

Twenty-Fifth Annual Report

of

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

and

Third Annual Report

of the

ALFRED HOSPITAL
CLINICAL RESEARCH UNIT

1951

ALFRED HOSPITAL, PRAHRAN
VICTORIA, AUSTRALIA

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 recognized 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.

BAKER MEDICAL RESEARCH INSTITUTE

Annual Report
1951

ALFRED HOSPITAL CLINICAL RESEARCH UNIT

ALFRED HOSPITAL, PRAHRAN
VICTORIA, AUSTRALIA

BAKER MEDICAL RESEARCH INSTITUTE

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DIRECTOR'S ANNUAL REPORT

This year the annual reports of the Baker Institute and the Clinical Research Unit are published in a common cover. This step has been taken because the activities of the two are so closely interwoven that any account of the work of one of necessity requires reference to the other. It is hoped that this new form of presentation will give a clear account of the scientific work in progress and also show how the two organisations are integrated to their mutual advantage.

As it is now three years since considerable changes were made in the scope of the work of the Baker Institute, and also since the Clinical Research Unit was established, it seems desirable to review their activities from the viewpoints of their objects and the extent to which these are being carried out.

Considered against the background of medical teaching and practice in Melbourne, such research groups as ours have three broad functions. First, the search for new ideas and facts about disease and its allied problems; secondly, to form a link between the practitioner and the scientist, enabling new ideas to be applied to the treatment of the sick; and thirdly, dissemination of new knowledge to other workers and practitioners.

Transfer to the Pathology Department of the Hospital of the responsibility for carrying out routine tests in various aspects of clinical pathology, which had in previous years formed an appreciable portion of the work of the Institute, was completed in 1949. This change left the staff of the Institute completely free to pursue research activities.

A glance at the last two annual reports and the scientific report of this year shows that research has been directed towards the elucidation of problems concerned with the coagulation of blood the metabolism of vitamin K, the metabolism of fatty acids and the metabolism of carbohydrates. In this last project special attention has been paid to endocrine influences and the changes seen in diabetes mellitus.

To date the workers of the Clinical Research Unit have been investigating in detail two basic problems concerned with diseases of the heart and blood vessels. This has led to studies of first, the mechanisms in man which control the total quantity water in the body, the disturbance of which leads to oedema; and secondly, the action on the blood vessels of various drugs and the possibility of using them in the treatment of high blood pressure. Further, in the past year, investigations have been commenced into some of the difficulties associated with present theories of electrocardiography. These difficulties hamper considerably the interpretation of electrocardiograms taken for the diagnosis of obscure heart diseases.

Although these research projects have been described as being carried out by members of one or the other organisation, in reality all the senior members of both staffs take some part in any investigation, for it is realised that most problems in medicine are so complex that their solution requires the combined efforts of many scientists with different fields of training. In the coming year the background of basic science experience available to any worker in either organisation will be further increased by the addition of a pharmacologist to the team.

In regard to the second object—namely, to form a link between the scientist and the practitioner—the present integration of Institute and Clinical Research

Unit is very satisfactory. The members of the Clinical Unit apply the findings of the research teams to the practice of medicine. Again, past annual reports show that this aspect of the work of both organisations has been steady. There has been the application of new knowledge gained from work on blood coagulation to the diagnosis and treatment of blood diseases, largely by co-operation with the Staff of the hospital Haematology sub-department, and also the use of anti-coagulant drugs in the treatment of myocardial infarction. The past three years have also seen the introduction of flame photometry as a method for the estimation of salts in body fluids; of the technique of vectorelectrocardiography, being developed as a clinical method of heart examination, and of several applications of continuous pressure recording methods to the study and diagnosis of disease. These last are venous occlusion plethysmography for the diagnosis of arterial obstruction in the limbs, balloon kymography for the study of diseases of the stomach and duodenum, and cystometric investigation of urinary bladder function in diseases of the prostate gland. Such methods have all been established as routine investigational procedures available to all members of the hospital Staff as required. Equipment is also being made and assembled to enable continuous pressure recordings to be taken from inside the heart and great blood vessels to assist in the diagnosis of various types of congenital heart disease, with a view to determination of suitability for surgery.

Concerning the third object mentioned, it is clear that new ideas and new facts must be passed on to other workers and to practitioners, both for criticism and application. If this be not done then the new knowledge is lost, and must await rediscovery. Broadly, this dissemination may be achieved by word of mouth or writing. The writing of papers for scientific journals has been practised by members of both organisations, as the lists of published papers in these reports show, and this method forms virtually the only means of spreading the information overseas.

In the local sphere, however, much can be done by word of mouth, and we have endeavoured to use this method to the full in three ways. First, by reading papers and joining in discussions of scientific bodies, both in Melbourne and other Australian cities. Secondly, by group discussions, held at the Institute or Clinical Research Unit, to which interested scientists from kindred institutions and the University have been invited, and I would like to take this opportunity to thank them for their assistance in our discussions. Thirdly, regular ward rounds are held at which visitors from other centres are frequently present.

As mentioned previously, a small group such as ours can only work in a very limited field. Also in a relatively small country such as Australia only a few people will be working on any one aspect of a subject. Most workers find discussion a great stimulus to their work, and unless they can travel it is difficult for them to compare notes with their fellow workers. In a similar way overseas travel for research workers seems desirable both for the stimulus received by discussing problems with other workers and to keep up to date with overseas developments. Scientific journals often take twelve months to publish papers, so that by the time they are read here the articles refer to work of nearly two years previously. For these reasons I wish to thank the Trustees of the Baker Institute and the members of the Board of Management for the generous facilities they have made available for senior members of our staffs to travel for such purposes.

BAKER MEDICAL RESEARCH INSTITUTE.

During the year the death occurred of Mr. J. Sutherland, a trustee of the Institute since 1929, and the staff of the Institute feel that they have lost a trusted friend and wise counsellor.

In August Dr. Fantl left for a three months visit of England and Europe to study the latest trends in biochemical research. He had a very profitable trip, and has returned with much information of value to us. I wish to express our appreciation of the facilities he was given at the various centres visited.

The research projects of the Institute have continued to be into problems connected with the coagulation of blood, the metabolism of fatty acids and vitamin K. The work on carbohydrate metabolism conducted by Dr. Bornstein and Miss Trehwella has been temporarily discontinued until the return of Dr. Bornstein from overseas. A detailed account of these projects is given in the scientific section of this report.

The library continues, as libraries must, to grow in size, and some structural alterations have been made to increase its accommodation. Gifts to the library are gratefully acknowledged from the following:—

Abbott Laboratories; Alfred Hospital Library; Bayer Products Ltd.; Bausch & Lomb Optical Co.; Hospitals and Charities Commission; Commonwealth Scientific and Industrial Research Organization; 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; Organization 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 also due to 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; National Health and Medical Research Council; 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 common with the other Clinical Research Units in Melbourne, the Unit has this year been recognized by the University of Melbourne as a suitable organization in which post-graduate students may study for certain senior degrees.

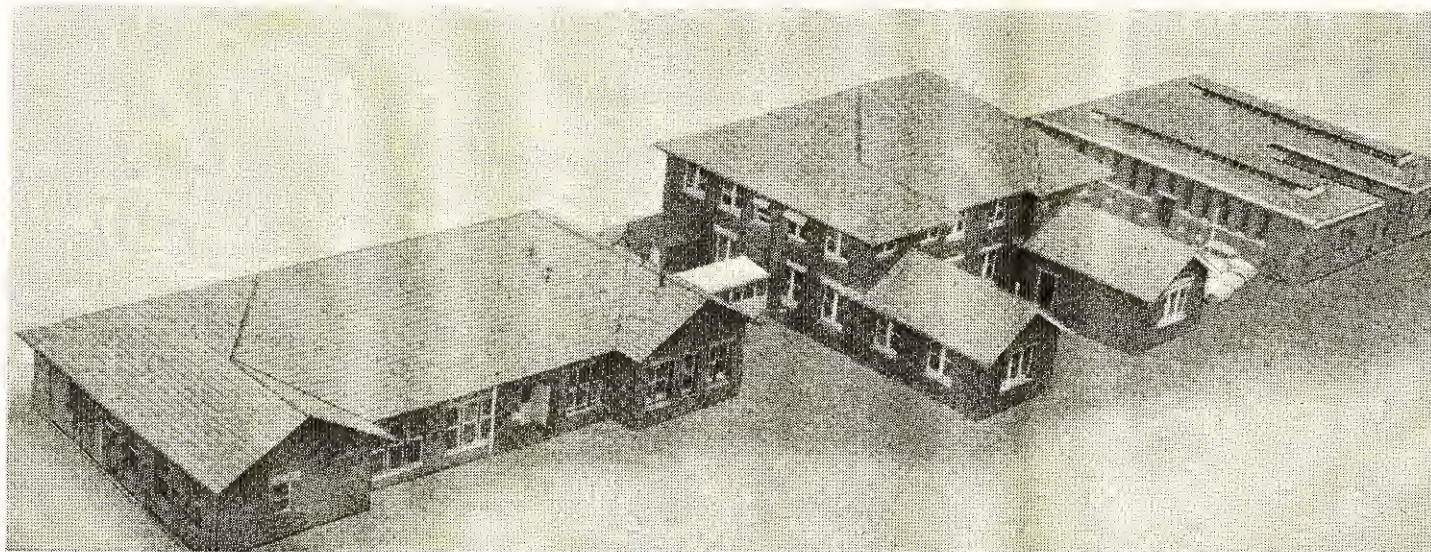
The research projects of the Unit are substantially the same as last year, and all have been considerably advanced and in some cases broadened. The study of congestive cardiac failure has led to a fuller appreciation of the problems of treatment of this condition and to an investigation of the control of the water content of the body in general and of other diseases (e.g., nephritis and cirrhosis of the liver) in which water retention occurs. The vectorelectrocardiograph has been used to study the electrical activity of the heart in normal individuals and a comprehensive report on this new method of cardiac investigation has been accepted for publication. Experiments are also in progress by which it is hoped to elucidate some of the difficulties encountered in the interpretation of electrocardiograms obtained in some cases of heart disease. The investigations into hypertension have been continued, and studies made of the efficacy of the methonium drugs in its treatment. Also the value of other new drugs in the diagnosis of the rarer causes of high blood pressure (e.g., tumours of the adrenal glands) is being investigated. Studies of the physiology and pathology of the stomach and duodenum and of urinary bladder function in patients with enlargement of the prostate gland have continued. Details of this work are 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 by members of the University staff. Particularly we wish to thank the Alfred Hospital Auxiliary who generously permitted funds, accumulated for another purpose, to be used in the purchase of a recording oscillograph which will be of great value in connection with the diagnosis of many heart conditions. Our thanks are due to Kodak (A/sia) Pty. Ltd. for the generous gift of a camera for the vectorelectrocardiograph.

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

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

RESEARCH DEPARTMENTS IN THE GROUNDS OF THE HOSPITAL.



Ward 8

Clinical Research Unit.

Contains: 2 Six-bed Wards and Ward Services
Examination Room
Biophysics Laboratory
Biochemistry Laboratory
Offices

Baker Medical Research Institute.

Contains: Biochemistry Laboratories
Physiology Laboratories
Library
Workshop
Offices

Animal Farm.

REPORT OF SCIENTIFIC INVESTIGATIONS

EXPERIENCE WITH INTRAMUSCULAR HEPARIN PREPARATIONS

P. Fantl and L. Ebbels.

Heparin is used widely in the prophylaxis and treatment of thrombo-embolic complications of diseases. The drug has to be given parenterally. Intravenous administration gives immediate results, but the effect is transitory, so that frequent injections are needed to maintain a therapeutic blood level. This disadvantage of intravenous administration can be partly overcome by intramuscular injection. A number of suggestions have been made to increase the efficacy of this procedure, and it was thought desirable to find the most effective manner of intramuscular administration for our experience showed that great variations in response to heparin occur from patient to patient, and may even be seen in the same patient at different times. In order to obtain reliable results it was decided to use one dosage of heparin, namely 20,000 international units. Two different preparations were tested. One was an aqueous solution and the other contained heparin dispersed in Pitkin's menstruum, which is a gelatin medium believed to retard heparin absorption. Each preparation was used on the same patient after the effect of a previous injection had worn off. The heparin concentration was measured by its effect on blood coagulation time. As the technique of this test is difficult to standardise, it was supplemented by the determination of heparin in the blood. Our experience is that aqueous heparin preparations are at least as effective as heparin in Pitkin's menstruum. We feel, therefore, that the latter preparation has no advantage over the former.

INVESTIGATION OF THE MECHANISM OF CLOT RETRACTION

P. Fantl, L. Ebbels and J. F. Nelson.

It has been known for a long time that the thrombocytes affect the structure of a fibrin clot. When present in sufficient numbers, they produce a shrinkage of the blood clot. This ability of the thrombocytes to alter the structure of the fibrin gel is thought to be of importance in haemostasis, and may also play some role in intravascular coagulation. It was therefore considered of interest to study the mechanism of clot retraction. This investigation was carried out on a system consisting of isolated thrombocytes and citrated human plasma from which the thrombocytes were removed. Clotting was induced by the addition of thrombin preparations. It was found that a variety of substances known to react with thiol groups have the ability to inactivate the thrombocytes with regard to fibrin gel contraction. However, these inactivated thrombocytes still show full thromboplastic activity. The experiments were extended to purified fibrinogen preparations. Here it was observed that thrombin and thrombocytes are insufficient to produce contraction of a fibrin gel. Additional factors are required for this phenomenon. These are present in plasma and serum, and it is suggested that these additional factors be called "contraction co-factors."

METABOLISM OF SUBSTANCES WITH VITAMIN K ACTIVITY

P. Fantl, J. F. Nelson and G. J. Lincoln.

Certain derivatives of 2-Methyl 1,4 naphthoquinone are used to treat bleeding tendencies due to a deficiency of prothrombin. In a previous report it was mentioned that a fraction of these drugs, after oral administration, is excreted in the urine. For the present investigation the diacetate of 2-Methyl 1,4 naphtho-hydroquinone (Acetomenaphthone), a compound with low toxicity and insolubility in aqueous medium, was selected.

Oral administration of acetomenaphthone to normal humans and rabbits is followed by the urinary excretion of a derivative of the drug which yields in the case of rabbits 30-40% and in case of humans 20-30% of 2-Methyl 1,4 naphtho-quinone.

Complete obstruction of the biliary flow produced by ligation and severance of the common bile duct in rabbits did not influence intestinal absorption and urinary excretion of acetomenaphthone, and no significant decrease in the prothrombin level could be detected. In patients suffering from obstructive jaundice, the first administration of acetomenaphthone was followed by marked variations from nil to normal excretion. In the cases of low urinary excretion, a second administration of the drug gave higher excretion rates. From these results it is concluded that bile is not required for the intestinal absorption of acetomenaphthone in humans.

A VITAMIN K SATURATION TEST

P. Fantl.

The results obtained in the patients with obstructive jaundice suggested the application of 2-Methyl 1,4 naphthoquinone derivatives as an indicator of Vitamin K deficiency.

The following technique was adopted: 50-60 mg of acetomenaphthone is given by mouth and a 24-hour urine specimen or two 12-hour specimens are collected over a preservative. The amount of 2-Methyl 1,4 naphthoquinone excreted is determined by a colorimetric procedure. Excretion of less than 15% in 24 hours following the administration of the drug is indicative of Vitamin K deficiency.

THE DETERMINATION OF CHOLIC ACID IN BLOOD AND BILE

P. Fantl and B. McQuade.

It seemed desirable to have direct evidence for our finding that acetomenaphthone does not require bile for its absorption from the intestinal tract. To this end an estimation of bile acids in blood and bile was carried out. A considerable amount of preliminary work was, however, necessary to establish reproducible analytical conditions. The principle of the technique adopted consists of treatment of the body fluid with alcohol to remove proteins. The alcoholic filtrates are evaporated in vacuum. The residue is taken up in diluted sodium hydroxide. Zinc sulphate solution is added. The zinc hydroxide removes pigments and water insoluble components. If the quantity of zinc hydroxide is not excessive the losses of bile

acids are not significant. The cholic acid in the filtrates has been measured by a modified Pettenkofer reaction, a colorimetric procedure and also by the fluorescence of cholates in concentrated sulphuric acid. Applying these techniques to gall bladder contents, it was observed that normal rabbit's bile gave a relatively high value for "cholic acid" by both procedures. After ligation of the common bile duct the value fell to very low figures. The tests for the detection of bile acids have given valuable information as an indicator in the change of bile acid concentration. However, there is some doubt about the specificity of these reactions.

ANTIDIURETIC SUBSTANCES IN BLOOD AND THEIR RELATION TO CONGESTIVE CARDIAC FAILURE

P. Trehella.

From previous studies on congestive cardiac failure, it seemed likely that some of the patients might have an excess of circulating antidiuretic substances. This hypothesis has been investigated by assaying the blood content of antidiuretic substances, and this has shown that some patients with congestive cardiac failure have an increased quantity of antidiuretic substances in their blood.

During this study it was noticed that, in normal young women, there was considerable daily variation in the amount of antidiuretic substance in their blood stream, whereas this phenomenon was not seen in males nor in one woman past the menopause. Further observations on a series of young women showed a relationship between the level of these substances in blood and their menstrual cycles. A minimum concentration of antidiuretic substances was found between the second and sixth day of the menstrual cycle. The time of highest concentration varied from one individual to another, but was towards the end of the cycle.

It seems possible that the occasional cyclical recurrence of congestive cardiac failure in the premenstrual period is related to the rise and fall of the amount of antidiuretic substances in the blood of women.

STUDIES ON ENDOCRINE INFLUENCES ON CARBOHYDRATE METABOLISM.

P. Trehella.

In last year's report on the work in this field it was noted that glucose utilization by isolated diaphragm muscle was appreciably increased by the previous intravenous injection of the receptor destroying enzyme (R.D.E.) of the cholera vibrio. Further, it seemed that R.D.E. had the power to partially inactivate *in vitro* adrenal cortical extract.

During the year this latter phenomenon has been studied, using a fresh adrenal cortical extract prepared in our laboratories and dried R.D.E. provided by Sir MacFarlane Burnet, of the Walter and Eliza Hall Institute. It has been shown that R.D.E. itself does not liberate formaldehyde when treated with periodic acid. Further, the reduction of activity of adrenal cortical extract by incubation with R.D.E. is not due to any enzymatic property, but to some heat stable factor, which is possibly an impurity in the R.D.E. preparation.

CONTROL OF BODY WATER VOLUME IN MAN

T. E. Lowe, T. Cullity, J. Upfill and B. McA. Sayers.

Previous studies on quantitative balances of water and sodium metabolism in patients under treatment for congestive cardiac failure have been continued, and have led to the tentative hypothesis that this condition represents a disturbance in control of body water volume rather than of electrolyte metabolism. It had been shown that the mechanism controlling the electrolyte pattern of body fluids in normal individuals was still functioning in a substantially normal manner. Water balance studies showed that another mechanism could be detected from the manner in which excess water was lost from the body during recovery from oedema. The typical response takes the form of alternate increasing and decreasing loss of water in cycles whose amplitude gets smaller and frequency greater until normal body volume is regained.

This typical behaviour has also been observed in patients' oedematous from nephritis and liver disease. The response is not altered in type by the exhibition of mercurial diuretics, but it is substantially altered by fever. In one patient, who was becoming oedematous, this typical response was seen in reverse.

It has been shown that the curves obtained in these balance studies can be described by one equation.

Working from the hypothesis that the curves obtained in the water balance studies described the behaviour of the volume-regulating mechanism, the problem has been analysed on the basis that the body represents a storage reservoir of water that is an "open" system. In such a system there would be a continuous flow of water into and out of the reservoir.

This analysis has led to the conclusion that the water volume-controlling mechanism has components that may be described as volume-disturbing and volume-restoring forces. Further, in the conditions analysed these forces do not seem to be grossly abnormal, but the sensitivity of the system is altered in oedematous states. Sensitivity is low in oedema, but gradually returns to normal during the recovery period.

Body Electrolyte Patterns in Oedema States

The observations made on sodium balances in congestive cardiac failure have been extended to give daily quantitative balance measurements for potassium and chloride metabolism. This has enabled electrolyte patterns in body fluids to be studied in more detail in these oedematous conditions and to follow fluid movements in the body during treatment. As yet the studies are not sufficiently advanced to allow conclusions to be reached, but they are proving valuable in studying the action of mercurial diuretics and the newly introduced "exchange resins."

STUDY OF HYPERTENSIVE STATES

Hypertension

A. J. Barnett.

Following early experience of the blood pressure lowering effect of the methonium* drugs in patients suffering from arterial hypertension, the effect of the injection of these compounds has been noted in a larger series of patients. Detailed observations have been made on the effects of intramuscular injection in some 30 persons.

The response has varied from patient to patient, in some cases the blood pressure being reduced to normotensive levels, in others the effect being very slight. The results suggest that the sympathetic nervous component in arterial hypertension varies greatly, and there may not be a uniform mechanism in essential hypertension.

Some seventeen persons have received continued treatment with methonium compounds, and it has been possible to form an opinion of the value of these drugs in the management of arterial hypertension. Persons with hypertension in the "malignant" phase have obtained marked relief of headache, and, in cases in which the therapy has been continued for three months or more, improvement in the condition of the ocular fundi.

However, in most cases a fairly rapid tolerance of the drugs has occurred, so that the early blood pressure lowering action is not maintained.

Unpleasant side of effects from the drugs—in the form of attacks of faintness, constipation, blurred vision, dryness of the mouth, sensitivity to glare—have been common.

The opinion has been formed that these drugs are valuable agents in the management of severe arterial hypertension with Grade IV hypertensive retinal changes, and headache. There is, however, no strong indication for their use in benign hypertension without severe hypertensive symptoms; in fact, the unpleasant side effects from the methonium therapy may be more objectionable than the symptoms of the arterial hypertension.

*The methonium drugs used were supplied to us by courtesy of May & Baker Ltd.

Adrenergic Blocking Agents

A. J. Barnett and R. Fowler.

A reliable and non-toxic blocking agent against noradrenaline would be of great value in the diagnosis and management of patients suffering from the adrenal medullary tumour, phaeochromocytoma. Previous experience with benzodioxane and "Dibenamine," recommended for this purpose, had shown disadvantages of these substances due either to unreliability or toxicity.

Investigations have been made on the effects of the newly introduced "Regitin" (Ciba 7337).^{*} The intravenous injection of this drug produced practically no change in the blood pressure of resting normal persons. In all of eight subjects in whom the blood pressure had been raised by continuous intravenous infusion of 1-noradrenaline, the intravenous injection of 10 mg. of "Regitin" produced a marked fall in blood pressure, this being more marked in the case of the diastolic than of the systolic pressure. In subjects receiving an intravenous infusion of adrenaline, the intravenous injection of "Regitin" produced variable and less marked effects on the blood pressure. Intravenous injections of 10 mg. "Regitin" have also been given to eight persons suffering from arterial hypertension. A definite fall in the blood pressure has occurred in some cases, but not to normotensive levels. No serious toxic effects have resulted from the injection of "Regitin." It is hoped that it will prove of value in diagnosis and management in patients suffering from phaeochromocytoma.

PLETHYSMOGRAPHY

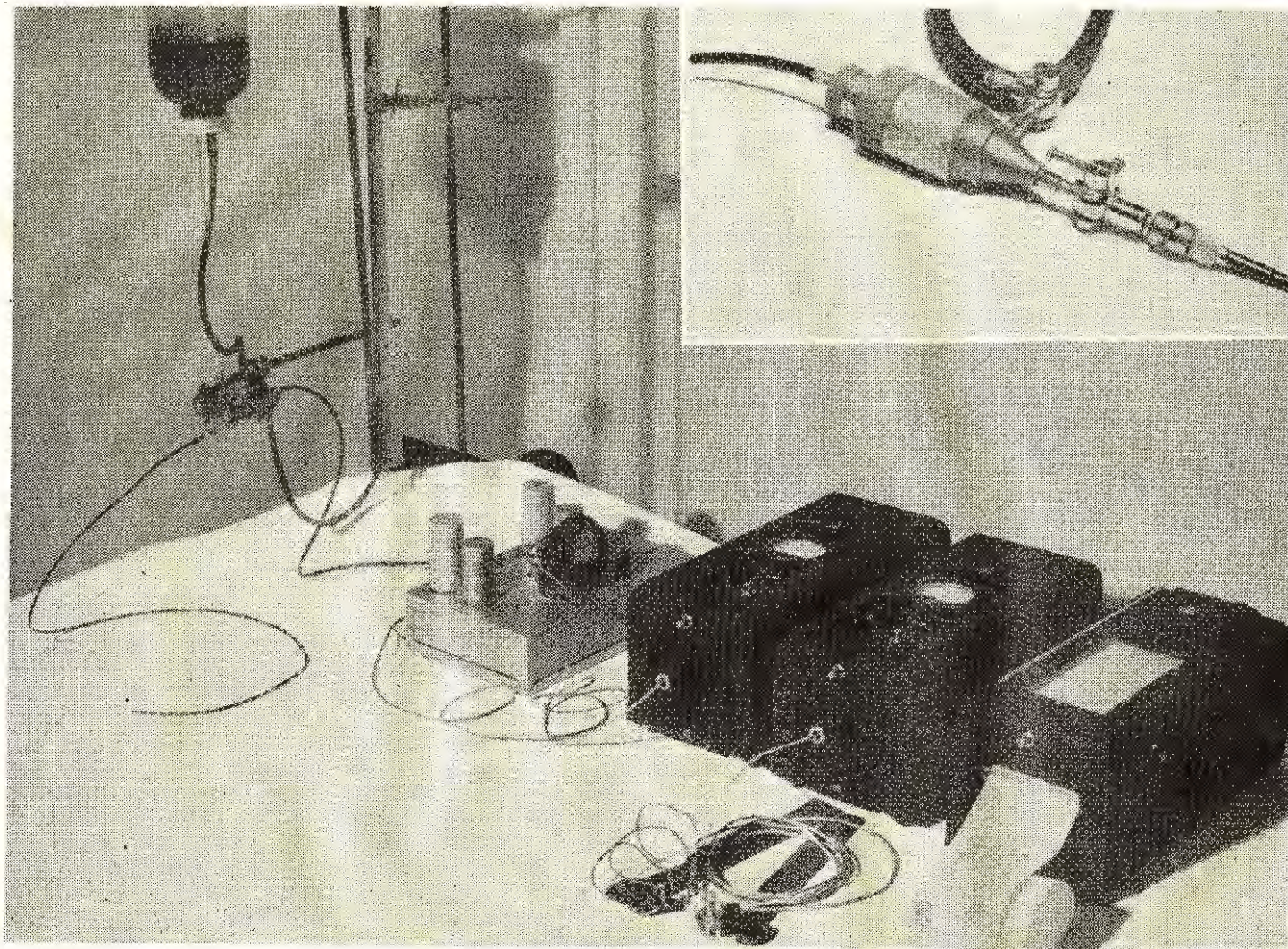
A. J. Barnett.

The technique of venous occlusion plethysmography, previously developed and used as a research method and clinical test, has been used in the investigation of patients suffering from occlusive vascular disease.

During the year 1951 venous occlusion plethysmography has been carried out on 33 patients, and by providing quantitative measurement of blood flow through the limb has proved of great help in diagnosis and prognosis.

Many of these patients were referred from other departments of the Hospital for this investigation.

^{*}The supply of Regitin was made available through the courtesy of the local representative of Ciba, S.A., Basle.



Apparatus for Continuous Recording of Intracardiac Pressures, illustrating a Hansen Condenser Manometer (inset) and a Recording Oscillograph.

VECTORELECTROCARDIOGRAPHY

T. E. Lowe and A. J. Goble.

Early this year construction of the first channel of the vectorelectrocardiograph was completed, and vectorelectrocardiograms, directly synthesized by electronic means, can be photographed from the fluorescent screen of the apparatus.

During the year observations were chiefly directed to establishing the appearances of the tracings in the normal individual. In this method of electrocardiography, instead of the conventional P, QRS and T complexes, each is replaced by a loop, and by combining loops taken in different planes a three dimensional model can be made. From the photographs of loops in various planes the tracings made from any of the conventional leads can be deduced. From a series of 104 normal individuals the range of values for the duration of the QRS loop, the direction of the long axis of the QRS loop, and the spatial angle between the long axes of the QRS and T loops were determined. The usual direction of inscription of the QRS loop, when viewed in various planes, and the variations in its contour were also studied. A detailed report of these findings has been accepted for publication in the "Medical Journal of Australia."

A start has been made on the study of the vectorelectrocardiogram in cardiac disease, and it is already clear that for many purposes this method gives less ambiguous and more readily interpreted records than the conventional methods of electrocardiography.

THEORY OF ELECTROCARDIOGRAPHY

B. McA. Sayers.

Interest has been focused recently upon the apparently inexplicable abnormalities occasionally found in electrocardiograms recorded both from apparently normal individuals and from those suffering from cardiac disabilities.

In an endeavour to clarify these abnormalities, close attention has been paid to the fundamental theory of electrocardiography upon which most clinical conclusions are based.

It was found experimentally that the theory presented by Einthoven only approximately agreed with the experimental conditions. Closer investigation showed that in the presence of irregularities of the medium (the body as an electrical conductor does not adhere to the classical assumption of a homogenous spherical medium), considerable uncertainty in interpretation of the E.C.G. recordings may exist. In fact, it has been shown that under some conditions the recorded electrocardiogram may give completely meaningless indications.

A technique for overcoming this difficulty is being developed, and experimental results thus far (a) confirm the presence of the uncertainty which was predicted theoretically, and (b) the techniques being developed show promise of avoiding

the trouble. Investigations to determine the validity and scope of application of the technique are progressing. It is hoped that some of the anomalies present in standard electrocardiographic theory may be removed.

Another field of interest surrounds a theory propounded in this laboratory concerning the relationship between the fluctuating establishment of charges within the heart, and the resulting electrical field in the body.

Application of this theory has resolved some of the theoretical physical contradictions and already throws new light upon the meaning of the electrocardiogram. Further development of the theory is progressing.

The inadequacy of present-day electrocardiographic theory and technique has highlighted the need for more satisfactory apparatus. To fill this need, a high speed electronic computing device is being developed. This will permit study of the time plot of the radius vector of the spatial vectorcardiograph signal. It seems possible that the record may prove to be a more sensitive indicator of significant change in the electrical activity of the heart than present records.

Study of the degree of homogeneity of the body as an electrical conductor is in progress. With the aid of artificial fields, the results of other workers have been investigated and conflicting results obtained. These experimental contradictions, however, may be explained in terms of the theory of irregularities mentioned earlier.

BIOPHYSICAL METHODS

B. McA. Sayers.

With the application of physical methods to medical research, certain new tools of study have become necessary. Some of these which are of especial interest, and which are being used in the laboratory, are mentioned below.

In the report on the studies on body water volume the importance of "open" systems in biological studies was indicated. A specific calculus equation is available to describe that system, and in order to solve this equation for practical purposes an electronic computing machine has been developed. This will make possible a study of internal conditions of the system where the external factors, such as input, and output, are known.

It is also interesting to note that a mechanical integrator, electronic multipliers and other processing units have been constructed in order to assist the extensive calculations often necessary in these biophysical problems.

Another device constructed is a non-linear biological amplifier. With a calibrated recording device, the amplifier, which is frequency-modulated, has a much greater sensitivity for small signals than for larger signals. The shape of the sensitivity-input-voltage curve may be controlled over a wide range, and it is possible to remove any component of the input voltage which is referable to magnitude, such as unwanted pulses from stimulated biological structures in the vicinity of the field of measurement.

BLADDER FUNCTION IN PROSTATOMEGALY

A. J. Barnett, K. Burnside and T. Cullity.

The investigation concerning the disturbance of bladder function in patients suffering from prostatomegaly, and the survey of results of treatment in these patients has been continued.

Determination of the intravesical volume—pressure relationship has been carried out in cases of prostatomegaly, and in some instances the test repeated after operation. Sixteen cystometric examinations were carried out during 1951.

Data has been collected concerning the clinical features, results of special tests, operation details, post-operative course and clinical result in patients admitted to the surgical wards with symptoms attributed to prostatomegaly. Detailed records have been obtained from 75 patients.

At present these data are being analysed to decide what lines the investigation will follow in the future.

STUDIES OF THE PHYSIOLOGY AND PATHOLOGY OF THE STOMACH AND DUODENUM

R. R. Andrew, P. J. Parsons and T. Cullity.

The study of gastric and duodenal activity in various conditions and in response to various drugs has been continued, using the technique of balloon kymography through a four-lumen Miller-Abbot tube. The conditions being investigated include peptic ulcer, anorexia nervosa, hiatus hernia, post-gastrectomy syndrome and steatorrhoea. Observations are also being made on the changes produced in motility by the drugs, atropine, morphine, insulin, banthine and hexamethonium.

Some observations on the effects of various drugs on gastric acidity have been made with the antimony-antimony oxide electrode previously described.

PAPERS ACCEPTED FOR PUBLICATION DURING 1951

- T. E. Lowe and A. J. Goble: "SPATIAL VECTORELECTROCARDIOGRAPHY: THE TECHNIQUE AND THE NORMAL VECTORELECTROCARDIOGRAM," (Med. J. Aust.).
- 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.).
- P. Fantl and J. F. Nelson: "THE SECRETION OF 3,3'-ETHYLIDENE BIS (4-HYDROXYCOUMARIN) IN MILK" (Med. J. Aust.).

LECTURES DELIVERED BY STAFF MEMBERS DURING 1951

- "FLUID BALANCE IN CONGESTIVE CARDIAC FAILURE" .. T. E. Lowe
Royal Australasian College of Physicians in Sydney.
- "THE ROLE OF THE SYMPATHETIC NERVOUS SYSTEM IN ESSENTIAL HYPERTENSION" .. A. J. Barnett
Royal Australasian College of Physicians in Perth.
- "VECTORELECTROCARDIOGRAPHY" .. A. J. Goble
Victorian Society for Pathology and Experimental Medicine.
- "SECRETORY AND MOTOR ASPECTS OF GASTRIC AND INTESTINAL DISEASES" .. R. R. Andrew, P. J. Parsons
Alfred Hospital Clinical Society.

GROUP DISCUSSIONS HELD DURING 1951

- "PROBLEMS OF BLOOD COAGULATION" .. P. Fantl
- "THEORY OF ELECTROCARDIOGRAPHY" .. B. McA. Sayers

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FINANCIAL STATEMENTS

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

Revenue Account for the Year ended 31st December, 1951.

EXPENDITURE.		INCOME.	
Salaries and Wages	£10,894 16 2	Donations—	
Drugs	243 11 4	Thomas Baker (Kodak), Alice Baker and Eleanor Shaw	
Instruments and Glassware	314 8 4	Benefactions	£7,200 0 0
Special Maintenance	588 0 9	Government Grants—	
Repairs and Renewals	124 0 11	National Health and Medical Research	
Miscellaneous and Administration—		Council	£2,975 16 6
Fuel and Lighting	£74 19 4	Department of Health Travelling Ex-	
Insurance	127 5 0	penses of Associate Director	600 0 0
Library Maintenance	389 1 3		
Printing and Stationery	78 9 7		3,575 16 6
Laundry	43 13 7	Interest from Investments—	
Telephone	106 15 3	Thomas Baker (Kodak), Alice Baker and	
Travelling Expenses	1,366 16 7	Eleanor Shaw Benefactions—	
Advertising	35 14 10	Australian Commonwealth Inscribed	
Sundries	97 5 11	Stock	552 10 0
	2,320 1 4	Endowment Investments—	
		Australian Commonwealth Inscribed	
		Stock	178 2 6
		Grain Elevators Board Inscribed Stock	93 15 0
		Australian Consolidated Treasury Bonds	16 5 0
			840 12 6
		Biochemistry Fees	5 4 6
		Balance—Deficiency for the Year	2,863 5 4
	£14,484 18 10		£14,484 18 10

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

Balance Sheet at 31st December, 1951

LIABILITIES.		ASSETS.	
Current Liabilities—		Current Assets—	
Commercial Bank of Australia Ltd.	£750 1 10	Sundry Debtors	£53 18 5
Sundry Creditors	794 13 1	Investments—	
	<u>£1,544 14 11</u>	Grain Elevators Board Inscribed Stock—	
Capital Grants and Gifts—		3½% due 1/5/1952	2,500 0 0
Balance, 31st December, 1950	372 16 7	Australian Commonwealth Inscribed	
Add Grants made during the year	450 0 0	Stock—	
	<u>822 16 7</u>	3½% due 15/10/1960	5,000 0 0
Endowment Fund	8,500 0 0	3½% due 15/10/1963	500 0 0
	<u>10,867 11 6</u>	Australian Commonwealth Treasury	
Revenue Account—		Bonds—	
Balance at 31st December, 1950	224 14 0	3½% due 15/9/1961	500 0 0
Add Recoup of Deficit for year ended 31st			
December, 1950, from The Thomas			
Baker, Alice Baker and Eleanor Shaw			
Benefactions	2,424 18 3		
	<u>2,649 12 3</u>	Fixed Assets, at cost—	
Less Deficiency for Year	2,863 5 4	Furniture and Fittings	2,100 0 0
Accumulated Deficiency	213 13 1		
	<u>£10,653 18 5</u>		
			<u>£10,653 18 5</u>

Note: In addition to receiving interest on the Investments as shown in the Balance Sheet, the Institute receives 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 required by us, we are of opinion that the Balance Sheet shows a true and fair view of the state of the Institute's affairs at 31st December, 1951, according to the best of our information and the explanations given to us and as shown by the Books of the Institute.

Melbourne,
28th March, 1952.

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

Spectator Publishing Co. Pty. Ltd.
Printers
134a Little Collins Street, Melbourne
