with intracerebral haemorrhage have had hypertension. The site of the haemorrhage is most frequently in the external capsular region, and a high proportion of the cases of primary supratentorial haemorrhages have secondary haemorrhages in the brain stem.

In subjects with subarachnoid haemorrhage, in the 40-65 years age group rupture of an aneurysm of the circle of Willis has been a common cause. Death seldom occurs after the first bleed, but frequently occurs following recurrent haemorrhage in the second week.

So far, histological investigations of arteries and brain tissue has not yielded any new data.

Now that a suitable plastic is available, it is hoped to extend the methods of research by infusion of the vascular tree of the brain.

DISEASE OF THE MITRAL AND AORTIC VALVES

H. B. Kay.

Mitral Stenosis.

So far 300 cases of rheumatic heart disease have been studied, in order to assess their suitability for surgical treatment. Of this number 100 had pure mitral stenosis, of which fifty have been subjected to operation. Previously it had been decided that patients showing the characteristic features of "obstructive" mitral stenosis in association with a clear, loud first sound, opening snap and diastolic murmur, an electrocardiogram tending to right ventricular enlargement, radiological evidence of moderate left auricular enlargement without much ventricular enlargement, and pulmonary venous congestion, were the most suited to surgical treatment. Subsequent experience has shown that these typical cases respond well to operation. More severe cases, however, have a variable response to operation, and the contraindications to surgical intervention which have been found agree closely with those detailed by overseas investigators. No additional information of value has been obtained by special investigations, such as cardiac catheterisation, which only confirm the relevant information gained from the symptoms and signs.

Aortic Valve Disease.

In view of the possibility that operative relief may ultimately be available in cases of aortic stenosis, some fifty cases with this disease have been studied. So far it appears that these patients may be divided into the following groups:—First, those with a tight aortic stenosis with classical signs—systolic murmur and

thrill, absent second heart sound in the aortic area, and occasionally a short diastolic murmur. The peripheral pulse in these patients is anacrotic. A number of these cases show marked calcification of the valves in fluoroscopy, and this will probably constitute a contra-indication to operation. Secondly, those with aortic stenosis and incompetence, particularly those patients with alterations in pulse tracings, such as pulsus bisferiens. Thirdly, aortic stenosis, without characteristic peripheral pulse changes, and often with wide pulse pressure.

Although the lesion in many of the cases in the third group is probably of atheromatous origin, most of the patients encountered in this series have had lesions of rheumatic origin. There have been a few indisputable cases of congenital origin—some with associated coarctation of the aorta.

Finally, an occasional patient has been seen with the rare condition of subaortic stenosis.

These surveys are being continued so that as surgical techniques develop, and should operative relief become available, the various categories into which the patients fall will be well established.

In addition, cases with dominant aortic incompetence are being surveyed with a view to possible surgical correction.

THE HEART'S ELECTRICAL ACTIVITY

VECTORELECTROCARDIOGRAPHY**

T. E. Lowe and J. M. Gardiner.†

During the year V.C.G. in patients with cardiac disease has been studied and a series of 68 cases with right ventricular hypertrophy were analysed in detail. These patients were suffering from mitral stenosis, congenital heart disease, pulmonary heart disease or primary pulmonary hypertension. The abnormalities in the vectorelectrocardiogram appeared in some cases in the auricular complex, the P loop. In general, it had an increased amplitude, its contour was markedly bifid or triangular, and sometimes there was a displacement of the P loop axis.

Two changes in the ventricular complex were commonly seen. First, in the QRS loop there was distortion of contour, especially to the right, forwards and sometimes upwards, of the centripetal limb. There was a change in the rate of inscription which was frequently slowed in the terminal portion of the loop which approached the junction (J) of the QRS and T from the right. Secondly, there was a shift of the long axis of the QRS loop, giving rise to a changed position in space which is particularly well seen as a forwards rotation in the horizontal projection.

J was frequently displaced from O, to the right, backwards and upwards.

Abnormalities of the JT segment and the spatial angle between its axis and that of the QRS loop were also seen, but many of these may have been due to the effect of digitalis administration. These abnormalities occurred in various combinations.

A comparison was also carried out between the vectorelectrocardiograms and the standard electrocardiograms done in all these patients. This comparison has led to the conclusion that in the case of left ventricular hypertrophy the vectorelectrocardiogram enables a more detailed and accurate investigation of

†Cardiovascular Diagnostic Service, Alfred Hospital.

the QRS portion of the ventricular complex to be made than with standard electrocardiographic methods. This is largely because standard electrocardiographic lead placements do not adequately investigate the sagittal plane of the body, in which the changes are most outstanding. In right ventricular hypertrophy the outstanding changes which occur in the frontal and horizontal planes are well investigated by standard limb and precordial leads.

In general the vector loop gives details of the QRS complex which can only be noted in scalar ECGs by an accurate comparison of tracings taken simultaneously from many positions.

THEORY OF ELECTROCARDIOGRAPHY

B. McA. Sayers.

The search for a three dimensional electrode placement system which shows fundamental errors less than those of conventional vectorcardiograph systems has led to a new system. This consists of a double electrode system with six electrodes giving a three channel output. One pair of electrodes in each of the frontal, sagital and horizontal planes was used. The additional leads permit estimation of the degree of geometrically produced error in each lead from which modifications to improve accuracy are feasible.

Investigation of the physical significance of the concept of ventricular gradient has led to the belief that the ventricular gradient represents some direct function of the total unbalanced charge structure induced as a result of the depolarisation and repolarisation of the heart. This has led to the hypothesis that the higher frequency components of the cardiac electrical activity have specific significance in terms of mechanical activity. Experimental verification of this feature has been achieved in the rabbit's heart.

An interesting feature has been the recording of the induction (magnetic) field of the electrical activity of the heart. This is minute, but the wave shape is closely parallel to that of the E.C.G. when the effect of inductive pickup (and hence time-differentiation) is compensated.

The existence of very high frequency circulating components of the E.C.G. were also demonstrated for the first time. Frequencies well in excess of 20,000 cps have been recorded. This offers further verification of the hypothesis that QRS and T waves are produced from vastly different source conditions and impedances, since the only other possibility is that the source impedance has extremely high shunt capacities.

SPATIAL MAGNITUDE ELECTROCARDIOGRAPHY

B. McA. Sayers, F. G. Silberberg and R. Fowler.

For experimental purposes a new type of E.C.G. has been designed and built during the year. This records the magnitude in space of the cardiac vector as a function of time. It requires the automatic solution of the Pythagoras theorem in three dimensions and apparatus for high speed squaring, adding and square root taking upon the three E.C.G. channels has been successfully operated for some time.

The initial phase of this work required extensive manual calculation of the spatial magnitude E.C.G. on 100 human cases and certain interesting results follow.

The existence of irregularities in spatial magnitude electrocardiograms has been verified and shown to be related to localised conduction abnormalities. Interesting and significant topographical correlation with these irregularities has been found. One of the conclusions is that the irregularities due to left bundle branch block are due to localised conduction defects.

This apparatus has been used for investigation of human cardiac activity, but more specifically for the topographic correlation with irregularity in the rabbit's heart. The application of potassium chloride pledglets and intramural phenol infarction, as well as intravenous digitalis, have been utilised to study conduction processes and irregularities. Particular attention has been paid to higher frequency E.C.G. components in the region above 100 cps. Impedence variations in the cardiac source have been shown to be responsible for irregularities in the high frequency components. The work is continuing.

ENERGY PRODUCTION IN THE MYOCARDIUM*

T. E. Lowe, G. A. Bentley, F. McCallum and B. McA. Sayers.

Late in the year a project to study the mechanical and electrical energy production in the intact heart was commenced.

For this purpose appartus is being constructed so that a recycling toad heart can be studied in a Warburg type of respiratory chamber with simultaneous measurements of oxygen consumption, intraventricular pressure, fluid output and electrical changes being made.

Preliminary experiments indicate that it is feasible to construct and operate such a preparation.

THE PHYSIOLOGY AND PATHOLOGY OF THE STOMACH AND SMALL BOWEL

R. R. Andrew, A. F. Rollo and C. I. Slade.

During the year the techniques previously developed for investigation of motility of various parts of the intestine, and of the secretions of these parts, have been used to study chronic gastritis and gall bladder disease, with particular reference to the association of these two conditions. In a few cases the physiological disturbances in the alimentary canal which follow the removal of the diseased gall bladder have also been recorded. To date two of the patients examined have been found to be suffering from both gastritis and gall bladder disease. One of these had a superficial gastritis, and the other a chronic atrophic gastritis.

As a complementary study, tests have been made on these patients to measure the duodenal secretion, and the therapeutic effects from morphine, atropine and amyl nitrite. In this procedure a four lumen Miller-Abbott tube with two balloons, one in the gastric antrum and one in the distal duodenum, is used. This gives a physiologically closed segment of gut from which the secretion can be aspirated through the remaining two channels of the tube.

In the course of this investigation opportunity was taken to study the effect of "Nulacin" on gastric acidity. Six patients suffering from duodenal ulceration were investigated, and it was shown that in all cases whilst the tablets were being sucked, there was a striking reduction in gastric acidity.

ACTH-INDUCED EOSINOPENIA

Bryan Hudson.

The cause of the eosinopenia that follows the administration of ACTH and Cortisone has not been elucidated.

Experiments have been performed which indicate that this phenomenon is not due to the lysis of cells by the hormone. Blood samples were incubated with cortisone and other adrenal steroids for periods of four to six hours. At the end of this time there was no significant drop in the number of eosinophiles. These findings are contrary to the claims of certain overseas workers.

It is possible that these cells become sequestrated in one or more organs of the body. To test this hypothesis the reticulo-endothelial system of guinea pigs was blockaded with India Ink and Trypan Blue. These procedures had no effect on the ability of cortisone to cause a disappearance of circulating eosinophiles.

At the present the lungs are being examined in the belief that the eosinophiles may become sequestrated in the pulmonary capillaries under the influence of these hormones.

PIGMENTATION IN ADDISON'S DISEASE

Bryan Hudson.

The brown pigmentation that is seen in patients with Addison's disease has not been adequately explained. It is believed that this pigmentation may result from excessive secretion of one of the pituitary hormones (melanophore-expanding hormone). This hormone can be assayed by the use of cold blooded vertebrates with chromatophores, and in these experiments the South African clawed toad, Xenopis Laevis, has been used as the test animal.

A standard preparation of this hormone has been made from beef posterior lobe. Commercial preparations of ACTH have been tested against this standard and assayed with regard to their content of melanophore expanding hormone.

At the present time various methods are being tried to extract this hormone from the blood of patients with various disorders of pigmentation.

DIABETES MELLITUS
PERIPHERAL NERVOUS AND VASCULAR LESIONS

H. D. Breidahl.

In this investigation an attempt has been made to determine the cause of the pains in the limbs complained of so frequently by diabetic patients in older age groups. In the short period which has elapsed since the investigation was started, it has been possible only to establish some criteria for the grouping of these patients.

TIGER-SNAKE VENOM
ATTEMPTED RESUSCITATION IN RABBITS

F. G. Silberberg.

Reports of human fatalities following the bites of Tiger and Taipan snakes initiated an attempt to show that the outcome in similar cases could be modified if the predominant lethal effect, that of respiratory paralysis, were combated.

Ten rabbits were given three minimum lethal doses of tiger snake venom subcutaneously, and when respiratory paralysis appeared a tracheotomy was done and manual control of the respiration instigated. As compared with a control group, this procedure prolonged life by some hours, but the animals eventually succumbed to circulatory failure. The exhibition of an anti-histamine drug and intravenous dextran failed to combat the shock-like syndrome. This fact and the persistent bradycardia with terminal arrhythmias indicated that the venom contained a potent cardiotoxin.

The benefit of controlled respiration in prolonging life was shown, but a fatal outcome was not prevented because no effective means were found to counteract the effect of the venom on the myocardium. It appeared that although antivenene is still the only effective treatment in cases of snake bite, respiratory aid should not be omitted in severe cases.

FUNGICIDES IN THE TREATMENT OF FUNGOUS INFECTIONS OF SKIN

E. S. Mancy.

Over the past two years a study has been made of the efficiency in vitro of various fungicides against specific types of dermatophytes isolated from superficial fungous infections of the human skin.

This survey involved in the first place the identification and tabulation of the common fungous infections of the skin seen in patients of this hospital.

It has been found that a very satisfactory technique for assessing the efficiency of fungicides in vitro is the use of a central disk of Sabouraud's dextrose agar in a petrie dish, surrounded by an annulus of the same medium containing various concentrations of the fungicide.

From this work it has been possible to determine the appropriate therapeutic agent to use in particular cases of skin infection with these fungi. It has also been possible to determine a number of circumstances which interfere with the efficiency of such therapy. For example, the abnormal condition of the skin may not be of fungous origin, or the fungicide preparation used does not penetrate the tissues, or structural anomalies of the skin, such as ichthyosis, are present and interfere directly with the therapeutic action of the fungicide of choice.

PUBLICATIONS DURING 1953

T. E. Lowe: "TREATMENT OF CONGESTIVE CARDIAC FAILURE," **Med. J. Aust.**, Vol. 2 (1953), p. 544.

T. E. Lowe: "INTAKE AND OUTPUT OF WATER IN THE CONTROL OF BODY WATER CONTENT," **A'sian Ann. Med.**, Vol. 2 (1953), p. 136.

P. Fantl and L. Ebbels: "INTERACTION OF THROMBIN WITH THE PLASMA COMPONENTS OF MAN AND EXPERIMENTAL ANIMALS," **Aust. J. exp. Biol. & Med. Sci.**, Vol. 31 (1953), p. 175.

P. Fantl and R. A. Hayes: "FORMATION OF THROMBOPLASTIN IN SHED MAMMALIAN BLOOD," **Nature**, Vol. 172 (1953), p. 303.

P. Fantl and J. F. Nelson: "COAGULATION IN LYMPH," **J. Physiol.**, Vol. 122 (1953), p. 33.

A. J. Barnett and G. R. Wigley: "CALORIMETRY: A METHOD OF ESTIMATING PERIPHERAL BLOOD FLOW," **Med. J. Aust.**, Vol. 2 (1953), p. 326.

J. M. Gardiner and T. E. Lowe: "THE SPATIAL VECTOR-ELECTROCARDIOGRAM IN THE LEFT VENTRICULAR HYPERTROPHY OF HYPERTENSION," **A'sian Ann. Med.**, Vol. 2 (1953), p. 22.

F. H. Shaw and G. A. Bentley: "THE PHARMACOLOGY OF SOME NEW ANTICHOLINESTERASES," **Aust. J. exp. Biol. & Med. Sci.**, Vol. 31 (1953), p. 573.

R. Andrew: "DUODENAL ULCER: THE EFFECT OF COLD WATER ON GASTRIC MOTILITY," **Alfred Hospital Clinical Reports**, Vol. 3 (1953), p. 47.

R. Andrew and A. J. Rollo: "THE EFFECT ON GASTRIC ACIDITY OF 'NULACIN' TABLETS," **Med. J. Aust.**, Vol. 2 (1953), p. 823.

H. D. Breidahl: "CATION EXCHANGE RESINS," **A'sian Ann. Med.**, Vol. 2 (1953), p. 186.

J. H. W. Birrell: "A NOTE ON LEPROSY AS AN AETIOLOGICAL FACTOR IN THE WEBER-CHRISTIAN SYNDROME," **Med. J. Aust.**, Vol. 2 (1953), p. 7.

P. J. Parsons and P. H. Cody: "PACHYPERIOSTOSIS WITH PACHYDERMIA FOLLOWING ENDOCRINE DISTURBANCE," **Alfred Hospital Clinical Reports**, Vol. 3 (1953), p. 83.

PAPERS ACCEPTED FOR PUBLICATION

P. Fantl: "THE USE OF SUBSTANCES DEPRESSING ANTITHROMBIN ACTIVITY IN THE ASSAY OF PROTHROMBIN." **Biochem. J.**

P. Fantl and R. J. Sawers: "B-PROTHROMBIN DEFICIENCY CAUSING A HAEMORRHAGIC TENDENCY RESEMBLING HAEMOPHILIA," **Med. J. Aust.**

A. J. Barnett and J. R. E. Fraser: "SECONAL SEDATION TEST IN ARTERIAL HYPERTENSION, LIMITATIONS OF ITS VALUE," **A'sian Ann. Med.**

"MECHANISM OF ARTERIAL HYPERTENSION. A COMPARISON OF THE EFFECTS OF HEXAMETHONIUM BROMIDE IN HYPERTENSIVE AND NORMOTENSIVE PERSONS," **A'sian Ann. Med.**

R. Andrew: "GASTRIC, DUODENAL AND JEJUNAL MOTILITY IN MAN: PHYSIOLOGICAL STUDIES BY BALLOON-KYMOGRAPHY" **Aust. J. exp. Biol. & Med. Sci.**

J. M. Gardiner: "THE EFFECT OF PRISCOL IN PULMONARY HYPERTENSION," **A'sian Ann. Med.**

J. M. Gardiner and T. E. Lowe: "THE SPATIAL VECTOR-ELECTROCARDIOGRAM IN RIGHT VENTRICULAR HYPERTROPHY." **A'sian Ann. Med.**

MONOGRAPH IN PUBLICATION

A. J. Barnett and J. R. E. Fraser: "PERIPHERAL VASCULAR DISEASE." **M.U.P.** (Stawell Memorial Prize Essay for 1952).

LECTURES DELIVERED DURING 1953

"VECTORELECTROCARDIOGRAPHY" . . . . . T. E. Lowe

(i) Australasian Cardiac Society, Hobart.

(ii) Alfred Hospital Clinical Society.

"INTAKE AND OUTPUT OF WATER IN CONTROL OF BODY WATER CONTENT" . . . . . T. E. Lowe

Royal Australasian College of Physicians, Hobart.

"A MODEL OF VOLUME REGULATION IN MAN" . . . . . T. E. Lowe

International Biometric Society, Victorian Branch.

"THE HAEMOPHILIAS" . . . . . P. Fantl

Alfred Hospital Clinical Society.

"A THEORY OF THROMBOPLASTIN FORMATION IN SHED BLOOD" . . . . . P. Fantl

Victorian Society for Pathology and Experimental Medicine.

"BIOCHEMISTRY OF NUTRITION" . . . . . P. Fantl

Victorian Dietetics Association.

"METHONIUM TREATMENT OF ARTERIAL HYPERTENSIVE DISEASE" . . . . . A. J. Barnett

Alfred Hospital Clinical Society.

"MECHANISM OF ARTERIAL HYPERTENSION: COMPARISON OF THE EFFECTS OF HEXAMETHONIUM BROMIDE IN HYPERTENSIVE AND NORMOTENSIVE PERSONS" . . . . . A. J. Barnett

Victorian Society for Pathology and Experimental Medicine.

"THE INFLUENCE OF CORTISONE ON THE EOSINOPHILES IN THE PERITONEAL CAVITY OF THE GUINEA PIG" . . . . . B. Hudson

Victorian Society for Pathology and Experimental Medicine.

"LABORATORY AIDS TO THE DIAGNOSIS OF ADDISON'S DISEASE" . . . . . B. Hudson

British Medical Association (Clinical Pathology Section).

"THE CLINICAL USEFULNESS OF ACTH AND CORTISONE" B. Hudson

Melbourne Permanent Post-Graduate Committee (Mildura Meeting).

FINANCIAL STATEMENTS

Baker Medical Research Institute

THE THOMAS BAKER, ALICE BAKER AND ELEANOR SHAW MEDICAL RESEARCH INSTITUTE

Balance Sheet at 31st December, 1953.

LIABILITIES.

Current Liabilities—						
Sundry Creditors				£1,116	0	6
Capital Grants and Gifts—						
Balance as at 31st December, 1952	£714	16	11			
Add Grants made during year	300	0	0			
	1,014	16	11			
Less Amount expended during year	241	18	9			
				772	18	5
Endowment Fund				8,500	0	0
Life Insurance Medical Research Fund of Australia and New Zealand—						
Grant made during year	1,050	0	0			
Less Amount expended	190	1	8			
				859	18	4
				11,248	17	3
Revenue Account—						
Recoup of Deficit for year ended 31st December 1952, from Thomas Baker (Kodak), Alice Baker and Eleanor Shaw Benefactions	2,724	3	9			
Less—						
Balance at 31st December, 1952	74	11	6			
Deficit for year ended 31st December, 1953	605	0	8			
	679	12	2			
				2,044	11	7
				£13,293	8	10

ASSETS.

Current Assets—						
Cash at Bank	£2,335	6	2			
Sundry Debtors	358	2	8			
				£2,693	8	10
Investments—						
Grain Elevators Board Inscribed Stock—						
4¼%, maturing 1/5/1964	2,500	0	0			
Commonwealth Government Inscribed Stock—						
3¼%, maturing 15/10/1960	5,000	0	0			
3½%, maturing 15/10/1963	500	0	0			
Australian Consolidated Treasury Bonds—						
3¼%, maturing 15/9/1961	500	0	0			
				8,500	0	0
Fixed Assets—						
Furniture and Fixtures				2,100	0	0
				£13,293	8	10

Note: In addition to receiving interest from the Investments as shown on the Balance Sheet, the Institute receives the income from 3¼% Commonwealth Government Inscribed Stock face value of £17,000, which is inscribed in the name of the Trustees of the Estate of the late Thomas Baker for the benefit of the Institute.

AUDITORS' REPORT TO THE TRUSTEES.

We have examined the above Balance Sheet with the books of the Institute and have obtained all the information and explanations we have required. In our opinion the Balance Sheet presents a true and fair view of the state of the affairs of the Institute at 31st December 1953, according to the best of our information and the explanations given to us and as shown by the books of the Institute.

FLACK & FLACK,
Chartered Accountants (Australia),
Honorary Auditors.

Melbourne,
16th February, 1954.

THE THOMAS BAKER, ALICE BAKER AND ELEANOR SHAW MEDICAL RESEARCH INSTITUTE

Balance Sheet at 31st December, 1953.

LIABILITIES.				ASSETS.			
Current Liabilities—				Current Assets—			
Sundry Creditors		£1,116 0 6		Cash at Bank	£2,335 6 2		
Capital Grants and Gifts—				Sundry Debtors	358 2 8		
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Add Grants made during year	300 0 0			Investments—			
	1,014 16 11			Grain Elevators Board Inscribed Stock—			
Less Amount expended during year	241 18 9			4½%, maturing 1/5/1964	2,500 0 0		
		772 18 5		Commonwealth Government Inscribed Stock—			
Endowment Fund		8,500 0 0		3¼%, maturing 15/10/1960	5,000 0 0		
Life Insurance Medical Research Fund of Australia and New Zealand—				3¾%, maturing 15/10/1963	500 0 0		
Grant made during year	1,050 0 0			Australian Consolidated Treasury Bonds—			
Less Amount expended	190 1 8			3¼%, maturing 15/9/1961	500 0 0		
		859 18 4				8,500 0 0	
		11,248 17 3		Fixed Assets—			
Revenue Account—				Furniture and Fixtures		2,100 0 0	
Recoup of Deficit for year ended 31st December 1952, from Thomas Baker (Kodak), Alice Baker and Eleanor Shaw Benefactions	2,724 3 9						
Less—							
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	679 12 2						
		2,044 11 7					
		£13,293 8 10				£13,293 8 10	

Note: In addition to receiving interest from the Investments as shown on the Balance Sheet, the Institute receives the income from 3¼% Commonwealth Government Inscribed Stock face value of £17,000, which is inscribed in the name of the Trustees of the Estate of the late Thomas Baker for the benefit of the Institute.

AUDITORS' REPORT TO THE TRUSTEES.

We have examined the above Balance Sheet with the books of the Institute and have obtained all the information and explanations we have required. In our opinion the Balance Sheet presents a true and fair view of the state of the affairs of the Institute at 31st December 1953, according to the best of our information and the explanations given to us and as shown by the books of the Institute.

FLACK & FLACK,
Chartered Accountants (Australia),
Honorary Auditors.

Melbourne,
16th February, 1954.

THE THOMAS BAKER, ALICE BAKER AND ELEANOR SHAW MEDICAL RESEARCH INSTITUTE

Revenue Account for the Year Ended 31st December, 1953.

EXPENDITURE.				INCOME.				
Salaries and Wages			£11,392 15 6	Donations—				
Drugs			219 2 7	Thomas Baker (Kodak), Alice Baker and Eleanor Shaw Benefactions		£9,600 0 0		
Instruments and Glassware			361 8 6	Mr. Edgar Rouse		60 0 0		
Special Maintenance			617 16 9	Life Insurance Medical Research Fund of Australia and New Zealand Grant	£1,050 0 0			
Repairs and Renewals			220 11 5	Less Amount Carried Forward	859 18 4			
Miscellaneous and Administration—						190 1 8		
Fuel and Lighting	£96 9 0						£9,850 1 8	
Insurance	52 7 11			Government Grants—				
Library	525 7 3			National Health and Medical Research Council			2,888 6 1	
Printing and Stationery	118 6 4			Interest from Investments—				
Telephone	67 15 11			Thomas Baker (Kodak), Alice Baker and Eleanor Shaw Benefactions—				
Laundry	74 19 0			Commonwealth Government Inscribed Stock		551 10 0		
Advertising	10 19 11			Endowment Investments—				
Sundries	471 5 1			Commonwealth Government Inscribed Stock		178 2 6		
			1,417 10 5	Australian Consolidated Treasury Bonds		16 5 0		
				Grain Elevators Board Inscribed Stock		103 2 6		
							849 0 0	
				Sundry Sales			36 16 9	
				Balance—Deficit for Year			605 0 8	
			£14,229 5 2				£14,229 5 2	

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