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.

Both bodies are accepted as "approved research Institutions" by the National Health and Medical Research Council, from whom grants are received for specific research work.

The Clinical Research Unit 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.

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

Twenty-Sixth Annual Report

of

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

and

Fourth Annual Report

of

ALFRED HOSPITAL CLINICAL RESEARCH UNIT

and

RESEARCH FELLOWS

1952

ALFRED HOSPITAL, PRAHRAN
VICTORIA, AUSTRALIA

BAKER MEDICAL RESEARCH INSTITUTE

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Resident Medical Officers	W. E. Hobart, M.B., B.S. (1/1/52 to 31/3/52) G. W. Wigley, M.B., B.S. (1/4/52 to 31/6/52) D. N. Fearon, M.B., B.S. (1/7/52 to 31/9/52) K. McNicol, M.B., B.S. (1/10/52 to 31/12/52)
Ward Sister	Sister J. E. Angus.
Biochemist	Miss J. Uffill, B.Sc.
Biophysicist	B. McA. Sayers, M.Sc., A.M.I.R.E.
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"Sol Green"	R. R. Andrew, M.D., M.R.C.P. H. D. Breidahl, M.D. D. G. Duffy, M.D., M.R.C.P., M.R.A.C.P. H. B. Kay, M.D., M.R.C.P., M.R.A.C.P. E. S. Mancy, M.D.

*Appointed from the University of Melbourne.

ANNUAL REPORT OF THE DIRECTOR

One of the functions of a research group attached to a hospital is the development of new techniques for the study of disease and when they have proved of lasting value to place them on a routine basis. Over the past few years several technical methods for the investigation of cardiovascular diseases have been studied by various members of the staff and proven to be of value in the management of patients. Towards the end of the year it was felt that these methods were of sufficient value to be grouped and made into a routine diagnostic service under the control of a specialist medical officer. The Board of Management of Alfred Hospital has therefore established a Cardiovascular Diagnostic Service as an autonomous unit and so has freed the research staff from a considerable amount of routine work. This will enable the value of other new techniques to be explored.

It will be seen from the details of the scientific work carried out that both the number of workers and the projects being studied are increasing, and with the increased research funds available for next year a further increase is to be anticipated. As these developments have taxed the laboratory space of the Baker Institute and the Clinical Research Unit, it is fortunate that funds have been available to enable extensions to be made to the Institute building. Two large laboratories, one for biophysics and one for biochemistry, are being erected and new storerooms will permit a better distribution of laboratory and office space.

I have mentioned that an increased number of workers is anticipated for 1953. This is partly due to an increase of funds available and partly to a welcome and far-sighted decision of the Board's Research Advisory Committee. In November this Committee recommended that portion of its funds should be used to support trainee research workers, and as a result two junior medical graduates have been given scholarships for 1953 to work under direction. This decision is important for it is now possible to give some of our young graduates a chance to find out whether they are suited for research work. This opportunity is necessary for the medical student has little opportunity in his course of training to acquaint himself with the disciplines of research. In fact, although he may be attracted by what he thinks the glamour of research, he may be quite unsuited temperamentally to carry it out. From the community point of view it is highly desirable that the small percentage of medical graduates who have a real flair for research should be sought out and encouraged for, as was written in an editorial in "Nature," "research is after all a product of the individual. It is a matter of imagination and intuition . . . no administration, no organisation can, of itself, turn it out." The individual must be encouraged and supported and it is now possible for the research group at the Hospital to provide facilities and to encourage workers at all levels of experience.

The facilities available to our workers have been increased this year by the establishment of a pharmacology laboratory under the direction of Dr. G. A. Bentley. This team has been actively engaged in one aspect of the problem of hypertension.

At the beginning of the year an outbreak of myxomatosis occurred in the rabbits in the animal farm. This was presumed to be transmitted by some insect

vector from wild rabbits in the neighbouring parks. At the time of the outbreak myxomatosis was present in these wild rabbits. With the assistance of Professor F. Fenner of the Australian National University it was possible to immunise all unaffected animals with fibroma virus. These measures proved adequate to control the disease, and we were fortunately able to save a majority of the stock. I thank Professor Fenner and his associates for their timely help.

During the year the Director General of Civil Aviation requested the assistance of the members of the Clinical Research Unit to investigate, on a research basis, a problem concerning the health of civil air line pilots. At first sight it appeared that there was an undue incidence of hypertension in these young men. More detailed investigation showed that this appearance was fictitious and that these men had, if anything, a lower incidence of hypertension than the general population.

It is a pleasure to thank the Trustees of the Institute and the Board of Management of the Hospital for the facilities they have given members of the staff to visit other centres. I attended a meeting of the Royal Australasian College of Physicians in Adelaide, Dr. Barnett visited the Medical School at Dunedin, New Zealand, and Dr. Bentley attended the ANZAAS conference in Sydney. From these visits many contacts and much information of value to all of us resulted.

BAKER MEDICAL RESEARCH INSTITUTE

This year three new senior workers have joined the staff of the Institute. Dr. G. A. Bentley commenced his appointment as pharmacologist. Dr. B. Hudson is working under a research scholarship awarded jointly by the Institute Trustees and Alfred Hospital. Dr. R. J. Sawers holds a part time scholarship awarded by the hospital.

The research projects in progress which are described in detail in the scientific section of the report may be briefly summarised. A study of biochemical problems related to the coagulation of blood continues and a closely related study of both the bleeding and heredity aspects of haemophilia has been commenced. The pharmacology team has been concerned in finding a suitable method whereby to assay adrenaline and noradrenaline in urine. It is hoped to apply this technique to the study of hypertension in man. Another project concerns the biological actions of ACTH and adrenal cortical hormones.

The continued support of various research projects by the National Health and Medical Research Council is gratefully acknowledged.

Gifts to the library were received from the following: Abbott Laboratories; Alfred Hospital Library; Bayer Products Ltd.; Bausch & Lomb Optical Co.; Hospitals and Charities Commission; Commonwealth Scientific and Industrial Research Organisation; Eastman Kodak Ltd.; Felton, Grimwade & Duerdins Ltd.; Imperial Chemical Industries of Australia and New Zealand Ltd.; International Anesthesia Research Society; Lilly Research Laboratories; Mayo Clinic; Medical Research Council, London; Middlesex Hospital Medical School; National Health and Medical Research Council, Canberra; Organisation for Scientific Research, Indonesia; Parke, Davis & Co.; Queensland Institute of Medical Research; Rockefeller Institute for Medical Research; U.S. Army Medical Library; Walter and Eliza Hall Institute.

Our thanks are expressed to them and to the various Libraries that have lent many journals to us, and particularly to the librarians, whose assistance is greatly valued.

As in previous years, much assistance, both professional and material, has been given to us by other organisations, and grateful acknowledgment for such is expressed to the following and their associates:

Members of the Honorary Medical Staff and of the various Departments of Alfred Hospital; Professor V. M. Trikojus (Biochemistry Department, University of Melbourne); Dr. F. G. Morgan (Director, Commonwealth Serum Laboratories); Dr. A. W. Turner (C.S.I.R.O.); The Red Cross Blood Transfusion Service; Dr. Lewis, Mr. Goble and other members of the staff of Kodak A/sia Pty. Ltd.

It is a pleasure for me to thank the Trustees for their wholehearted support and assistance during the year.

Also, I wish to thank the members of the Advisory Committee, who have been very ready to help whenever their assistance has been sought.

CLINICAL RESEARCH UNIT

In general the subjects of research in the unit are similar to those that have been pursued in previous years and in all of them considerable progress has been made. The study of congestive cardiac failure has led to a study of the wider problem of the control of the body water in man. Examination of the electrical activity of the heart continues. The practical applications of vectorelectrocardiography are still being studied and much work has been done on the basic theory of electrocardiography. Further observations both physiological and clinical have been made on patients with high blood pressure and clinical trials of hypotensive drugs continue. Diseases of the peripheral blood vessels are being investigated by various techniques and therapeutic and physiological studies are being made.

Throughout the year facilities have been made available to enable several research fellows to pursue their work.

The work of the Unit and of the Hospital Research Fellows is detailed in the scientific section of this report.

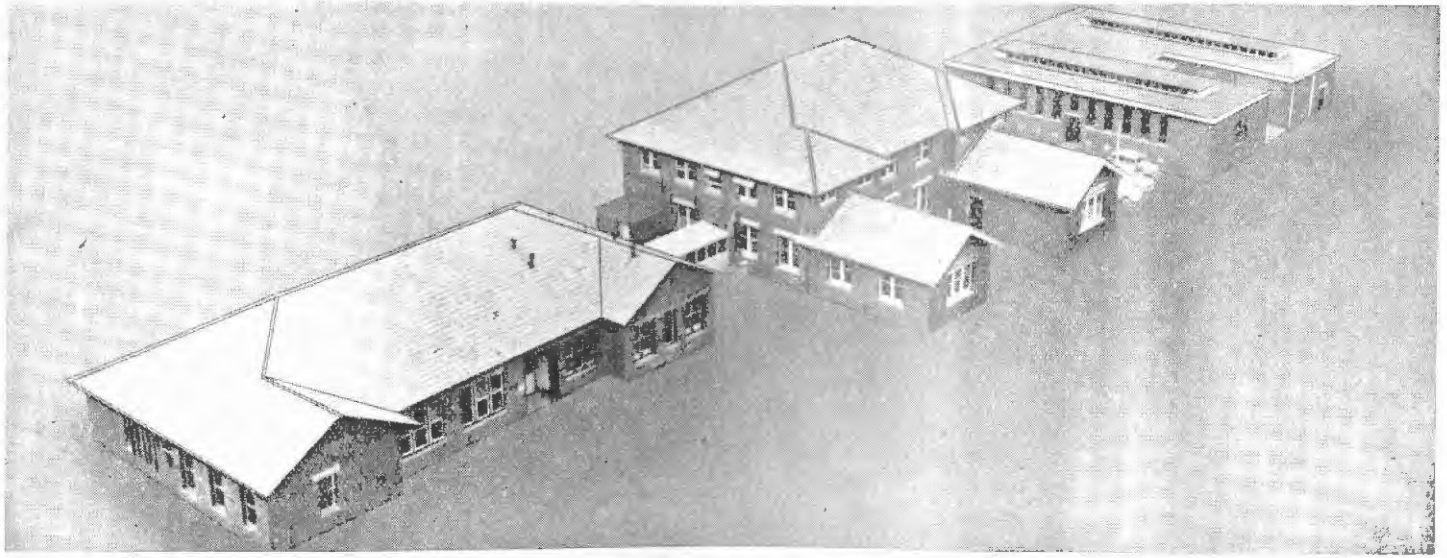
It is a pleasure to record the assistance rendered to the Unit by members of the Honorary Medical Staff, by all Hospital departments, and members of the University staff.

Grateful acknowledgment is made to the National Health and Medical Research Council for continuation of a grant toward expenses and apparatus.

Personally, I thank the Board of Management for their continued generous support of the Unit.

31st December, 1952. T. E. LOWE, Director.

RESEARCH DEPARTMENTS IN THE GROUNDS OF THE HOSPITAL



Ward 8

Clinical Research Unit.

Two Six-bed Wards and Ward Services
Examination Rooms
Biophysics Laboratory
Biochemistry Laboratory
Offices

Baker Medical Research Institute.

Biochemistry Laboratories
Physiology Laboratories
Library
Workshop
Offices

Animal Farm

REPORT OF SCIENTIFIC INVESTIGATIONS

THE REACTION OF THROMBIN WITH PLASMA COMPONENTS*

P. Fantl, L. Ebbels and M. Pearce.

The addition of thrombin to plasma gives rise to several effects, one of which is the production of fibrin. It was observed in plasma from patients suffering from a variety of diseases, including obstructive jaundice and multiple myelomata, that the time of appearance of a clot (fibrin formation) is longer than in normal plasma. The cause of this delay in the thrombin clotting time is not known. Since this phenomenon may have a bearing on the pathology of the conditions mentioned, an investigation of the factors determining the thrombin clotting time of plasma has been carried out.

As it was observed that animal plasma (guinea pig and rat) showed likewise a delayed thrombin clotting time in comparison to normal human plasma, thrombin was prepared from the plasma of several mammals. Clotting time was shown to be dependent on the activity of the preparations but to be independent of the source of thrombin. However all thrombins showed a greater affinity to normal human plasma than to animal plasma. This might explain the high incidence of thrombo-embolic attacks in humans.

Tests for Inhibitors of Thrombin

In order to explain the delayed thrombin clotting time of pathological and animal plasma, the presence of thrombin inhibitors was considered. It was established that thrombin inhibitors were absent from the different plasmas and further that the power of plasma to inactivate thrombin added to serum was not significantly different in the different species investigated.

Species Specificity of Native Fibrinogen

The above experimental results suggested that the varying reaction of thrombin with plasma may depend upon properties of fibrinogen being different in the various species. It was found that separation of fibrinogen from plasma by the use of the known procedures led to an alteration of its reactivity towards thrombin. This indicated that certain surface properties of the native fibrinogen had been altered during the isolation procedures.

It is thought that the delayed thrombin clotting time in patients suffering from obstructive jaundice is likewise due to an altered fibrinogen. Apparently the liver produces under certain pathological conditions an abnormal type of fibrinogen.

Reaction of Phenols with the Coagulation Components of Plasma

Additional evidence for the species specificity of native fibrinogen has been provided by the following experiments. A number of compounds are known to potentiate the thrombin-fibrinogen reaction. Pyrocatechol is very active in this respect. A comparison of the thrombin clotting time of plasma mixtures with and without the addition of pyrocatechol indicated that this substance abolished the time lag observed between human and animal plasma.

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.

THE COAGULATION MECHANISM OF LYMPH*

P. Fantl and J. F. Nelson.

This investigation was carried out in connection with the problem of the initial stages of the clotting process. Lymph contains all the plasma soluble factors but is lacking in thrombocytes. Since the role thrombocytes in blood coagulation is controversial a comparison between the clotting process of blood and lymph seemed desirable. Both fluids were obtained from dogs. It was observed that thoracic duct lymph clots in a far shorter time when in contact with glass than when in contact with a water repellent siliconised surface. The concentration of the coagulation factors is approximately half that of blood plasma. The initial stages of the clotting process of lymph are explained by the presence of a soluble precursor termed prothromboplastin. The rate of conversion of prothromboplastin into active thromboplastin depends on the surface properties of the container.

THROMBOPLASTIN FORMATION IN BLOOD*

P. Fantl and R. A. Hayes†

In connection with the coagulation studies carried out in lymph it was found that a shortening of the whole blood coagulation time of normal blood occurred after incubation with sodium citrate in glass containers. Since thrombocytes have been connected with the supply and activation of clotting components, thrombocyte counts were carried out simultaneously with the coagulation experiments. Statistical evaluation of the counts indicated that incubation of citrated blood at 37°C for 15 minutes did not produce a significant change in the number of thrombocytes. The reported results are consistent with the assumption that normal blood plasma contains a soluble precursor of the thromboplastin complex which in contact with glass becomes activated at calcium ion concentrations as low as 10^{-5} molar. The above technique will be applied to the study of the clotting defect in haemophilia.

†Department of Pathology, Alfred Hospital.

HAEMOPHILIA

R. J. Sawers.

In the latter part of the year a programme of research into several aspects of haemophilia and allied haemorrhagic diseases was commenced.

It was felt opportune to study bleeding tendencies because new techniques for investigating the coagulation mechanisms have been developed recently. To make the study as complete as possible, both the clinical and laboratory aspects are being examined in parallel.

Through the courtesy of hospital authorities a search has been begun in the medical record libraries of the metropolitan hospitals to obtain cases for investigation. All cases of abnormal bleeding treated during the last twenty years are being registered and about seventy cases have been collected to date.

A personal and family history is obtained and an examination is made for deformities and any stigma of haemophilia or other bleeding diseases. Tests are made to exclude vascular and cellular causes of bleeding and samples of blood are obtained by a standard technique for investigation of coagulation factors.

Certain points of interest have been noted. In the group of "haemophilics" it is evident that a family history of the disease is frequently lacking. Review of the pedigree of these cases suggests that they are spontaneous cases of the disease. This is usually regarded as occurring rarely. However in our series almost half of the patients give no family history of the disease.

Another point of interest is the occasional lack of correlation between the degree of prolongation of the coagulation time and the clinical severity of the disease.

Finally, some haemophilics have been diagnosed as such for the first time during the investigation. These have been adults, with no family history of the disease, who have been admitted to hospital at some time on account of abnormal bleeding but in whom the previously available laboratory tests have given normal results. From the clinical side alone it appears probable that certain changes in the definition of the disease might be made with advantage.

CONTROL OF BODY WATER VOLUME IN MAN*

Clinical Studies

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

In previous studies quantitative observations have been made of the way in which the water content of the body changes during diuresis from oedema and during the formation of oedema. It was found that the curve representing the daily water balance of these patients undergoes cyclic variations and that under certain conditions its rhythm is suddenly changed. Detailed examination of these curves led to the conclusion that early changes in water balance 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 disturbance 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. Further it has been apparent from these studies 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 laws of an "open" system.

During this year attention has been paid to two aspects of this problem. First, many oedematous patients were treated with mercurial diuretics and their fluid balances recorded. The usual clinical responses were seen, some patients had a good diuresis following each injection of mercurial diuretic, others developed a steady diuresis over the period during which injections were given and in a few the mercurial diuretic had no action. It was concluded from these studies that mercurial diuretics partially block one of the factors controlling water balance in body and that the varying clinical response depends upon the phase of activity of the system at the time of exhibition of the diuretic.

Secondly, it was considered that the forces of this water balance system must control body water volume by their control of the intake and output of water. The records of the patients studied showed that several types of change in intake and output of water could be discerned.

As theoretical analysis of the "open" storage system representing the body's water volume control is difficult, a mechanical model was constructed. This model consisted of a reservoir in which both the volume of water in the reservoir and the difference in height of water in two parts of the reservoir control both the intake and output of water. This model was capable of reproducing many of the types of behaviour seen in man.

From the observations made on patients with oedema of cardiac origin and study of the mechanical model it has been concluded that at least three separate mechanisms control the intake and output of water in man.

The effector agents of these mechanisms are represented by thirst and urinary water output. The receptor mechanisms are possibly actuated in one case by the volume of some portion of the body and in a second by the osmotic pressure of some body fluid. Observations in a patient with cardiac tamponade show clearly that the heart is intimately connected with these mechanisms.

Physical Studies

B. McA. Sayers.

In addition to the clinical studies outlined above the problem has been studied analytically in two ways.

First, the effects of climatic factors on the storage of water in man and rabbits have been investigated. It appears from these observations that there is a quantitative relation between ambient temperature and pressure and intake and output of body water. The relationship appears to alter in a roughly linear fashion with the instantaneous excess of body storage of water. The sensitivity of the response to climatic changes appears to alter with the amount of excess storage of water above normal.

Secondly, automatic computing apparatus has been constructed which allows study of a formal equation which represents factors and mechanisms operating in maintaining the body water equilibrium. This study indicates that the internal sensitivity of one of the control mechanisms varies with time in a regular and possibly predictable manner. The possibility of correlation between this and climatic effects is being investigated.

STUDY OF HYPERTENSIVE STATES

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

Mechanism of Hypertension

One hypothesis advanced as to the cause of arterial hypertension is that an abnormal vasoconstrictor response to normal stimuli occurs in blood vessels. In particular it is suggested that there is an abnormal response to sympathetic nervous control of vessels.

In the course of treatment of patients with hypertension 27 persons have been given intramuscular injections of hexamethonium in doses of 2 mgm per Kgm of body weight. This procedure has also been carried out in 13 normotensive persons.

Following these injections both the systolic and diastolic blood pressure fell in the hypertensive subjects to a greater degree than in the normotensive subjects. As hexamethonium is a sympatholytic agent these results are in accord with the hypothesis mentioned. They could however be explained on other grounds.

As the sympathetic hormone is believed to be noradrenaline the effect of intravenous infusion of noradrenalin in patients with Addison's Disease is being studied as opportunity arises. It is hoped that this study may shed some light on the problem of the responsiveness of blood vessels to noradrenaline, for the amount of circulating noradrenaline must be greatly reduced in Addison's Disease.

Clinical Trial of Hypotensive Drugs

The clinical trial of methonium* compounds as therapeutic agents for patients with severe and malignant hypertension has been continued during the year and the series of patients now numbers thirty-six.

Administration of the drugs by intermittent subcutaneous injection is being studied and is thought to be more effective than oral administration. By this method it is found that the dose can be increased to a level giving a satisfactory lowering of blood pressure without at the same time producing severe reactions or bromide intoxication. Twenty patients have been taught to give themselves these injections.

*The methonium drugs were in part supplied by courtesy of May & Baker Ltd.

In a few patients who have not been in a malignant phase of hypertension, the drugs have been used for the treatment of left ventricular failure.

Hydrazinophthalazine† has been used as an adjunct to methonium treatment in 11 patients in whom it was difficult to obtain a satisfactory lowering of blood pressure with methonium alone. With a combination of the two drugs adequate lowering of blood pressure was obtained in all cases.

The opinion previously formed that these drugs are valuable agents in the management of patients with severe arterial hypertension with Grade IV hypertensive retinal changes has been reinforced by the further year's experience.

PULMONARY HYPERTENSION

J. M. Gardiner and R. E. Fraser.

During the year a study has been made of the effect of the vasodilator drug "Priscol" on pulmonary hypertension. Seven patients have been investigated by cardiac catheterisation and the recording of pulmonary arterial pressure by an electromanometer and the measurement of pulmonary blood flow by the Fick principle. In these patients "Priscol" was administered directly into the pulmonary circulation through the intra-cardiac catheter. Measurements of the pulmonary arterial pressure and pulmonary blood flow showed that the drug lowered the peripheral resistance of the lung vessels, lowered pressures and increased the pulmonary blood flow. One of these patients was considered to be suffering from primary pulmonary hypertension and in this case the response to the drug was the most satisfactory of the series. This patient is being treated with "Priscol" given orally and the results of treatment are being observed.

ASSAY OF ADRENALINE AND NOR-ADRENALINE IN URINE

G. A. Bentley.

In studying the mechanism of hypertensive states in man it is considered of importance to determine the urinary excretion of adrenaline and noradrenaline which is known to be excessive in some cases of phaeochromocytoma. Normally some 10-30 microgrammes of noradrenaline are excreted in the urine per day and the present study has been devoted to finding a suitable method of assay for such amounts in urine.

Two problems are present in this project. First, the active material must be freed from interfering substances and secondly the assay method must be sufficiently sensitive.

The recognised methods of isolation of the active material which are based on adsorption of the active material on ion exchange resins, aluminium hydroxide or aluminium oxide and subsequent elution with acids all give satisfactory recovery from water. Only one appears from our experience to be practical in the presence of urine. This method involves adsorption of the active material on aluminium oxide and its subsequent elution by acid.

The methods of assay of adrenaline and noradrenaline are biological, colourimetric or fluorimetric. The biological assay is extremely sensitive but cannot be adequately controlled for the present purposes. The colourimetric methods have proved too insensitive as the minimum quantity which can be assayed is some 25 microgrammes. At present it appears that Pekkarincu's fluorimetric method of assay is able to distinguish adrenaline and noradrenaline and is sufficiently sensitive for this project.

†Hydrazinophthalazine was supplied by courtesy of Ciba Ltd.

THE SYMPTOMATOLOGY OF SYSTEMIC HYPERTENSION

D. G. Duffy.

This investigation has been directed to the cause of breathlessness in patients suffering from systemic hypertension. The patients selected for observation all had diastolic blood pressures in excess of 110 mms. Hg. They suffered from essential hypertension, chronic type 1 nephritis, chronic pyelonephritis or polycystic disease of the kidneys.

Under standard conditions measurements of the patient's tidal air and vital capacity were made both before and after a standard exercise test. The patients were then instructed in breathing exercises and after two weeks' training were retested.

Forty-three patients have been studied in detail and of these 28 showed symptomatic improvement. Their tolerance to exercise had increased so that they complained of breathlessness only after unusual effort.

It was found that measurements of the volume of tidal air gave a better indication of the patients' condition than did measurements of vital capacity.

It is considered important to note that breathlessness, commonly attributed to hypertension per se or to incipient cardiac failure, can be relieved in these patients by measures which lay no claim to lowering of blood pressure.

STUDY OF DISEASES OF THE PERIPHERAL BLOOD VESSELS

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

Diagnostic Methods.

Venous occlusion plethysmography continues to be a valuable diagnostic aid for suspected occlusive arterial disease in the lower limbs. During the year 49 patients were examined by this technique.

In conjunction with the staff of the X-ray department the technique of arteriography of peripheral vessels has been established as a valuable diagnostic method for these conditions. Using this technique it has been possible to demonstrate in a number of patients that their Raynaud's phenomenon was due to blockage, rather than to spasm, of the digital arteries. This diagnosis is of considerable practical importance in deciding upon the treatment to be used.

Hand Calorimetry. In order to estimate blood flow through the hand a calorimeter has been constructed. This method is used in preference to plethysmography because it gives more readily an estimate of the average blood flow in the hand which, in contrast to the foot, fluctuates greatly from moment to moment. This instrument has been found of value in the diagnosis of vascular disturbances in the upper limbs. In the establishment of this method considerable assistance was given to us by Drs. G. W. Wigley and D. N. Fearon.

Therapeutic Studies

In a number of patients who had intermittent claudication sympathectomy has been carried out. This procedure markedly improved the blood flow through the skin of the limbs but did not influence the distance the patient could walk over standard steps before claudication developed. In a few patients intra-arterial injections of histamine into the affected limb have been given at weekly intervals. The results so far are encouraging but enough time has not yet elapsed for an opinion to be expressed as to its value as a therapeutic agent.

Physiological Studies

The apparatus necessary for the continuous recording of intra-arterial pressure pulses has been assembled. This is based on a capacitance manometer (Hansen type) which actuates an amplifier and pen recorder. With this apparatus some preliminary studies of pulse wave form and of the rate of decay of arterial pressure following arterial occlusion have been made. By these means it is hoped to estimate the peripheral vascular resistance in a limb and to assess the changes in this which may follow sympathectomy.

Hand calorimetry is being used to examine the vascular changes in "reflex" hyperaemia following the exposure of the body to heat or the immersion of one hand and forearm in hot water.

MITRAL STENOSIS

Selection of Cases for Surgical Treatment

H. B. Kay.

Several problems arise in the selection of cases of mitral stenosis that are suitable for surgical treatment. Ninety patients have so far been studied and it is considered that patients showing the characteristic features of "obstructive" mitral stenosis in association with a clear loud first sound, opening snap and diastolic murmur, radiological evidence of moderate left auricular enlargement without much ventricular enlargement and pulmonary venous congestion, are the most suited to surgical treatment.

Attention is being directed to methods of diagnosis of associated mitral incompetence, and to the problem of associated pulmonary hypertension.

THE USE OF CATION EXCHANGE RESINS IN THE TREATMENT OF OEDEMA

H. D. Breidahl and J. Upfill.

This work was an enquiry into the uses of cation exchange resins for the relief of oedematous states. It has been known for many years that a retention of sodium in the body is in some way connected with clinical oedema, and it has been shown that lowering the intake of sodium will diminish the water retention. As, however, a diet of low sodium content is difficult to prepare in the home and is extremely unpalatable, cation exchange resins have been suggested as a means of immobilising sodium in the bowel and excreting it in the faeces. Theoretically this is a satisfactory procedure but in practice there are certain drawbacks. Although the patient is able to have a more palatable diet, the ingestion of the large amounts of cation exchange resin necessary to produce the therapeutic effect causes a considerable degree of nausea and in some cases vomiting. Also the resins produce unwanted side effects on other systems of the body and are not completely safe for routine use without biochemical control.

Biochemical studies made on the patients treated with resins showed that sodium was withdrawn from the body by an increased excretion in the faeces with a diminished urinary excretion. Potassium was similarly affected but to a much greater extent and potassium depletion developed rapidly in one patient.

Detailed studies have been made in 19 patients and from this experience it is concluded that provided one is aware of the contraindications to and the complications of the use of resins they may be valuable adjuncts in the treatment of oedema for patients in whom other forms of therapy are unprocurable or unavailing.

VECTORELECTROCARDIOGRAPHY*

T. E. Lowe and J. M. Gardiner.

The second channel of the vectorelectrocardiograph was completed early in the year and the machine has been used to study the VCG in patients with cardiac disease.

A series of 68 cases of left ventricular hypertrophy in Hypertension were studied in detail and the abnormalities of the VCG determined. These have three features.

Abnormalities of the QRS component of the ventricular complex may be of position, especially rotation horizontally and back, or of contour, especially distortion upwards and backwards of the whole or part of the centripetal limb.

There is frequently a shift of the junction of the QRS component with the rest of the complex. Finally there may be abnormalities of the JT segment, in particular in the spatial angle between this and the QRS loop.

VCGs of considerable number of cases with other conditions have been made but as yet not sufficient have been obtained for analysis.

It appears from our studies that VCGs provide in many cases additional information about the electrical activity of the heart, because that activity is portrayed in a form in which recognition of the abnormalities is easier than in the conventional scalar electrocardiogram.

THEORY OF ELECTROCARDIOGRAPHY

B. McA. Sayers.

Experiments designed to test the absolute accuracy of the electrical field formulae applied to human electrocardiography have shown irregularities in the pattern of generally good agreement between predicted and observed potentials at various parts of the body. Theoretically the presence of a small inhomogeneity in the electrical conducting medium of the human body should produce such irregularities. These should be most noticeable when certain geometrical conditions of lead placements are used for the recording of scalar ECGs. This effect has been confirmed experimentally.

It appears, however, that placement of leads recommended by Duchosal and Sulzer for VCGs may give less evidence of these irregularities than that of other systems.

In a number of cases the spatial magnitude of the manifest electrical vector has been calculated for successive intervals of time during the cardiac cycle. The results obtained suggest that such records may provide a simple diagnosis of some cardiac abnormalities. Owing to the labour of calculation, it will be necessary to perform this step by electronic synthesis and a start has been made on the construction of the necessary apparatus.

STUDIES OF THE PHYSIOLOGY AND PATHOLOGY OF THE STOMACH, DUODENUM AND SMALL BOWEL

R. R. Andrew.

During the year these studies have been directed to the following three problems.

The normal motility of stomach, duodenum and small bowel has been investigated using the technique of balloon kymography through a four-lumen Miller-Abbott tube. It has been found that contrary to the usual teaching, there is both a very complex relationship, and independence, of intestinal motility in the regions studied. Harmony of these parts is often observed, but at different times gastric or duodenal activity may be quite autonomous. A proper understanding of the normal physiology in this region may advance our knowledge of the exceedingly large and common group of gastro-intestinal disorders of which so little at present is known.

Utilising the same technique the effects of various drugs on these organs have been studied and confirmation has been obtained of the effects others have observed with atropine, hexamethonium bromide and banthine. Some light has been thrown on the action of morphine, about which there is still considerable controversy.

Similar procedures have also been used to note the effect of acid-induced pain on the motility of stomach, duodenum and jejunum in patients with active duodenal ulceration. Considerable technical difficulties have emerged with these studies and further work is necessary. It would appear that contrary to the published work, there is little or no correlation between the occurrence of peptic ulcer pain and motility patterns.

BIOLOGICAL ACTION OF A.C.T.H.

B. Hudson.

A consistent biological effect of the adrenocorticotrophic hormone of the pituitary gland (ACTH) when injected into an intact animal is to cause the disappearance from the blood of eosinophile leucocytes. This effect is probably the result of the production of compounds E (cortisone) or F by the adrenal cortex in response to the ACTH. This phenomenon can also be induced by the administration of either compounds E or F. This response to the injection of ACTH has now been generally accepted as a qualitative index of adrenocortical function.

At present very little is known concerning the nature of this response. During the past year investigations have been directed towards discovering the fate of eosinophiles which disappear from the circulation under the influence of ACTH. These investigations have proceeded along two lines.

(1) Do the eosinophiles become sequestrated in one or more internal organs? It has been suggested that the spleen may be the responsible organ. In two patients there was no detectable change in the eosinophil response to ACTH before and after splenectomy. In both patients there was a 90-100% fall in circulating eosinophiles both before and after splenectomy.

(2) Do the adrenal hormones cause disappearance of eosinophiles by a direct lytic effect on these cells? This phenomenon was investigated by incubating, in vitro, blood samples with cortisone and compound F at two different dose levels. Eosinophile counts were made before and four hours after incubation. At high dose levels (0.33 mgm. ml) there was a highly significant fall in the numbers of eosinophiles at the end of four hours. At lower, and more physiological dose levels (40 micrograms/ml) there was no significant difference between treated and control samples.

Whether or not these hormones have any lytic effect on eosinophiles in vivo has not yet been precisely determined. Further experiments are in progress to ascertain by in vivo methods the effects of cortisone and compound F on eosinophiles.

FUNGICIDES IN THE TREATMENT OF FUNGUS INFECTIONS OF THE SKIN

E. S. Mancy.†

The relative efficiency of a number of fungicides in vitro against specific types of dermatophytes isolated from superficial fungus infections of the human skin is being investigated.

A satisfactory method of testing the efficiency of fungicides in vitro has been developed using a central disc of Sabouraud's dextrose agar in a Petrie dish surrounded by an annulus of the same medium containing the required concentration of fungicides.

It has been found that many fungicides, when added to artificial media in high dilution will prevent the growth of all the species of dermatophytes when using native material for inoculation. A somewhat higher concentration of these fungicides will prevent progressive growth from an actively growing culture.

The use of these fungicides clinically is at times ineffective in restoring skin, hair and nails to normality. Frequently this is due to the abnormal condition not being of fungus origin, or that the fungicide preparation used does not penetrate the tissues or that structural anomalies of the skin such as ichthyosis are present.

†This work was carried out in the Pathology Department, Alfred Hospital.

PUBLICATIONS DURING 1952

T. E. Lowe: "INFLUENCE OF A MERCURIAL DIURETIC ON THE MECHANISM OF DIURESIS IN CONGESTIVE CARDIAC FAILURE," Lancet, Vol. 2 (1952) p. 1238.

T. E. Lowe: "MEDICAL RESEARCH," Hosp. Admin., Vol. 1 No. 2 (1952), p. 11.

T. E. Lowe and B. McA. Sayers: "CONTROL OF THE WATER CONTENT OF THE BODY," A'sian. Ann. Med., Vol 1 (1952), p. 51.

P. Fantl, L. Ebbels and J. F. Nelson, "THE PRESENCE OF THIOL GROUPS IN THROMBOCYTES AND THEIR SIGNIFICANCE IN THE CONTRACTION OF FIBRIN GEL," Brit. J. Exper. Path., Vol. 32 (1951), p. 538.

P. Fantl and J. F. Nelson: "THE SECRETION OF 3,3'—ETHYLIDENE BIS (4-HYDROXYCOUMARIN) IN MILK," Med. J. Aust., Vol. 1 (1952), p. 404.

P. Fantl and L. Ebbels: "EXPERIENCE WITH INTRAMUSCULAR ADMINISTRATION OF HEPARIN PREPARATIONS: A COMPARISON BETWEEN AQUEOUS AND RETARD HEPARIN," A'sian. Ann. Med., Vol. 1 (1952), p. 135.

A. J. Barnett: "OCULAR EFFECTS OF METHONIUM COMPOUNDS," Brit. J. Ophthal., Vol. 36 (1952), p. 593.

A. J. Barnett and R. Fowler: "THE ACTION OF 'REGITINE' IN MAN WITH SPECIAL REFERENCE TO ITS ADRENERGIC BLOCKING ACTION," A'sian. Ann. Med., Vol 1 (1952), p. 109.

B. McA. Sayers: "ON THE IMPORTANCE OF 'OPEN SYSTEMS' IN THE MEDICAL SCIENCES," Aust. J. Sc., Vol. 14 (1952), p. 174.

B. McA. Sayers: "UNCERTAINTIES IN EINTHOVEN'S HYPOTHESIS ON ELECTROCARDIOGRAPHY," Aust. J. Sc., Vol. 14 (1952), p. 195.

B. McA. Sayers: "COMPARATIVE STUDIES IN VECTOR AND LINEAR ELECTROCARDIOGRAPHY," A'sian. Ann. Med., Vol. 1 (1952), p. 154.

P. J. Parson: "FAMILIAL CARDIAC ENLARGEMENT: REPORT OF TWO CASES," Med. J. Aust., Vol. 2 (1952), p. 435.

J. H. W. Birrell: "WEBER-CHRISTIAN SYNDROME: REPORT OF A CASE," Med. J. Aust., Vol. 2 (1952), p. 124.

E. S. Mancy: "SUPERFICIAL FUNGOUS INFECTION IN VICTORIA," Med. J. Aust., Vol. 1 (1952), p. 883.

PAPERS ACCEPTED FOR PUBLICATION

P. Fantl and R. A. Hayes: "THROMBOPLASTIN FORMATION IN SHED MAMALIAN BLOOD." Nature.

P. Fantl and J. F. Nelson: "THE COAGULATION MECHANISM OF LYMPH." J. Physiol.

P. Fantl and L. Ebbels: "THE INTERACTION OF THROMBIN WITH THE PLASMA COMPONENTS OF MAN AND EXPERIMENTAL ANIMALS." Aust. J. Exper. Biol. & Med. Sc.

J. H. W. Birrell: "A NOTE ON LEPROSY AS AN AETIOLOGICAL FACTOR IN THE WEBER-CHRISTIAN SYNDROME." Med. J. Aust.

J. M. Gardiner and T. E. Lowe: "THE SPATIAL VECTORELECTROCARDIOGRAM IN THE LEFT VENTRICULAR HYPERTROPHY OF HYPERTENSION." A'sian. Ann. Med.

H. D. BREIDAHL: "CATION EXCHANGE RESINS: A CLINICAL AND BIOCHEMICAL STUDY OF THEIR USE IN OEDEMA." A'sian. Ann. Med.

LECTURES DELIVERED DURING 1952

"PHYSIOLOGY OF CARDIAC FAILURE" . . . . . T. E. Lowe
Sprent Memorial Lecture—Hobart.
Tasmanian Section, Royal Australasian College of Physicians.

"CONTROL OF THE WATER CONTENT OF THE BODY" . . T. E. Lowe
Victorian Section, Royal Australasian College of Physicians.

"MODE OF ACTION OF MERCURIAL DIURETICS IN CONGESTIVE CARDIAC FAILURE" . . . . . T. E. Lowe
Victorian Society for Pathology and Experimental Medicine.

"MEDICAL RESEARCH" . . . . . T. E. Lowe
Annual Meeting, Alfred Hospital.

"INTERACTION OF THROMBIN WITH PLASMA COMPONENTS IN MAN AND EXPERIMENTAL ANIMALS" . . . . . P. Fantl
Victorian Society for Pathology and Experimental Medicine.

"SERUM FACTORS IN BLOOD COAGULATION" . . . . . P. Fantl
Alfred Hospital Clinical Society.

"SPECIES SPECIFICITY OF THROMBINS" . . . . . P. Fantl
Victorian Society for Pathology and Experimental Medicine.

"DANGERS OF INTRAVENOUS IONIC THERAPY" . . . A. J. Barnett
Alfred Hospital Clinical Society.

"DISCREPANCIES BETWEEN SCALAR AND VECTORELECTROCARDIOGRAMS" . . . . . B. McA. Sayers
Victorian Society for Pathology and Experimental Medicine.

"PULMONARY HYPERTENSION" . . . . . J. M. Gardiner
Alfred Hospital Clinical Society.

"BIOLOGICAL ACTION OF A.C.T.H." . . . . . B. Hudson
Victorian Section, Royal Australasian College of Physicians.

FINANCIAL STATEMENTS

Baker Medical Research Institute

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

Revenue Account for the Year Ended 31st December, 1952.

EXPENDITURE.				INCOME.				
Salaries and Wages			£10,901 2 11	*Donations*—				
Drugs			208 6 0	Thomas Baker (Kodak), Alice Baker and Eleanor Shaw Benefactions	£7,200 0 0			
Instruments and Glassware			136 14 1	George H. Little Estate	333 7 10			
Special Maintenance			642 12 11				£7,533 7 10	
Repairs and Renewals			192 14 7	Government Grants—				
Miscellaneous and Administration—				National Health and Medical Research Council			2,286 0 0	
Fuel and Lighting	£123 1 1			Interest from Investments—				
Insurance	73 14 7			Trustees of the Thomas Baker Estate—Commonwealth Government Inscribed Stock held for the Benefit of the Institute	552 0 0			
Library Maintenance	578 16 1			Endowment Investments—				
Printing and Stationery	101 13 10			Australian Commonwealth Government Inscribed Stock	178 2 6			
Laundry	67 9 8			Australian Consolidated Treasury Bonds	16 5 0			
Telephone	104 7 4			Grain Elevators Board Inscribed Stock	98 8 9			
Travelling Expenses	7 3 2						844 16 3	
Advertising	1 7 6			Sundry Sales			97 0 0	
Sundry	346 4 1			Balance—Deficiency for the Year			2,724 3 9	
			1,403 17 4					
			£13,485 7 10				£13,485 7 10	

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

Balance Sheet at 31st December, 1952.

LIABILITIES.

Current Liabilities—			
Commercial Bank of Australia Ltd.	£1,051 0 4		
Sundry Creditors	622 9 10		
		£1,673 10 2	
Capital Grants and Gifts—			
Balance at 31st December, 1951	822 16 7		
Add Grants Made During Year	300 0 0		
	£1,122 16 7		
Less Amount Expended on Fixed Assets During Year	407 19 8		
		714 16 11	
Endowment Fund		8,500 0 0	
Net Revenue Account			
Balance at 1st January, 1952 Dr.	213 13 1		
Donation, Recoup of Deficit for Year Ended 31st December, 1951, from the Thomas Baker, Alice Baker and Eleanor Shaw Benefactions	2,863 5 4		
Cr.	2,649 12 3		
Less Deficit for Year Ended 31st December, 1952 Dr.	2,724 3 9		
Balance Dr. (as per contra)	74 11 6		
		£10,888 7 1	

ASSETS.

Current Assets—			
Sundry Debtors			£213 15 7
Investments—			
Grain Elevators Board Inscribed Stock—			
4½% Due 1/5/1964	£2,500 0 0		
Australian Commonwealth Inscribed Stock—			
3½% Due 15/10/1960	£5,000 0 0		
3½% Due 15/10/1963	500 0 0		
Australian Consolidated Treasury Bonds—			
3½% Due 15/9/1961	500 0 0		
			8,500 0 0
Fixed Assets, at Cost—			
Furniture and Fixtures			2,100 0 0
Net Revenue Account (as per Contra)			74 11 6
			£10,888 7 1

Note: In addition to receiving interest on the Investments as shown in in the Balance Sheet, the Institute received the income from 3½% 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, having obtained all the information and explanations we have required, we are of opinion that the Balance Sheet presents a true and fair view of the state of the affairs of the Institute at 31st December, 1952, according to the best of our information and the explanations given to us and as shown by the books of the Institute.

Melbourne,
2nd April, 1953.

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

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